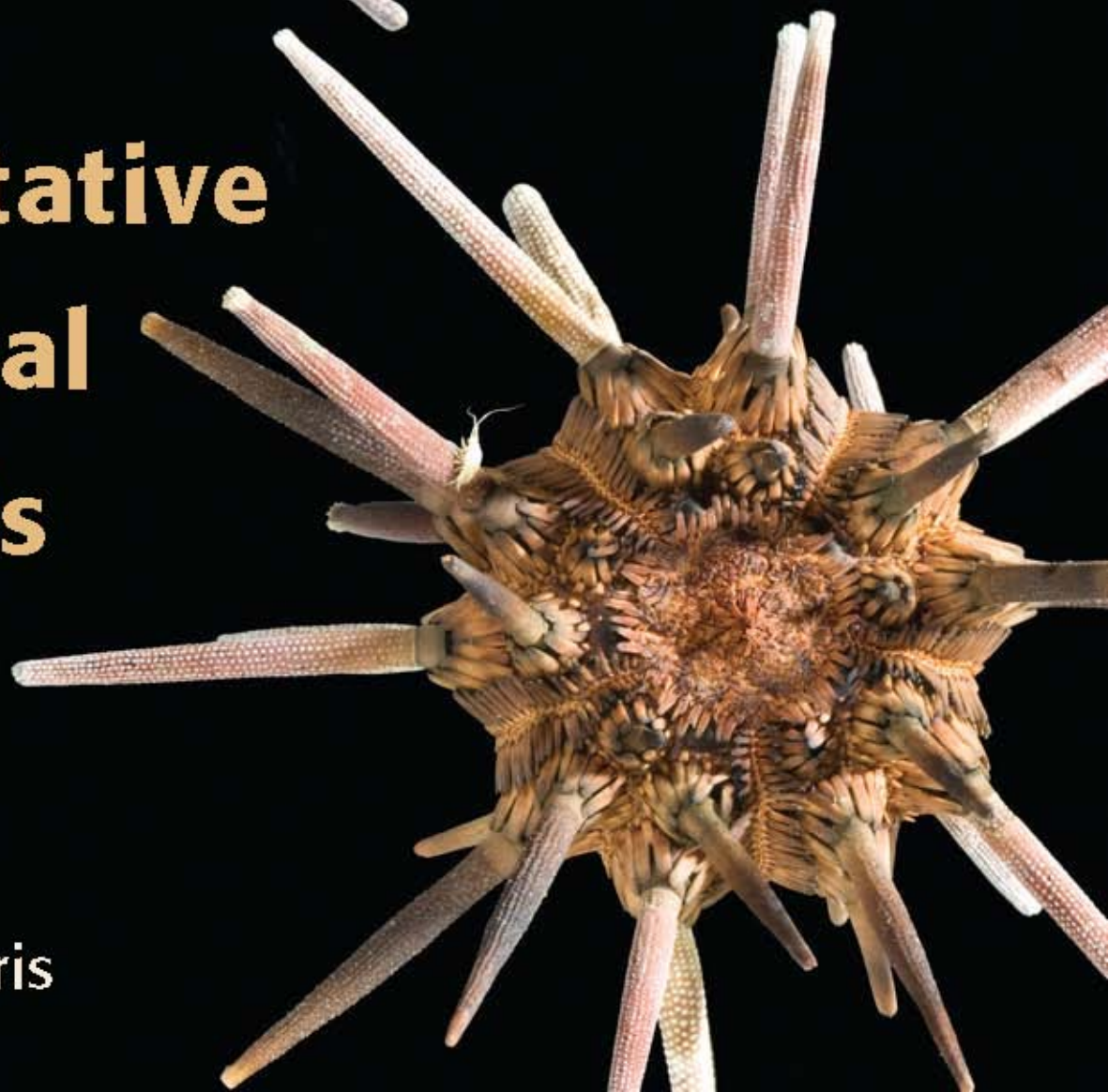
Eighth Edition

Quantitative Chemical Analysis



Daniel C. Harris

"The Experiment" by Sempé © C. Charillon, Paris

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Eighth Edition

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Michelson Laboratory
China Lake, California

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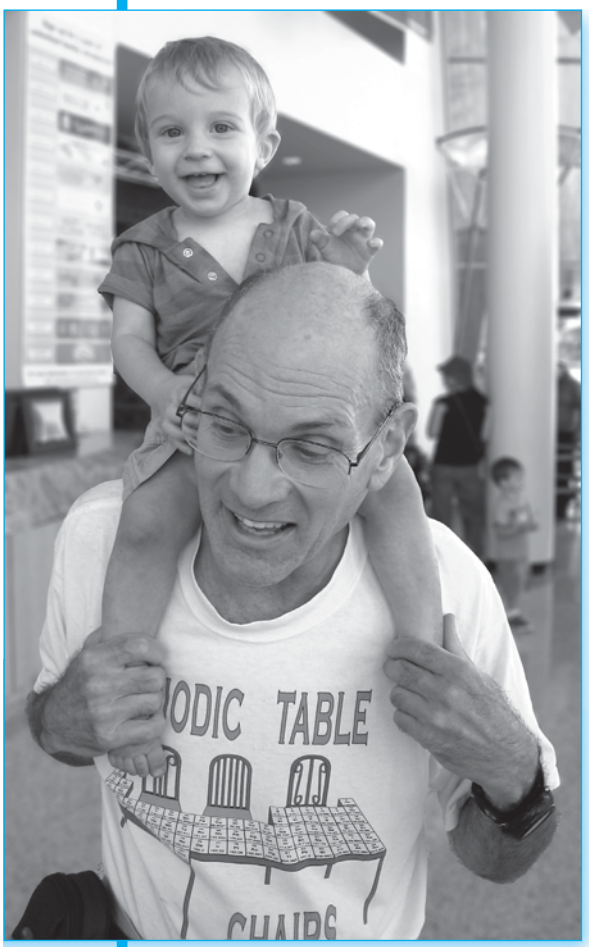


Dan's grandson Samuel discovers that the periodic table can take you to great places.

PREFACE

Goals of This Book

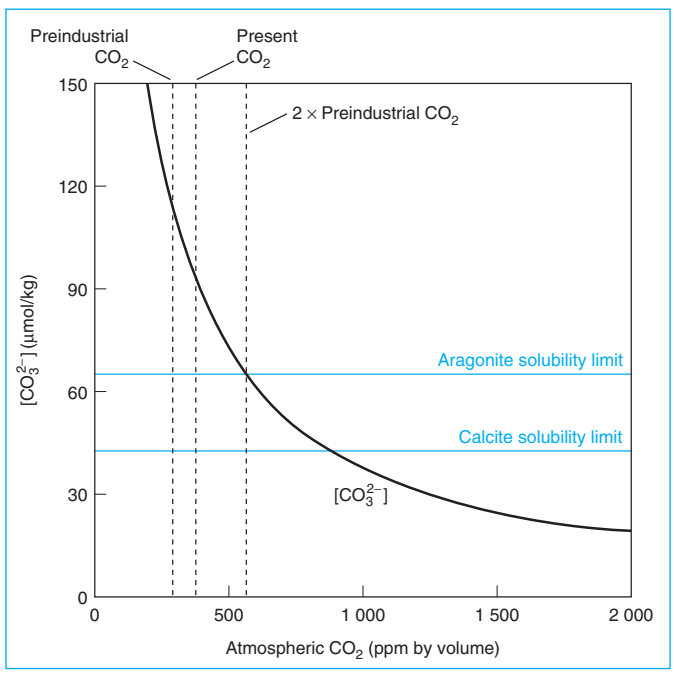
My goals are to provide a sound physical understanding of the principles of analytical chemistry and to show how these principles are applied in chemistry and related disciplines—especially in life sciences and environmental science. I have attempted to present the subject in a rigorous, readable, and interesting manner that will appeal to students whether or not their primary interest is chemistry. I intend the material to be lucid enough for nonchemistry majors, yet to contain the depth required by advanced undergraduates. This book grew out of an introductory analytical chemistry course that I taught mainly for nonmajors at the University of California at Davis and from a course for third-year chemistry students at Franklin and Marshall College in Lancaster, Pennsylvania.

What's New?

A significant change in this edition that instructors will discover is that the old Chapter 7 on titrations from earlier editions is missing, but its content is dispersed throughout this edition. My motive was to remove precipitation titrations from the critical learning path. Precipitation titrations have decreased in importance and they have not appeared in the last two versions of the American Chemical Society examination in quantitative analysis.* The introduction to titrations comes in Chapter 1. Kjeldahl analysis is grouped with acid-base titrations in Chapter 10. Spectrophotometric titrations appear in Chapter 17 with spectrophotometry. Efficiency in titrimetric experimental design is now with quality assurance in Chapter 5. Precipitation titrations appear with gravimetric analysis in Chapter 26. Gravimetric analysis and precipitation titrations remain self-contained topics that can be covered at any point in the course.

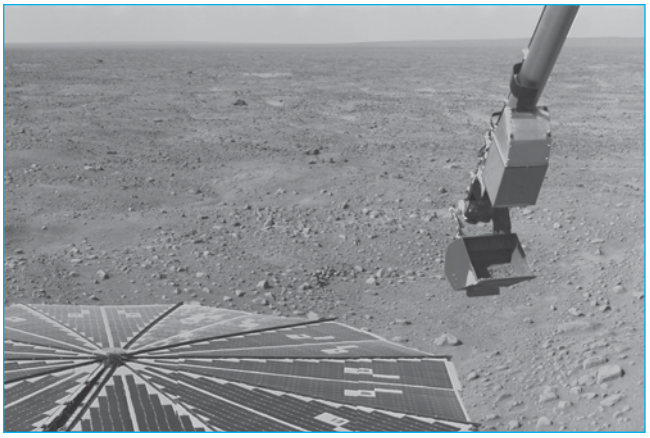
A new feature of this edition is a short "Test Yourself" question at the end of each worked example. If you understand the worked example, you should be able to answer the Test Yourself question. Compare your answer with mine to see if we agree.

Chapter 0 begins with a biographical account of Charles David Keeling's measurement of atmospheric carbon dioxide. His results have been described as "the single most important environmental data set taken in the 20th century." Boxes in Chapters 3 and 19 provide detail on Keeling's precise manometric and spectrometric techniques. Box 9-1 discusses ocean acidification by atmospheric carbon dioxide.



Effect of increasing atmospheric CO_2 on the ability of marine organisms to make calcium carbonate shells and skeletons (Box 9-1).

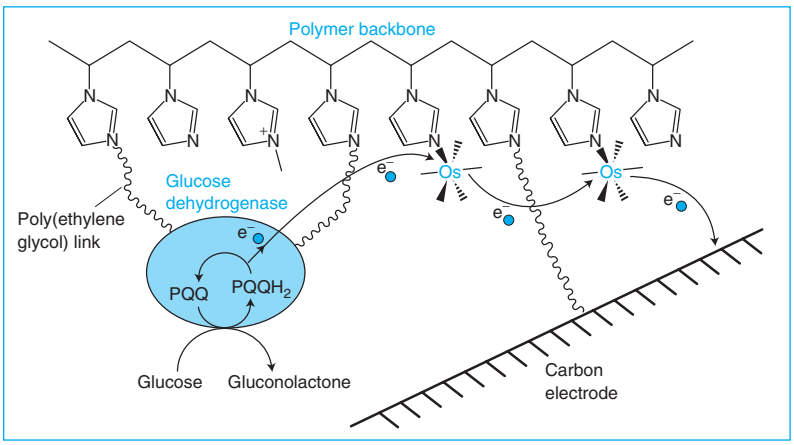
*P. R. Griffiths, "Whither 'Quant'? An Examination of the Curriculum and Testing Methods for Quantitative Analysis Courses Taught in Universities and Colleges in the Western USA," *Anal. Bioanal. Chem.* **2008,** *391*, 875.



Phoenix Mars Lander discovered perchlorate in Martian soil with ion-selective electrodes (Chapter 14).

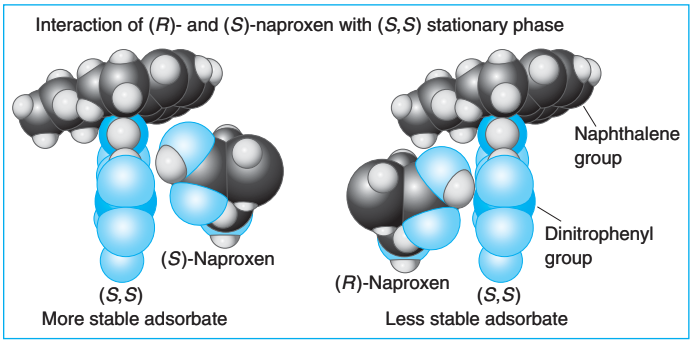
New boxed applications include biochemical measurements with a nanoelectrode (Chapter 1), the quartz crystal microbalance in medical diagnosis (Chapter 2), a case study of systematic error (Chapter 3), choosing the null hypothesis in epidemiology (Chapter 4), a lab-on-a-chip example of isoelectric focusing (Chapter 9), Kjeldahl nitrogen analysis in the headlines (Chapter 10), lithium-ion batteries (Chapter 13), measuring selectivity coefficients of ion-selective electrodes (Chapter 14), how perchlorate was discovered on Mars (Chapter 14), an updated description of the Clark oxygen electrode (Chapter 16), Rayleigh and Raman scattering (Chapter 17), spectroscopic upconversion (Chapter 18), trace elements in the ocean (Chapter 20), phase transfer agents (Chapter 22), gas chromatography on a chip (Chapter 23), paleothermometry (Chapter 24), structure of the solvent-bonded phase interface (Chapter 24), and measuring illicit drug use by analyzing river water (Chapter 27).

Spreadsheet instructions are updated to Excel 2007, but instructions for earlier versions of Excel are retained. A new section in Chapter 2 describes how electronic balances work. Rectangular and triangular uncertainty distributions for systematic error are introduced in Chapter 3. Chapter 4 includes discussion of standard deviation of the mean and "tails" in probability distributions. The Grubbs test replaces the Dixon Q test for outliers in Chapter 4. Reporting limits are illustrated with *trans* fat analysis in food in Chapter 5. Elementary discussion of the systematic treatment of equilibrium in Chapter 7 is enhanced with a discussion of ammonia acid-base chemistry. Chapter 8 and the appendix now include pK_a for acids at an ionic strength of 0.1 M in addition to an ionic strength of 0. Discussion of selectivity coefficients was improved in Chapter 14 and the iridium oxide pH electrode is introduced. "Wired" enzymes and mediators for coulometric blood glucose monitoring are described in Chapter 16. Voltammetry in Chapter 16 now includes a microelectrode array for biological measurements. There is a completely new section on flow injection analysis and sequential injection in Chapter 18, and these techniques appear again in later examples. Chapter 19 on spectrophotometers is heavily updated. Laser-induced breakdown and dynamic reaction cells for atomic spectrometry are introduced in Chapter 20. Mass spectrometry in Chapter 21 now includes the linear ion trap and the orbitrap, electron-transfer dissociation for protein sequencing, and open-air sampling methods.

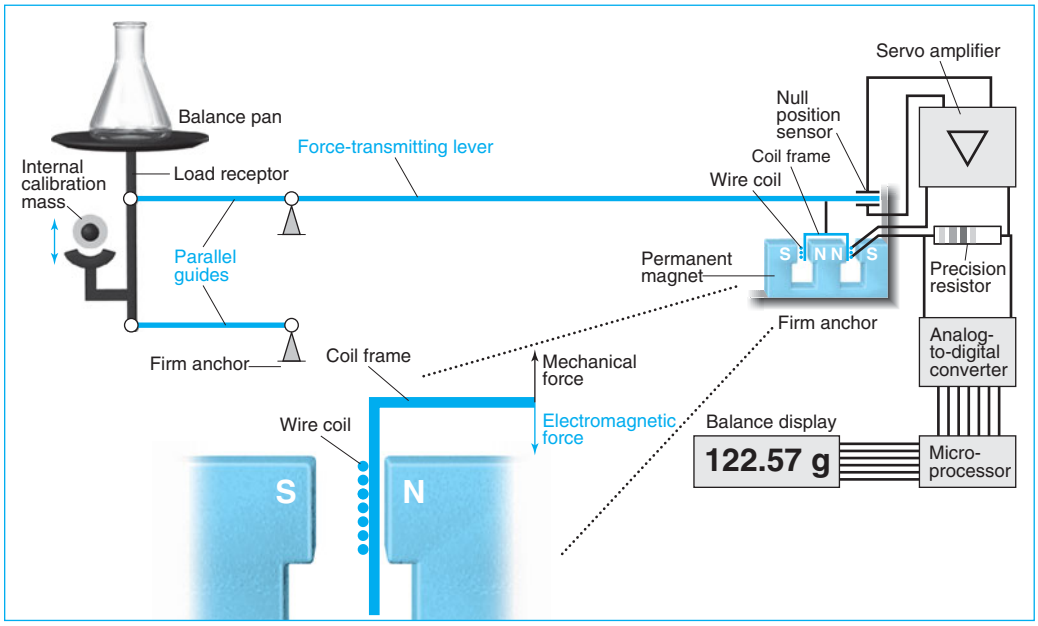


"Wired" enzymes described in Section 16-4 are at the heart of sensitive personal blood glucose monitors.

Numerous chromatography updates are found throughout Chapters 22–25. Stir-bar sorption was added to sample preparation in Chapter 23. Polar embedded group stationary phases, hydrophilic interaction chromatography, and the charged aerosol detector were added to Chapter 24. There is a discussion of the linear solvent strength model in liquid chromatography and a new section that teaches how to use a spreadsheet to predict the effect of solvent composition in isocratic elution. The supplement at **www.whfreeman.com/qca** gives a spreadsheet for simulating gradient elution. Chapter 25 describes hydrophilic interaction chromatography for ion exchange, hydrophobic interaction chromatography for protein purification, analyzing heparin contamination by electrophoresis, wall charge control in electrophoresis, an update on DNA sequencing by electrophoresis, and microdialysis/electrophoresis of neurotransmitters with a lab-on-a-chip. Data from a round-robin study of precision and accuracy of combustion analysis are included in Chapter 26. The 96-well plate for solid-phase extraction sample preparation was added to Chapter 27.



Chiral stationary phase separates enantiomers of the drug naproxen by high-performance liquid chromatography (Figure 24-10).



There is a new discussion of the operation of an electronic balance in Chapter 2, Tools of the Trade.

Applications

A basic tenet of this book is to introduce and illustrate topics with concrete, interesting examples. In addition to their pedagogic value, Chapter Openers, Boxes, Demonstrations, and Color Plates are intended to help lighten the load of a very dense subject. I hope you will find these features interesting and informative. **Chapter Openers** show the relevance of analytical chemistry to the real world and to other disciplines of science. I can't come to your classroom to present **Chemical Demonstrations,** but I can tell you about some of my favorites and show you color photos of how they look. **Color Plates** are located near the center of the book. **Boxes** discuss interesting topics related to what you are studying or amplify points in the text.

Problem Solving

Nobody can do your learning for you. The two most important ways to master this course are to work problems and to gain experience in the laboratory. **Worked Examples** are a principal pedagogic tool designed to teach problem solving and to illustrate how to apply what you have just read. Each worked example ends with a **Test Yourself** question that asks you to apply what you learned in the example. **Exercises** are the minimum set of problems that apply most major concepts of each chapter. Please struggle mightily with an Exercise before consulting the solution at the back of the book. **Problems** at the end of the chapter cover the entire content of the book. **Short answers** to numerical problems are at the back of the book and complete solutions appear in the **Solutions Manual** that can be made available for purchase if your instructor so chooses.

EXAMPLE **How Many Tablets Should We Analyze?**

In a gravimetric analysis, we need enough product to weigh accurately. Each tablet provides ~15 mg of iron. How many tablets should we analyze to provide 0.25 g of Fe_2O_3?

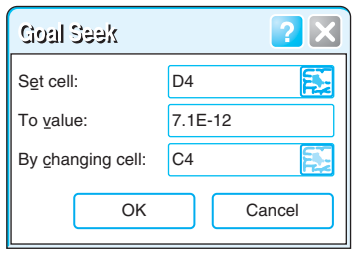
⋮

Test Yourself If each tablet provides ~20 mg of iron, how many tablets should we analyze to provide ~0.50 g of Fe_2O_3? (***Answer:*** 18)

Spreadsheets are indispensable tools for science and engineering. You can cover this book without using spreadsheets, but you will never regret taking the time to learn to use them. The text explains how to use spreadsheets and some problems ask you to apply them. If you are comfortable with spreadsheets, you will use them even when the problem does not ask you to. A few of the powerful built-in features of Microsoft Excel are described as they are needed. These features include graphing in Chapters 2 and 4, statistical functions and regression in Chapter 4,

	A	B	C	D
1	$Mg(OH)_2$ Solubility			
2				
3	K_{sp} =		$[OH^-]_{guess}$ =	$[OH^-]^3/(2 + K_1[OH^-])$ =
4	7.1E-12		0.0002459	7.1000E-12
5	K_1 =			
6	3.8E+02		$[Mg^{2+}]$ =	$[MgOH^+]$ =
7			0.0001174	0.0000110
8				
9	D4 = C4^3/(2+A6*C4)			
10	C7 = A4/C4^2			
11	D8 = A6*C7*C4			

Spreadsheets are introduced as an important problem-solving tool.



multiple regression for experimental design in Chapter 5, solving equations with Goal Seek in Chapters 7, 8, and 12, Solver in Chapters 12 and 18, and matrix operations in Chapter 18.

Other Features of This Book

Terms to Understand Essential vocabulary, highlighted in **bold** in the text, is collected at the end of the chapter. Other unfamiliar or new terms are *italic* in the text, but not listed at the end of the chapter.

Glossary All bold vocabulary terms and many of the italic terms are defined in the glossary.

Appendixes Tables of solubility products, acid dissociation constants, redox potentials, and formation constants appear at the back of the book. You will also find discussions of logarithms and exponents, equations of a straight line, propagation of error, balancing redox equations, normality, and analytical standards.

Notes and References Citations in the chapters appear at the end of the book.

Supplements

The ***Solutions Manual for Quantitative Chemical Analysis*** (ISBN 1-4292-3123-8) contains complete solutions to all problems.

The **student Web site, www.whfreeman.com/qca8e**, has **directions for experiments,** which may be reproduced for your use. "Green chemistry" is introduced in Chapter 2 of the textbook and "green profiles" of student experiments are included in the instructions for experiments at the Web site. There are instructions for two new experiments on fitting an acid-base titration curve with a spreadsheet and liquid carbon dioxide extraction of lemon peel oil. At the Web site, you will also find **lists of experiments** from the *Journal of Chemical Education*. **Supplementary topics** at the Web site include spreadsheets for precipitation titrations, microequilibrium constants, spreadsheets for redox titrations curves, analysis of variance, and spreadsheet simulation of gradient liquid chromatography. **Online quizzing** helps students reinforce their understanding of the chapter content.

The **instructors' Web site, www.whfreeman.com/qca8e**, has all **artwork** and **tables** from the book in preformatted PowerPoint slides and as JPG files, an online quizzing gradebook, and more.

WebAssign Premium logo.

For instructors interested in online homework management, W. H. Freeman and WebAssign have partnered to deliver **WebAssign Premium.** WebAssign Premium combines over 600 questions with a fully interactive DynamicBook at an affordable price. To learn more or sign up for a faculty demo account, visit **www.webassign.net**.

DynamicBook for *Quantitative Chemical Analysis, Eighth Edition,* is an electronic version of the text that gives you the flexibility to fully tailor content to your presentation of course material. It can be used in conjunction with the printed text, or it can be adopted on its own. Please go to **www.dynamicbooks.com** for more information, or speak with your W. H. Freeman sales representative.

The People

A book of this size and complexity is the work of many people. Jodi Simpson—the most thoughtful and meticulous copy editor—read every word with a critical eye and improved the exposition in innumerable ways. At W. H. Freeman and Company, Jessica Fiorillo provided overall guidance and was especially helpful in ferreting out opinions from instructors. Mary Louise Byrd shepherded the manuscript through production with her magic wand. Kristina Treadway managed the process of moving the book into production, and Anthony Petrites coordinated the reviewing of every chapter. Ted Sczcepanski located several hard-to-find photographs for the book. Dave Quinn made sure that the supplements were out on time and that the Web site was up and running with all its supporting resources active. Katalin Newman, at Aptara, did an outstanding job of proofreading.

At the Scripps Institution of Oceanography, Ralph Keeling, Peter Guenther, David Moss, Lynne Merchant, and Alane Bollenbacher shared their knowledge of atmospheric CO_2 measurements and graciously provided access to Keeling family photographs. I am especially delighted to have had feedback from Louise Keeling on my story of her husband, Charles David Keeling. This material opens the book in Chapter 0. Sam Kounaves of Tufts University

devoted a day to telling me about the *Phoenix Mars Lander* Wet Chemistry Laboratory, which is featured in Chapter 14. Jarda Ruzika of the University of Washington brought the importance of flow injection and sequential injection to my attention, provided an excellent tutorial, and reviewed my description of these topics in Chapters 18 and 19. David Sparkman of the University of the Pacific had detailed comments and suggestions for Chapter 21 on mass spectrometry. Joerg Barankewitz of Sartorius AG provided information and graphics on balances that you will find in Chapter 2.

Solutions to problems and exercises were checked by two wonderfully careful students, Cassandra Churchill and Linda Lait of the University of Lethbridge in Canada. Eric Erickson and Greg Ostrom provided helpful information and discussions at Michelson Lab.

My wife, Sally, works on every aspect of every edition of this book and the Solutions Manual. She contributes mightily to whatever clarity and accuracy we have achieved.

In Closing

This book is dedicated to the students who use it, who occasionally smile when they read it, who gain new insight, and who feel satisfaction after struggling to solve a problem. I have been successful if this book helps you develop critical, independent reasoning that you can apply to new problems. I truly relish your comments, criticisms, suggestions, and corrections. Please address correspondence to me at the Chemistry Division (Mail Stop 6303), Research Department, Michelson Laboratory, China Lake CA 93555.

Acknowledgments

I am indebted to many people who asked questions and provided suggestions and new information for this edition. They include Robert Weinberger *(CE Technologies)*, Tom Betts *(Kutztown University)*, Paul Rosenberg *(Rochester Institute of Technology)*, Barbara Belmont *(California State University, Dominguez Hills)*, David Chen *(University of British Columbia)*, John Birks *(2B Technologies)*, Bob Kennedy *(University of Michigan)*, D. Brynn Hibbert *(University of New South Wales)*, Kris Varazo *(Francis Marion University)*, Chongmok Lee *(Ewha Womans University, Korea)*, Michael Blades *(University of British Columbia)*, D. J. Asa *(ESA, Inc.)*, F. N. Castellano and T. N. Singh-Rachford *(Bowling Green State University)*, J. M. Kelly and D. Ledwith *(Trinity College, University of Dublin)*, Justin Ries *(University of North Carolina)*, Gregory A. Cutter *(Old Dominion University)*, Masoud Agah *(Virginia Tech)*, Michael E. Rybak *(U.S. Centers for Disease Control and Prevention)*, James Harnly *(U.S. Department of Agriculture),* Andrew Shalliker *(University of Western Sydney),* R. Graham Cooks *(Purdue University)*, Alexander Makarov *(Thermo Fisher Scientific, Bremen)*, Richard Mathies *(University of California, Berkeley)*, A. J. Pezhathinal and R. Chan-Yu-King *(University of Science and Arts of Oklahoma)*, Peter Licence *(University of Nottingham)*, and Geert Van Biesen *(Memorial University of Newfoundland)*.

People who reviewed parts of the eighth edition manuscript or who reviewed the seventh edition to make suggestions for the eighth edition include Rosemari Chinni *(Alvernia College)*, Shelly Minteer *(St. Louis University)*, Charles Cornett *(University of Wisconsin–Platteville)*, Anthony Borgerding *(St. Thomas College)*, Jeremy Mitchell-Koch *(Emporia State University)*, Kenneth Metz *(Boston College)*, John K. Young *(Mississippi State University)*, Abdul Malik *(University of Southern Florida)*, Colin F. Poole *(Wayne State University)*, Marcin Majda *(University of California, Berkeley)*, Carlos Garcia *(University of Texas, San Antonio)*, Elizabeth Binamira-Soriaga *(Texas A&M University)*, Erin Gross *(Creighton University)*, Dale Wood *(Bishop's University)*, Xin Wen *(California State University, Los Angeles)*, Benny Chan *(The College of New Jersey)*, Pierre Herckes *(Arizona State University)*, Daniel Bombick *(Wright State University)*, Sidney Katz *(Rutgers University)*, Nelly Matteva *(Florida A&M University)*, Michael Johnson *(University of Kansas)*, Dmitri Pappas *(Texas Tech University)*, Jeremy Lessmann *(Washington State University)*, Alexa Serfis *(Saint Louis University)*, Stephen Wolf *(Indiana State University)*, Stuart Chalk *(University of North Florida)*, Barry Lavine *(Oklahoma State University)*, Katherine Pettigrew *(George Mason University)*, Blair Miller *(Grand Valley State University)*, Nathalie Wall *(Washington State University)*, Kris Varazo *(Francis Marion University)*, Carrie Brennan *(Austin Peay State University)*, Lisa Ponton *(Elon University)*, Feng Chen *(Rider University)*, Eric Ball *(Metropolitan State College of Denver)*, Russ Barrows *(Metropolitan State College of Denver)*, and Mary Sohn *(Florida Institute of Technology)*.

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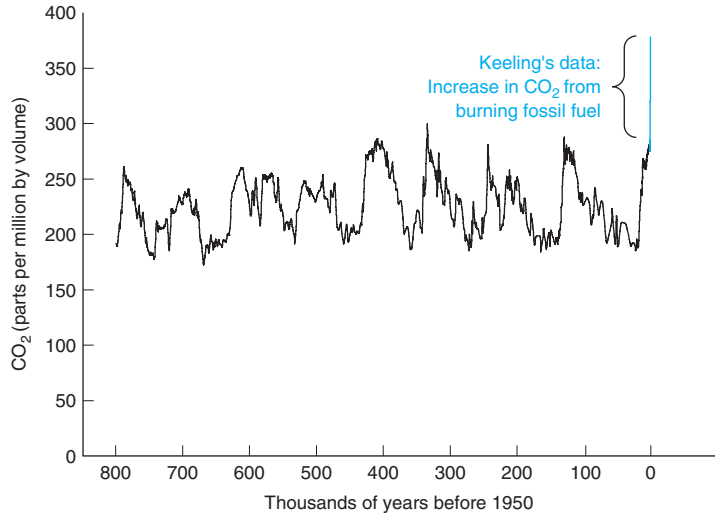
0 The Analytical Process

THE "MOST IMPORTANT" ENVIRONMENTAL DATA SET OF THE TWENTIETH CENTURY

Atmospheric CO_2 has been measured since 1958 at Mauna Loa Observatory, 3 400 meters above sea level on a volcano in Hawaii. [Forrest M. Mims III, www.forrestmims.org/maunaloaobservatory.html, photo taken in 2006.]



Historic atmospheric CO_2 data are derived from analyzing air bubbles trapped in ice drilled from Antarctica. Keeling's measurements of atmospheric CO_2 give the vertical line at the right side of the graph. [Ice core data from D. Lüthi et al., *Nature*, **2008**, *453*, 379. Mauna Loa data from http://scrippsco2.ucsd.edu/data/in_situ_co2/monthly_mlo.csv.]

In 1958, Charles David Keeling began a series of precise measurements of atmospheric carbon dioxide that have been called "the single most important environmental data set taken in the 20th century."* A half century of observations now shows that human beings have increased the amount of CO_2 in the atmosphere by more than 40% over the average value that existed for the last 800 000 years. On a geologic time scale, we are unlocking all of the carbon sequestered in coal and oil in one brief moment, an outpouring that is jarring the Earth away from its previous condition.

The vertical line at the upper right of the graph shows what we have done. This line will continue on its vertical trajectory until we have consumed all of the fossil fuel on Earth. The consequences will be discovered by future generations, beginning with yours.

*C. F. Kennel, Scripps Institution of Oceanography.

In the last century, humans abruptly changed the composition of Earth's atmosphere. We begin our study of quantitative chemical analysis with a biographical account of how Charles David Keeling came to measure atmospheric CO_2. Then we proceed to discuss the general nature of the analytical process.

0-1 Charles David Keeling and the Measurement of Atmospheric CO_2

Notes and references appear after the last chapter of the book.

Charles David Keeling (1928–2005, Figure 0-1) grew up near Chicago during the Great Depression.[1] His investment banker father excited an interest in astronomy in 5-year-old Keeling. His mother gave him a lifelong love of music. Though "not predominantly interested in science," Keeling took all the science available in high school, including a wartime course in aeronautics that exposed him to aerodynamics and meteorology. In 1945, he enrolled in a

FIGURE 0-1 Charles David Keeling and his wife, Louise, circa 1970. [Courtesy Ralph Keeling, Scripps Institution of Oceanography, University of California, San Diego.]

summer session at the University of Illinois prior to his anticipated draft into the army. When World War II ended that summer, Keeling continued at Illinois, where he "drifted into chemistry."

Upon graduation in 1948, Professor Malcolm Dole of Northwestern University, who had known Keeling as a precocious child, offered him a graduate fellowship in chemistry. On Keeling's second day in the lab, Dole taught him how to make careful measurements with an analytical balance. Keeling went on to conduct research in polymer chemistry, though he had no special attraction to polymers or to chemistry.

A requirement for graduate study was a minor outside of chemistry. Keeling noticed the book *Glacial Geology and the Pleistocene Epoch* on a friend's bookshelf. It was so interesting that he bought a copy and read it between experiments in the lab. He imagined himself "climbing mountains while measuring the physical properties of glaciers." In graduate school, Keeling completed most of the undergraduate curriculum in geology and twice interrupted his research to hike and climb mountains.

In 1953, Ph.D. polymer chemists were in demand for the new plastics industry. Keeling had job offers from manufacturers in the eastern United States, but he "had trouble seeing the future this way." He had acquired a working knowledge of geology and loved the outdoors. Professor Dole considered it "foolhardy" to pass up high-paying jobs for a low-paying postdoctoral position. Nonetheless, Keeling wrote letters seeking a postdoctoral position as a chemist "exclusively to geology departments west of the North American continental divide." He became the first postdoctoral fellow in the new Department of Geochemistry in Harrison Brown's laboratory at Caltech in Pasadena, California.

One day, "Brown illustrated the power of applying chemical principles to geology. He suggested that the amount of carbonate in surface water . . . might be estimated by assuming the water to be in chemical equilibrium with both limestone [$CaCO_3$] and atmospheric carbon dioxide." Keeling decided to test this idea. He "could fashion chemical apparatus to function in the real environment" and "the work could take place outdoors."

Keeling built a vacuum system to isolate CO_2 from air or acidified water. The CO_2 in dried air was trapped as a solid in the vacuum system by using liquid nitrogen, "which had recently become available commercially." Keeling built a manometer to measure gaseous CO_2 by confining the gas in a known volume at a known pressure and temperature (Figure 0-2 and Box 3-2). The measurement was precise (reproducible) to 0.1%, which was as good or better than other procedures for measuring CO_2.

Keeling prepared for a field experiment at Big Sur. The area is rich in calcite ($CaCO_3$), which would, presumably, be in contact with groundwater. Keeling "began to worry . . . about assuming a specified concentration for CO_2 in air." This concentration had to be known for his experiments. Published values varied widely, so he decided to make his own

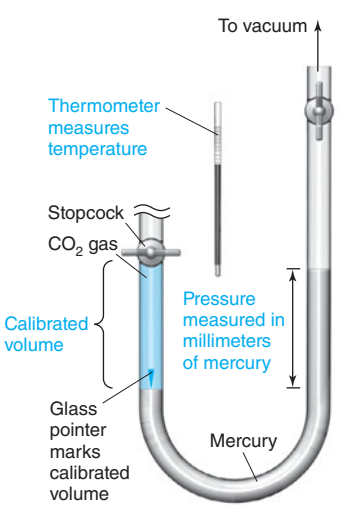


FIGURE 0-2 A manometer made from a glass U-tube. The difference in height between the mercury on the left and the right gives the pressure of the gas in millimeters of mercury. Box 3-2 provides more detail.

measurements. He had a dozen 5-liter flasks built with stopcocks that would hold a vacuum. He weighed each flask empty and filled with water. From the mass of water it held, he could calculate the volume of each flask. To rehearse for field experiments, Keeling measured air samples in Pasadena. Concentrations of CO_2 varied significantly, apparently affected by urban emissions.

Not being certain that CO_2 in pristine air next to the Pacific Ocean at Big Sur would be constant, he collected air samples every few hours over a full day and night. He also collected water samples and brought everything back to the lab to measure CO_2. At the suggestion of Professor Sam Epstein, Keeling provided samples of CO_2 for Epstein's group to measure carbon and oxygen isotopes with their newly built isotope ratio mass spectrometer. "I did not anticipate that the procedures established in this first experiment would be the basis for much of the research that I would pursue over the next forty-odd years," recounted Keeling. Contrary to hypothesis, Keeling found that river water and groundwater contained more dissolved CO_2 than expected if the dissolved CO_2 were in equilibrium with the CO_2 in the air.

Diurnal means the pattern varies between night and day.

Keeling's attention was drawn to the diurnal pattern that he observed in atmospheric CO_2. Air in the afternoon had an almost constant CO_2 content of 310 parts per million (ppm) by volume of dry air. The concentration of CO_2 at night was higher and variable. Also, the higher the CO_2 content, the lower the $^{13}C/^{12}C$ ratio. It was thought that photosynthesis by plants would draw down atmospheric CO_2 near the ground during the day and respiration would restore CO_2 to the air at night. However, samples collected in daytime from many locations had nearly the same 310 ppm CO_2.

Keeling found an explanation in a book entitled *The Climate Near the Ground*. All of his samples were collected in fair weather, when solar heating induces afternoon turbulence that mixes air near the ground with air higher in the atmosphere. At night, air cools and forms a stable layer near the ground that becomes rich in CO_2 from respiration of plants. Keeling had discovered that CO_2 is near 310 ppm in the free atmosphere over large regions of the Northern Hemisphere. By 1956, his findings were firm enough to be told to others, including Dr. Oliver Wulf of the U.S. Weather Bureau, who was working at Caltech.

Wulf passed Keeling's results to Harry Wexler, Head of Meteorological Research at the Weather Bureau. Wexler invited Keeling to Washington, DC, where he explained that the International Geophysical Year commencing in July 1957 was intended to collect worldwide geophysical data for a period of 18 months. The Bureau had just built an observatory near the top of Mauna Loa volcano in Hawaii, and Wexler was anxious to put it to use. The Bureau wanted to measure atmospheric CO_2 at remote locations around the world.

Scripps pier, wafted by a gentle sea breeze.

Keeling explained that measurements in the scientific literature might be unreliable. He proposed to measure CO_2 with an infrared spectrometer that would be precisely calibrated with gas measured by a manometer. The manometer is the most reliable way to measure CO_2, but each measurement requires half a day of work. The spectrometer could measure several samples per hour but must be calibrated with reliable standards.

Wexler liked Keeling's proposal and declared that infrared measurements should be made on Mauna Loa and in Antarctica. The next day, Wexler offered Keeling a job. Keeling described what happened next: "I was escorted to where I might work . . . in the dim basement of the Naval Observatory where the only activity seemed to be a cloud-seeding study being conducted by a solitary scientist."

Fortunately, Keeling's CO_2 results had also been brought to the attention of Roger Revelle, Director of the Scripps Institution of Oceanography near San Diego, California. Revelle invited Keeling for a job interview. He was given lunch outdoors "in brilliant sunshine wafted by a gentle sea breeze." Keeling thought to himself, "dim basement or brilliant sunshine and sea breeze?" He chose Scripps, and Wexler graciously provided funding to support CO_2 measurements.

Keeling identified several continuous gas analyzers and tested one from "the only company in which [he] was able to get past a salesman and talk directly with an engineer." He went to great lengths to calibrate the infrared instrument with precisely measured gas standards. Keeling painstakingly constructed a manometer whose results were reproducible to 1 part in 4 000 (0.025%), thus enabling atmospheric CO_2 measurements to be reproducible to 0.1 ppm. Contemporary experts questioned the need for such precision because existing literature indicated that CO_2 in the air varied by a factor of 2. Furthermore, there was concern that measurements on Mauna Loa would be confounded by CO_2 emitted by the volcano.

Roger Revelle of Scripps believed that the main value of the measurements would be to establish a "snapshot" of CO_2 around the world in 1957, which could be compared with

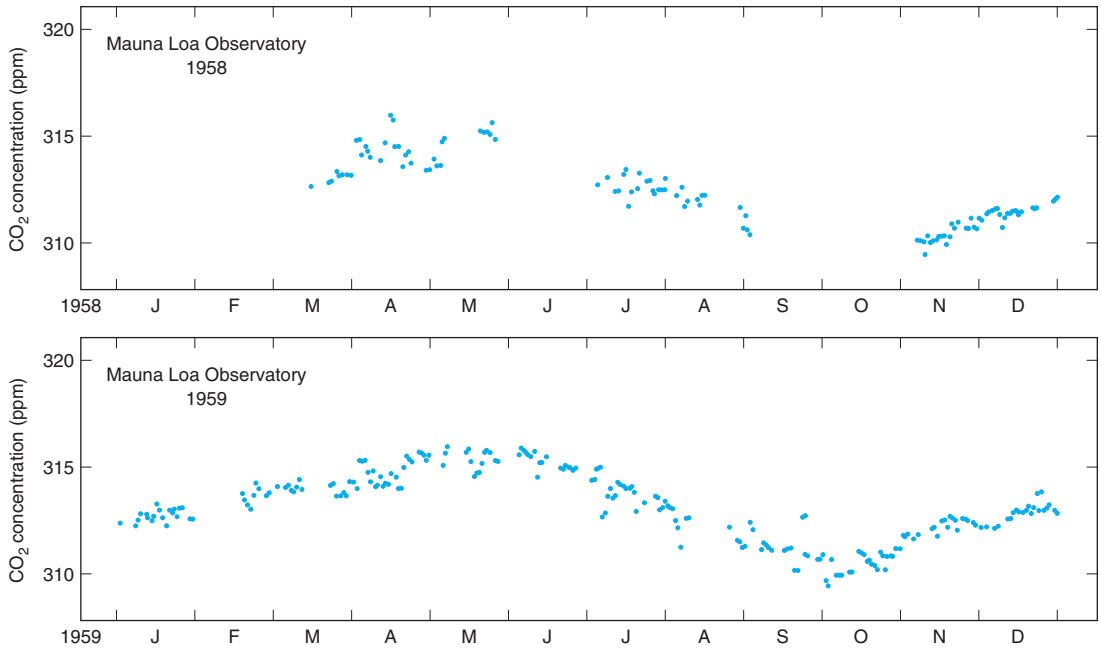


FIGURE 0-3 Atmospheric CO_2 measurements from Mauna Loa in 1958–1959. [J. D. Pales and C. D. Keeling, "The Concentration of Atmospheric Carbon Dioxide in Hawaii," *J. Geophys. Res.* **1965**, *70*, 6053.]

another snapshot taken 20 years later to see if CO_2 concentration was changing. People had considered that burning of fossil fuel could increase atmospheric CO_2, but it was thought that a good deal of this CO_2 would be absorbed by the ocean. No meaningful measurements existed to evaluate any hypothesis.

In March 1958, Ben Harlan of Scripps and Jack Pales of the Weather Bureau installed Keeling's infrared instrument on Mauna Loa. The first day's reading was within 1 ppm of the 313-ppm value expected by Keeling from his measurements made on the pier at Scripps. Concentrations in Figure 0-3 rose between March and May, when operation was interrupted by a power failure. Concentrations were falling in September when power failed again. Keeling was then allowed to make his first trip to Mauna Loa to restart the equipment. Concentrations steadily rose from November to May 1959, before gradually falling again. Data for the full year 1959 in Figure 0-3 reproduced the pattern from 1958. *These patterns could not have been detected if Keeling's measurements had not been made so carefully.*

Maximum CO_2 was observed just before plants in the temperate zone of the Northern Hemisphere put on new leaves in May. Minimum CO_2 was observed at the end of the growing season in October. Keeling concluded that "we were witnessing for the first time nature's withdrawing CO_2 from the air for plant growth during the summer and returning it each succeeding winter."

Figure 0-4, known as the *Keeling curve*, shows the results of half a century of CO_2 monitoring on Mauna Loa. Seasonal oscillations are superimposed on a steady rise.

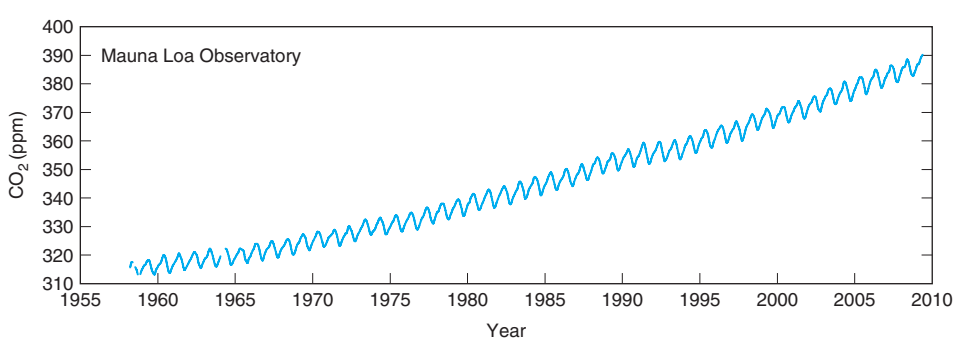


FIGURE 0-4 Monthly average atmospheric CO_2 measured on Mauna Loa. This graph, known as the *Keeling curve*, shows seasonal oscillations superimposed on rising CO_2. [Data from http://scrippsco2.ucsd.edu/data/in_situ_co2/monthly_mlo.csv.]

Approximately half of the CO_2 produced by the burning of fossil fuel (principally coal, oil, and natural gas) in the last half century resides in the atmosphere. Most of the remainder was absorbed by the ocean.

In the atmosphere, CO_2 absorbs infrared radiation from the surface of the Earth and reradiates part of that energy back to the ground (Figure 0-5). This *greenhouse effect* warms the Earth's surface and might produce climate change. In the ocean, CO_2 forms carbonic acid, H_2CO_3, which makes the ocean more acidic. Fossil fuel burning has already lowered the pH of ocean surface waters by 0.1 unit from preindustrial values. Combustion during the twenty-first century is expected to acidify the ocean by another 0.3–0.4 pH units—threatening marine life whose calcium carbonate shells dissolve in acid (Box 9-1). The entire ocean food chain is jeopardized by ocean acidification.[2]

The significance of the Keeling curve is apparent by appending Keeling's data to the 800 000-year record of atmospheric CO_2 and temperature preserved in Antarctic ice. Figure 0-6 shows that temperature and CO_2 experienced peaks roughly every 100 000 years, as marked by arrows.

Cyclic changes in Earth's orbit and tilt cause cyclic temperature change. Small increases in temperature drive CO_2 from the ocean into the atmosphere. Increased atmospheric CO_2 further increases warming by the greenhouse effect. Cooling brought on by orbital changes redissolves CO_2 in the ocean, thereby causing further cooling. Temperature and CO_2 have followed each other for 800 000 years.

Burning fossil fuel in the last 150 years increased CO_2 from its historic cyclic peak of 280 ppm to today's 380 ppm. No conceivable action in the present century will prevent CO_2 from climbing to several times its historic high, which might significantly affect climate. The longer we take to reduce fossil fuel use, the longer this unintended global experiment will continue. Increasing population exacerbates this and many other problems.

Keeling's CO_2 measurement program was jeopardized many times by funding decisions at government agencies. His persistence ensured the continuity and quality of the measurements. Manometrically measured calibration standards are labor intensive and costly. Funding agencies tried to reduce the cost by finding substitutes for manometry, but no method provided the same precision. The analytical quality of Keeling's data has enabled subtle trends, such as the effect of El Niño ocean temperature patterns, to be teased out of the overriding pattern of increasing CO_2 and seasonal oscillations.

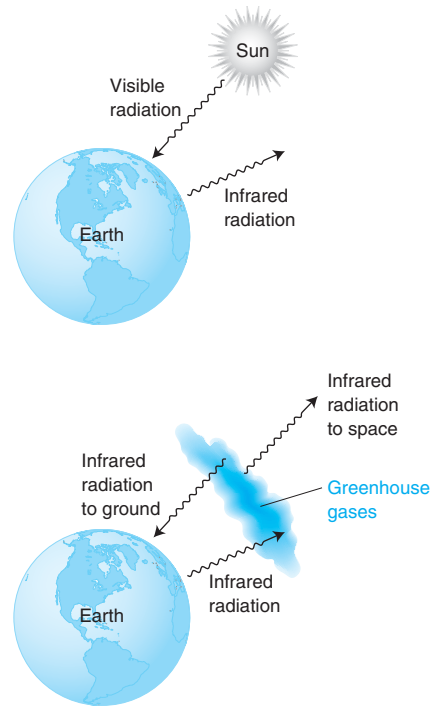


FIGURE 0-5 *Greenhouse effect.* The sun warms the Earth mainly with visible radiation. Earth emits infrared radiation, which would all go into space in the absence of the atmosphere. Greenhouse gases in the atmosphere absorb some of the infrared radiation and emit some of that radiation back to the Earth. Radiation directed back to Earth by greenhouse gases keeps the Earth warmer than it would be in the absence of greenhouse gases.

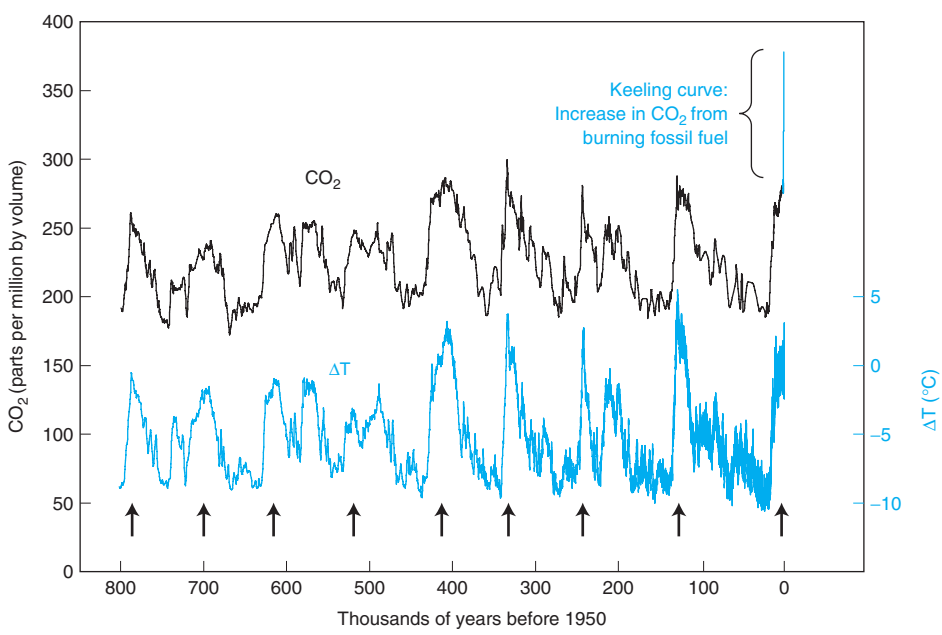
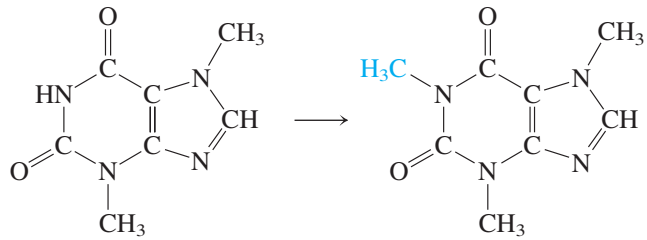


FIGURE 0-6 Significance of the Keeling curve (upper right, color) is shown by plotting it on the same graph with atmospheric CO_2 measured in air bubbles trapped in ice cores drilled from Antarctica. Atmospheric temperature at the level where precipitation forms is deduced from hydrogen and oxygen isotopic composition of the ice. [Vostok ice core data from J. M. Barnola, D. Raynaud, C. Lorius, and N. I. Barkov, http://cdiac.esd.ornl.gov/ftp/trends/co2/vostok.icecore.co2.]

Chocolate is great to eat, but not so easy to analyze. [W. H. Freeman photo by K. Bendo.]

0-2 The Analytical Chemist's Job

Chocolate[3] has been the savior of many a student on the long night before a major assignment was due. My favorite chocolate bar, jammed with 33% fat and 47% sugar, propels me over mountains in California's Sierra Nevada. In addition to its high energy content, chocolate packs an extra punch with the stimulant caffeine and its biochemical precursor, theobromine.



Theobromine (from Greek "food of the gods")
A diuretic, smooth muscle relaxant, cardiac stimulant, and vasodilator

Caffeine
A central nervous system stimulant

A *diuretic* makes you urinate.
A *vasodilator* enlarges blood vessels.

Too much caffeine is harmful for many people, and even small amounts cannot be tolerated by some unlucky individuals. How much caffeine is in a chocolate bar? How does that amount compare with the quantity in coffee or soft drinks? At Bates College in Maine, Professor Tom Wenzel teaches his students chemical problem solving through questions such as these.[4]

Chemical Abstracts is the most comprehensive source for locating articles published in chemistry journals. *SciFinder* is software that accesses *Chemical Abstracts*.

But, how *do* you measure the caffeine content of a chocolate bar? Two students, Denby and Scott, began their quest with a computer search for analytical methods. Searching with the key words "caffeine" and "chocolate," they uncovered numerous articles in chemistry journals. Two reports entitled "High-Pressure Liquid Chromatographic Determination of Theobromine and Caffeine in Cocoa and Chocolate Products"[5] described a procedure suitable for the equipment in their laboratory.[6]

Sampling

Bold terms should be learned. They are listed at the end of the chapter and in the Glossary at the back of the book. *Italicized* words are less important, but many of their definitions are also found in the Glossary.

The first step in any chemical analysis is procuring a representative sample to measure—a process called **sampling.** Is all chocolate the same? Of course not. Denby and Scott bought one chocolate bar in the neighborhood store and analyzed pieces of it. If you wanted to make broad statements about "caffeine in chocolate," you would need to analyze a variety of chocolates from different manufacturers. You would also need to measure multiple samples of each type to determine the range of caffeine in each kind of chocolate.

Homogeneous: same throughout
Heterogeneous: differs from region to region

A pure chocolate bar is fairly **homogeneous,** which means that its composition is the same everywhere. It might be safe to assume that a piece from one end has the same caffeine content as a piece from the other end. Chocolate with a macadamia nut in the middle is an example of a **heterogeneous** material—one whose composition differs from place to place. The nut is different from the chocolate. To sample a heterogeneous material, you need to use a strategy different from that used to sample a homogeneous material. You would need to know the average mass of chocolate and the average mass of nuts in many candies. You would need to know the average caffeine content of the chocolate and of the macadamia nut (if it has any caffeine). Only then could you make a statement about the average caffeine content of macadamia chocolate.

Sample Preparation

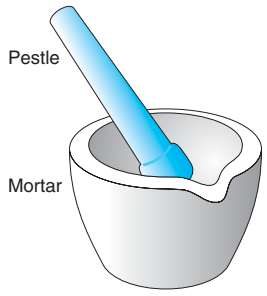


FIGURE 0-7 Ceramic mortar and pestle used to grind solids into fine powders.

The first step in the procedure calls for weighing out some chocolate and extracting fat from it by dissolving the fat in a hydrocarbon solvent. Fat needs to be removed because it would interfere with chromatography later in the analysis. Unfortunately, if you just shake a chunk of chocolate with solvent, extraction is not very effective, because the solvent has no access to the inside of the chocolate. So, our resourceful students sliced the chocolate into small bits and placed the pieces into a mortar and pestle (Figure 0-7), thinking they would grind the solid into small particles.

Imagine trying to grind chocolate! The solid is too soft to be ground. So Denby and Scott froze the mortar and pestle with its load of sliced chocolate. Once the chocolate was cold, it was brittle enough to grind. Then small pieces were placed in a preweighed 15-milliliter (mL) centrifuge tube, and their mass was noted.

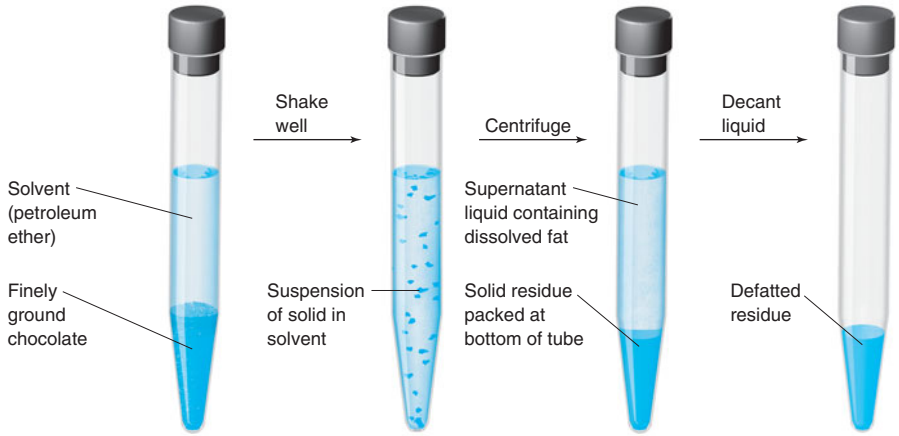


FIGURE 0-8 Extracting fat from chocolate to leave defatted solid residue for analysis.

Figure 0-8 shows the next part of the procedure. A 10-mL portion of the solvent, petroleum ether, was added to the tube, and the top was capped with a stopper. The tube was shaken vigorously to dissolve fat from the solid chocolate into the solvent. Caffeine and theobromine are insoluble in this solvent. The mixture of liquid and fine particles was then spun in a centrifuge to pack the chocolate at the bottom of the tube. The clear liquid, containing dissolved fat, could now be **decanted** (poured off) and discarded. Extraction with fresh portions of solvent was repeated twice more to ensure complete removal of fat from the chocolate. Residual solvent in the chocolate was finally removed by heating the centrifuge tube in a beaker of boiling water. The mass of chocolate residue could be calculated by weighing the centrifuge tube plus its content of defatted chocolate residue and subtracting the known mass of the empty tube.

Substances being measured—caffeine and theobromine in this case—are called **analytes.** The next step in the sample preparation procedure was to make a **quantitative transfer** (a complete transfer) of the fat-free chocolate residue to an Erlenmeyer flask and to dissolve the analytes in water for the chemical analysis. If any residue were not transferred from the tube to the flask, then the final analysis would be in error because not all of the analyte would be present. To perform the quantitative transfer, Denby and Scott added a few milliliters of pure water to the centrifuge tube and used stirring and heating to dissolve or suspend as much of the chocolate as possible. Then they poured the **slurry** (a suspension of solid in a liquid) into a 50-mL flask. They repeated the procedure several times with fresh portions of water to ensure that every bit of chocolate was transferred from the centrifuge tube to the flask.

To complete the dissolution of analytes, Denby and Scott added water to bring the volume up to about 30 mL. They heated the flask in a boiling water bath to extract all the caffeine and theobromine from the chocolate into the water. To compute the quantity of analyte later, the total mass of solvent (water) must be accurately known. Denby and Scott knew the mass of chocolate residue in the centrifuge tube and they knew the mass of the empty Erlenmeyer flask. So they put the flask on a balance and added water drop by drop until there were exactly 33.3 g of water in the flask. Later, they would compare known solutions of pure analyte in water with the unknown solution containing 33.3 g of water.

A solution of anything in water is called an **aqueous** solution.

Before Denby and Scott could inject the unknown solution into a chromatograph for the chemical analysis, they had to clean up the unknown even further (Figure 0-9). The slurry of chocolate residue in water contained tiny solid particles that would surely clog their expensive chromatography column and ruin it. So they transferred a portion of the slurry to a centrifuge tube and centrifuged the mixture to pack as much of the solid as possible at the bottom of the tube. The cloudy, tan, **supernatant liquid** (liquid above the packed solid) was then filtered in a further attempt to remove tiny particles of solid from the liquid.

It is critical to avoid injecting solids into a chromatography column, but the tan liquid still looked cloudy. So Denby and Scott took turns between classes to repeat the centrifugation and filtration five times. After each cycle in which the supernatant liquid was filtered and centrifuged, it became a little cleaner. But the liquid was never completely clear. Given enough time, more solid always seemed to precipitate from the filtered solution.

Real-life samples rarely cooperate with you!

The tedious procedure described so far is called **sample preparation**—transforming a sample into a state that is suitable for analysis. In this case, fat had to be removed from the chocolate, analytes had to be extracted into water, and residual solid had to be separated from the water.

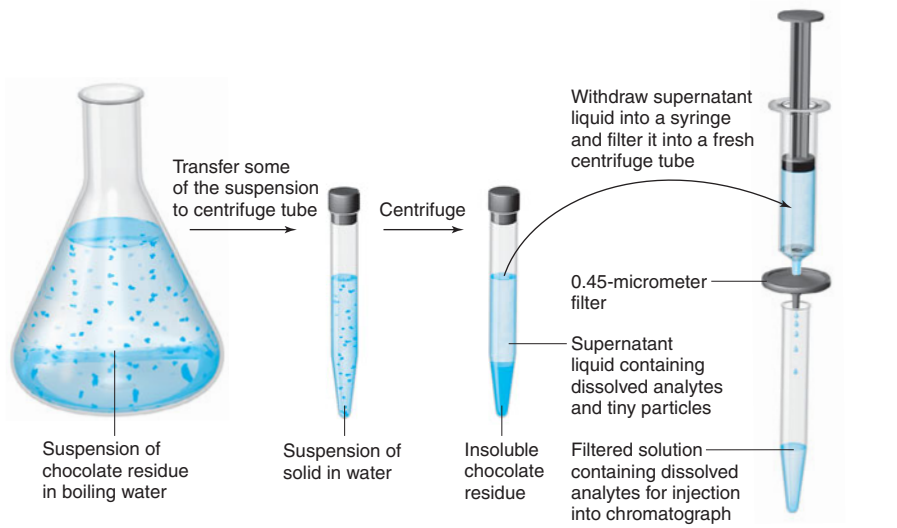


FIGURE 0-9 Centrifugation and filtration are used to separate undesired solid residue from the aqueous solution of analytes.

The Chemical Analysis (At Last!)

Chromatography solvent is selected by a systematic trial-and-error process described in Chapter 24. Acetic acid reacts with negative oxygen atoms on the silica surface. When not neutralized, these oxygen atoms tightly bind a small fraction of caffeine and theobromine.

$$\underset{\text{Binds analytes very tightly}}{\text{silica-O}^-} \xrightarrow{\text{acetic acid}} \underset{\text{Does not bind analytes strongly}}{\text{silica-OH}}$$

Denby and Scott finally decided that the solution of analytes was as clean as they could make it in the time available. The next step was to inject solution into a *chromatography* column, which would separate the analytes and measure the quantity of each. The column in Figure 0-10a is packed with tiny particles of silica (SiO_2) to which are attached long hydrocarbon molecules. Twenty microliters (20.0×10^{-6} liters) of the chocolate extract were injected into the column and washed through with a solvent made by mixing 79 mL of pure water, 20 mL of methanol, and 1 mL of acetic acid. Caffeine is more soluble than theobromine in the hydrocarbon on the silica surface. Therefore, caffeine "sticks" to the coated silica particles in the column more strongly than theobromine does. When both

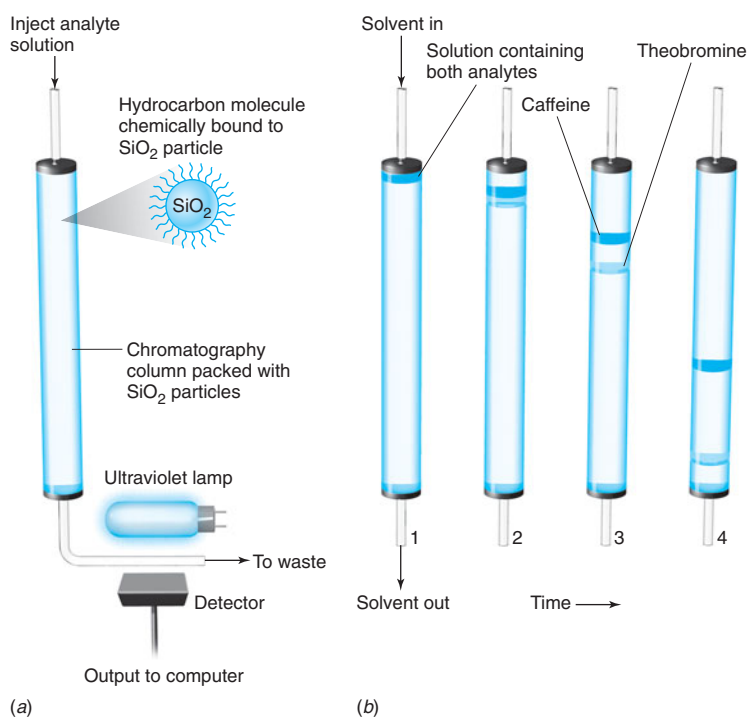


FIGURE 0-10 Principle of liquid chromatography. (*a*) Chromatography apparatus with an ultraviolet absorbance monitor to detect analytes at the column outlet. (*b*) Separation of caffeine and theobromine by chromatography. Caffeine is more soluble than theobromine in the hydrocarbon layer on the particles in the column. Therefore, caffeine is retained more strongly and moves through the column more slowly than theobromine.

analytes are flushed through the column by solvent, theobromine reaches the outlet before caffeine (Figure 0-10b).

Analytes are detected at the outlet by their ability to absorb ultraviolet radiation from the lamp in Figure 0-10a. The graph of detector response versus time in Figure 0-11 is called a *chromatogram*. Theobromine and caffeine are the major peaks in the chromatogram. Small peaks arise from other substances extracted from the chocolate.

The chromatogram alone does not tell us what compounds are present. One way to identify individual peaks is to measure spectral characteristics of each one as it emerges from the column. Another way is to add an authentic sample of either caffeine or theobromine to the unknown and see whether one of the peaks grows in magnitude.

Identifying *what* is in an unknown is called **qualitative analysis.** Identifying *how much* is present is called **quantitative analysis.** The vast majority of this book deals with quantitative analysis.

In Figure 0-11, the *area* under each peak is proportional to the quantity of compound passing through the detector. The best way to measure area is with a computer that receives output from the chromatography detector. Denby and Scott did not have a computer linked to their chromatograph, so they measured the *height* of each peak instead.

Only substances that absorb ultraviolet radiation at a wavelength of 254 nanometers are observed in Figure 0-11. The major components in the aqueous extract are sugars, but they are not detected in this experiment.

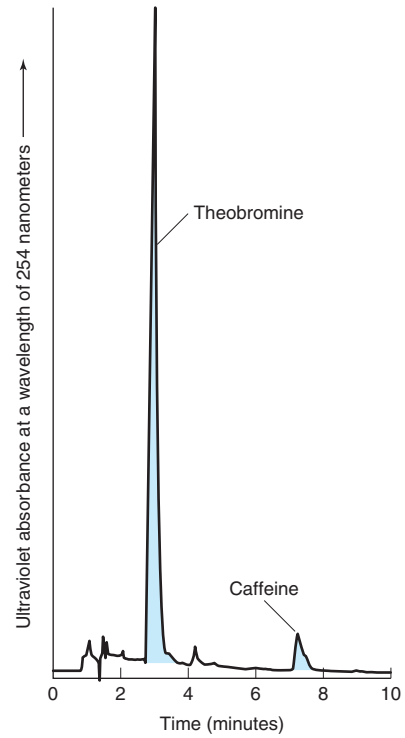


FIGURE 0-11 Chromatogram of 20.0 microliters of dark chocolate extract. A 4.6-mm-diameter × 150-mm-long column, packed with 5-micrometer particles of Hypersil ODS, was eluted (washed) with water:methanol:acetic acid (79:20:1 by volume) at a rate of 1.0 mL per minute.

Calibration Curves

In general, analytes with equal concentrations give different detector responses. Therefore, the response must be measured for known concentrations of each analyte. A graph of detector response as a function of analyte concentration is called a **calibration curve** or a *standard curve*. To construct such a curve, **standard solutions** containing known concentrations of pure theobromine or caffeine were prepared and injected into the column, and the resulting peak heights were measured. Figure 0-12 is a chromatogram of one of the standard solutions, and Figure 0-13 shows calibration curves made by injecting solutions containing 10.0, 25.0, 50.0, or 100.0 micrograms of each analyte per gram of solution.

Straight lines drawn through the calibration points could then be used to find the concentrations of theobromine and caffeine in an unknown. From the equation of the theobromine line in Figure 0-13, we can say that, if the observed peak height of theobromine from an unknown solution is 15.0 cm, then the concentration is 76.9 micrograms per gram of solution.

Interpreting the Results

Knowing how much analyte is in the aqueous extract of the chocolate, Denby and Scott could calculate how much theobromine and caffeine were in the original chocolate. Results for dark and white chocolates are shown in Table 0-1. The quantities found in white chocolate are only about 2% as great as the quantities in dark chocolate.

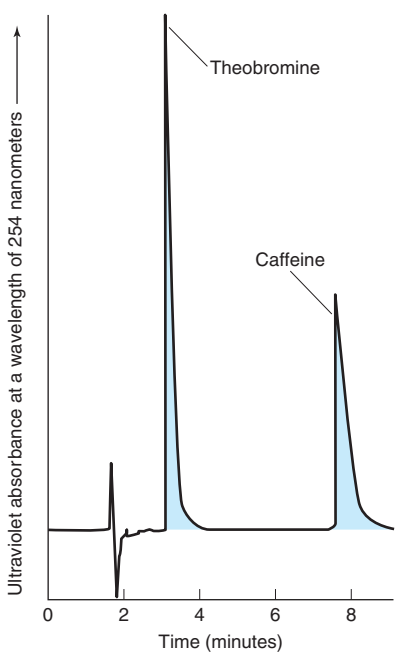


FIGURE 0-12 Chromatogram of 20.0 microliters of a standard solution containing 50.0 micrograms of theobromine and 50.0 micrograms of caffeine per gram of solution.

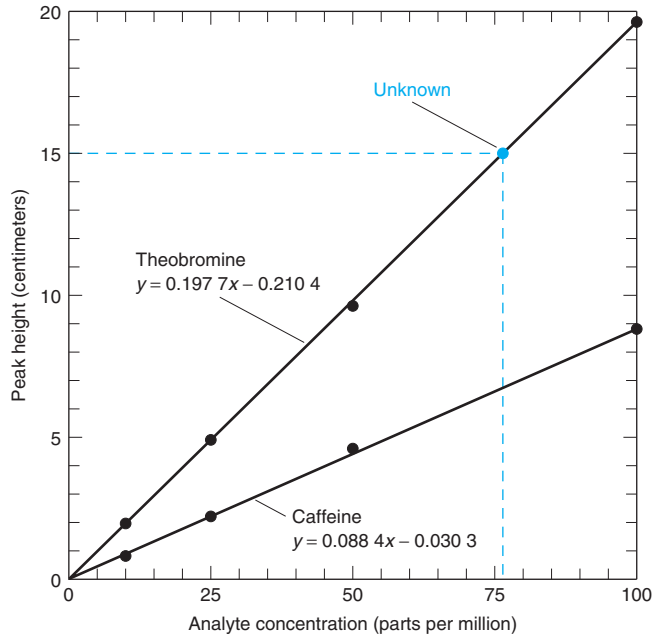


FIGURE 0-13 Calibration curves, showing observed peak heights for known concentrations of pure compounds. One *part per million* is one microgram of analyte per gram of solution. Equations of the straight lines drawn through the experimental data points were determined by the *method of least squares* described in Chapter 4.

The table also reports the *standard deviation* of three replicate measurements for each sample. Standard deviation, discussed in Chapter 4, is a measure of the reproducibility of the results. If three samples were to give identical results, the standard deviation would be 0. If results are not very reproducible, then the standard deviation is large. For theobromine in dark chocolate, the standard deviation (0.002) is less than 1% of the average (0.392), so we say the measurement is reproducible. For theobromine in white chocolate, the standard deviation (0.007) is nearly as great as the average (0.010), so the measurement is poorly reproducible.

TABLE 0-1 Analyses of dark and white chocolate

	Grams of analyte per 100 grams of chocolate	
Analyte	**Dark chocolate**	**White chocolate**
Theobromine	0.392 ± 0.002	0.010 ± 0.007
Caffeine	0.050 ± 0.003	0.000 9 ± 0.001 4

Average ± standard deviation of three replicate injections of each extract.

The purpose of an analysis is to reach some conclusion. The questions posed earlier were "How much caffeine is in a chocolate bar?" and "How does it compare with the quantity in coffee or soft drinks?" After all this work, Denby and Scott discovered how much caffeine is in the *one* particular chocolate bar that they analyzed. It would take a great deal more work to sample many chocolate bars of the same type and many different types of chocolate to gain a more universal view. Table 0-2 compares results from analyses of different sources of caffeine. A can of soft drink or a cup of tea contains less than one-half of the caffeine in a small cup

TABLE 0-2 Caffeine content of beverages and foods

Source	Caffeine (milligrams per serving)	Serving size[a] (ounces)
Regular coffee	106–164	5
Decaffeinated coffee	2–5	5
Tea	21–50	5
Cocoa beverage	2–8	6
Baking chocolate	35	1
Sweet chocolate	20	1
Milk chocolate	6	1
Caffeinated soft drinks	36–57	12
Red Bull	80	8.2

a. 1 ounce = 28.35 grams.
SOURCES: http://www.holymtn.com/tea/caffeine_content.htm. Red Bull from http://wilstar.com/caffeine.htm.

of coffee. Chocolate contains even less caffeine, but a hungry backpacker eating enough baking chocolate can get a pretty good jolt!

0-3 General Steps in a Chemical Analysis

The analytical process often begins with a question that is not phrased in terms of a chemical analysis. The question could be "Is this water safe to drink?" or "Does emission testing of automobiles reduce air pollution?" A scientist translates such questions into the need for particular measurements. An analytical chemist then chooses or invents a procedure to carry out those measurements.

When the analysis is complete, the analyst must translate the results into terms that can be understood by others—preferably by the general public. A most important feature of any result is its limitations. What is the statistical uncertainty in reported results? If you took samples in a different manner, would you obtain the same results? Is a tiny amount (a *trace*) of analyte found in a sample really there or is it contamination? Only after we understand the results and their limitations can we draw conclusions.

We can now summarize general steps in the analytical process:

Formulating the question — Translate general questions into specific questions to be answered through chemical measurements.

Selecting analytical procedures — Search the chemical literature to find appropriate procedures or, if necessary, devise new procedures to make the required measurements.

Sampling — *Sampling* is the process of selecting representative material to analyze. Box 0-1 provides some ideas on how to do so. If you begin with a poorly chosen sample or if the sample changes between the time it is collected and the time it is analyzed, the results are meaningless. "Garbage in, garbage out!"

Sample preparation — *Sample preparation* is the process of converting a representative sample into a form suitable for chemical analysis, which usually means dissolving the sample. Samples with a low concentration of analyte may need to be concentrated prior to analysis. It may be necessary to remove or *mask* species that interfere with the chemical analysis. For a chocolate bar, sample preparation consisted of removing fat and dissolving the desired analytes. Fat was removed because it would interfere with chromatography.

Analysis — Measure the concentration of analyte in several identical **aliquots** (portions). The purpose of *replicate measurements* (repeated measurements) is to assess the variability (uncertainty) in the analysis and to guard against a gross error in the analysis of a single aliquot. *The uncertainty of a measurement is as important as the measurement itself,* because it tells us how reliable the measurement is. If necessary, use different analytical methods on similar samples to make sure that all methods give the same result and that the choice of analytical method is not biasing the result. You may also wish to construct and analyze several different bulk samples to see what variations arise from your sampling procedure.

Reporting and interpretation — Deliver a clearly written, complete report of your results, highlighting any limitations that you attach to them. Your report might be written to be read only by a specialist (such as your instructor), or it might be written for a general audience (perhaps your mother). Be sure the report is appropriate for its intended audience.

Drawing conclusions — Once a report is written, the analyst might not be involved in what is done with the information, such as modifying the raw material supply for a factory or creating new laws to regulate food additives. The more clearly a report is written, the less likely it is to be misinterpreted by those who use it.

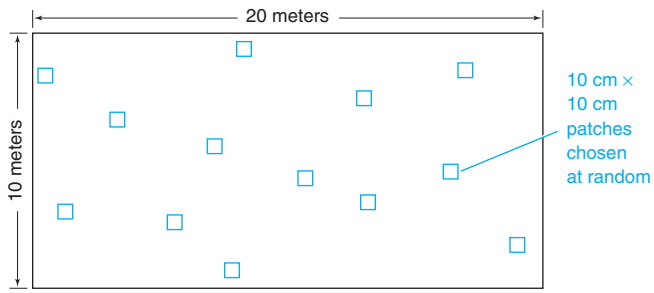
Chemists use the term **species** to refer to any chemical of interest. Species is both singular and plural. **Interference** occurs when a species other than analyte increases or decreases the response of the analytical method and makes it appear that there is more or less analyte than is actually present. **Masking** is the transformation of an interfering species into a form that is not detected. For example, Ca^{2+} in lake water can be measured with a reagent called EDTA. Al^{3+} interferes with this analysis because it also reacts with EDTA. Al^{3+} can be masked with excess F^- to form AlF_6^{3-}, which does not react with EDTA.

Most of this book deals with measuring chemical concentrations in homogeneous aliquots of an unknown. The analysis is meaningless unless you have collected the sample properly, you have taken measures to ensure the reliability of the analytical method, and you communicate your results clearly and completely. The chemical analysis is only the middle portion of a process that begins with a question and ends with a conclusion.

BOX 0-1 Constructing a Representative Sample

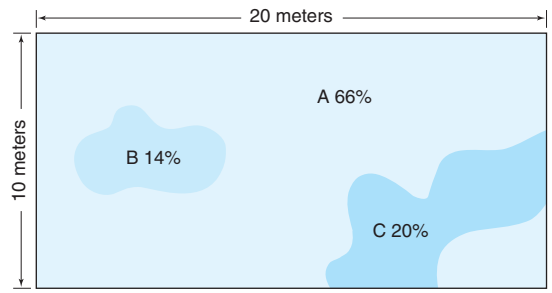
In a **random heterogeneous material,** differences in composition occur randomly and on a fine scale. When you collect a portion of the material for analysis, you obtain some of each of the different compositions. To construct a representative sample from a heterogeneous material, you can first visually divide the material into segments. A **random sample** is collected by taking portions from the desired number of segments chosen at random. If you want to measure the magnesium content of the grass in the 10-meter × 20-meter field in panel *a*, you could divide the field into 20 000 small patches that are 10 centimeters on a side. After assigning a number to each small patch, you could use a computer program to pick 100 numbers at random from 1 to 20 000. Then harvest and combine the grass from each of these 100 patches to construct a representative bulk sample for analysis.

For a **segregated heterogeneous material** (in which large regions have obviously different compositions), a representative **composite sample** must be constructed. For example, the field in panel *b* has three different types of grass segregated into regions A, B, and C. You could draw a map of the field on graph paper and measure the area in each region. In this case, 66% of the area lies in region A, 14% lies in region B, and 20% lies in region C. To construct a representative bulk sample from this segregated material, take 66 of the small patches from region A, 14 from region B, and 20 from region C. You could do so by drawing random numbers from 1 to 20 000 to select patches until you have the desired number from each region.



Random heterogeneous material

(*a*)



Segregated heterogeneous material

(*b*)

Terms to Understand

Terms are introduced in **bold** type in the chapter and are also defined in the Glossary.

aliquot
analyte
aqueous
calibration curve
composite sample
decant
heterogeneous
homogeneous
interference
masking
qualitative analysis
quantitative analysis
quantitative transfer
random heterogeneous material
random sample
sample preparation
sampling
segregated heterogeneous material
slurry
species
standard solution
supernatant liquid

Problems

Complete solutions to Problems can be found in the *Solutions Manual*. Short answers to numerical problems are at the back of the book.

0-1. What is the difference between *qualitative* and *quantitative* analysis?

0-2. List the steps in a chemical analysis.

0-3. What does it mean to *mask* an interfering species?

0-4. What is the purpose of a calibration curve?

0-5. (a) What is the difference between a homogeneous material and a heterogeneous material?

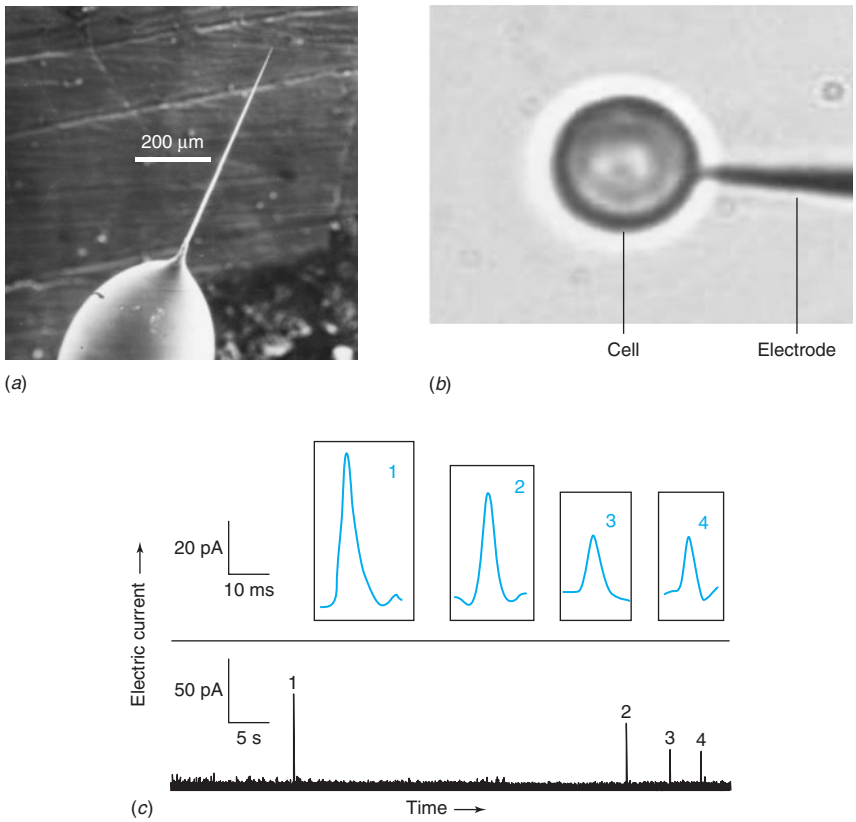
(b) After reading Box 0-1, state the difference between a segregated heterogeneous material and a random heterogeneous material.

(c) How would you construct a representative sample from each type of material?

0-6. The iodide (I^-) content of a commercial mineral water was measured by two methods that produced wildy different results.[7] Method A found 0.23 milligrams of I^- per liter (mg/L) and method B found 0.009 mg/L. When Mn^{2+} was added to the water, the I^- content found by method A increased each time more Mn^{2+} was added, but results from method B were unchanged. Which of the *Terms to Understand* describes what is occurring in these measurements?

1 Chemical Measurements

BIOCHEMICAL MEASUREMENTS WITH A NANOELECTRODE



(*a*) Carbon-fiber electrode with a 100-nanometer-diameter (100×10^{-9} meter) tip extending from glass capillary. The marker bar is 200 micrometers (200×10^{-6} meter). [From W.-H. Huang, D.-W. Pang, H. Tong, Z.-L. Wang, and J.-K. Cheng, *Anal. Chem.* **2001**, *73*, 1048.] (*b*) Electrode positioned adjacent to a cell detects release of the neurotransmitter, dopamine, from the cell. A nearby, larger counterelectrode is not shown. (*c*) Bursts of electric current detected when dopamine is released. Insets are enlargements. [From W.-Z. Wu, W.-H. Huang, W. Wang, Z.-L. Wang, J.-K. Cheng, T. Xu, R.-Y. Zhang, Y. Chen, and J. Liu, *J. Am. Chem. Soc.* **2005**, *127*, 8914.]

An electrode with a tip smaller than a single cell allows us to measure neurotransmitter molecules released by a nerve cell in response to a chemical stimulus. We call the electrode a *nanoelectrode* because its active region has dimensions of nanometers (10^{-9} meters). Neurotransmitter molecules released from one *vesicle* (a small compartment) of a nerve cell diffuse to the electrode, where they donate or accept electrons, thereby generating an electric current measured in picoamperes (10^{-12} amperes) for a period of milliseconds (10^{-3} seconds). This chapter discusses units that describe chemical and physical measurements of objects ranging in size from atoms to galaxies.

Neurotransmitter measurements illustrate the need for units of measurement covering many *orders of magnitude* (powers of 10) in range. This chapter introduces those units and reviews chemical concentrations, solution preparation, stoichiometry, and fundamentals of titrations.

For readability, we insert a space after every third digit on either side of the decimal point. Commas are not used, because in some parts of the world a comma has the same meaning as a decimal point. Examples:

Speed of light: 299 792 458 m/s

Avogadro's number: $6.022\ 141\ 79 \times 10^{23}$ mol^{-1}

1-1 SI Units

SI units of measurement, used by scientists around the world, derive their name from the French *Système International d'Unités*. *Fundamental units* (base units) from which all others are derived are listed in Table 1-1. Standards of length, mass, and time are the *meter* (m), *kilogram* (kg), and *second* (s), respectively. Temperature is measured in *kelvins* (K), amount of substance in *moles* (mol), and electric current in *amperes* (A).

TABLE 1-1 Fundamental SI units

Quantity	Unit (symbol)	Definition
Length	meter (m)	One meter is the distance light travels in a vacuum during $\frac{1}{299\,792\,458}$ of a second.
Mass	kilogram (kg)	One kilogram is the mass of the Pt-Ir alloy prototype kilogram made in 1885 and kept under an inert atmosphere at Sèvres, France. This object has been removed from its protective enclosure only in 1890, 1948, and 1992 to weigh secondary standards kept in several countries. Unfortunately, the mass of the prototype kilogram can change slowly over time by chemical reaction with the atmosphere or from mechanical wear. Work in progress will replace the prototype kilogram with a standard based on unchanging properties of nature that can be measured within an uncertainty of 1 part in 10^8. See I. Robinson, "Weighty Matters," *Scientific American*, December 2006, p.102.
Time	second (s)	One second is the duration of 9 192 631 770 periods of the radiation corresponding to a certain atomic transition of ^{133}Cs.
Electric current	ampere (A)	One ampere of current produces a force of 2×10^{-7} newtons per meter of length when maintained in two straight, parallel conductors of infinite length and negligible cross section, separated by 1 meter in a vacuum.
Temperature	kelvin (K)	Temperature is defined such that the triple point of water (at which solid, liquid, and gaseous water are in equilibrium) is 273.16 K, and the temperature of absolute zero is 0 K.
Luminous intensity	candela (cd)	Candela is a measure of luminous intensity visible to the human eye.
Amount of substance	mole (mol)	One mole is the number of particles equal to the number of atoms in exactly 0.012 kg of ^{12}C (approximately 6.022×10^{23}).
Plane angle	radian (rad)	There are 2π radians in a circle.
Solid angle	steradian (sr)	There are 4π steradians in a sphere.

Pressure is force per unit area: 1 pascal (Pa) = 1 N/m^2. The pressure of the atmosphere is approximately 100 000 Pa.

Table 1-2 lists some quantities that are defined in terms of the fundamental quantities. For example, force is measured in *newtons* (N), pressure in *pascals* (Pa), and energy in *joules* (J), each of which can be expressed in terms of length, time, and mass.

Using Prefixes as Multipliers

Rather than using exponential notation, we often use prefixes from Table 1-3 to express large or small quantities. As an example, consider the pressure of ozone (O_3) in the upper atmosphere (Figure 1-1). Ozone is important because it absorbs ultraviolet radiation from the sun that damages many organisms and causes skin cancer. Each spring, a great deal of ozone disappears from the Antarctic stratosphere, thereby creating what is called an ozone "hole." The opening of Chapter 17 discusses the chemistry behind this process.

At an altitude of 1.7×10^4 meters above the Earth's surface, the pressure of ozone over Antarctica reaches a peak of 0.019 Pa. Let's express these numbers with prefixes from Table 1-3. We customarily use prefixes for every third power of ten (10^{-9}, 10^{-6}, 10^{-3}, 10^3,

TABLE 1-2 SI-derived units with special names

Quantity	Unit	Symbol	Expression in terms of other units	Expression in terms of SI base units
Frequency	hertz	Hz		1/s
Force	newton	N		$m \cdot kg/s^2$
Pressure	pascal	Pa	N/m^2	$kg/(m \cdot s^2)$
Energy, work, quantity of heat	joule	J	$N \cdot m$	$m^2 \cdot kg/s^2$
Power, radiant flux	watt	W	J/s	$m^2 \cdot kg/s^3$
Quantity of electricity, electric charge	coulomb	C		$s \cdot A$
Electric potential, potential difference, electromotive force	volt	V	W/A	$m^2 \cdot kg/(s^3 \cdot A)$
Electric resistance	ohm	Ω	V/A	$m^2 \cdot kg/(s^3 \cdot A^2)$
Electric capacitance	farad	F	C/V	$s^4 \cdot A^2/(m^2 \cdot kg)$

Frequency is the number of cycles per unit time for a repetitive event. Force is the product mass × acceleration. Pressure is force per unit area. Energy or work is force × distance = mass × acceleration × distance. Power is energy per unit time. The electric potential difference between two points is the work required to move a unit of positive charge between the two points. Electric resistance is the potential difference required to move one unit of charge per unit time between two points. The electric capacitance of two parallel surfaces is the quantity of electric charge on each surface when there is a unit of electric potential difference between the two surfaces.

TABLE 1-3 Prefixes

Prefix	Symbol	Factor	Prefix	Symbol	Factor
yotta	Y	10^{24}	deci	d	10^{-1}
zetta	Z	10^{21}	centi	c	10^{-2}
exa	E	10^{18}	milli	m	10^{-3}
peta	P	10^{15}	micro	μ	10^{-6}
tera	T	10^{12}	nano	n	10^{-9}
giga	G	10^{9}	pico	p	10^{-12}
mega	M	10^{6}	femto	f	10^{-15}
kilo	k	10^{3}	atto	a	10^{-18}
hecto	h	10^{2}	zepto	z	10^{-21}
deca	da	10^{1}	yocto	y	10^{-24}

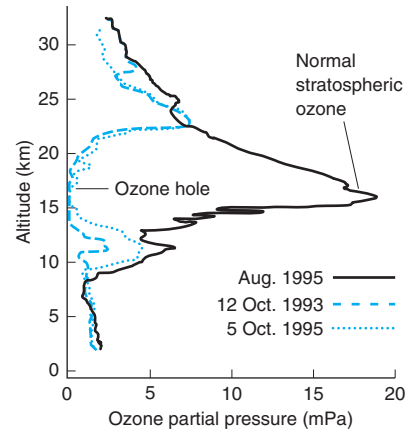


FIGURE 1-1 An ozone "hole" forms each year in the stratosphere over the South Pole at the beginning of spring in October. The graph compares ozone pressure in August, when there is no hole, with the pressure in October, when the hole is deepest. Less severe ozone loss is observed at the North Pole. [Data from National Oceanic and Atmospheric Administration.]

10^6, 10^9, and so on). The number 1.7×10^4 m is more than 10^3 m and less than 10^6 m, so we use a multiple of 10^3 m (= kilometers, km):

$$1.7 \times 10^4\ \cancel{\text{m}} \times \frac{1\ \text{km}}{10^3\ \cancel{\text{m}}} = 17\ \text{km}$$

The number 0.019 Pa is more than 10^{-3} Pa and less than 10^0 Pa, so we use a multiple of 10^{-3} Pa (= millipascals, mPa):

$$0.019\ \cancel{\text{Pa}} \times \frac{1\ \text{mPa}}{10^{-3}\ \cancel{\text{Pa}}} = 19\ \text{mPa}$$

Of course you recall that $10^0 = 1$.

Figure 1-1 is labeled with km on the *y*-axis and mPa on the *x*-axis. The *y*-axis of a graph is called the **ordinate** and the *x*-axis is called the **abscissa.**

It is a fabulous idea to write units beside each number in a calculation and to cancel identical units in the numerator and denominator. This practice ensures that you know the units for your answer. If you intend to calculate pressure and your answer comes out with units other than pascals (N/m^2 or $kg/[m \cdot s^2]$ or other units of force/area), then you have made a mistake.

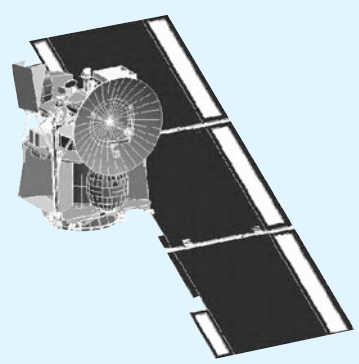
Converting Between Units

Although SI is the internationally accepted system of measurement in science, other units are encountered. Useful conversion factors are found in Table 1-4. For example, common non-SI

TABLE 1-4 Conversion factors

Quantity	Unit	Symbol	SI equivalent[a]
Volume	liter	L	$*10^{-3}\ m^3$
	milliliter	mL	$*10^{-6}\ m^3$
Length	angstrom	Å	$*10^{-10}$ m
	inch	in.	*0.025 4 m
Mass	pound	lb	*0.453 592 37 kg
	metric ton		*1 000 kg
Force	dyne	dyn	$*10^{-5}$ N
Pressure	bar	bar	$*10^{5}$ Pa
	atmosphere	atm	*101 325 Pa
	atmosphere	atm	*1.013 25 bar
	torr (= 1 mm Hg)	Torr	133.322 Pa
	pound/in.^{2}	psi	6 894.76 Pa
Energy	erg	erg	$*10^{-7}$ J
	electron volt	eV	$1.602\ 176\ 487 \times 10^{-19}$ J
	calorie, thermochemical	cal	*4.184 J
	Calorie (with a capital C)	Cal	*1 000 cal = 4.184 kJ
	British thermal unit	Btu	1 055.06 J
Power	horsepower		745.700 W
Temperature	centigrade (= Celsius)	°C	*K − 273.15
	Fahrenheit	°F	*1.8(K − 273.15) + 32

a. An asterisk (*) indicates that the conversion is exact (by definition).



Oops! In 1999, the $125 million Mars Climate Orbiter spacecraft was lost when it entered the Martian atmosphere 100 km lower than planned. *The navigation error would have been avoided if people had written their units of measurement.* Engineers who built the spacecraft calculated thrust in the English unit, pounds of force. Jet Propulsion Laboratory engineers thought they were receiving the information in the metric unit, newtons. Nobody caught the error.

One *calorie* is the energy required to heat 1 gram of water from 14.5° to 15.5°C.

One *joule* is the energy expended when a force of 1 newton acts over a distance of 1 meter. This much energy can raise 102 g (about $\frac{1}{4}$ pound) by 1 meter.

$$1 \text{ cal} = 4.184 \text{ J}$$

1 pound (mass) ≈ 0.453 6 kg
1 mile ≈ 1.609 km
The symbol ≈ is read "is approximately equal to."

units for energy are the *calorie* (cal) and the *Calorie* (written with a capital C and standing for 1 000 calories, or 1 kcal). Table 1-4 states that 1 cal is exactly 4.184 J (joules).

Your *basal metabolism* uses approximately 46 Calories per hour (h) per 100 pounds (lb) of body mass just to carry out basic functions required for life, apart from doing any kind of exercise. A person walking at 2 miles per hour on a level path uses approximately 45 Calories per hour per 100 pounds of body mass beyond basal metabolism. The same person swimming at 2 miles per hour consumes 360 Calories per hour per 100 pounds beyond basal metabolism.

EXAMPLE **Unit Conversions**

Express the rate of energy used by a person walking 2 miles per hour (46 + 45 = 91 Calories per hour per 100 pounds of body mass) in kilojoules per hour per kilogram of body mass.

Solution We will convert each non-SI unit separately. First, note that 91 Calories = 91 kcal. Table 1-4 states that 1 cal = 4.184 J; so 1 kcal = 4.184 kJ, and

$$91 \text{ kcal} \times 4.184 \frac{\text{kJ}}{\text{kcal}} = 3.8 \times 10^2 \text{ kJ}$$

Table 1-4 also says that 1 lb is 0.453 6 kg; so 100 lb = 45.36 kg. The rate of energy consumption is therefore

$$\frac{91 \text{ kcal/h}}{100 \text{ lb}} = \frac{3.8 \times 10^2 \text{kJ/h}}{45.36 \text{ kg}} = 8.4 \frac{\text{kJ/h}}{\text{kg}}$$

Significant figures are discussed in Chapter 3. For multiplication and division, the number with the fewest digits determines how many digits should be in the answer. The number 91 kcal at the beginning of this problem limits the answer to 2 digits.

We could have written this as one long calculation:

$$\text{Rate} = \frac{91 \text{ kcal/h}}{100 \text{ lb}} \times 4.184 \frac{\text{kJ}}{\text{kcal}} \times \frac{1 \text{ lb}}{0.453\,6 \text{ kg}} = 8.4 \frac{\text{kJ/h}}{\text{kg}}$$

Test Yourself A person swimming at 2 miles per hour requires 360 + 46 Calories per hour per 100 pounds of body mass. Express the energy use in kJ/h per kg of body mass. (***Answer:*** 37 kJ/h per kg)

1-2 Chemical Concentrations

A *homogeneous* substance has a uniform composition. Sugar dissolved in water is homogeneous. A mixture that is not the same everywhere (such as orange juice, which has suspended solids) is *heterogeneous*.

A *solution* is a *homogeneous* mixture of two or more substances. A minor species in a solution is called **solute**, and the major species is the **solvent**. In this book, most discussions concern *aqueous solutions*, in which the solvent is water. **Concentration** states how much solute is contained in a given volume or mass of solution or solvent.

Molarity and Molality

Avogadro's number = number of atoms in 12 g of ^{12}C

$$\text{Molarity (M)} = \frac{\text{moles of solute}}{\text{liters of solution}}$$

Atomic masses are shown in the periodic table inside the cover of this book. Physical constants such as Avogadro's number are also listed inside the cover.

A **mole** (mol) is *Avogadro's number* of particles (atoms, molecules, ions, or anything else). **Molarity** (M) is the number of moles of a substance per liter of solution. A **liter** (L) is the volume of a cube that is 10 cm on each edge. Because 10 cm = 0.1 m, 1 L = $(0.1 \text{ m})^3 = 10^{-3} \text{ m}^3$. Chemical concentrations, denoted with square brackets, are usually expressed in moles per liter (M). Thus "$[H^+]$" means "the concentration of H^+."

The **atomic mass** of an element is the number of grams containing Avogadro's number of atoms.[1] The **molecular mass** of a compound is the sum of atomic masses of the atoms in the molecule. It is the number of grams containing Avogadro's number of molecules.

Strong electrolyte: mostly dissociated into ions in solution

Weak electrolyte: partially dissociated into ions in solution

An **electrolyte** is a substance that dissociates into ions in solution. In general, electrolytes are more dissociated in water than in other solvents. We refer to a compound that is mostly dissociated into ions as a *strong electrolyte*. One that is partially dissociated is called a *weak electrolyte*.

$MgCl^+$ is called an *ion pair*. See Box 7-1.

Magnesium chloride is a strong electrolyte. In 0.44 M $MgCl_2$ solution, 70% of the magnesium is free Mg^{2+} and 30% is $MgCl^+$. The concentration of $MgCl_2$ molecules is close to 0. Sometimes the molarity of a strong electrolyte is called the **formal concentration** (F), to emphasize that the substance is really converted into other species in solution. When we

say that the "concentration" of $MgCl_2$ is 0.054 M in seawater, we are really speaking of its formal concentration (0.054 F). The "molecular mass" of a strong electrolyte is called the **formula mass** (FM), because it is the sum of atomic masses of atoms in the formula, even though there are very few molecules with that formula. *We are going to use the abbreviation FM for both formula mass and molecular mass.*

EXAMPLE Molarity of Salts in the Sea

(a) Typical seawater contains 2.7 g of salt (sodium chloride, NaCl) per 100 mL ($= 100 \times 10^{-3}$ L). What is the molarity of NaCl in the ocean? **(b)** $MgCl_2$ has a concentration of 0.054 M in the ocean. How many grams of $MgCl_2$ are present in 25 mL of seawater?

Solution **(a)** The molecular mass of NaCl is 22.99 g/mol (Na) + 35.45 g/mol (Cl) = 58.44 g/mol. The moles of salt in 2.7 g are (2.7 g)/(58.44 g/mol) = 0.046 mol, so the molarity is

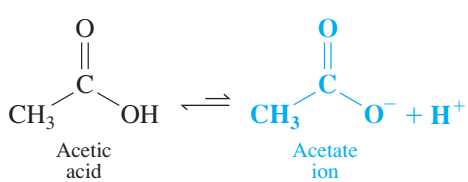
$$\text{Molarity of NaCl} = \frac{\text{mol NaCl}}{\text{L of seawater}} = \frac{0.046\ \text{mol}}{100 \times 10^{-3}\ \text{L}} = 0.46\ \text{M}$$

(b) The molecular mass of $MgCl_2$ is 24.30 g/mol (Mg) + 2 × 35.45 g/mol (Cl) = 95.20 g/mol. The number of grams in 25 mL is

$$\text{Grams of MgCl}_2 = \left(0.054\,\frac{\cancel{\text{mol}}}{\cancel{\text{L}}}\right)\left(95.20\,\frac{\text{g}}{\cancel{\text{mol}}}\right)(25 \times 10^{-3}\ \cancel{\text{L}}) = 0.13\ \text{g}$$

Test Yourself Calculate the formula mass of $CaSO_4$. What is the molarity of $CaSO_4$ in a solution containing 1.2 g of $CaSO_4$ in a volume of 50 mL? How many grams of $CaSO_4$ are in 50 mL of 0.086 M $CaSO_4$? (***Answer:*** 136.14 g/mol, 0.18 M, 0.59 g)

For a *weak electrolyte* such as acetic acid, CH_3CO_2H, some of the molecules dissociate into ions in solution:



Formal concentration	Percent dissociated
0.10 F	1.3%
0.010 F	4.1%
0.001 0 F	12%

Molality (m) is concentration expressed as moles of substance per kilogram of solvent (not total solution). Molality is independent of temperature. Molarity changes with temperature because the volume of a solution usually increases when it is heated.

Confusing abbreviations:
mol = moles

$$\text{M} = \text{molarity} = \frac{\text{mol solute}}{\text{L solution}}$$

$$m = \text{molality} = \frac{\text{mol solute}}{\text{kg solvent}}$$

Percent Composition

The percentage of a component in a mixture or solution is usually expressed as a **weight percent** (wt%):

$$\text{Weight percent} = \frac{\text{mass of solute}}{\text{mass of total solution or mixture}} \times 100 \qquad \textbf{(1-1)}$$

A common form of ethanol (CH_3CH_2OH) is 95 wt%; this expression means 95 g of ethanol per 100 g of total solution. The remainder is water. **Volume percent** (vol%) is defined as

$$\text{Volume percent} = \frac{\text{volume of solute}}{\text{volume of total solution}} \times 100 \qquad \textbf{(1-2)}$$

Although units of mass or volume should always be expressed to avoid ambiguity, mass is usually implied when units are absent.

$$\text{Density} = \frac{\text{mass}}{\text{volume}} = \frac{\text{g}}{\text{mL}}$$

A closely related dimensionless quantity is

$$\text{Specific gravity} = \frac{\text{density of a substance}}{\text{density of water at 4°C}}$$

The density of water at 4°C is close to 1 g/mL, so specific gravity is nearly the same as density.

EXAMPLE Converting Weight Percent into Molarity and Molality

Find the molarity and molality of 37.0 wt% HCl. The **density** of a substance is the mass per unit volume. The table inside the back cover of this book tells us that the density of the reagent is 1.19 g/mL.

Solution For *molarity*, we need to find the moles of HCl per liter of solution. The mass of a liter of solution is $(1.19\ \text{g}/\cancel{\text{mL}})(1\,000\ \cancel{\text{mL}}) = 1.19 \times 10^3$ g. The mass of HCl in a liter is

$$\text{Mass of HCl per liter} = \left(1.19 \times 10^3 \frac{\cancel{\text{g solution}}}{\text{L}}\right)\underbrace{\left(0.370 \frac{\text{g HCl}}{\cancel{\text{g solution}}}\right)}_{\text{This is what 37.0 wt\% means}} = 4.40 \times 10^2 \frac{\text{g HCl}}{\text{L}}$$

The molecular mass of HCl is 36.46 g/mol, so the molarity is

$$\text{Molarity} = \frac{\text{mol HCl}}{\text{L solution}} = \frac{4.40 \times 10^2\ \cancel{\text{g HCl}}/\text{L}}{36.46\ \cancel{\text{g HCl}}/\text{mol}} = 12.1 \frac{\text{mol}}{\text{L}} = 12.1\ \text{M}$$

For *molality*, we need to find the moles of HCl per kilogram of solvent (which is H_2O). The solution is 37.0 wt% HCl, so we know that 100.0 g of solution contains 37.0 g of HCl and $100.0 - 37.0 = 63.0$ g of H_2O (= 0.063 0 kg). But 37.0 g of HCl contains $37.0\ \cancel{\text{g}}/(36.46\ \cancel{\text{g}}/\text{mol}) = 1.01$ mol. The molality is therefore

$$\text{Molality} = \frac{\text{mol HCl}}{\text{kg of solvent}} = \frac{1.01\ \text{mol HCl}}{0.063\,0\ \text{kg}\ H_2O} = 16.1\ m$$

If you divide 1.01/0.063 0, you get 16.0. Dan got 16.1 because he kept all the digits in his calculator and did not round off until the end. The number 1.01 was really 1.014 8 and (1.014 8)/(0.063 0) = 16.1.

Test Yourself Calculate the molarity and molality of 49.0 wt% HF, using the density given inside the back cover of this book. (***Answer:*** 31.8 M, 48.0 *m*)

Figure 1-2 illustrates a weight percent measurement in the application of analytical chemistry to archaeology. Gold and silver are found together in nature. Dots in Figure 1-2 show the weight percent of gold in more than 1 300 silver coins minted over a 500-year period. Prior to A.D. 500, it was rare for the gold content to be below 0.3 wt%. By A.D. 600, people developed techniques for removing more gold from the silver, so some coins had as little as 0.02 wt% gold. Colored squares in Figure 1-2 represent known, modern forgeries made from silver whose gold content is always less than the prevailing gold content in the years A.D. 200 to 500. Chemical analysis makes it easy to detect the forgeries.

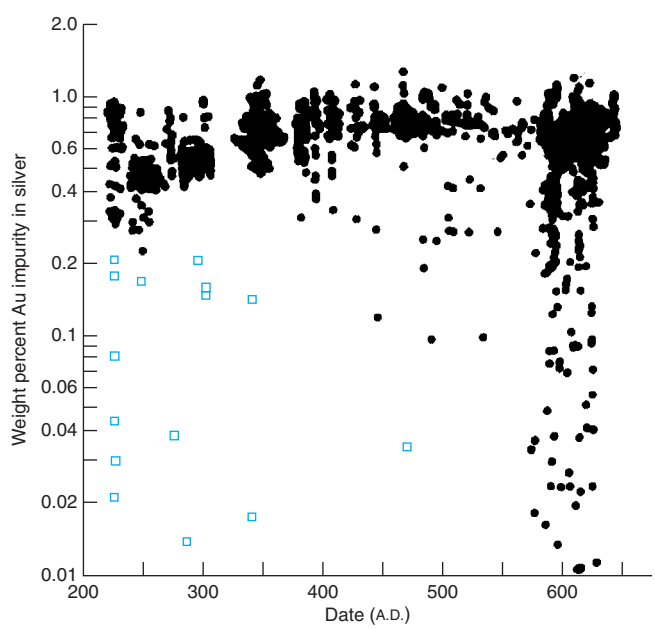


FIGURE 1-2 Weight percent of gold impurity in silver coins from Persia. Colored squares are known, modern forgeries. Note that the ordinate scale is logarithmic. [A. A. Gordus and J. P. Gordus, *Archaeological Chemistry*, *Adv. Chem*. No. 138, American Chemical Society, Washington, DC, 1974, pp. 124–147.]

Parts per Million and Parts per Billion

Sometimes composition is expressed as **parts per million** (ppm) or **parts per billion** (ppb), which mean grams of substance per million or billion grams of total solution or mixture. Because the density of a dilute aqueous solution is close to 1.00 g/mL, *we frequently equate 1 g of water with 1 mL of water*, although this equivalence is only approximate. Therefore, 1 ppm corresponds to 1 μg/mL (= 1 mg/L) and 1 ppb is 1 ng/mL (= 1 μg/L). For gases, ppm usually refers to volume rather than mass. Atmospheric CO_2 has a concentration near 380 ppm, which means 380 μL CO_2 per liter of air. It is best to label units to avoid confusion.

$$\text{ppm} = \frac{\text{mass of substance}}{\text{mass of sample}} \times 10^6$$

$$\text{ppb} = \frac{\text{mass of substance}}{\text{mass of sample}} \times 10^9$$

Question What does one part per thousand mean?

EXAMPLE Converting Parts per Billion into Molarity

Normal alkanes are hydrocarbons with the formula C_nH_{2n+2}. Plants selectively synthesize alkanes with an odd number of carbon atoms. The concentration of $C_{29}H_{60}$ in summer rainwater collected in Hannover, Germany is 34 ppb. Find the molarity of $C_{29}H_{60}$ and express the answer with a prefix from Table 1-3.

Solution A concentration of 34 ppb means there are 34 ng of $C_{29}H_{60}$ per gram of rainwater, a value that we equate to 34 ng/mL. Multiplying nanograms and milliliters by 1 000 gives 34 μg of $C_{29}H_{60}$ per liter of rainwater. The molecular mass of $C_{29}H_{60}$ is 408.8 g/mol, so the molarity is

$$\text{Molarity of } C_{29}H_{60} \text{ in rainwater} = \frac{34 \times 10^{-6}\,\text{g/L}}{408.8\,\text{g/mol}} = 8.3 \times 10^{-8}\,\text{M}$$

An appropriate prefix from Table 1-3 would be nano (n), which is a multiple of 10^{-9}:

$$8.3 \times 10^{-8}\,\text{M}\left(\frac{1\,\text{nM}}{10^{-9}\,\text{M}}\right) = 83\,\text{nM}$$

nM = nanomoles per liter

Test Yourself How many ppm of $C_{29}H_{60}$ are in 23 μM $C_{29}H_{60}$? (***Answer:*** 9.4 ppm)

1-3 Preparing Solutions

To prepare a solution with a desired molarity from a pure solid or liquid, we weigh out the correct mass of reagent and dissolve it in a *volumetric flask* (Figure 1-3).

EXAMPLE Preparing a Solution with a Desired Molarity

Copper(II) sulfate pentahydrate, $CuSO_4 \cdot 5H_2O$, has 5 moles of H_2O for each mole of $CuSO_4$ in the solid crystal. The formula mass of $CuSO_4 \cdot 5H_2O$ (= $CuSO_9H_{10}$) is 249.68 g/mol. (Copper(II) sulfate without water in the crystal has the formula $CuSO_4$ and is said to be **anhydrous.**) How many grams of $CuSO_4 \cdot 5H_2O$ should be dissolved in a volume of 500.0 mL to make 8.00 mM Cu^{2+}?

Solution An 8.00 mM solution contains 8.00×10^{-3} mol/L. We need

$$8.00 \times 10^{-3}\,\frac{\text{mol}}{\text{L}} \times 0.5000\,\text{L} = 4.00 \times 10^{-3}\,\text{mol } CuSO_4 \cdot 5H_2O$$

The mass of reagent is $(4.00 \times 10^{-3}\,\text{mol}) \times (249.68\,\text{g/mol}) = 0.999$ g.

Using a volumetric flask: The procedure is to place 0.999 g of solid $CuSO_4 \cdot 5H_2O$ into a 500-mL volumetric flask, add about 400 mL of distilled water, and swirl to dissolve the reagent. Then dilute with distilled water up to the 500-mL mark and invert the flask several times to ensure complete mixing.

Test Yourself Find the formula mass of anhydrous $CuSO_4$. How many grams should be dissolved in 250.0 mL to make a 16.0 mM solution? (***Answer:*** 159.61 g/mol, 0.638 g)

FIGURE 1-3 A *volumetric flask* contains a specified volume when the liquid level is adjusted to the middle of the mark in the thin neck of the flask. Use of this flask is described in Section 2-5.

Dilution

Dilute solutions can be prepared from concentrated solutions. A volume of the concentrated solution is transferred to a fresh vessel and diluted to the desired final volume. The number of moles of reagent in V liters containing M moles per liter is the product $M \cdot V = \text{mol}/\cancel{L} \cdot \cancel{L}$, so we equate the number of moles in the concentrated (conc) and dilute (dil) solutions:

In Equation 1-3, you can use any units for concentration per unit volume (such as mmol/L or g/mL) and any units for volume (such as mL or μL), as long as you use the same units on both sides. We frequently use mL for volume.

Dilution formula:

$$\underbrace{M_{conc} \cdot V_{conc}}_{\text{Moles taken from concentrated solution}} = \underbrace{M_{dil} \cdot V_{dil}}_{\text{Moles placed in dilute solution}} \qquad (1\text{-}3)$$

EXAMPLE Preparing 0.100 M HCl

The molarity of "concentrated" HCl purchased for laboratory use is approximately 12.1 M. How many milliliters of this reagent should be diluted to 1.000 L to make 0.100 M HCl?

Solution The dilution formula handles this problem directly:

The symbol ⇒ is read "implies that."

$$M_{conc} \cdot V_{conc} = M_{dil} \cdot V_{dil}$$
$$(12.1\ \text{M})(x\ \text{mL}) = (0.100\ \text{M})(1\ 000\ \text{mL}) \Rightarrow x = 8.26\ \text{mL}$$

To make 0.100 M HCl, we would dilute 8.26 mL of concentrated HCl up to 1.000 L. The concentration will not be exactly 0.100 M because the reagent is not exactly 12.1 M. A table inside the cover of this book gives volumes of common reagents required to make 1.0 M solutions.

Test Yourself With information on the inside cover of the book, calculate how many mL of 70.4 wt% nitric acid should be diluted to 0.250 L to make 3.00 M HNO_3. (***Answer:*** 47.5 mL)

EXAMPLE A More Complicated Dilution Calculation

A solution of ammonia in water is called "ammonium hydroxide" because of the equilibrium

In a chemical reaction, species on the left side are called **reactants** and species on the right are called **products**. NH_3 is a reactant and NH_4^+ is a product in Reaction 1-4.

$$\underset{\text{Ammonia}}{NH_3} + H_2O \rightleftharpoons \underset{\text{Ammonium}}{NH_4^+} + \underset{\text{Hydroxide}}{OH^-} \qquad (1\text{-}4)$$

The density of concentrated ammonium hydroxide, which contains 28.0 wt% NH_3, is 0.899 g/mL. What volume of this reagent should be diluted to 500.0 mL to make 0.250 M NH_3?

Solution To use Equation 1-3, we need to know the molarity of the concentrated reagent. The solution contains 0.899 g of solution per milliliter and there is 0.280 g of NH_3 per gram of solution (28.0 wt%), so we can write

$$\text{Molarity of } NH_3 = \frac{899\dfrac{\cancel{\text{g solution}}}{\text{L}} \times 0.280\dfrac{\cancel{\text{g } NH_3}}{\cancel{\text{g solution}}}}{17.03\dfrac{\cancel{\text{g } NH_3}}{\text{mol } NH_3}} = 14.8\ \text{M}$$

Now we find the volume of 14.8 M NH_3 required to prepare 500.0 mL of 0.250 M NH_3:

$$M_{conc} \cdot V_{conc} = M_{dil} \cdot V_{dil}$$
$$14.8\ \cancel{\text{M}} \times V_{conc} = 0.250\ \cancel{\text{M}} \times 500.0\ \text{mL} \Rightarrow V_{conc} = 8.46\ \text{mL}$$

The procedure is to place 8.46 mL of concentrated reagent in a 500-mL volumetric flask, add about 400 mL of water, and swirl to mix. Then dilute to exactly 500 mL with water and invert the flask many times to mix well.

Test Yourself From the density of 70.4 wt% HNO_3 on the inside cover, calculate the molarity of HNO_3. (***Answer:*** 15.8 M)

1-4 Stoichiometry Calculations for Gravimetric Analysis

Chemical analysis based on weighing a final product is called **gravimetric analysis.** Iron from a dietary supplement tablet can be measured by dissolving the tablet and then converting the iron into solid Fe_2O_3. From the mass of Fe_2O_3, we can calculate the mass of iron in the original tablet.

Here are the steps in the procedure:

Step 1 Tablets containing iron(II) fumarate ($Fe^{2+}C_4H_2O_4^{2-}$) and inert binder are mixed with 150 mL of 0.100 M HCl to dissolve the Fe^{2+}. The solution is filtered to remove insoluble binder.

Step 2 Iron(II) in the clear liquid is oxidized to iron(III) with excess hydrogen peroxide:

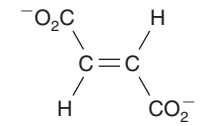
$$\underset{\substack{\text{Iron(II)}\\\text{(ferrous ion)}}}{2Fe^{2+}} + \underset{\substack{\text{Hydrogen peroxide}\\\text{FM 34.01}}}{H_2O_2} + 2H^+ \rightarrow \underset{\substack{\text{Iron(III)}\\\text{(ferric ion)}}}{2Fe^{3+}} + 2H_2O \qquad \textbf{(1-5)}$$

Step 3 Ammonium hydroxide is added to precipitate hydrous iron(III) oxide, which is a gel. The gel is filtered and heated in a furnace to convert it to pure solid Fe_2O_3.

$$\underset{\text{Hydroxide}}{Fe^{3+} + 3OH^-} + (x-1)H_2O \longrightarrow \underset{\text{Hydrous iron(III) oxide}}{FeOOH \cdot xH_2O(s)} \xrightarrow{900°C} \underset{\substack{\text{Iron(III) oxide}\\\text{FM 159.69}}}{Fe_2O_3(s)} \qquad \textbf{(1-6)}$$

We now work through some practical laboratory calculations for this analysis.

Stoichiometry is the calculation of quantities of substances involved in a chemical reaction. It is derived from the Greek *stoicheion* (simplest components) and *metrisi* (to measure).



Fumarate anion, $C_4H_2O_4^{2-}$

The units of formula mass (FM) are g/mol.

$Fe_2O_3(s)$ means that Fe_2O_3 is a *solid*. Other abbreviations for phases are (*l*) for *liquid*, (*g*) for *gas*, and (*aq*) for *aqueous* (meaning "dissolved in water").

EXAMPLE How Many Tablets Should We Analyze?

In a gravimetric analysis, we need enough product to weigh accurately. Each tablet provides ~15 mg of iron. How many tablets should we analyze to provide 0.25 g of Fe_2O_3 product?

The symbol ~ is read "approximately."

Solution We can answer the question if we know how many grams of iron are in 0.25 g of Fe_2O_3. The formula mass of Fe_2O_3 is 159.69 g/mol, so 0.25 g is equal to

$$\text{mol } Fe_2O_3 = \frac{0.25\ \cancel{g}}{159.69\ \cancel{g}/\text{mol}} = 1.6 \times 10^{-3} \text{ mol}$$

$$\text{mol} = \frac{\text{grams}}{\text{grams per mol}} = \frac{\text{grams}}{\text{formula mass}}$$

Each mol of Fe_2O_3 has 2 mol of Fe, so 0.25 g of Fe_2O_3 contains

$$1.6 \times 10^{-3}\ \cancel{\text{mol } Fe_2O_3} \times \frac{2 \text{ mol Fe}}{1\ \cancel{\text{mol } Fe_2O_3}} = 3.2 \times 10^{-3} \text{ mol Fe}$$

The mass of Fe is

$$3.2 \times 10^{-3}\ \cancel{\text{mol Fe}} \times \frac{55.845 \text{ g Fe}}{\cancel{\text{mol Fe}}} = 0.18 \text{ g Fe}$$

The atomic mass of Fe, 55.845 g/mol, is in the periodic table inside the cover.

If each tablet contains 15 mg Fe, the number of tablets required is

$$\text{Number of tablets} = \frac{0.18\ \cancel{\text{g Fe}}}{0.015\ \cancel{\text{g Fe}}/\text{tablet}} = 12 \text{ tablets}$$

Test Yourself If each tablet provides ~20 mg of iron, how many tablets should we analyze to provide ~0.50 g of Fe_2O_3? (***Answer:*** 18)

EXAMPLE How Much H_2O_2 Is Required?

What mass of 3.0 wt% H_2O_2 solution is required to provide a 50% excess of reagent for Reaction 1-5 with 12 dietary iron tablets?

Solution Twelve tablets provide 12 $\cancel{\text{tablets}}$ × (0.015 g Fe^{2+}/$\cancel{\text{tablet}}$) = 0.18 g Fe^{2+}, or (0.18 g $\cancel{Fe^{2+}}$)/(55.845 g $\cancel{Fe^{2+}}$/mol Fe^{2+}) = 3.2×10^{-3} mol Fe^{2+}. Reaction 1-5 requires 1 mol of H_2O_2 for every 2 mol of Fe^{2+}. Therefore 3.2×10^{-3} mol Fe^{2+} requires (3.2×10^{-3} $\cancel{\text{mol } Fe^{2+}}$)(1 mol H_2O_2/2 $\cancel{\text{mol } Fe^{2+}}$) = 1.6×10^{-3} mol H_2O_2. A 50% excess means

$$\text{Moles} = \frac{\text{grams}}{\text{formula mass}} = \frac{\text{g}}{\text{g/mol}}$$

You should be able to use this relationship in your sleep.

that we want to use 1.50 times the stoichiometric quantity: $(1.50)(1.6 \times 10^{-3}$ mol $H_2O_2) = 2.4 \times 10^{-3}$ mol H_2O_2. The formula mass of H_2O_2 is 34.01 g/mol, so the required mass of pure H_2O_2 is $(2.4 \times 10^{-3}$ ~~mol~~)(34.01 g/~~mol~~) = 0.082 g. But hydrogen peroxide is available as a 3.0 wt% solution, so the required mass of solution is

$$\text{Mass of } H_2O_2 \text{ solution} = \frac{0.082 \text{ g } \cancel{H_2O_2}}{0.030 \text{ g } \cancel{H_2O_2}/\text{g solution}} = 2.7 \text{ g solution}$$

Test Yourself What mass of 3.0 wt% H_2O_2 solution is required to provide a 25% excess of reagent for Reaction 1-5 with 12 dietary iron tablets? (***Answer:*** 2.3 g)

EXAMPLE **The Gravimetric Calculation**

The mass of Fe_2O_3 isolated at the end of the experiment was 0.277 g. What is the average mass of iron per dietary tablet?

Solution The moles of isolated Fe_2O_3 are (0.277 g)/(159.69 g/mol) = 1.73×10^{-3} mol. There are 2 mol Fe per formula unit, so the moles of Fe in the product are

$$(1.73 \times 10^{-3} \text{ mol } \cancel{Fe_2O_3})\left(\frac{2 \text{ mol Fe}}{1 \text{ mol } \cancel{Fe_2O_3}}\right) = 3.47 \times 10^{-3} \text{ mol Fe}$$

The mass of Fe is $(3.47 \times 10^{-3}$ ~~mol Fe~~)(55.845 g Fe/~~mol Fe~~) = 0.194 g Fe. Each of the 12 tablets therefore contains an average of (0.194 g Fe)/12 = 0.016 1 g = 16.1 mg.

Test Yourself If the mass of isolated Fe_2O_3 were 0.300 g, what is the average mass of iron per tablet? (***Answer:*** 17.5 mg)

Retain all digits in your calculator during a series of calculations. The product 1.73 × 2 is not 3.47; but, with extra digits in the calculator, the answer is 3.47.

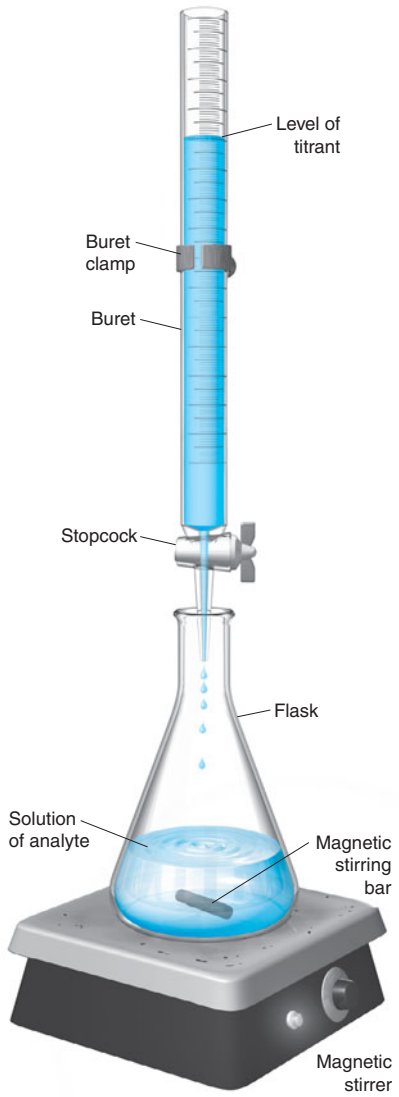


FIGURE 1-4 Typical setup for a titration. Analyte is contained in the flask, and titrant is in the buret. The stirring bar is a magnet coated with Teflon, which is inert to most solutions. The bar is spun by a rotating magnet inside the stirring motor. Burets are described in Section 2-4.

1-5 Introduction to Titrations

Procedures in which we measure the volume of reagent needed to react with *analyte* (the substance being measured) are called **volumetric analysis.** A **titration** is a form of volumetric analysis in which increments of reagent solution—the **titrant**—are added to analyte until their reaction is complete. From the quantity of titrant required, we calculate the quantity of analyte that must have been present. Titrant is usually delivered from a *buret*, which is a glass tube with marks indicating volume (Figure 1-4). Each increment of titrant is completely and quickly consumed by analyte until analyte is used up.

The **equivalence point** occurs when the quantity of added titrant is the exact amount necessary for stoichiometric reaction with the analyte. For example, 5 mol of oxalic acid react with 2 mol of permanganate in hot acidic solution:

$$5HO{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}OH + 2MnO_4^- + 6H^+ \longrightarrow 10CO_2 + 2Mn^{2+} + 8H_2O \qquad (1\text{-}7)$$

Analyte	**Titrant**		
Oxalic acid	Permanganate		
colorless	purple	colorless	colorless

If the unknown contains 5.000 mmol of oxalic acid, the equivalence point is reached when 2.000 mmol of MnO_4^- have been added.

The equivalence point is the ideal (theoretical) result we seek in a titration. What we actually measure is the **end point,** which is marked by a sudden change in a physical property of the solution. In Reaction 1-7, a convenient end point is the abrupt appearance of the purple color of permanganate in the flask. Prior to the equivalence point, permanganate is consumed by oxalic acid, and the titration solution remains colorless. After the equivalence point, unreacted MnO_4^- accumulates until there is enough to see. The *first trace* of purple color is the end point. The better your eyes, the closer will be your measured end point to the true equivalence point. Here, the end point cannot exactly equal the equivalence point, because extra MnO_4^-—some small amount beyond that needed to react with oxalic acid—is required to exhibit purple color.

Methods for determining when analyte has been consumed include (1) detecting a sudden change in the voltage or current between a pair of electrodes, (2) monitoring absorp-

BOX 1-1 Reagent Chemicals and Primary Standards

Chemicals are sold in many grades of purity. For analytical chemistry, we usually use **reagent grade** chemicals with purity set by the American Chemical Society (ACS) Committee on Analytical Reagents.[2] Sometimes "reagent grade" simply meets purity standards set by the manufacturer. A lot analysis for specified impurities should appear on the reagent bottle. Here is a lot analysis from a bottle of zinc sulfate:

$ZnSO_4$	ACS Reagent	Lot Analysis:
Assay: 100.6%	Fe: 0.000 5%	Ca: 0.001%
Insoluble matter: 0.002%	Pb: 0.002 8%	Mg: 0.000 3%
pH of 5% solution at 25°C: 5.6	Mn: 0.6 ppm	K: 0.002%
Ammonium: 0.000 8%	Nitrate: 0.000 4%	Na: 0.003%
Chloride: 1.5 ppm		

The assay value of 100.6% means that a specified analysis for one of the major components produced 100.6% of the theoretical value. If $ZnSO_4$ is contaminated with the lower-molecular-mass $Zn(OH)_2$, the assay for Zn^{2+} will be higher than the value for pure $ZnSO_4$. Less pure chemicals, generally unsuitable for analytical chemistry, carry designations such as "chemically pure" (CP), "practical," "purified," or "technical."

A few chemicals have high enough purity to be *primary standard grade*. Whereas reagent grade potassium dichromate has a lot assay of $\geq 99.0\%$, primary standard grade $K_2Cr_2O_7$ is in the range 99.95–100.05%. Primary standards must be indefinitely stable.

For **trace analysis** (ppm and lower levels), impurities in reagent chemicals must be extremely low. For this purpose, we use very-high-purity, expensive grades of acids such as "trace metal grade" HNO_3 or HCl to dissolve samples. We must pay careful attention to reagents and vessels whose impurity levels could be greater than the quantity of analyte we seek to measure.

To protect the purity of chemical reagents, you should

- Avoid putting a spatula into a bottle. Instead, pour chemical out of the bottle into a clean container (or onto weighing paper) and dispense the chemical from the clean container.
- Never pour unused chemical back into the reagent bottle.
- Replace the cap on the bottle immediately to keep dust out.
- Never put a stopper from a liquid-reagent container down on the lab bench. Either hold the stopper or place it in a clean beaker or watchglass while you dispense reagent.
- Store chemicals in a cool, dark place away from sunlight.

tion of light by reactants or products, and (3) observing an indicator color change. An **indicator** is a compound with a physical property (usually color) that changes abruptly near the equivalence point. The change is caused by disappearance of analyte or appearance of excess titrant.

The difference between the end point and the equivalence point is an inescapable **titration error.** We estimate the titration error with a **blank titration,** in which we carry out the same procedure *without* analyte. For example, we can titrate a solution containing no oxalic acid to see how much MnO_4^- is needed to produce observable purple color. We then subtract this volume of MnO_4^- from the volume observed in the analytical titration.

The validity of an analytical result depends on knowing the amount of one of the reactants used. If titrant is prepared by dissolving a weighed amount of pure reagent in a known volume of solution, its concentration can be calculated. We call such a reagent a **primary standard,** because it is pure enough to be weighed and used directly. A primary standard should be 99.9% pure, or better. It should not decompose under ordinary storage, and it should be stable when dried by heat or vacuum, because drying is required to remove traces of water adsorbed from the atmosphere. Primary standards for many elements are given in Appendix K. Box 1-1 discusses reagent purity.

Many reagents used as titrants, such as HCl, are not available as primary standards. Instead, we prepare titrant with approximately the desired concentration and use it to titrate an analyte that is a primary standard. By this procedure, called **standardization,** we determine the concentration of titrant. We then say that the titrant is a **standard solution.** The validity of the analytical result ultimately depends on knowing the composition of a primary standard. Sodium oxalate ($Na_2C_2O_4$) is a commercially available primary standard for generating oxalic acid to standardize permanganate in Reaction 1-7.

In a **direct titration,** we add titrant to analyte until the reaction is complete. Occasionally, we perform a **back titration,** in which we add a known *excess* of one standard reagent to the analyte. (A "standard" reagent is one whose concentration is known.) Then we titrate the excess reagent with a second standard reagent. A back titration is useful when its end point is clearer than the end point of the direct titration, or when an excess of the first reagent is required for complete reaction with analyte. To appreciate the difference between direct and back titrations, consider first the addition of permanganate titrant to oxalic acid analyte in Reaction 1-7; this reaction is a direct titration. Alternatively, to perform a back titration, we

could add a known *excess* of permanganate to consume oxalic acid. Then we could back titrate the excess permanganate with standard Fe^{2+} to measure how much permanganate was left after reaction with the oxalic acid.

In a **gravimetric titration,** titrant is measured by mass, not volume. Titrant can be delivered from a pipet. Titrant concentration is expressed as moles of reagent per kilogram of solution. Precision is improved from 0.3% attainable with a buret to 0.1% with a balance. Experiments by Guenther and by Butler and Swift at the Web site for this book (www.whfreeman.com/qca) provide examples. "Gravimetric titrations should become the gold standard, and volumetric glassware should be seen in museums only."[3]

1-6 Titration Calculations

Here is an example to illustrate stoichiometry calculations in volumetric analysis. The key step is to *relate moles of titrant to moles of analyte*.

EXAMPLE Standardization of Titrant Followed by Analysis of Unknown

The calcium content of urine can be determined by the following procedure:

Step 1 Precipitate Ca^{2+} with oxalate in basic solution:

$$Ca^{2+} + \underset{\text{Oxalate}}{C_2O_4^{2-}} \rightarrow \underset{\text{Calcium oxalate}}{Ca(C_2O_4)\cdot H_2O(s)}$$

Step 2 Wash the precipitate with ice-cold water to remove free oxalate and then dissolve the solid in acid to obtain Ca^{2+} and $H_2C_2O_4$ in solution.

Step 3 Heat the solution to 60°C and titrate the oxalate with standardized potassium permanganate until the purple end point of Reaction 1-7 is observed.

Standardization Suppose that 0.356 2 g of $Na_2C_2O_4$ is dissolved in a 250.0-mL volumetric flask. If 10.00 mL of this solution require 48.36 mL of $KMnO_4$ solution for titration by Reaction 1-7, what is the molarity of the permanganate solution?

Retain all digits in your calculator during a calculation. Chapter 3 discusses rounding to the proper number of digits at the end of the calculation. In this example, extra digits beyond those justified by the measurements are subscripted.

Solution The concentration of oxalate solution is

$$\frac{0.356\,2 \text{ g } Na_2C_2O_4/(134.00 \text{ g } Na_2C_2O_4/\text{mol})}{0.250\,0 \text{ L}} = 0.010\,63_3 \text{ M}$$

The moles of $C_2O_4^{2-}$ in 10.00 mL are $(0.010\,63_3 \text{ mol/L})(0.010\,00 \text{ L}) = 1.063_3 \times 10^{-4}$ mol = 0.106 3_3 mmol. Reaction 1-7 requires 2 mol of permanganate for 5 mol of oxalate, so the MnO_4^- delivered must have been

Reaction 1-7 requires 2 mol MnO_4^- for 5 mol $C_2O_4^{2-}$.

$$\text{Moles of } MnO_4^- = \left(\frac{2 \text{ mol } MnO_4^-}{5 \text{ mol } C_2O_4^{2-}}\right)(\text{mol } C_2O_4^{2-}) = 0.042\,53_1 \text{ mmol}$$

The concentration of MnO_4^- in the titrant is therefore

Note that $\frac{\text{mmol}}{\text{mL}}$ is the same as $\frac{\text{mol}}{\text{L}}$.

$$\text{Molarity of } MnO_4^- = \frac{0.042\,53_1 \text{ mmol}}{48.36 \text{ mL}} = 8.794_7 \times 10^{-4} \text{ M}$$

Analysis of Unknown Calcium in a 5.00-mL urine sample was precipitated with $C_2O_4^{2-}$ and redissolved. The redissolved $C_2O_4^{2-}$ required 16.17 mL of standard MnO_4^- solution to reach the end point. Find the concentration of Ca^{2+} in the urine.

Solution In 16.17 mL of MnO_4^-, there are $(0.016\,17 \text{ L})(8.794_7 \times 10^{-4} \text{ mol/L}) = 1.422_1 \times 10^{-5}$ mol MnO_4^-. This quantity will react with

$$\text{Moles of } C_2O_4^{2-} = \left(\frac{5 \text{ mol } C_2O_4^{2-}}{2 \text{ mol } MnO_4^-}\right)(\text{mol } MnO_4^-) = 0.035\,55_3 \text{ mmol}$$

Reaction 1-7 requires 5 mol $C_2O_4^{2-}$ for 2 mol MnO_4^-.

Because there is one oxalate ion for each calcium ion in $Ca(C_2O_4) \cdot H_2O$, there must have been 0.035 55_3 mmol of Ca^{2+} in 5.00 mL of urine:

$$[Ca^{2+}] = \frac{0.035\,55_3 \text{ mmol}}{5.00 \text{ mL}} = 0.007\,11_1 \text{ M}$$

Test Yourself In standardization, 10.00 mL of $Na_2C_2O_4$ solution required 39.17 mL of $KMnO_4$. Find the molarity of $KMnO_4$. The unknown required 14.44 mL of MnO_4^-. Find $[Ca^{2+}]$ in the urine. (***Answer:*** 1.086×10^{-3} M, 7.840×10^{-3} M)

Terms to Understand

Terms are introduced in **bold** type in the chapter and are also defined in the Glossary.

abscissa
anhydrous
atomic mass
back titration
blank titration
concentration
density
direct titration
electrolyte
end point
equivalence point
formal concentration
formula mass
gravimetric analysis
gravimetric titration
indicator
liter
molality
molarity
mole
molecular mass
ordinate
ppb (parts per billion)
ppm (parts per million)
primary standard
product
reactant
reagent grade chemical
SI units
solute
solvent
standardization
standard solution
stoichiometry
titrant
titration
titration error
trace analysis
volume percent
volumetric analysis
weight percent

Summary

SI base units include the meter (m), kilogram (kg), second (s), ampere (A), kelvin (K), and mole (mol). Derived quantities such as force (newton, N), pressure (pascal, Pa), and energy (joule, J) can be expressed in terms of base units. In calculations, units should be carried along with the numbers. Prefixes such as kilo- and milli- are used to denote multiples of units. Common expressions of concentration are molarity (moles of solute per liter of solution), molality (moles of solute per kilogram of solvent), formal concentration (formula units per liter), percent composition, and parts per million. To calculate quantities of reagents needed to prepare solutions, the relation $M_{conc} \cdot V_{conc} = M_{dil} \cdot V_{dil}$ is useful because it equates the moles of reagent removed from a stock solution to the moles delivered into a new solution. You should be able to use stoichiometry relationships to calculate required masses or volumes of reagents for chemical reactions. From the mass of the product of a reaction, you should be able to compute how much reactant was consumed.

The volume of titrant required for stoichiometric reaction of analyte is measured in volumetric analysis. The stoichiometric point of the reaction is the equivalence point. What we measure by an abrupt change in a physical property (such as indicator color or electrode potential) is the end point. The difference between the end point and the equivalence point is a titration error. This error can be reduced by either subtracting results of a blank titration, in which the same procedure is carried out in the absence of analyte, or standardizing the titrant by using the same reaction and a similar volume as that used for analyte.

The validity of an analytical result depends on knowing the amount of a primary standard. A solution with an approximately desired concentration can be standardized by titrating a primary standard. In a direct titration, titrant is added to analyte until the reaction is complete. In a back titration, a known excess of reagent is added to analyte, and the excess is titrated with a second standard reagent. Calculations of volumetric analysis relate known moles of titrant to unknown moles of analyte.

Exercises

Complete solutions to *Exercises* are provided at the back of the book, whereas only numerical answers to *Problems* are provided. Complete solutions to *Problems* are in the *Solutions Manual*. *Exercises* cover many of the major ideas in each chapter.

1-A. A solution with a final volume of 500.0 mL was prepared by dissolving 25.00 mL of methanol (CH_3OH, density = 0.791 4 g/mL) in chloroform.

(a) Calculate the *molarity* of methanol in the solution.

(b) The solution has a density of 1.454 g/mL. Find the *molality* of methanol.

1-B. A 48.0 wt% solution of HBr in water has a density of 1.50 g/mL.

(a) Find the formal concentration of HBr.

(b) What mass of solution contains 36.0 g of HBr?

(c) What volume of solution contains 233 mmol of HBr?

(d) How much solution is required to prepare 0.250 L of 0.160 M HBr?

1-C. A solution contains 12.6 ppm of dissolved $Ca(NO_3)_2$ (which dissociates into $Ca^{2+} + 2NO_3^-$). Find the concentration of NO_3^- in parts per million.

1-D. Ascorbic acid (vitamin C, page 354) reacts with I_3^- according to the equation

$$\underset{C_6H_8O_6}{\text{Ascorbic acid}} + I_3^- + H_2O \rightarrow \underset{C_6H_8O_7}{\text{dehydroascorbic acid}} + 3I^- + 2H^+$$

Starch is used as an indicator in the reaction. The end point is marked by the appearance of a deep blue starch-iodine complex when the first fraction of a drop of unreacted I_3^- remains in the solution.

(a) Use atomic masses from the periodic table on the inside cover of this book to find the formula mass of ascorbic acid.

(b) If 29.41 mL of I_3^- solution are required to react with 0.197 0 g of pure ascorbic acid, what is the molarity of the I_3^- solution?

(c) A vitamin C tablet containing ascorbic acid plus inert binder was ground to a powder, and 0.424 2 g was titrated by 31.63 mL of I_3^-. Find the weight percent of ascorbic acid in the tablet.

1-E. A solution of NaOH was standardized by titration of a known quantity of the primary standard, potassium hydrogen phthalate (page 223):

$$\underset{\text{Potassium hydrogen phthalate (FM 204.221)}}{C_8H_5O_4K} + NaOH \longrightarrow C_8H_4O_4NaK + H_2O$$

The NaOH was then used to find the concentration of an unknown solution of H_2SO_4:

$$H_2SO_4 + 2NaOH \longrightarrow Na_2SO_4 + 2H_2O$$

(a) Titration of 0.824 g of potassium hydrogen phthalate required 38.314 g of NaOH solution to reach the end point detected by phenolphthalein indicator. Find the concentration of NaOH (mol NaOH/kg solution).

(b) A 10.00-mL aliquot of H_2SO_4 solution required 57.911 g of NaOH solution to reach the phenolphthalein end point. Find the molarity of H_2SO_4.

Problems

Units and Conversions

1-1. (a) List the SI units of length, mass, time, electric current, temperature, and amount of substance; write the abbreviation for each.

(b) Write the units and symbols for frequency, force, pressure, energy, and power.

1-2. Write the names and abbreviations for each of the prefixes from 10^{-24} to 10^{24}. Which abbreviations are capitalized?

1-3. Write the name and number represented by each symbol. For example, for kW you should write kW = kilowatt = 10^3 watts.

(a) mW **(c)** kΩ **(e)** TJ **(g)** fg
(b) pm **(d)** μF **(f)** ns **(h)** dPa

1-4. Express the following quantities with abbreviations for units and prefixes from Tables 1-1 through 1-3:

(a) 10^{-13} joules **(d)** 10^{-10} meters
(b) $4.317\,28 \times 10^{-8}$ farads **(e)** 2.1×10^{13} watts
(c) $2.997\,9 \times 10^{14}$ hertz **(f)** 48.3×10^{-20} moles

1-5. During the 1980s, the average emission of carbon from burning fossil fuels on Earth was 5.4 petagrams (Pg) of carbon per year in the form of CO_2.[4]

(a) How many kg of C were placed in the atmosphere each year?

(b) How many kg of CO_2 were placed in the atmosphere each year?

(c) A metric ton is 1 000 kg. How many metric tons of CO_2 were placed in the atmosphere each year? If there were 5 billion people on Earth, how many tons of CO_2 were produced for each person?

1-6. How many joules per second and how many calories per hour are produced by a 100.0-horsepower engine?

1-7. A 120-pound woman working in an office consumes about 2.2×10^3 kcal/day, whereas the same woman climbing a mountain needs 3.4×10^3 kcal/day.

(a) Express these numbers in terms of joules per second per kilogram of body mass (= watts per kilogram).

(b) Which consumes more power (watts), the office worker or a 100-W light bulb?

1-8. How many joules per second (J/s) are used by a device that requires 5.00×10^3 British thermal units per hour (Btu/h)? How many watts (W) does this device use?

1-9. The table shows fuel efficiency for several automobiles.

Car model	Fuel consumption (L/100 km)	CO_2 emission (g CO_2/km)
Gasoline Engine		
Peugeot 107	4.6	109
Audi Cabriolet	11.1	266
Chevrolet Tahoe	14.6	346
Diesel Engine		
Peugeot 107	4.1	109
Audi Cabriolet	8.4	223

SOURCE: *M. T. Oliver-Hoyo and G. Pinto, "Using the Relationship Between Vehicle Fuel Consumption and CO_2 Emissions to Illustrate Chemical Principles," J. Chem. Ed.* ***2008****, 85, 218.*

(a) A mile is 5 280 feet and a foot is 12 inches. Use Table 1-4 to find how many miles are in 1 km.

(b) The gasoline-engine Peugeot 107 consumes 4.6 L of fuel per 100 km. Express the fuel efficiency in miles per gallon. A U.S. liquid gallon is 3.785 4 L.

(c) The diesel Cabriolet is more efficient than the gasoline Cabriolet. How many metric tons of CO_2 are produced by the diesel and gasoline Cabriolets in 15 000 miles of driving? A metric ton is 1 000 kg.

1-10. Newton's law states that force = mass × acceleration. Acceleration has the units m/s^2. You also know that energy = force × distance and pressure = force/area. From these relations, derive the dimensions of newtons, joules, and pascals in terms of the fundamental SI units in Table 1-1. Check your answers in Table 1-2.

1-11. Dust falls on Chicago at a rate of 65 mg m^{-2} day^{-1}. Major metallic elements in the dust include Al, Mg, Cu, Zn, Mn, and Pb.[5] Pb accumulates at a rate of 0.03 mg m^{-2} day^{-1}. How many metric tons (1 metric ton = 1 000 kg) of Pb fall on the 535 square kilometers of Chicago in 1 year?

Chemical Concentrations

1-12. Define the following terms:

(a) molarity **(e)** volume percent
(b) molality **(f)** parts per million
(c) density **(g)** parts per billion
(d) weight percent **(h)** formal concentration

1-13. Why is it more accurate to say that the concentration of a solution of acetic acid is 0.01 F rather than 0.01 M? (Despite this distinction, we will usually write 0.01 M.)

1-14. What is the formal concentration (expressed as mol/L = M) of NaCl when 32.0 g are dissolved in water and diluted to 0.500 L?

1-15. How many grams of methanol (CH_3OH, FM 32.04) are contained in 0.100 L of 1.71 M aqueous methanol (i.e., 1.71 mol CH_3OH/L solution)?

1-16. The concentration of a gas is related to its pressure by the *ideal gas law:*

$$\text{Concentration}\left(\frac{\text{mol}}{\text{L}}\right) = \frac{n}{V} = \frac{P}{RT},$$

$$R = \text{gas constant} = 0.083\,14\,\frac{\text{L}\cdot\text{bar}}{\text{mol}\cdot\text{K}}$$

where n is the number of moles, V is volume (L), P is pressure (bar), and T is temperature (K).

(a) The maximum pressure of ozone in the Antarctic stratosphere in Figure 1-1 is 19 mPa. Convert this pressure into bars.

(b) Find the molar concentration of ozone in part **(a)** if the temperature is −70°C.

1-17. Any dilute aqueous solution has a density near 1.00 g/mL. Suppose the solution contains 1 ppm of solute; express the concentration of solute in g/L, μg/L, μg/mL, and mg/L.

1-18. The concentration of the alkane $C_{20}H_{42}$ (FM 282.55) in a particular sample of rainwater is 0.2 ppb. Assume that the density of rainwater is close to 1.00 g/mL and find the molar concentration of $C_{20}H_{42}$.

1-19. How many grams of perchloric acid, $HClO_4$, are contained in 37.6 g of 70.5 wt% aqueous perchloric acid? How many grams of water are in the same solution?

1-20. The density of 70.5 wt% aqueous perchloric acid is 1.67 g/mL. Recall that grams refers to grams of *solution* (= g $HClO_4$ + g H_2O).

(a) How many grams of solution are in 1.000 L?

(b) How many grams of $HClO_4$ are in 1.000 L?

(c) How many moles of $HClO_4$ are in 1.000 L?

1-21. An aqueous solution containing 20.0 wt% KI has a density of 1.168 g/mL. Find the molality (m, not M) of the KI solution.

1-22. A cell in your adrenal gland has about 2.5×10^4 tiny compartments called *vesicles* that contain the hormone epinephrine (also called adrenaline).

(a) An entire cell has about 150 fmol of epinephrine. How many attomoles (amol) of epinephrine are in each vesicle?

(b) How many molecules of epinephrine are in each vesicle?

(c) The volume of a sphere of radius r is $\frac{4}{3}\pi r^3$. Find the volume of a spherical vesicle of radius 200 nm. Express your answer in cubic meters (m^3) and liters, remembering that 1 L = 10^{-3} m^3.

(d) Find the molar concentration of epinephrine in the vesicle if it contains 10 amol of epinephrine.

1-23. The concentration of sugar (glucose, $C_6H_{12}O_6$) in human blood ranges from about 80 mg/100 mL before meals to 120 mg/100 mL after eating. Find the molarity of glucose in blood before and after eating.

1-24. An aqueous solution of antifreeze contains 6.067 M ethylene glycol ($HOCH_2CH_2OH$, FM 62.07) and has a density of 1.046 g/mL.

(a) Find the mass of 1.000 L of this solution and the number of grams of ethylene glycol per liter.

(b) Find the molality of ethylene glycol in this solution.

1-25. Protein and carbohydrates provide 4.0 Cal/g, whereas fat gives 9.0 Cal/g. (Remember that 1 Calorie, with a capital C, is really 1 kcal.) The weight percent of these components in some foods are

Food	wt% protein	wt% carbohydrate	wt% fat
Shredded wheat	9.9	79.9	—
Doughnut	4.6	51.4	18.6
Hamburger (cooked)	24.2	—	20.3
Apple	—	12.0	—

Calculate the number of calories per gram and calories per ounce in each of these foods. (Use Table 1-4 to convert grams into ounces, remembering that there are 16 ounces in 1 pound.)

1-26. It is recommended that drinking water contain 1.6 ppm fluoride (F^-) for prevention of tooth decay. Consider a reservoir with a diameter of 4.50×10^2 m and a depth of 10.0 m. (The volume is $\pi r^2 h$, where r is the radius and h is the height.) How many grams of F^- should be added to give 1.6 ppm? Fluoride is provided by hydrogen hexafluorosilicate, H_2SiF_6. How many grams of H_2SiF_6 contain this much F^-?

1-27. Noble gases (Group 18 in the periodic table) have the following volume concentrations in dry air: He, 5.24 ppm; Ne, 18.2 ppm; Ar, 0.934%; Kr, 1.14 ppm; Xe, 87 ppb.

(a) A concentration of 5.24 ppm He means 5.24 μL of He per liter of air. Using the ideal gas law in Problem 1-16, find how many moles of He are contained in 5.24 μL at 25.00°C (298.15 K) and 1.000 bar. This number is the molarity of He in the air.

(b) Find the molar concentrations of Ar, Kr, and Xe in air at 25°C and 1 bar.

Preparing Solutions

1-28. How many grams of boric acid, $B(OH)_3$ (FM 61.83), should be used to make 2.00 L of 0.050 0 M solution? What kind of flask is used to prepare this solution?

1-29. Describe how you would prepare approximately 2 L of 0.050 0 m boric acid, $B(OH)_3$.

1-30. What is the maximum volume of 0.25 M sodium hypochlorite solution (NaOCl, laundry bleach) that can be prepared by dilution of 1.00 L of 0.80 M NaOCl?

1-31. How many grams of 50 wt% NaOH (FM 40.00) should be diluted to 1.00 L to make 0.10 M NaOH? (Answer with two digits.)

1-32. A bottle of concentrated aqueous sulfuric acid, labeled 98.0 wt% H_2SO_4, has a concentration of 18.0 M.

(a) How many milliliters of reagent should be diluted to 1.000 L to give 1.00 M H_2SO_4?

(b) Calculate the density of 98.0 wt% H_2SO_4.

1-33. What is the density of 53.4 wt% aqueous NaOH (FM 40.00) if 16.7 mL of the solution diluted to 2.00 L gives 0.169 M NaOH?

Stoichiometry Calculations

1-34. How many milliliters of 3.00 M H_2SO_4 are required to react with 4.35 g of solid containing 23.2 wt% $Ba(NO_3)_2$ if the reaction is $Ba^{2+} + SO_4^{2-} \rightarrow BaSO_4(s)$?

1-35. How many grams of 0.491 wt% aqueous HF are required to provide a 50% excess to react with 25.0 mL of 0.023 6 M Th^{4+} by the reaction $Th^{4+} + 4F^- \rightarrow ThF_4(s)$?

Titrations

1-36. Explain the following statement: "The validity of an analytical result ultimately depends on knowing the composition of some primary standard."

1-37. Distinguish between the terms *end point* and *equivalence point*.

1-38. How does a blank titration reduce titration error?

1-39. What is the difference between a direct titration and a back titration?

1-40. What is the difference between a reagent grade chemical and a primary standard?

1-41. Why are ultrapure acid solvents required to dissolve samples for trace analysis?

1-42. How many milliliters of 0.100 M KI are needed to react with 40.0 mL of 0.040 0 M $Hg_2(NO_3)_2$ if the reaction is $Hg_2^{2+} + 2I^- \rightarrow Hg_2I_2(s)$?

1-43. For Reaction 1-7, how many milliliters of 0.165 0 M $KMnO_4$ are needed to react with 108.0 mL of 0.165 0 M oxalic acid? How many milliliters of 0.165 0 M oxalic acid are required to react with 108.0 mL of 0.165 0 M $KMnO_4$?

1-44. Ammonia reacts with hypobromite, OBr^-, by the reaction $2NH_3 + 3OBr^- \rightarrow N_2 + 3Br^- + 3H_2O$. What is the molarity of a hypobromite solution if 1.00 mL of the OBr^- solution reacts with 1.69 mg of NH_3?

1-45. Sulfamic acid is a primary standard that can be used to standardize NaOH.

$$\underset{\substack{\text{Sulfamic acid}\\ \text{FM 97.094}}}{{}^{+}H_3NSO_3^-} + OH^- \longrightarrow H_2NSO_3^- + H_2O$$

What is the molarity of a sodium hydroxide solution if 34.26 mL react with 0.333 7 g of sulfamic acid?

1-46. Limestone consists mainly of the mineral calcite, $CaCO_3$. The carbonate content of 0.541 3 g of powdered limestone was measured by suspending the powder in water, adding 10.00 mL of 1.396 M HCl, and heating to dissolve the solid and expel CO_2:

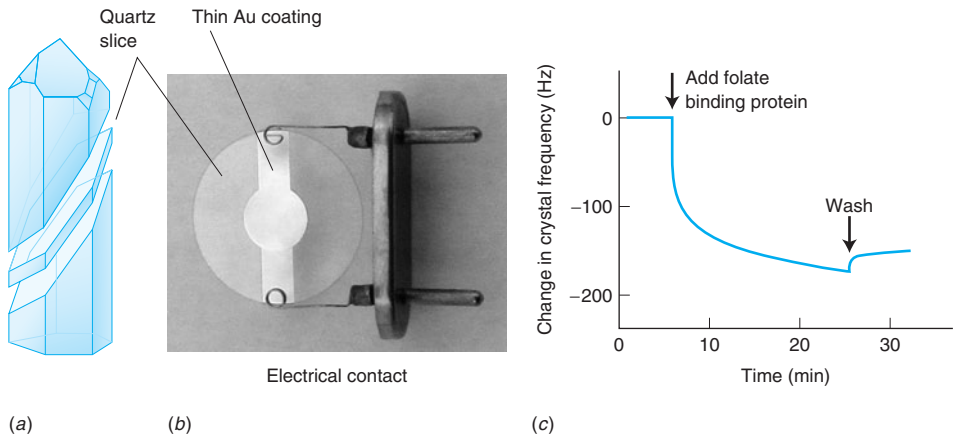
$$\underset{\substack{\text{Calcium carbonate}\\ \text{FM 100.087}}}{CaCO_3(s)} + 2H^+ \longrightarrow Ca^{2+} + CO_2\uparrow + H_2O$$

The excess acid required 39.96 mL of 0.100 4 M NaOH for complete titration. Find the weight percent of calcite in the limestone.

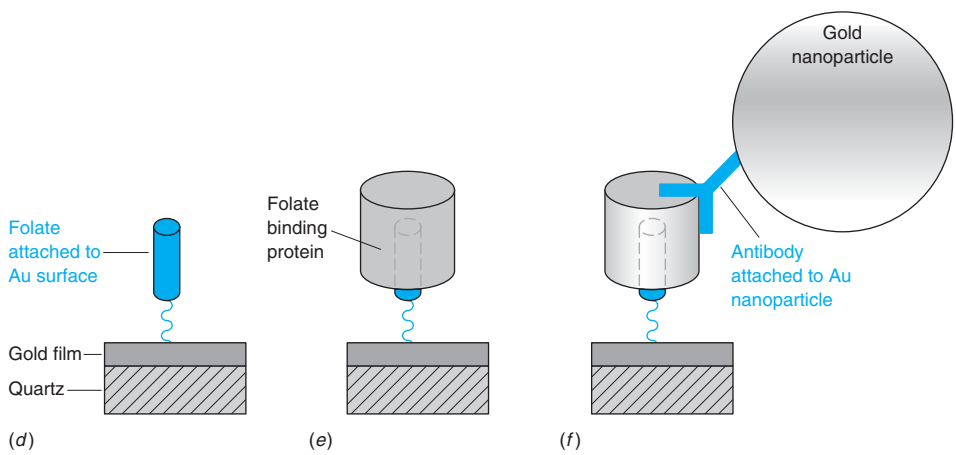
2 Tools of the Trade

QUARTZ CRYSTAL MICROBALANCE IN MEDICAL DIAGNOSIS

Slice of quartz (*a*) used to make microbalance (*b*). (*c*) Change in quartz oscillator frequency when 1 μM folate binding protein binds to folate attached to Au surface. After washing, most protein remains irreversibly bound to folate [Photo courtesy Dave Garvey/LapTech. Graph from W. A. Henne, D. D. Doorneweerd, J. Lee, P. S. Low, and C. Savran, "Detection of Folate Binding Protein with Enhanced Sensitivity Using a Functionalized Quartz Crystal Microbalance Sensor," *Anal. Chem.* **2006**, *78*, 4880.]



Measuring folate binding protein with quartz crystal microbalance. Folate is attached to Au surface in (*d*). Folate binding protein then binds to folate in (*e*). To increase mass, an antibody tethered to a gold nanoparticle binds to folate binding protein in (*f*).



Folic acid is a vitamin essential to many metabolic pathways. Folate binding protein expressed by cancer cells appears in blood at elevated levels not found in healthy people. Measurement of folate binding protein is a tool for cancer diagnosis, but "elevated" levels are only ~20 pM (pM = picomolar = 10^{-12} M) and are difficult to measure.

A quartz crystal vibrating at its resonant frequency keeps time in your wristwatch. A quartz crystal microbalance consists of a slice of quartz sandwiched between two thin Au electrodes.[1,2] Application of an oscillating electric field causes the quartz to oscillate. Binding of 10 ng (nanograms = 10^{-9} g) of matter to a 1 cm^2 area of a gold electrode lowers the 5-MHz resonant frequency of the quartz by an observable 1 Hz.[3,4] A substance whose dimensions change when an electric field is applied is said to be *piezoelectric*.

To measure folate binding protein, folate is attached to the Au surface in panel (*d*). When exposed to serum containing folate binding protein, the protein binds to the folate, increasing the mass on the Au surface and decreasing the oscillation frequency of the quartz. The mass of protein is too little to provide a sufficiently low detection level. So, clever chemists then add an antibody that binds specifically to folate binding protein (*e*). The antibody is covalently attached to a 20-nm-diameter Au particle (*f*). The combined mass of antibody and Au nanoparticle lowers the detection limit from 30 nM to 50 pM. Another factor-of-10 decrease in detection limit is still required to reach a clinically meaningful level.

FIGURE 2-1 Goggles or safety glasses should be worn at all times in the lab.

Why we wear lab coats: In 2008, 23-year-old University of California research assistant Sheharbano Sangji was withdrawing *t*-butyllithium with a syringe from a bottle. The plunger came out of the syringe and the pyrophoric liquid burst into flames, igniting her sweater and gloves. Burns on 40% of her body proved fatal. A flame-resistant coat might have protected her.

Limitations of gloves: In 1997, Dartmouth College professor Karen Wetterhahn, age 48, died from a drop of dimethylmercury absorbed through her latex gloves. Many organic compounds readily penetrate latex. Wetterhahn was an expert in the biochemistry of metals, the first female professor of chemistry at Dartmouth, and played a major role in bringing more women into science.

Analytical chemistry extends from simple "wet" chemical procedures to elaborate instrumental methods. This chapter describes basic laboratory apparatus and manipulations associated with chemical measurements.[5] We also introduce spreadsheets, which have become essential to everyone who manipulates quantitative data.

2-1 Safe, Ethical Handling of Chemicals and Waste

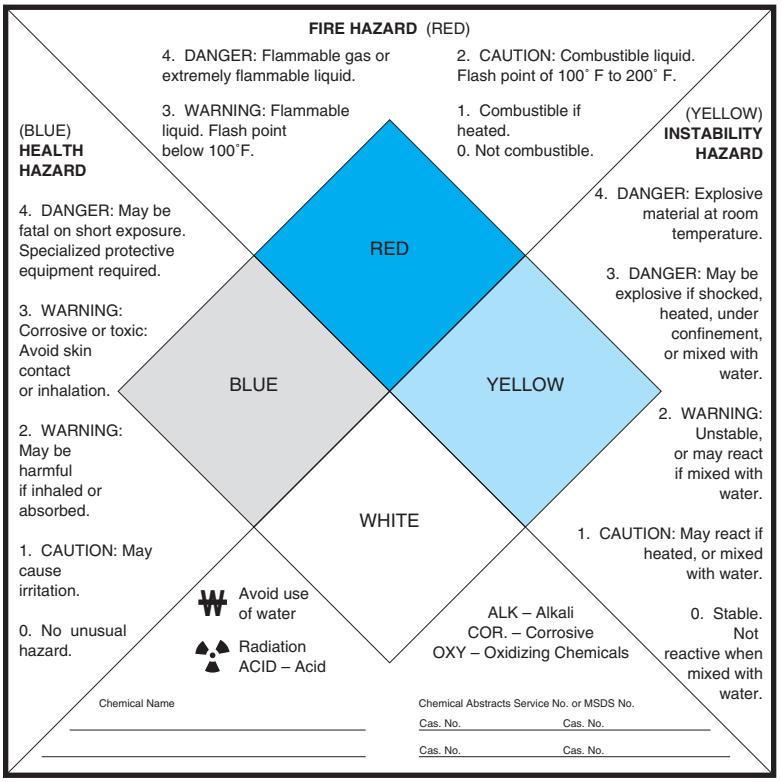
Chemical experimentation, like driving a car or operating a household, creates hazards. *The primary safety rule is to familiarize yourself with the hazards and then to do nothing that you (or your instructor or supervisor) consider to be dangerous.* If you believe that an operation is hazardous, discuss it first and do not proceed until sensible precautions are in place.

Before working, familiarize yourself with safety features of your laboratory. You should wear goggles (Figure 2-1) or safety glasses with side shields at all times in the lab to protect your eyes from liquids and glass, which fly around when least expected. Contact lenses are not recommended in the lab because vapors can be trapped between the lens and your eye. You can protect your skin from spills and flames by wearing a flame-resistant lab coat. Use rubber gloves when pouring concentrated acids. Do not eat or drink in the lab.

Organic solvents, concentrated acids, and concentrated ammonia should be handled in a fume hood. Air flowing into the hood keeps fumes out of the lab and dilutes the fumes before expelling them from the roof. Never generate large quantities of toxic fumes that are allowed to escape through the hood. Wear a respirator when handling fine powders, which could produce a cloud of dust that might be inhaled.

Clean up spills immediately to prevent accidental contact by the next person who comes along. Treat spills on your skin first by flooding with water. In anticipation of splashes on your body or in your eyes, know where to find and how to operate the emergency shower and eyewash. If the sink is closer than an eyewash, use the sink first for splashes in your eyes. Know how to operate the fire extinguisher and how to use an emergency blanket to extinguish burning clothing. A first aid kit should be available, and you should know how and where to seek emergency medical assistance.

Label all vessels to indicate what they contain. An unlabeled bottle left and forgotten in a refrigerator or cabinet presents an expensive disposal problem, because the contents must be analyzed before they can be legally discarded. National Fire Protection Association labels (Figure 2-2) identify hazards associated with reagents. A Material Safety Data Sheet provided



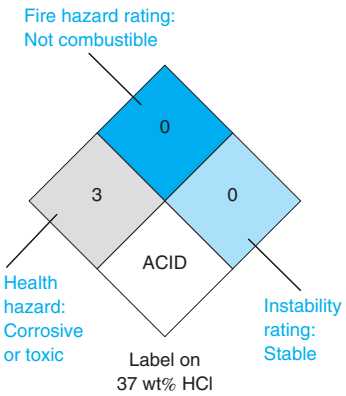


FIGURE 2-2 Chemical hazards label used by the National Fire Protection Association.

with each chemical sold in the United States lists hazards and precautions for that chemical. It gives first aid procedures and instructions for handling spills.

If we want our grandchildren to inherit a habitable planet, we need to minimize waste production and dispose of chemical waste in a responsible manner. When it is economically feasible, recycling of chemicals is preferable to waste disposal.[6] Carcinogenic dichromate ($Cr_2O_7^{2-}$) waste provides an example of an accepted disposal strategy. Cr(VI) from dichromate should be reduced to the less toxic Cr(III) with sodium hydrogen sulfite ($NaHSO_3$) and precipitated with hydroxide as insoluble $Cr(OH)_3$. The solution is evaporated to dryness and the solid is discarded in an approved landfill that is lined to prevent escape of the chemicals. Wastes such as silver and gold that can be economically recycled should be chemically treated to recover the metal.[7]

Compact fluorescent lights, which reduce energy use, must be treated as hazardous waste because they contain mercury. *Fluorescent bulbs must not be discarded as ordinary waste*. Light-emitting diodes (LEDs) are even more efficient than fluorescent lamps, contain no mercury, and will replace fluorescent lights soon.

Green chemistry is a set of principles intended to change our behavior to help sustain a habitable planet.[8] Examples of unsustainable behavior are consumption of a limited resource and careless disposal of waste. Green chemistry seeks to design chemical products and processes to reduce the use of resources and energy and the generation of hazardous waste. It is better to design a process to prevent waste than to dispose of waste. For example, NH_3 can be measured with an ion-selective electrode instead of using the spectrophotometric Nessler procedure, which generates HgI_2 waste. "Microscale" classroom experiments are encouraged to reduce the cost of reagents and the generation of waste.

2-2 The Lab Notebook

The critical functions of your lab notebook are to state *what you did* and *what you observed*, and it should be *understandable by a stranger*. The greatest error, made even by experienced scientists, is writing incomplete or unintelligible notebooks. Using *complete sentences* is an excellent way to prevent incomplete descriptions.

The lab notebook must

1. State what was done
2. State what was observed
3. Be understandable to someone else

Beginning students often find it useful to write a complete description of an experiment, with sections dealing with purpose, methods, results, and conclusions. Arranging a notebook to accept numerical data prior to coming to the lab is an excellent way to prepare for an experiment. It is good practice to write a balanced chemical equation for every reaction you use. This practice helps you understand what you are doing and may point out what you do not understand about what you are doing.

The measure of scientific "truth" is the ability of different people to reproduce an experiment. A good lab notebook will state everything that was done and what you observed and will allow you or anyone else to repeat the experiment.

One fine future day, you or one of your classmates will make an important discovery and will seek a patent. The lab notebook is your legal record of your discovery. For this purpose, each page in your notebook should be signed and dated. Anything of potential importance should also be signed and dated by a second person.

Record in your notebook the names of computer files where programs and data are stored. Paste hard copies of important data into your notebook. The lifetime of a printed page is 10 to 100 times longer than that of a computer file.

2-3 Analytical Balance

An *electronic balance* uses electromagnetic force compensation to balance the load on the pan. Figure 2-3 shows a typical analytical balance with a capacity of 100–200 g and a readability of 0.01–0.1 mg. *Readability* is the smallest increment of mass that can be indicated. A *microbalance* weighs milligram quantities with a readability of 1 μg.

To weigh a chemical, first place a clean receiving vessel on the balance pan. The mass of the empty vessel is called the **tare**. On most balances, you can press a button to reset the tare to 0. Add the chemical to the vessel and read its mass. If there is no automatic tare operation, subtract the tare mass from that of the filled vessel. To protect the balance from corrosion, *chemicals should never be placed directly on the weighing pan*. Also, be careful never to spill chemicals into the mechanism below the balance pan.

An alternate procedure, called *weighing by difference,* is necessary for **hygroscopic** reagents, which rapidly absorb moisture from the air. First weigh a capped bottle containing dry reagent. Then quickly pour some reagent from the weighing bottle into a receiver. Cap the weighing bottle and weigh it again. The difference is the mass of reagent delivered from the weighing bottle. With an electronic balance, set the initial mass of the weighing bottle to 0 with the tare button. Then deliver reagent from the bottle and reweigh the bottle. The negative reading on the balance is the mass of reagent delivered from the bottle.[9]

FIGURE 2-3 Electronic analytical balance measures mass down to 0.1 mg. [Courtesy Fisher Scientific, Pittsburgh, PA.]

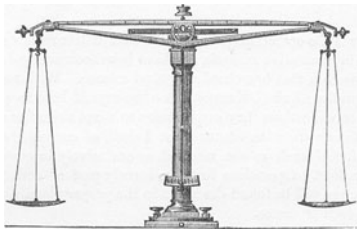


FIGURE 2-4 Equal-long-arm nineteenth-century balance. [Reproduced from *Fresenius' Quantitative Chemical Analysis*, 2nd American ed., 1881.]

How a Mechanical Balance Works

The classic *mechanical balance* in Figure 2-4 has two pans suspended on opposite ends of an equal-arm lever balanced at its center on a knife edge. An unknown mass is placed on one pan and standard masses are placed on the other pan. When the balance is restored to its level position, the mass of the standards is equal to the mass of the unknown.

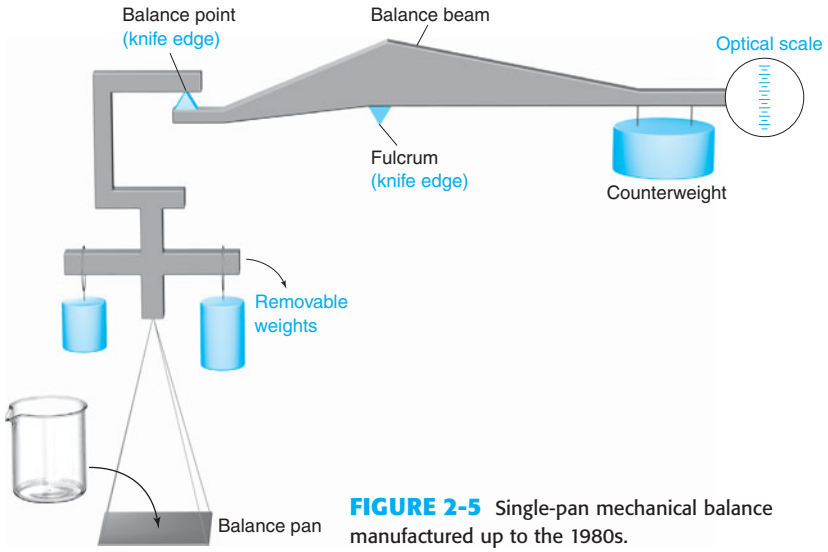


FIGURE 2-5 Single-pan mechanical balance manufactured up to the 1980s.

The single-pan mechanical balance in Figure 2-5 evolved from the two-pan balance and operates by the substitution principle. The mass of the pan at the left is balanced by a counterweight at the right. An object to be weighed is placed on the pan. We then rotate mechanical knobs to detach calibrated internal weights until the balance beam is restored as close as possible to its original position. The remaining small deflection is read on the optical scale and this reading is added to that of the removed weights.

A mechanical balance should be in its arrested position when you load or unload the pan and in the half-arrested position when you are dialing weights. This practice minimizes wear on the knife edges in Figure 2-5.

How an Electronic Balance Works

An object placed on the electronic balance in Figure 2-3 pushes the pan down with a force $m \times g$, where m is the mass of the object and g is the acceleration of gravity. Figure 2-6

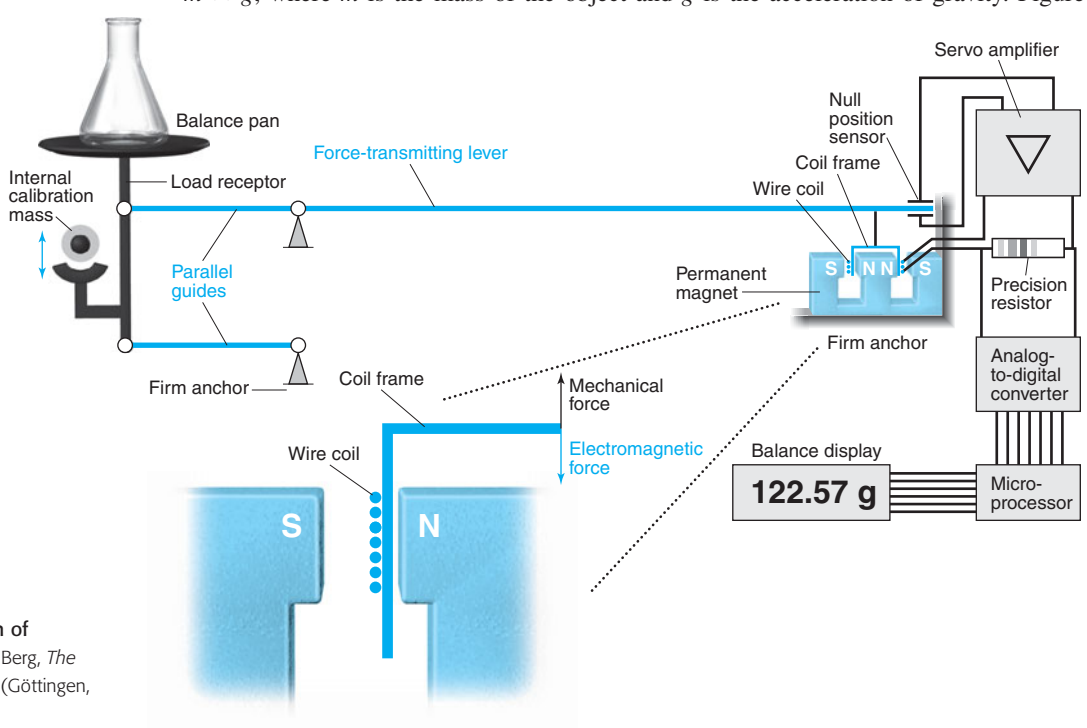
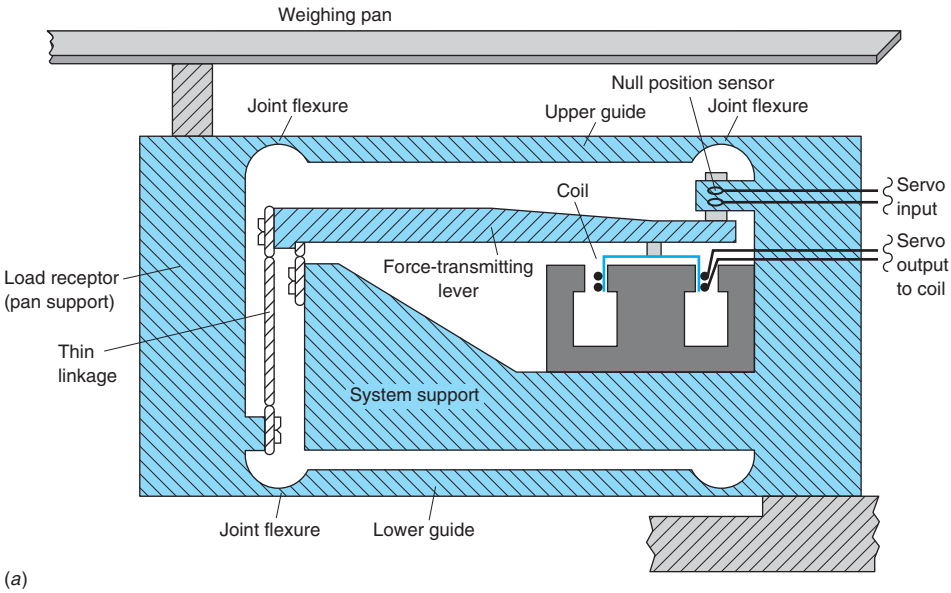
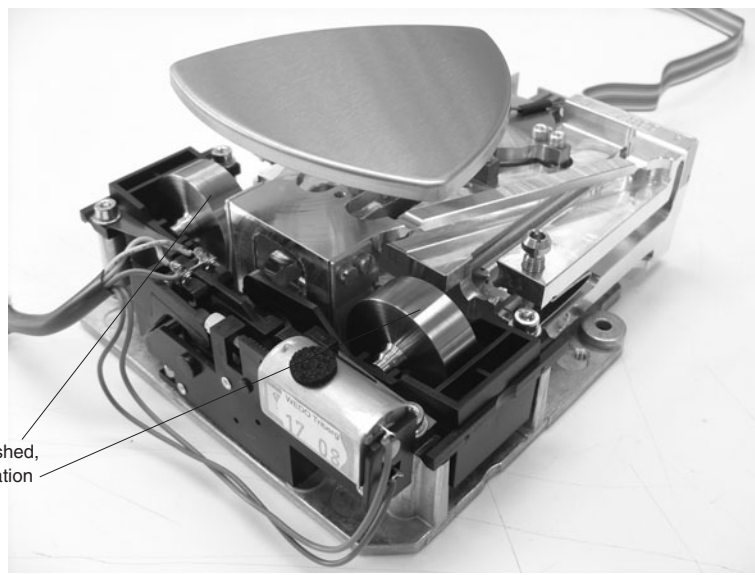


FIGURE 2-6 Schematic diagram of electronic balance. [Adapted from C. Berg, *The Fundamentals of Weighing Technology* (Göttingen, Germany: Sartorius AG, 1996).]



(*a*)



(*b*)

FIGURE 2-7 (*a*) Mechanical layout of an electronic balance. The lever ratio is such that the electromagnetic force must be only ~10% of the load on the pan. [Adapted from C. Berg, *The Fundamentals of Weighing Technology* (Göttingen, Germany: Sartorius AG, 1996).] (*b*) Internal components of Sartorius analytical balance with a capacity of 300 g and readability of 0.1 mg. The monolithic (one-piece) metal weighing system has nonmagnetic calibration weights, which are placed gently on the load receptor by a microprocessor-activated motor. Calibration is automatically activated by temperature changes. [Courtesy J. Barankewitz, Sartorius AG, Göttingen, Germany.]

shows how the balance works. The pan pushes down on a load receptor attached to parallel guides. The force of the sample pushes the left side of the force-transmitting lever down and moves the right side of the lever up. The null position sensor on the far right detects the smallest movement of the lever arm away from its equilibrium (null) position. When the null sensor detects displacement of the lever arm, the servo amplifier sends electric current through the force compensation wire coil in the field of a permanent magnet. The enlargement at the lower left shows part of the coil and magnet. Electric current in the coil interacts with the magnetic field to produce a downward force. The servo amplifier provides current that exactly compensates for the upward force on the lever arm to maintain a null position. Current flowing through the coil creates a voltage across the precision resistor, which is converted to a digital signal and ultimately to a readout in grams. The conversion between current and mass is accomplished by measuring the current required to balance an internal calibration mass. Figure 2-7 shows the layout of components inside a balance.

Weighing Errors

Samples must be at *ambient temperature* (the temperature of the surroundings) to prevent errors due to convective air currents. Warm samples might appear lighter and cool samples might appear heavier than their actual mass. The warmth of your hand and your fingerprints can affect the apparent mass of an object, so tweezers or a tissue are recommended for placing objects on a balance. A sample that has been dried in an oven takes about 30 min to cool

to room temperature. Place the sample in a desiccator during cooling to prevent accumulation of moisture. Close the glass doors of the balance in Figure 2-3 to prevent drafts from affecting the reading. Many top-loading balances have a plastic fence around the pan to protect against drafts. Analytical balances should be located on a heavy table, such as a marble slab, to minimize vibrations. The balance has adjustable feet and a bubble meter that allow you to keep it level. If the balance is not level, force is not transmitted directly down the load receptor in Figure 2-6 and an error results. The balance must be recalibrated after the level is adjusted. Keep the object to be weighed close to the center of the pan.

Errors in weighing magnetic objects might be evident from a change of the indicated mass as the object is moved around on the weighing pan.[10] It is best to weigh magnetic objects on a spacer such as an upside-down beaker to minimize attraction to the stainless steel parts of the balance. Electrostatic charge on the object being weighed interferes with the measurement and could be evident from unidirectional drift of the indicated mass as the object slowly discharges.

TABLE 2-1 Tolerances for laboratory balance weights[a]

Denomination	Tolerance (mg)		Denomination	Tolerance (mg)	
Grams	Class 1	Class 2	Milligrams	Class 1	Class 2
500	1.2	2.5	500	0.010	0.025
200	0.50	1.0	200	0.010	0.025
100	0.25	0.50	100	0.010	0.025
50	0.12	0.25	50	0.010	0.014
20	0.074	0.10	20	0.010	0.014
10	0.050	0.074	10	0.010	0.014
5	0.034	0.054	5	0.010	0.014
2	0.034	0.054	2	0.010	0.014
1	0.034	0.054	1	0.010	0.014

a. Tolerances are defined in ASTM (American Society for Testing and Materials) Standard E 617. Classes 1 and 2 are the most accurate. Larger tolerances exist for Classes 3–6, which are not given in this table.

Analytical balances have built-in calibration. A motor gently places an internal mass on the load receptor beneath the balance pan (see Figure 2-7b). Electric current required to balance this mass is measured. For external calibration, you should periodically weigh standard masses and verify that the reading is within allowed limits. *Tolerances* (allowable deviations) for standard masses are listed in Table 2-1. Another test for a balance is to weigh a standard mass six times and calculate the standard deviation (Section 4-1). Variations are partly from the balance but also reflect factors such as drafts and vibrations.

Linearity error (or *linearity*) of a balance is the maximum error that can occur as a result of nonlinear response of the system to added mass after the balance has been calibrated (Figure 2-8). A balance with a capacity of 220 g and a readability of 0.1 mg might have a linearity of ±0.2 mg. Even though the scale can be read to 0.1 mg, the error in mass can be as large as ±0.2 mg in some part of the allowed range.

After a balance is calibrated, the reading might drift if room temperature changes. If a balance has a temperature coefficient of sensitivity of 2 ppm/°C, and temperature changes by 4°C, the apparent mass will change by (4°C)(2 ppm/°C) = 8 ppm. For a mass of 100 g, 8 ppm is $(100\text{ g})(8 \times 10^{-6}) = 0.8$ mg. You can recalibrate the balance at its current temperature by pressing the calibrate button. For temperature stability, it is best to leave a balance in its standby mode when not in use.

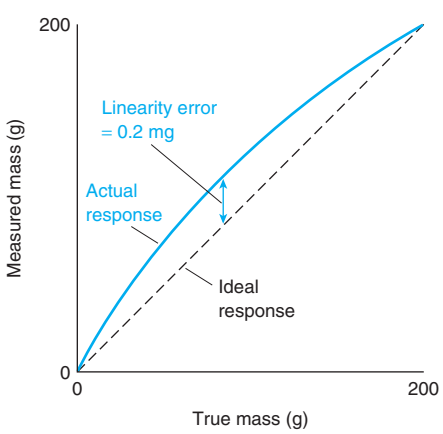


FIGURE 2-8 *Linearity error*. Dashed line is ideal, linear response proportional to mass on the balance, which has been calibrated at 0 and 200 g. Real response deviates from the straight line. Linearity error is the maximum deviation, which is greatly exaggerated in this drawing.

Buoyancy

You can float in water because your weight when swimming is nearly zero. **Buoyancy** is the upward force exerted on an object in a liquid or gaseous fluid.[11] An object weighed in air appears lighter than its actual mass by an amount equal to the mass of air that it displaces. True mass is the mass measured in vacuum. A standard mass in a balance is also affected by buoyancy, so it weighs less in air than in vacuum. A buoyancy error occurs whenever the density of the object being weighed is not equal to the density of the standard mass.

If mass m' is read on a balance, the true mass m of the object weighed in vacuum is[12]

Buoyancy equation:

$$m = \frac{m'\left(1 - \dfrac{d_a}{d_w}\right)}{\left(1 - \dfrac{d_a}{d}\right)} \qquad \textbf{(2-1)}$$

where d_a is the density of air (0.001 2 g/mL near 1 bar and 25°C),[13] d_w is the density of the calibration weights (8.0 g/mL), and d is the density of the object being weighed.

EXAMPLE Buoyancy Correction

A pure compound called "tris" is used as a *primary standard* to measure concentrations of acids. The volume of acid that reacts with a known mass of tris tells us the concentration of acid. Find the true mass of tris (density = 1.33 g/mL) if the apparent mass weighed in air is 100.00 g.

Solution If the density of air is 0.001 2 g/mL, we find the true mass by using Equation 2-1:

$$m = \frac{100.00\ g\left(1 - \dfrac{0.001\ 2\ \text{g/mL}}{8.0\ \text{g/mL}}\right)}{1 - \dfrac{0.001\ 2\ \text{g/mL}}{1.33\ \text{g/mL}}} = 100.08\ \text{g}$$

Unless we correct for buoyancy, we would think that the mass of tris is 0.08% less than its actual mass and we would think that the molarity of acid reacting with the tris is 0.08% less than the actual molarity.

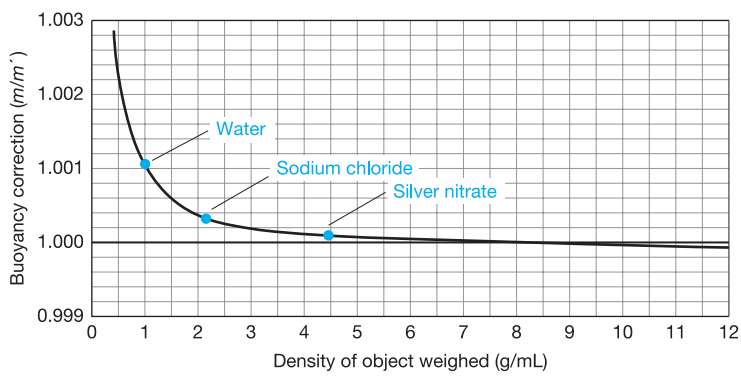


FIGURE 2-9 Buoyancy correction, assuming d_a = 0.001 2 g/mL and d_w = 8.0 g/mL. The apparent mass measured in air (1.000 0 g) is multiplied by the buoyancy correction to find the true mass.

Figure 2-9 shows buoyancy corrections for several substances. When you weigh water with a density of 1.00 g/mL, the true mass is 1.001 1 g when the balance reads 1.000 0 g. The error is 0.11%. For NaCl with a density of 2.16 g/mL, the error is 0.04%; and for $AgNO_3$ with a density of 4.45 g/mL, the error is only 0.01%.

2-4 Burets

The **buret** in Figure 2-10 is a precisely manufactured glass tube with graduations enabling you to measure the volume of liquid delivered through the stopcock (the valve) at the bottom. The 0-mL mark is near the top. If the initial liquid level is 0.83 mL and the final level is 27.16 mL, then you have delivered 27.16 − 0.83 = 26.33 mL. Class A burets (the most accurate grade) are certified to meet tolerances in Table 2-2. If the reading of a 50-mL buret is 27.16 mL, the true volume can be anywhere in the range 27.21 to 27.11 mL and still be within the tolerance of ±0.05 mL.

When reading the liquid level in a buret, your eye should be at the same height as the top of the liquid. If your eye is too high, the liquid seems to be higher than it really is. If your eye

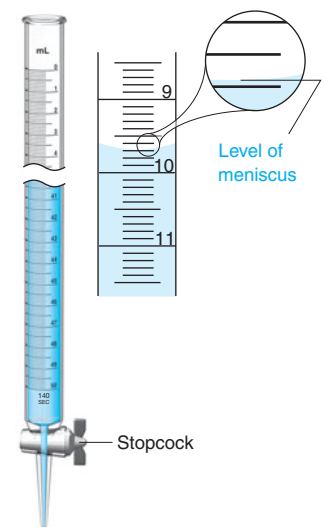


FIGURE 2-10 Glass buret with Teflon stopcock. Enlargement shows meniscus at 9.68 mL. Estimate the reading of any scale to the nearest tenth of a division. This buret has 0.1-mL divisions, so we estimate the reading to the nearest 0.01 mL.

TABLE 2-2 Tolerances of Class A burets

Buret volume (mL)	Smallest graduation (mL)	Tolerance (mL)
5	0.01	±0.01
10	0.05 *or* 0.02	±0.02
25	0.1	±0.03
50	0.1	±0.05
100	0.2	±0.10

Operating a buret:

- Wash buret with new solution
- Eliminate air bubble before use
- Drain liquid slowly
- Deliver fraction of a drop near end point
- Read bottom of concave meniscus
- Estimate reading to 1/10 of a division
- Avoid parallax
- Account for graduation thickness in readings

is too low, the liquid appears too low. The error that occurs when your eye is not at the same height as the liquid is called **parallax.**

The surface of most liquids forms a concave **meniscus** like that shown at the right side of Figure 2-10.[14] It is helpful to use black tape on a white card as a background for locating the precise position of the meniscus. Move the black strip up the buret to approach the meniscus. The bottom of the meniscus turns dark as the black strip approaches, thus making the meniscus more easily readable. Highly colored solutions may appear to have two meniscuses; either one may be used. Because volumes are determined by subtracting one reading from another, the important point is to read the position of the meniscus reproducibly. Estimate the reading to the nearest tenth of a division between marks.

The thickness of the markings on a 50-mL buret corresponds to about 0.02 mL. For best accuracy, select one portion of the marking to be called zero. For example, you can say that the liquid level is *at* the mark when the bottom of the meniscus just touches the top of the mark. When the meniscus is at the *bottom* of the same mark, the reading is 0.02 mL greater.

In a *titration,* increments of reagent in the buret are added to analyte until reaction is complete. From the volume delivered, we calculate the quantity of analyte.

For precise location of the end of a *titration*, we deliver less than one drop at a time from the buret near the end point. (A drop from a 50-mL buret is about 0.05 mL.) To deliver a fraction of a drop, carefully open the stopcock until part of a drop is hanging from the buret tip. (Some people prefer to rotate the stopcock rapidly through the open position to expel part of a drop.) Then touch the inside glass wall of the receiving flask to the buret tip to transfer the droplet to the wall of the flask. Carefully tip the flask so that the main body of liquid washes over the newly added droplet. Swirl the flask to mix the contents. Near the end of a titration, tip and rotate the flask often to ensure that droplets on the wall containing unreacted analyte contact the bulk solution.

Liquid should drain evenly down the wall of a buret. The tendency of liquid to stick to glass is reduced by draining the buret slowly (<20 mL/min). If many droplets stick to the wall, then clean the buret with detergent and a buret brush. If this cleaning is insufficient, soak the buret in peroxydisulfate–sulfuric acid cleaning solution,[15] which eats clothing and people as well as grease in the buret. Never soak volumetric glassware in alkaline solutions, which attack glass. A 5 wt% NaOH solution at 95°C dissolves Pyrex glass at a rate of 9 μm/h.

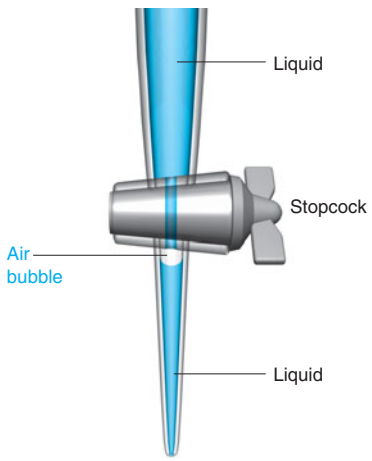


FIGURE 2-11 An air bubble trapped beneath the stopcock should be expelled before you use the buret.

Error can be caused by failure to expel the bubble of air often found directly beneath the stopcock (Figure 2-11). If the bubble becomes filled with liquid during the titration, then some volume that drained from the graduated portion of the buret did not reach the titration vessel. The bubble can be dislodged by draining the buret for a second or two with the stopcock wide open. You can expel a tenacious bubble by abruptly shaking the buret while draining it into a sink.

Before you fill a buret with fresh solution, it is a wonderful idea to rinse the buret several times with small portions of the new solution, discarding each wash. It is not necessary to fill the buret with wash solution. Simply tilt the buret to allow all surfaces to contact the wash liquid. This same technique should be used with any vessel (such as a spectrophotometer cuvet or a pipet) that is reused without drying.

The labor of conducting a titration is greatly reduced by using an autotitrator (Figure 2-12) instead of a buret. This device delivers reagent from a reservoir and records the volume of

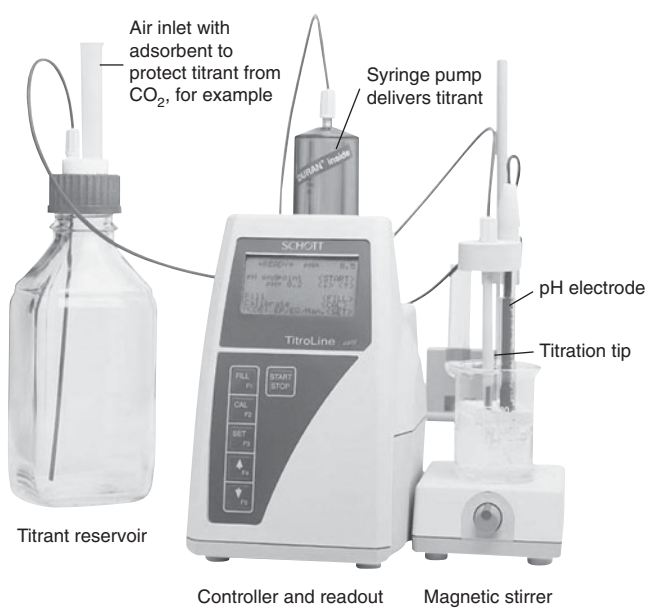


FIGURE 2-12 Autotitrator delivers reagent from the bottle at the left to the beaker at the right. The electrode immersed in the beaker monitors pH or the concentrations of specific ions. Volume and pH readings can go directly to a spreadsheet. [Schott Instruments, Mainz, Germany, and Cole-Parmer Instruments, Vernon Hills, IL.]

reagent and the response of an electrode immersed in the solution being titrated. Output can go directly to a computer for manipulation in a spreadsheet.

Mass Titrations and Microscale Titrations

For best precision, measure the *mass* of reagent, instead of the volume, delivered from a buret or syringe.[16] Mass can be measured more precisely than can volume.

Precision refers to reproducibility.

For procedures that can tolerate poor precision, "microscale" student experiments reduce consumption of reagents and generation of waste. An inexpensive student buret can be constructed from a 2-mL pipet graduated in 0.01-mL intervals.[17] Volume can be read to 0.001 mL, and titrations can be carried out with a precision of 1%.

2-5 Volumetric Flasks

A **volumetric flask** is calibrated to contain a particular volume of solution at 20°C when the bottom of the meniscus is adjusted to the center of the mark on the neck of the flask (Figure 2-13, Table 2-3). Most flasks bear the label "TC 20°C," which means *to contain* at 20°C. (Pipets and burets are calibrated *to deliver*, "TD," their indicated volume.) The temperature of the container is relevant because both liquid and glass expand when heated.

Volumetric glassware made of Pyrex, Kimax, or other low-expansion glass can be safely dried in an oven heated to at least 320°C without harm,[18] although there is rarely reason to go above 150°C.

To use a volumetric flask, dissolve the desired mass of reagent in the flask by swirling with *less* than the final volume of liquid. Then add more liquid and swirl the solution again. Adjust the final volume with as much well-mixed liquid in the flask as possible. (When two different liquids are mixed, there is generally a small volume change. The total volume is *not* the sum of the two volumes that were mixed. By swirling the liquid in a nearly full volumetric flask before liquid reaches the thin neck, you minimize the change in volume when the last liquid is added.) For good control, add the final drops of liquid with a pipet, *not a squirt bottle*. After adjusting the liquid to the correct level, hold the cap firmly in place and invert the flask several times to complete mixing. Before the liquid is homogeneous, we observe streaks (called *schlieren*) arising from regions that refract light differently. After the schlieren are gone, invert the flask a few more times to ensure complete mixing.

Figure 2-13 shows how liquid appears when it is at the *center* of the mark of a volumetric flask or a pipet. Adjust the liquid level while viewing the flask from above or below the level of the mark. The front and back of the mark describe an ellipse with the meniscus at the center.

Glass is notorious for *adsorbing* traces of chemicals—especially cations. **Adsorption** is the process in which a substance sticks to a surface. (In contrast, **absorption** is the process in which a substance is taken inside another, as water is taken into a sponge.) For critical work, you should **acid wash** glassware to replace low concentrations of cations on the surface with H^+. To do this, soak already thoroughly cleaned glassware in 3–6 M HCl or HNO_3 (in a fume hood) for >1 h. Then rinse it well with distilled water and, finally, soak it in distilled water. Acid can be

Example of acid washing: High-purity HNO_3 delivered from an acid-washed glass pipet had no detectable level of Ti, Cr, Mn, Fe, Co, Ni, Cu, and Zn (<0.01 ppb). The same acid delivered from a clean—but not acid-washed—pipet contained each metal at a level of 0.5 to 9 ppb.[19]

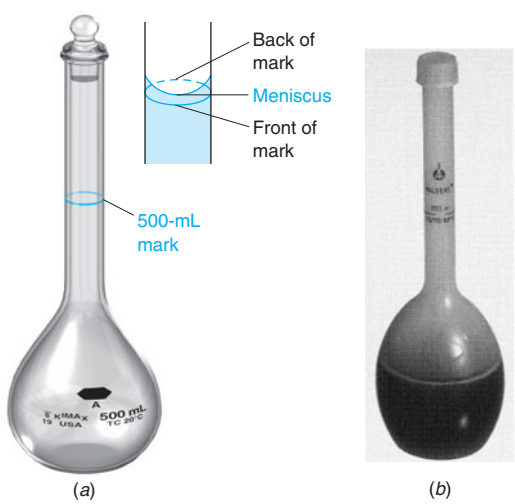


FIGURE 2-13 (*a*) Class A glass volumetric flask showing proper position of the meniscus—at the center of the ellipse formed by the front and back of the calibration mark when viewed from above or below. Volumetric flasks and transfer pipets are calibrated to this position. (*b*) Class B polypropylene plastic volumetric flask for trace analysis. [Courtesy Fisher Scientific, Pittsburgh, PA.] Class A flasks meet tolerances of Table 2-3. Class B tolerances are twice as big as Class A tolerances.

TABLE 2-3 Tolerances of Class A volumetric flasks

Flask capacity (mL)	Tolerance (mL)
1	±0.02
2	±0.02
5	±0.02
10	±0.02
25	±0.03
50	±0.05
100	±0.08
200	±0.10
250	±0.12
500	±0.20
1 000	±0.30
2 000	±0.50

reused many times, as long as it is only used for clean glassware. Acid washing is *especially* appropriate for new glassware, which you should assume is not clean. The polypropylene plastic volumetric flask in Figure 2-13b is designed for trace analysis (parts per billion concentrations) in which analyte might be lost by adsorption on the walls of a glass flask.

2-6 Pipets and Syringes

Do not blow the last drop out of a transfer pipet.

Pipets deliver known volumes of liquid. The *transfer pipet* in Figure 2-14a is calibrated to deliver one fixed volume. The last drop does not drain out of the pipet and *should not be blown out*. The *measuring pipet* in Figure 2-14b is calibrated like a buret. It is used to deliver a variable volume, such as 5.6 mL by starting delivery at the 1.0-mL mark and terminating at the 6.6-mL mark. The transfer pipet is more accurate, with tolerances listed in Table 2-4.

FIGURE 2-14 (*a*) Transfer pipet and (*b*) measuring (Mohr) pipet. [Courtesy A. H. Thomas Co., Philadelphia, PA.]

TABLE 2-4 Tolerances of Class A transfer pipets

Volume (mL)	Tolerance (mL)
0.5	±0.006
1	±0.006
2	±0.006
3	±0.01
4	±0.01
5	±0.01
10	±0.02
15	±0.03
20	±0.03
25	±0.03
50	±0.05
100	±0.08

Using a Transfer Pipet

Using a rubber bulb or other pipet suction device, *not your mouth*, suck liquid up past the calibration mark. Discard one or two pipet volumes of liquid to rinse traces of previous reagents from the pipet. After taking up a third volume past the calibration mark, quickly replace the bulb with your index finger at the end of the pipet. Gently pressing the pipet against the bottom of the vessel while removing the rubber bulb helps prevent liquid from draining below the mark while you put your finger in place. (Alternatively, you can use an automatic suction device that remains attached to the pipet.) Wipe the excess liquid off the outside of the pipet with a clean tissue. *Touch the tip of the pipet to the side of a beaker* and drain the liquid until the bottom of the meniscus just reaches the center of the mark, as in Figure 2-13. Touching the beaker draws liquid from the pipet without leaving part of a drop hanging when the liquid reaches the calibration mark.

Transfer the pipet to a receiving vessel and drain it by gravity *while holding the tip against the wall of the vessel*. After liquid stops draining, hold the pipet to the wall for a few more seconds to complete draining. *Do not blow out the last drop*. The pipet should be nearly vertical at the end of delivery. When you finish with a pipet, you should rinse it with distilled water or soak it until you are ready to clean it. Solutions should never be allowed to dry inside a pipet because removing internal deposits is very difficult.

An *aerosol* is a suspension of fine liquid droplets or solid particles in the gas phase.

Micropipets

Micropipets (Figure 2-15) deliver volumes of 1 to 1 000 μL (1 μL = 10^{-6} L). Liquid is contained in the disposable polypropylene tip, which is stable to most aqueous solutions and many organic solvents except chloroform ($CHCl_3$). The tip also is not resistant to concentrated nitric or sulfuric acids. To prevent aerosols from entering the pipet shaft, tips are available with polyethylene filters. Aerosols can corrode mechanical parts of the pipet or cross-contaminate biological experiments.

Sources of error for micropipets:[20]

- Use tip recommended by manufacturer. Other tips might make inadequate seal.
- Take up and expel liquid three times before delivery to wet pipet tip and equilibrate the inside with vapor.
- Unnecessary wiping of the tip can cause loss of sample.
- Liquid must be at same temperature as pipet. Less than the indicated volume of cold liquid is delivered and more than the indicated volume of warm liquid is delivered. Errors are greatest for smallest volumes.
- Micropipets are calibrated at sea level pressure. They are out of calibration at higher elevations. Errors are greatest for smallest volumes. Calibrate your pipet at your elevation.

To use a micropipet, place a fresh tip tightly on the barrel. Keep tips in their package or dispenser so that you do not contaminate the tips with your fingers. Set the desired volume with the knob at the top of the pipet. Depress the plunger to the first stop, which corresponds to the selected volume. Hold the pipet *vertically*, dip it 3–5 mm into the reagent solution, and *slowly* release the plunger to suck up liquid. Leave the tip in the liquid for a few seconds to allow the aspiration of liquid into the tip to go to completion. Withdraw the pipet vertically from the liquid without touching the tip to the side of the vessel. The volume of liquid taken into the tip depends on the angle at which the pipet is held and how far beneath the liquid surface the tip is held during uptake. To dispense liquid, touch the tip to the wall of the receiver and gently depress the plunger to the first stop. Wait a few seconds to allow liquid to drain down the tip, and then depress the plunger further to squirt out the last liquid. Prior to dispensing liquid, clean and wet a fresh tip by taking up and discarding three squirts of

reagent. The tip can be discarded or rinsed well with a squirt bottle and reused. A tip with a filter (Figure 2-15b) cannot be cleaned for reuse.

The procedure we just described for *aspirating* (sucking in) and delivering liquids is called "forward mode." The plunger is depressed to the first stop and liquid is then taken up. To expel liquid, the plunger is depressed beyond the first stop. In "reverse mode," the plunger is depressed beyond the first stop and *excess* liquid is taken in. To deliver the correct volume, depress the plunger to the first stop and *not beyond*. Reverse mode is good for foamy (protein or surfactant solutions) and viscous (syrupy) liquids.[21]

Table 2-5 lists tolerances for micropipets from one manufacturer. As internal parts wear out, both precision and accuracy can decline by an order of magnitude. In a study[22] of 54 micropipets in use at a biomedical lab, 12 were accurate and precise to ≤1%. Five of 54 had errors ≥10%. When 54 quality control technicians at four pharmaceutical companies used a properly functioning micropipet, 10 people were accurate and precise to ≤1%. Six were inaccurate by ≥10%. Micropipets require periodic calibration and maintenance (cleaning, seal replacement, and lubrication), and operators require certification. If the mean time between falling out of tolerance for micropipets is 2 years, calibration is required every *2 months* to be confident that 95% of the micropipets in a laboratory are operating within specifications.[23] You can calibrate a micropipet by measuring the mass of water it delivers, as described in Section 2-9, or with a commercial colorimetric kit.[24]

TABLE 2-5 Manufacturer's tolerances for micropipets

	At 10% of pipet volume		At 100% of pipet volume	
Pipet volume (μL)	Accuracy (%)	Precision (%)	Accuracy (%)	Precision (%)
Adjustable Volume				
0.2–2	±8	±4	±1.2	±0.6
1–10	±2.5	±1.2	±0.8	±0.4
2.5–25	±4.5	±1.5	±0.8	±0.2
10–100	±1.8	±0.7	±0.6	±0.15
30–300	±1.2	±0.4	±0.4	±0.15
100–1 000	±1.6	±0.5	±0.3	±0.12
Fixed Volume				
10			±0.8	±0.4
25			±0.8	±0.3
100			±0.5	±0.2
500			±0.4	±0.18
1 000			±0.3	±0.12

SOURCE: *Data from Hamilton Co., Reno, NV.*

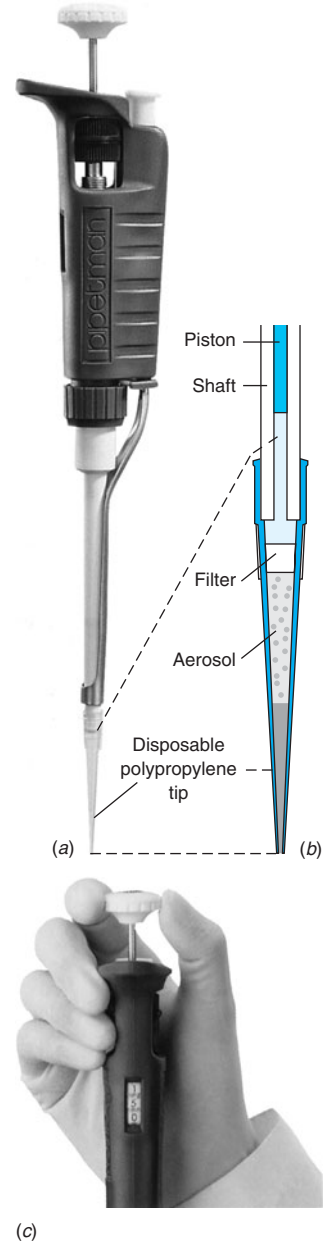


FIGURE 2-15 (*a*) Micropipet with disposable plastic tip. (*b*) Enlarged view of disposable tip containing polyethylene filter to prevent aerosol from contaminating the shaft of the pipet. (*c*) Volume selection dial set to 150 μL. [Courtesy Rainin Instrument Co., Emeryville, CA.]

Accuracy refers to nearness to the true value. *Precision* refers to reproducibility.

Syringes

Microliter *syringes*, such as that in Figure 2-16, come in sizes from 1 to 500 μL and have an accuracy and precision near 1%. When using a syringe, take up and discard several volumes of liquid to wash the glass walls and to remove air bubbles from the barrel. The steel needle is attacked by strong acid and will contaminate strongly acidic solutions with iron. A syringe is more reliable than a micropipet, but the syringe requires more care in handling and cleaning.

FIGURE 2-16 Hamilton syringe with a volume of 1 μL and divisions of 0.02 μL on the glass barrel. [Courtesy Hamilton Co., Reno, NV.]

2-7 Filtration

In *gravimetric analysis*, the mass of product from a reaction is measured to determine how much unknown was present. Precipitates from gravimetric analyses are collected by filtration, washed, and then dried. Most precipitates are collected in a *fritted-glass funnel* (also called a Gooch filter crucible), with suction applied to speed filtration (Figure 2-17). The porous glass plate in the funnel allows liquid to pass but retains solids. The empty funnel is first dried at 110°C and weighed. After collecting solid and drying again, the funnel and its contents are weighed a second time to determine the mass of collected solid. Liquid from which a substance precipitates or crystallizes is called the **mother liquor.** Liquid that passes through the filter is called **filtrate.**

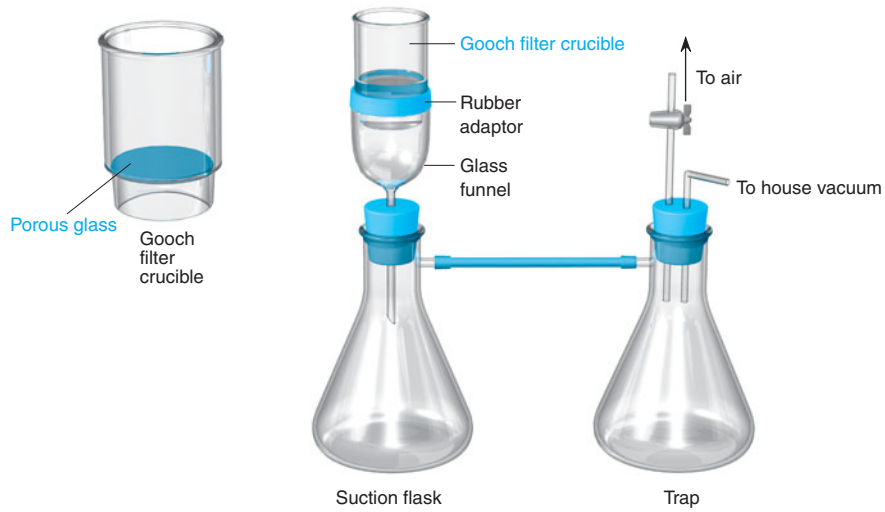


FIGURE 2-17 Filtration with a Gooch crucible that has a porous (*fritted*) glass disk through which liquid can pass. The trap prevents liquid from being accidentally sucked into the vacuum system.

In some gravimetric procedures, **ignition** (heating at high temperature over a burner or in a furnace) is used to convert a precipitate into a known, constant composition. For example, Fe^{3+} precipitates as hydrous ferric oxide, $FeOOH \cdot xH_2O$, with variable composition. Ignition converts it into pure Fe_2O_3 prior to weighing. When a precipitate is to be ignited, it is collected in **ashless filter paper,** which leaves little residue when burned.

To use filter paper with a conical glass funnel, fold the paper into quarters, tear off one corner (to allow a firm fit into the funnel), and place the paper in the funnel (Figure 2-18). The filter paper should fit snugly and be seated with some distilled water. When liquid is poured in, an unbroken stream of liquid should fill the stem of the funnel (Figure 2-19). The weight of liquid in the stem helps speed filtration.

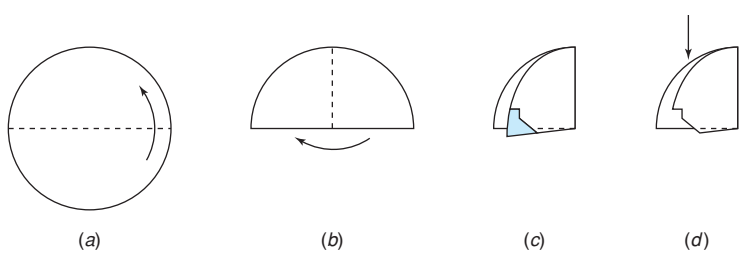


FIGURE 2-18 Folding filter paper for a conical funnel. (*a*) Fold the paper in half. (*b*) Then fold it in half again. (*c*) Tear off a corner to allow better seating of the paper in the funnel. (*d*) Open the side that was not torn when fitting the paper in the funnel.

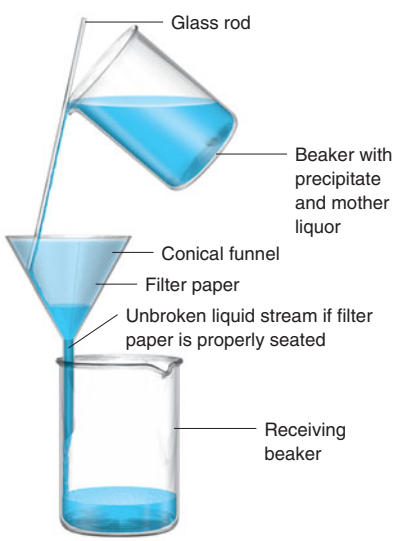


FIGURE 2-19 Filtering a precipitate. The conical funnel is supported by a metal ring attached to a ring stand, neither of which is shown.

For filtration, pour the slurry of precipitate down a glass rod to prevent splattering (Figure 2-19). (A **slurry** is a suspension of solid in liquid.) Particles adhering to the beaker or rod can be dislodged with a *rubber policeman*, which is a flattened piece of rubber at the end of a glass rod. Use a jet of appropriate wash liquid from a squirt bottle to transfer particles from the rubber and glassware to the filter. If the precipitate is going to be ignited, particles remaining in the beaker should be wiped onto a small piece of moist filter paper. Add that paper to the filter to be ignited.

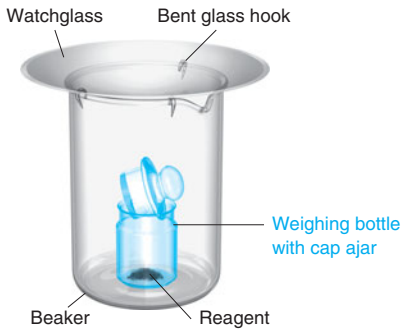


FIGURE 2-20 Use a watchglass as a dust cover while drying reagents or crucibles in the oven.

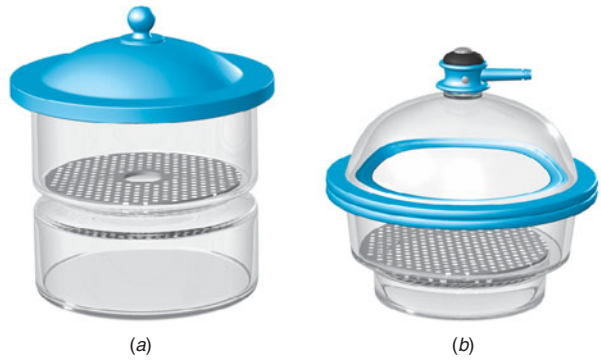


FIGURE 2-21 (*a*) Ordinary desiccator. (*b*) Vacuum desiccator that can be evacuated through the side arm at the top and then sealed by rotating the joint containing the side arm. Drying is more efficient at low pressure. [Courtesy A. H. Thomas Co., Philadelphia, PA.]

2-8 Drying

Reagents, precipitates, and glassware are conveniently dried in an oven at 110°C. (Some chemicals require other temperatures.) *Anything that you put in the oven should be labeled.* Use a beaker and watchglass (Figure 2-20) to minimize contamination by dust during drying. It is good practice to cover all vessels on the benchtop to prevent dust contamination.

Dust is a source of contamination in all experiments, so . . .

Cover all vessels whenever possible.

The mass of a gravimetric precipitate is measured by weighing a dry, empty filter crucible before the procedure and reweighing the same crucible filled with dry product after the procedure. To weigh the empty crucible, first bring it to "constant mass" by drying it in the oven for 1 h or longer and then cooling it for 30 min in a desiccator. Weigh the crucible and then heat it again for about 30 min. Cool it and reweigh it. When successive weighings agree to ±0.3 mg, the filter has reached "constant mass." If the crucible is warm when it is weighed, it creates convection currents that give a false weight. You can use a microwave oven instead of an electric oven for drying reagents and crucibles. Try an initial heating time of 4 min, with subsequent 2-min heatings. Use a 15-min cooldown before weighing.

A **desiccator** (Figure 2-21) is a closed chamber containing a drying agent called a **desiccant** (Table 2-6). The lid is greased to make an airtight seal, and desiccant is placed in the bottom beneath the perforated disk. Another useful desiccant that is not in the table is 98 wt% sulfuric acid. After placing a hot object in the desiccator, leave the lid cracked open for a minute until the object has cooled slightly. This practice prevents the lid from popping open when the air inside warms up. To open a desiccator, slide the lid sideways rather than trying to pull it straight up.

TABLE 2-6 Efficiencies of drying agents

Agent	Formula	Water left in atmosphere (μg H_2O/L)[a]
Magnesium perchlorate, anhydrous	$Mg(ClO_4)_2$	0.2
"Anhydrone"	$Mg(ClO_4)_2 \cdot 1-1.5H_2O$	1.5
Barium oxide	BaO	2.8
Alumina	Al_2O_3	2.9
Phosphorus pentoxide	P_4O_{10}	3.6
Calcium sulfate (Drierite)[b]	$CaSO_4$	67
Silica gel	SiO_2	70

a. Moist nitrogen was passed over each desiccant, and the water remaining in the gas was condensed and weighed. [A. I. Vogel, A Textbook of Quantitative Inorganic Analysis, 3rd ed. (New York: Wiley. 1961), p. 178.] For drying gases, the gas can be passed through a 60-cm-long Nafion tube. At 25°C, the residual moisture is 10 μg/L. If the drier is held at 0°C, the residual moisture is 0.8 μg/L. [K. J. Leckrone and J. M. Hayes, "Efficiency and Temperature Dependence of Water Removal by Membrane Dryers," Anal. Chem. ***1997,*** *69, 911.]*

b. Used Drierite can be regenerated by irradiating 1.5-kg batches in a 100 × 190 mm Pyrex crystallizing dish in a microwave oven for 15 min. Stir the solid, heat a second time for 15 min. and place the hot, dry material back in its original container. Use small glass spacers between the crystallizing dish and the glass tray of the oven to protect the tray. [J. A. Green and R. W. Goetz, "Recycling Drierite," J. Chem. Ed. ***1991,*** *68, 429.]*

2-9 Calibration of Volumetric Glassware

Each instrument that we use has a scale of some sort to measure a quantity such as mass, volume, force, or electric current. Manufacturers usually certify that the indicated quantity lies within a certain *tolerance* from the true quantity. For example, a Class A transfer pipet is certified to deliver 10.00 ± 0.02 mL when you use it properly. Your individual pipet might always deliver 10.016 ± 0.004 mL in a series of trials. That is, your pipet delivers an average of 0.016 mL more than the indicated volume in repeated trials. **Calibration** is the process of measuring the actual quantity that corresponds to an indicated quantity on the scale of an instrument.

Page 49 gives a detailed procedure for calibrating a buret.

For greatest accuracy, we calibrate volumetric glassware to measure the volume actually contained in or delivered by a particular piece of equipment. We do this by measuring the mass of water contained or delivered by the vessel and using the density of water to convert mass into volume.

In the most careful work, it is necessary to account for thermal expansion of solutions and glassware with changing temperature. For this purpose, you should know the lab temperature when a solution was prepared and when it is used. Table 2-7 shows that water expands 0.02% per degree near 20°C. Because the concentration of a solution is proportional to its density, we can write

Concentration decreases when the temperature increases.

Correction for thermal expansion:

$$\frac{c'}{d'} = \frac{c}{d} \tag{2-2}$$

where c' and d' are the concentration and density at temperature T', and c and d apply at temperature T.

TABLE 2-7 Density of water

Temperature (°C)	Density (g/mL)	Volume of 1 g of water (mL): At temperature shown[a]	Volume of 1 g of water (mL): Corrected to 20°C[b]
10	0.999 702 6	1.001 4	1.001 5
11	0.999 608 4	1.001 5	1.001 6
12	0.999 500 4	1.001 6	1.001 7
13	0.999 380 1	1.001 7	1.001 8
14	0.999 247 4	1.001 8	1.001 9
15	0.999 102 6	1.002 0	1.002 0
16	0.998 946 0	1.002 1	1.002 1
17	0.998 777 9	1.002 3	1.002 3
18	0.998 598 6	1.002 5	1.002 5
19	0.998 408 2	1.002 7	1.002 7
20	0.998 207 1	1.002 9	1.002 9
21	0.997 995 5	1.003 1	1.003 1
22	0.997 773 5	1.003 3	1.003 3
23	0.997 541 5	1.003 5	1.003 5
24	0.997 299 5	1.003 8	1.003 8
25	0.997 047 9	1.004 0	1.004 0
26	0.996 786 7	1.004 3	1.004 2
27	0.996 516 2	1.004 6	1.004 5
28	0.996 236 5	1.004 8	1.004 7
29	0.995 947 8	1.005 1	1.005 0
30	0.995 650 2	1.005 4	1.005 3

a. Corrected for buoyancy with Equation 2-1.

b. Corrected for buoyancy and expansion of borosilicate glass (0.001 0% K^{-1}).

EXAMPLE **Effect of Temperature on Solution Concentration**

A 0.031 46 M aqueous solution was prepared in winter when the lab temperature was 17°C. What is the molarity of the solution on a warm day when the temperature is 25°C?

Solution We assume that the thermal expansion of a dilute solution is equal to the thermal expansion of pure water. Then, using Equation 2-2 and densities from Table 2-7, we write

$$\frac{c' \text{ at } 25°\text{C}}{0.997\,05 \text{ g/mL}} = \frac{0.031\,46 \text{ M}}{0.998\,78 \text{ g/mL}} \quad \Rightarrow \quad c' = 0.031\,41 \text{ M}$$

The concentration has decreased by 0.16% on the warm day.

Pyrex and other borosilicate glasses expand by 0.001 0% per degree near room temperature. If the temperature increases by 10°C, the volume of a piece of glassware increases by (10°C)(0.001 0%/°C) = 0.010%. For most work, this expansion is insignificant.

To calibrate a 25-mL transfer pipet, first weigh an empty weighing bottle like the one in Figure 2-20. Then fill the pipet to the mark with distilled water, drain it into the weighing bottle, and cap the bottle to prevent evaporation. Weigh the bottle again to find the mass of water delivered from the pipet. Finally, use Equation 2-3 to convert mass into volume.

Small or odd-shaped vessels can be calibrated with Hg, which is easier than water to pour out of glass and is 13.6 times denser than water. This procedure is for researchers, not students.

$$\text{True volume} = (\text{grams of water}) \times (\text{volume of 1 g of } H_2O \text{ in Table 2-7}) \qquad (2\text{-}3)$$

EXAMPLE **Calibration of a Pipet**

An empty weighing bottle had a mass of 10.313 g. After the addition of water from a 25-mL pipet, the mass was 35.225 g. If the lab temperature was 27°C, find the volume of water delivered by the pipet.

Solution The mass of water is 35.225 − 10.313 = 24.912 g. From Equation 2-3 and the next-to-last column of Table 2-7, the volume of water is (24.912 g)(1.004 6 mL/g) = 25.027 mL at 27°C. The last column in Table 2-7 tells us what the volume would be if the pipet were at 20°C. This pipet would deliver (24.912 g)(1.004 5 mL/g) = 25.024 mL at 20°C.

The pipet delivers less volume at 20°C than at 27°C because glass contracts slightly as the temperature is lowered. Volumetric glassware is usually calibrated at 20°C.

2-10 Introduction to Microsoft Excel®

If you already use a spreadsheet, you can skip this section. The computer spreadsheet is an essential tool for manipulating quantitative information. In analytical chemistry, spreadsheets can help us with calibration curves, statistical analysis, titration curves, and equilibrium problems. Spreadsheets allow us to conduct "what if" experiments such as investigating the effect of a stronger acid or a different ionic strength on a titration curve. We use Microsoft Excel in this book as a tool for solving problems in analytical chemistry.[25] Although you can skip over spreadsheets with no loss of continuity, spreadsheets will enrich your understanding of chemistry and provide a valuable tool for use outside this course.

Getting Started: Calculating the Density of Water

Let's prepare a spreadsheet to compute the density of water from the equation

$$\text{Density (g/mL)} = a_0 + a_1{*}T + a_2{*}T^2 + a_3{*}T^3 \qquad (2\text{-}4)$$

where T is temperature (°C) and $a_0 = 0.999\,89$, $a_1 = 5.332\,2 \times 10^{-5}$, $a_2 = -7.589\,9 \times 10^{-6}$, and $a_3 = 3.671\,9 \times 10^{-8}$.

This equation is accurate to five decimal places over the range 4° to 40°C.

The blank spreadsheet in Figure 2-22a has columns labeled A, B, C and rows numbered 1, 2, 3, . . . , 12. The box in column B, row 4 is called *cell* B4.

Begin each spreadsheet with a title to help make the spreadsheet more readable. In Figure 2-22b, we click in cell A1 and type "Calculating Density of H2O with Equation 2-4". Then we click in cell A2 and write "(from the delightful book by Dan Harris)" without quotation marks. The computer automatically spreads the text to adjoining cells. To save your worksheet, click on the Office button at the upper left and select Save As. Give your

Columns

Rows

	A	B	C
1			
2			
3			
4		cell B4	
5			
6			
7			
8			
9			
10			
11			
12			

(*a*)

	A	B	C
1	Calculating Density of H2O with Equation 2-4		
2	(from the delightful book by Dan Harris)		
3			
4	Constants:		
5	a0 =		
6	0.99989		
7	a1 =		
8	5.3322E-05		
9	a2 =		
10	-7.5899E-06		
11	a3 =		
12	3.6719E-08		

(*b*)

	A	B	C
1	Calculating Density of H2O with Equation 2-4		
2	(from the delightful book by Dan Harris)		
3			
4	Constants:	Temp (°C)	Density (g/mL)
5	a0 =	5	0.99997
6	0.99989	10	
7	a1 =	15	
8	5.3322E-05	20	
9	a2 =	25	
10	-7.5899E-06	30	
11	a3 =	35	
12	3.6719E-08	40	

(*c*)

	A	B	C
1	Calculating Density of H2O with Equation 2-4		
2	(from the delightful book by Dan Harris)		
3			
4	Constants:	Temp (°C)	Density (g/mL)
5	a0 =	5	0.99997
6	0.99989	10	0.99970
7	a1 =	15	0.99911
8	5.3322E-05	20	0.99821
9	a2 =	25	0.99705
10	-7.5899E-06	30	0.99565
11	a3 =	35	0.99403
12	3.6719E-08	40	0.99223
13			
14	Formula:		
15	C5 = $A$6+$A$8*B5+$A$10*B5^2+$A$12*B5^3		

(*d*)

FIGURE 2-22 Evolution of a spreadsheet for computing the density of water.

spreadsheet a descriptive name that will tell you what is in it long after you have forgotten about it. File it in a location that you can find in the future. Information in your computer is only as good as your ability to retrieve it. In earlier versions of Excel, select the File menu to find Save As.

We adopt a convention in this book in which constants are collected in column A. Type "Constants:" in cell A4. Then select cell A5 and type "a0 =". Now select cell A6 and type the number 0.99989 (without extra spaces). In cells A7 to A12, enter the remaining constants. Powers of 10 are written, for example, as E-5 for 10^{-5}.

After you type "5.3322E-5" in cell A8, the spreadsheet probably displays "5.33E-5" even though additional digits are kept in memory. To display a desired number of digits in scientific format, click in cell A8 and select the Home ribbon at the top of the spreadsheet in Excel 2007. Go to the part of the ribbon that says Number and click on the little arrow at the lower right. The Format Cells window should appear. Select Scientific and 4 decimal places. When you click OK, the entry in cell A8 will be "5.3322E-5". If you need more room for the number of digits, grab the vertical line at the top of the column with your mouse and resize the column. In earlier versions of Excel, go to Format and then select Cells to obtain the formatting window. You can format all numbers in column A by clicking on the top of the column before setting the format. Your spreadsheet should now look like Figure 2-22b.

In cell B4, write the heading "Temp (°C)". In Excel 2007, you can find the degree sign on the Insert ribbon by clicking Symbol. In earlier versions of Excel, go to the Insert

menu and select Symbol. Now enter temperatures from 5 through 40 in cells B5 through B12. This is our *input* to the spreadsheet. The *output* will be computed values of density in column C.

In cell C4, enter the heading "Density (g/mL)". Cell C5 is the most important one in the table. In this one, you will write the *formula*

$$= \$A\$6 + \$A\$8*B5 + \$A\$10*B5\text{^}2 + \$A\$12*B5\text{^}3$$

Formulas begin with an equal sign. Arithmetic operations in a spreadsheet are

+ addition
− subtraction
* multiplication
/ division
^ exponentiation

It doesn't matter whether or not you use spaces around the arithmetic operators. When you hit Return, the number 0.99997 appears in cell C5. The formula above is the spreadsheet translation of Equation 2-4. $A$6 refers to the constant in cell A6. We will explain the dollar signs shortly. B5 refers to the temperature in cell B5. The times sign is * and the exponentiation sign is ^. For example, the term "$A$12*B5^3" means "(contents of cell A12) × (contents of cell B5)^3."

Now comes the most magical property of a spreadsheet. Highlight cell C5 and the empty cells below it from C6 to C12. In the Home ribbon, at the right side above Editing, click on the down arrow and select Down. In earlier versions of Excel, go to the Edit menu and select Fill Down. Excel copies the formula from C5 into the cells below it and evaluates the numbers in each of the selected cells. The density of water at each temperature now appears in column C in Figure 2-22d. You can make numbers appear as decimals, rather than scientific notation, by clicking on the arrow at the lower right in Number in the Home ribbon. In Format Cells, select Number and 5 decimal places.

In this example, we made three types of entries. *Labels* such as "a0 =" were typed in as text. An entry that does not begin with a digit or an equal sign is treated as text. *Numbers*, such as 25, were typed in some cells. The spreadsheet treats a number differently from text. In cell C5, we entered a *formula* that necessarily begins with an equal sign.

Three kinds of entries:

label	a3 =
number	4.4E-05
formula	= $A$8*B5

Arithmetic Operations and Functions

Addition, subtraction, multiplication, division, and exponentiation have the symbols +, −, *, /, and ^. *Functions* such as Exp(·) can be typed or can be selected from the Formula ribbon in Excel 2007. In earlier versions of Excel, select the Insert menu and choose Function. Exp(·) raises e to the power in parentheses. Other functions such as Ln(·), Log(·), Sin(·), and Cos(·) are also available.

The order of arithmetic operations in formulas is negation first, followed by ^, followed by * and / (evaluated in order from left to right as they appear), finally followed by + and – (also evaluated from left to right). Make liberal use of parentheses to be sure that the computer does what you intend. The contents of parentheses are evaluated first, before carrying out operations outside the parentheses. Here are some examples:

Order of operations:

1. Negation (a minus sign before a term)
2. Exponentiation
3. Multiplication and division (in order from left to right)
4. Addition and subtraction (in order from left to right)

Operations within parentheses are evaluated first, from the innermost set.

$$9/5*100+32 = (9/5)*100+32 = (1.8)*100+32 = (1.8*100)+32 = (180)+32 = 212$$
$$9/5*(100+32) = 9/5*(132) = (1.8)*(132) = 237.6$$
$$9+5*100/32 = 9+(5*100)/32 = 9+(500)/32 = 9+(500/32) = 9+(15.625) = 24.625$$
$$9/5\text{^}2+32 = 9/(5\text{^}2)+32 = (9/25)+32 = (0.36)+32 = 32.36$$
$$-2\text{^}2 = 4 \quad \text{but} \quad -(2\text{^}2) = -4$$

When in doubt about how an expression will be evaluated, use parentheses to force what you intend.

Documentation and Readability

The first important *documentation* in the spreadsheet is the name of the file. A name such as "Expt 10 Gran Plot" is more meaningful than "Chem Lab". The next important feature is a title at the top of the spreadsheet, which tells its purpose. To tell what formulas were used in the spreadsheet, we added text (labels) at the bottom. In cell A14, write "Formula:" and in cell A15 write "C5 = $A$6+$A$8*B5+$A$10*B5^2+$A$12*B5^3". The surest way to document a formula is to copy the text from the formula bar for cell C5. Go to cell A15, type "C5" and then paste in the text you copied.

Documentation means labeling. If your spreadsheet cannot be read by another person without your help, it needs better documentation. (The same is true of your lab notebook!)

We improved the *readability* of data in the spreadsheet by selecting the number (decimal) or scientific format and specifying how many decimal places would be shown. The spreadsheet retains more digits in its memory, even though just 5 might be displayed.

Absolute reference: $A$8
Relative reference: B5

Save your files frequently while you are working and make a backup file of anything that you don't want to lose.

Absolute and Relative References

The formula "= $A$8*B5" refers to cells A8 and B5 in different manners. $A$8 is an *absolute reference* to the contents of cell A8. No matter where cell $A$8 is called from in the spreadsheet, the computer goes to cell A8 to look for a number. "B5" is a *relative reference* in the formula in cell C5. When called from cell C5, the computer goes to cell B5 to find a number. When called from cell C6, the computer goes to cell B6 to look for a number. If called from cell C19, the computer would look in cell B19. This is why the cell written without dollar signs is called a relative reference. If you want the computer to always look only in cell B5, then you should write "$B$5".

2-11 Graphing with Microsoft Excel

Graphs are critical to understanding quantitative relations. To make a graph in Excel 2007 from the spreadsheet in Figure 2-22d, go to the Insert ribbon and select Chart. Click on Scatter and select the icon for Scatter with Smooth Lines and Markers. The other most common graph we will make is Scatter with only Markers. Grab the blank chart with your mouse and move it to the right of the data. In Chart Tools, select Design and click on Select Data. Click on Add. For Series name, write "Density" (without quotation marks). For X values, highlight cells B5:B12. For Y values, delete what was in the box and highlight cells C5:C12. Click OK twice. Click inside the plot area and select the Chart Tools Format ribbon. In Plot Area, Format Selection provides options for the border and fill color of the graph. For Fill, select Solid fill and Color white. For Border Color, select Solid line and Color black. We now have a white graph surrounded by a black border.

To add an X axis title, select Chart Tools Layout. Click on Axis Titles and Primary Horizontal Axis Title. Click on Title Below Axis. A generic axis title appears on the graph. Highlight it and type "Temperature (°C)" over the title. Get the degree sign from Insert Symbol. To put a title on the Y axis, select Chart Tools Layout again. Click on Axis Titles and Primary Vertical Axis Title. Click on Rotated Title. Then type "Density (g/mL)" for the title. Select the title that appears above the graph and remove it with the delete key. Your graph probably looks like the one in Figure 2-23 now.

Let's change the graph so that it looks like Figure 2-24. Click on the curve on the graph to highlight all data points. If only one point is highlighted, click elsewhere on the line. Select Chart Tools Format. In Current Selection, choose Format Selection. A Format Data Series window appears. For Marker Options, choose Built-in. Select the Type circle and Size 6. For Marker Fill, select Solid fill and a Color of your choice. Select Marker Line Color, then Solid line, then the same Color as the marker. To change the appearance of the curve on the graph, use Line Color and Line Style. Create a solid black line with a width of 1.5 points.

	A	B	C
1	Calculating Density of H2O with Equation 2-4		
2	(from the delightful book by Dan Harris)		
3			
4	Constants:	Temp (C)	Density (g/mL)
5	a0 =	5	0.99997
6	0.99989	10	0.99970
7	a1 =	15	0.99911
8	5.3322E-05	20	0.99821
9	a2 =	25	0.99705
10	–7.5899E-06	30	0.99565
11	a3 =	35	0.99403
12	3.6719E-08	40	0.99223
13			
14	Formula:		
15	C5 = $A$6+$A$8*B5+$A$10*B5^2+$A$12*B5^3		
16			
17			

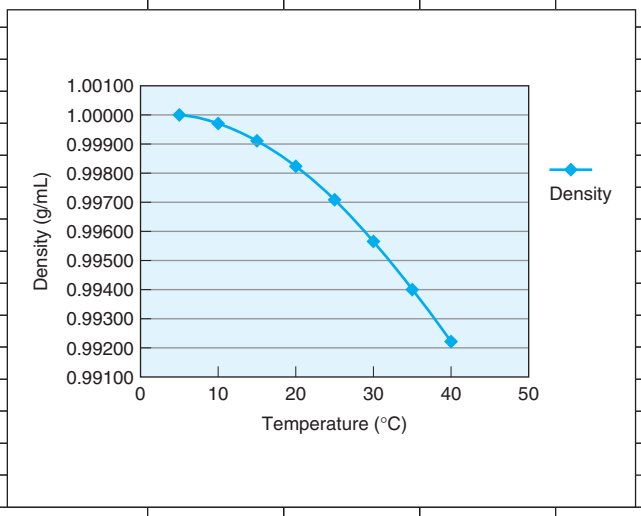


FIGURE 2-23 Initial density chart drawn by Excel.

To change the appearance of the Y axis, click any number on the Y axis and they will all be highlighted. Select Chart Tools and Format and Format Selection. The Format Axis box appears. For Axis Options, Minimum, click on Fixed and set the value to 0.992. For Axis Options, Maximum, click on Fixed and set the value to 1.000. For Major unit, click on Fixed and set the value to 0.002. For Minor unit, click on Fixed and set the value to 0.0004. Set Minor tick mark type to Outside. In the Format Axis window, select Number and set a display of 3 decimal places. Close the Format Axis window to finish with the vertical axis.

In a similar manner, select a number on the X axis and change the appearance so that it looks like Figure 2-24 with a Minimum of 0, Maximum of 40, Major unit of 10, and Minor unit of 5. Place Minor tick marks Outside. To add vertical grid lines, go to Chart Tools and select Layout and Grid Lines. Select Primary Vertical Gridlines and Major Gridlines.

Add a title back to the chart. In Chart Tools Layout, select Chart Title and highlight Above Chart. Type "Density of Water". In the Home ribbon, select a font size of 10 points. Your chart ought to look much like Figure 2-24 now. You can resize the chart from its lower right corner. To draw on an Excel worksheet, select Insert and then Shapes.

To write on the chart, go to the Insert ribbon and select Text Box. Click in the chart and begin typing. Drag the text box where you want it to be. To format the box, click on its border. Go to the Format ribbon and use Shape Fill and Shape Outline. To add arrows or lines, go to the Insert ribbon and select Shapes. To change the data point symbol, click on one point. On the Format Ribbon, click on Format Selection. The box that apppears lets you change the appearance of the points and the line.

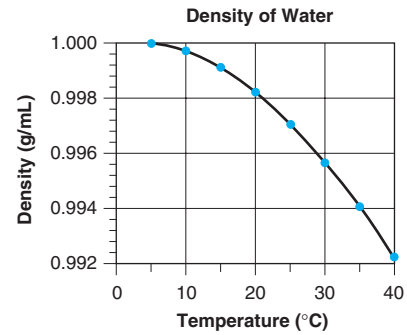


FIGURE 2-24 Density chart after reformatting.

Graphing in Earlier Versions of Excel

To make a graph from the spreadsheet in Figure 2-22d, go to the Insert menu and select Chart. A window appears with a variety of options. The one you will almost always want is XY (Scatter). Highlight XY (Scatter) and several options appear. Select the one that shows data points connected by a smooth curve. Click Next to move to a window called Chart Source Data. Click on the Series tab and click Add. Boxes appear for three inputs. For Name, type "Density" (without quotation marks). For X Values, enter B5:B12 or just highlight those cells on the spreadsheet and they will be automatically entered. For Y Values, highlight cells C5:C12. Click Next.

Now a small graph of your data appears. If it does not look as expected, make sure you selected the correct data, with *x* before *y*. The new window asks you for axis labels and an optional title for the graph. For the title, write "Density of Water". For the *x*-axis, enter "Temperature (°C)" and for the *y*-axis write "Density (g/mL)". Click Next.

Now you are given the option of drawing the graph on a new sheet or on the same sheet that is already open. Select "As object in Sheet 1". Click Finish and the chart will appear on your spreadsheet. Grab the chart with your mouse and move it to the right of the data.

Excel gives us many options for changing features of the graph. Here are a few, but you should experiment with the graph to discover other formatting options. Double click on the *y*-axis and a window appears. Select the Patterns tab. Change Minor tick mark type from None to Outside and click OK. You will see new tick marks appear on the *y*-axis. Double click on the *y*-axis again and select the Number tab. Change the decimal places to 3 and click OK. Double click on the *y*-axis again and select the Scale tab. Set the minimum to 0.992 and the maximum to 1.000 and click OK.

Double click on the *x*-axis and select Patterns. Change the Minor tick mark type from None to Outside. Select Scale and set the maximum to 40, the major unit to 10, the minor unit to 5, and click OK.

Double click on the gray area of the graph and a window called Patterns appears. Select Automatic for the Border and None for the Area. This removes the gray background and gives a solid line around the graph. To add vertical lines at the major tick marks, select the graph with the mouse. Then go to the Chart menu and select Chart Options. In the window that appears, select Gridlines. For the Value (X) axis, check Major gridlines. Then select the tab for Legend and remove the check mark from Show Legend. The legend will disappear. Click OK. You should be getting the idea that you can format virtually any part of the chart.

Click on the outer border of the chart and handles appear. Grab the one on the right and resize the chart so that it does not extend past column F of the spreadsheet. Grab the handle at the bottom and resize the chart so that it does not extend below row 15. When you resized the chart, letters and numbers shrank. Double click on each set of numbers and change the font to 8 points. Double click on the labels and change the letters to 9 points. Your chart should look much like the one in Figure 2-24.

To write on the chart, go to View and select Toolbars and Drawing. Select Text Box from the Drawing toolbar, click inside your chart, and begin typing. Draw arrows with the Arrow tool. Double click on a data point to get options to change plotting symbols.

Terms to Understand

absorption
acid wash
adsorption
ashless filter paper
buoyancy
buret
calibration
desiccant
desiccator
filtrate
green chemistry
hygroscopic
ignition
meniscus
mother liquor
parallax
pipet
slurry
tare
volumetric flask

Summary

Safety requires you to think in advance about what you will do; never do anything that seems dangerous. Know how to use safety equipment such as goggles, fume hood, lab coat, gloves, emergency shower, eyewash, and fire extinguisher. Chemicals should be stored and used in a manner that minimizes contact of solids, liquids, and vapors with people. Environmentally acceptable disposal procedures should be established in advance for every chemical that you use. Your lab notebook tells what you did and what you observed; it should be understandable to other people. It also should allow you to repeat an experiment in the same manner in the future. You should understand the principles of operation of balances and treat them as delicate equipment. Buoyancy corrections are required in accurate work. Burets should be read in a reproducible manner and drained slowly for best results. Always interpolate between markings to obtain accuracy one decimal place beyond the graduations. Volumetric flasks are used to prepare solutions with known volume. Transfer pipets deliver fixed volumes; less accurate measuring pipets deliver variable volumes. Do not be lulled into complacency by the nice digital reading on a micropipet. Unless your pipet has been calibrated recently and your personal technique tested, micropipets can have gross errors. Filtration and collection of precipitates require careful technique, as does the drying of reagents, precipitates, and glassware in ovens and desiccators. Volumetric glassware is calibrated by weighing water contained in or delivered by the vessel. In the most careful work, solution concentrations and volumes of vessels should be corrected for changes in temperature.

If you plan to use spreadsheets in this course, you should know how to enter formulas in a spreadsheet and how to draw a graph of data from a spreadsheet.

Exercises

2-A. What is the true mass of water if the measured mass in the atmosphere is 5.397 4 g? When you look up the density of water, assume that the lab temperature is **(a)** 15°C and **(b)** 25°C. Take the density of air to be 0.001 2 g/mL and the density of balance weights to be 8.0 g/mL.

2-B. A sample of ferric oxide (Fe_2O_3, density = 5.24 g/mL) obtained from ignition of a gravimetric precipitate weighed 0.296 1 g in the atmosphere. What is the true mass in vacuum?

2-C. A solution of potassium permanganate ($KMnO_4$) was found by titration to be 0.051 38 M at 24°C. What is the molarity when the lab temperature drops to 16°C?

2-D. Water was drained from a buret between the 0.12- and 15.78-mL marks. The apparent volume delivered was 15.78 − 0.12 = 15.66 mL. Measured in the air at 22°C, the mass of water delivered was 15.569 g. What was the true volume?

2-E. Reproduce the spreadsheet in Figure 2-23 and the graph in Figure 2-24.

Problems

Safety and Lab Notebook

2-1. What is the primary safety rule and what is your implied responsibility to make it work?

2-2. After safety features and safety procedures in your laboratory have been explained to you, make a list of them.

2-3. For chemical disposal, why is dichromate converted to $Cr(OH)_3(s)$?

2-4. Explain what each of the three numbered hazard ratings means for 37 wt% HCl in Figure 2-2.

2-5. State three essential attributes of a lab notebook.

Analytical Balance

2-6. Explain the principles of operation of electronic and mechanical balances.

2-7. Why is the buoyancy correction equal to 1 in Figure 2-9 when the density of the object being weighed is 8.0 g/mL?

2-8. Pentane (C_5H_{12}) is a liquid with a density of 0.626 g/mL near 25°C. Find the true mass of pentane when the mass in air is 14.82 g. Assume air density = 0.001 2 g/mL.

2-9. The densities (g/mL) of several substances are: acetic acid, 1.05; CCl_4, 1.59; S, 2.07; Li, 0.53; Hg, 13.5; PbO_2, 9.4; Pb, 11.4; Ir, 22.5. From Figure 2-9, predict which substances will have the smallest and largest buoyancy corrections.

2-10. Potassium hydrogen phthalate is a primary standard used to measure the concentration of NaOH solutions. Find the true mass of potassium hydrogen phthalate (density = 1.636 g/mL) if the mass weighed in air is 4.236 6 g. If you did not correct the mass for buoyancy, would the calculated molarity of NaOH be too high or too low? By what percentage?

2-11. (a) Use the ideal gas law (Problem 1-16) to calculate the density (g/mL) of helium at 20°C and 1.00 bar.

(b) Find the true mass of Na (density = 0.97 g/mL) weighed in a glove box with a He atmosphere, if the apparent mass is 0.823 g.

2-12. (a) The equilibrium vapor pressure of water at 20°C is 2 330 Pa. What is the vapor pressure of water in the air at 20°C if the relative humidity is 42%? (*Relative humidity* is the percentage of the equilibrium water vapor pressure in the air.)

(b) Use note 13 for Chapter 2 at the end of the book to find the air density (g/mL, not g/L) under the conditions of part **(a)** if the barometric pressure is 94.0 kPa.

(c) What is the true mass of water in part **(b)** if the mass in air is 1.000 0 g?

2-13. *Effect of altitude on electronic balance*. If an object weighs m_a grams at distance r_a from the center of the Earth, it will weigh $m_b = m_a(r_a^2/r_b^2)$ when raised to r_b. An object weighs 100.000 0 g on the first floor of a building at r_a = 6 370 km. How much will it weigh on the tenth floor, which is 30 m higher?

Glassware and Thermal Expansion

2-14. What do the symbols "TD" and "TC" mean on volumetric glassware?

2-15. Describe how to prepare 250.0 mL of 0.150 0 M K_2SO_4 with a volumetric flask.

2-16. When is it preferable to use a plastic volumetric flask instead of a more accurate glass flask?

2-17. (a) Describe how to deliver 5.00 mL of liquid by using a transfer pipet.

(b) Which is more accurate, a transfer pipet or a measuring pipet?

2-18. (a) Describe how to deliver 50.0 μL by using a 100-μL adjustable micropipet.

(b) What would you do differently in **(a)** if the liquid foams.

2-19. What is the purpose of the trap in Figure 2-17 and the watchglass in Figure 2-20?

2-20. Which drying agent is more efficient, Drierite or phosphorus pentoxide?

2-21. An empty 10-mL volumetric flask weighs 10.263 4 g. When the flask is filled to the mark with distilled water and weighed again in the air at 20°C, the mass is 20.214 4 g. What is the true volume of the flask at 20°C?

2-22. By what percentage does a dilute aqueous solution expand when heated from 15° to 25°C? If a 0.500 0 M solution is prepared at 15°C, what would its molarity be at 25°C?

2-23. The true volume of a 50-mL volumetric flask is 50.037 mL at 20°C. What mass of water measured **(a)** in vacuum and **(b)** in air at 20°C would be contained in the flask?

2-24. You want to prepare 500.0 mL of 1.000 M KNO_3 at 20°C, but the lab (and water) temperature is 24°C at the time of preparation. How many grams of solid KNO_3 (density = 2.109 g/mL) should be dissolved in a volume of 500.0 mL at 24°C to give a concentration of 1.000 M at 20°C? What apparent mass of KNO_3 weighed in air is required?

2-25. A simple model for the fraction of micropipets that operate within specifications after time t is

$$\text{Fraction within specifications} = e^{-t(\ln 2)/t_m}$$

where t_m is the mean time between failure (the time when the fraction within specifications is reduced to 50%). Suppose that t_m = 2.00 years.

(a) Show that the equation predicts that the time at which 50% remain within specifications is 2 yr if t_m = 2.00 yr.

(b) Find the time t at which pipets should be recalibrated (and repaired, if necessary) so that 95% of all pipets will operate within specifications.

2-26. Glass is a notorious source of metal ion contamination. Three glass bottles were crushed and sieved to collect 1-mm pieces.[26] To see how much Al^{3+} could be extracted, 200 mL of a 0.05 M solution of the metal-binding compound EDTA were stirred with 0.50 g of ~1-mm glass particles in a polyethylene flask. The Al content of the solution after 2 months was 5.2 μM. The total Al content of the glass, measured after completely dissolving some glass in 48 wt% HF with microwave heating, was 0.80 wt%. What fraction of the Al was extracted from glass by EDTA?

2-27. The efficiency of a gas chromatography column is measured by a parameter called plate height (H, mm) which is related to the gas flow rate (u, mL/min) by the van Deemter equation: $H = A + B/u + Cu$, where A, B, and C are constants. Prepare a spreadsheet with a graph showing values of H as a function of u for u = 4, 6, 8, 10, 20, 30, 40, 50, 60, 70, 80, 90, and 100 mL/min. Use the values A = 1.65 mm, B = 25.8 mm · mL/min, and C = 0.023 6 mm · min/mL.

Reference Procedure: Calibrating a 50-mL Buret

This procedure tells how to construct a graph such as Figure 3-3 to convert the measured volume delivered by a buret to the true volume delivered at 20°C.

0. Measure the temperature in the laboratory. Distilled water for this experiment must be at laboratory temperature.

1. Fill the buret with distilled water and force any air bubbles out the tip. See whether the buret drains without leaving drops on the walls. If drops are left, clean the buret with soap and water or soak it with cleaning solution.[15] Adjust the meniscus to be at or slightly below 0.00 mL, and touch the buret tip to a beaker to remove the suspended drop of water. Allow the buret to stand for 5 min while you weigh a 125-mL flask fitted with a rubber stopper. (Hold the flask with a tissue or paper towel, not with your hands, to prevent fingerprint residue from changing its mass.) If the level of the liquid in the buret has changed, tighten the stopcock and repeat the procedure. Record the level of the liquid.

2. Drain approximately 10 mL of water at a rate <20 mL/min into the weighed flask, and cap it tightly to prevent evaporation. Allow about 30 s for the film of liquid on the walls to descend before you read the buret. Estimate all readings to the nearest 0.01 mL. Weigh the flask again to determine the mass of water delivered.

3. Now drain the buret from 10 to 20 mL, and measure the mass of water delivered. Repeat the procedure for 30, 40, and 50 mL. Then do the entire procedure (10, 20, 30, 40, 50 mL) a second time.

4. Use Table 2-7 to convert the mass of water into the volume delivered. Repeat any set of duplicate buret corrections that do not agree to within 0.04 mL. Prepare a calibration graph like that in Figure 3-3, showing the correction factor at each 10-mL interval.

EXAMPLE Buret Calibration

When draining the buret at 24°C, you observe the following values:

Final reading	10.01		10.08 mL
Initial reading	0.03		0.04
Difference	9.98		10.04 mL
Mass	9.984		10.056 g
Actual volume delivered	10.02		10.09 mL
Correction	+0.04		+0.05 mL
Average correction		+0.045 mL	

To calculate the actual volume delivered when 9.984 g of water are delivered at 24°C, look at the column of Table 2-7 headed "Corrected to 20°C." In the row for 24°C, you find that 1.000 0 g of water occupies 1.003 8 mL. Therefore, 9.984 g occupies (9.984 g)(1.003 8 mL/g) = 10.02 mL. The average correction for both sets of data is +0.045 mL.

To obtain the correction for a volume greater than 10 mL, add successive masses of water collected in the flask. Suppose that the following masses were measured:

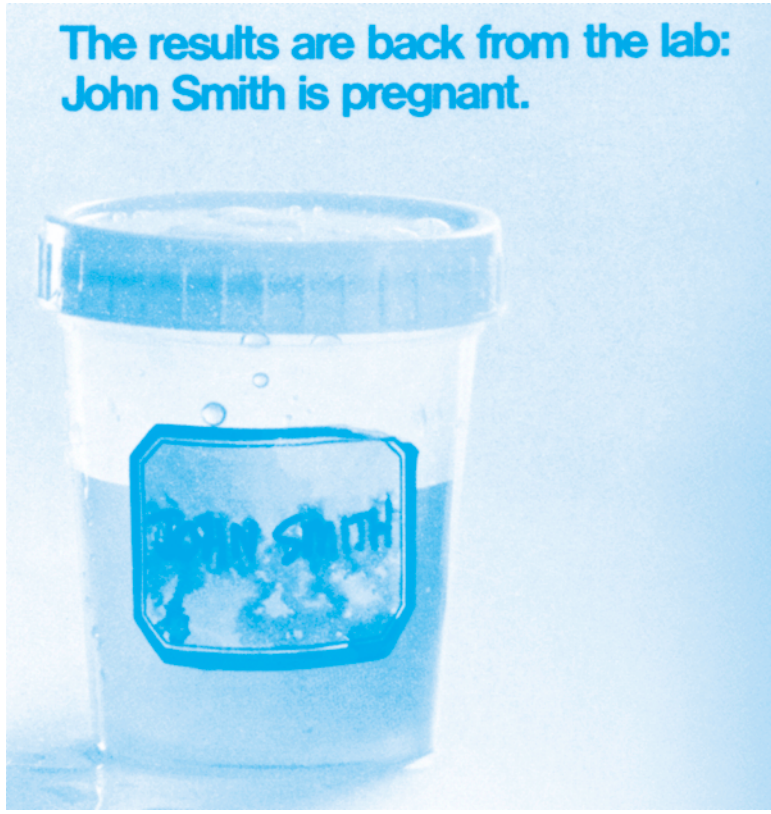
Volume interval (mL)	Mass delivered (g)
0.03–10.01	9.984
10.01–19.90	9.835
19.90–30.06	10.071
Sum 30.03 mL	29.890 g

The total volume of water delivered is (29.890 g)(1.003 8 mL/g) = 30.00 mL. Because the indicated volume is 30.03 mL, the buret correction at 30 mL is −0.03 mL.

What does this mean? Suppose that Figure 3-3 applies to your buret. If you begin a titration at 0.04 mL and end at 29.00 mL, you would deliver 28.96 mL if the buret were perfect. Figure 3-3 tells you that the buret delivers 0.03 mL less than the indicated amount, so only 28.93 mL were actually delivered. To use the calibration curve, either begin all titrations near 0.00 mL or correct both the initial and the final readings. Use the calibration curve whenever you use your buret.

3 Experimental Error

EXPERIMENTAL ERROR



[Courtesy 3M Company, St. Paul, MN.]

Some laboratory errors are more obvious than others, but there is error associated with every measurement. There is no way to measure the "true" value of anything. The best we can do in a chemical analysis is to carefully apply a technique that experience tells us is reliable. Repetition of one method of measurement several times tells us the *precision* (reproducibility) of the measurement. If the results of measuring the same quantity by different methods agree with one another, then we become confident that the results are *accurate*, which means they are near the "true" value.

Suppose that you determine the density of a mineral by measuring its mass (4.635 ± 0.002 g) and volume (1.13 ± 0.05 mL). Density is mass per unit volume: 4.635 g/1.13 mL = 4.101 8 g/mL. The uncertainties in measured mass and volume are ±0.002 g and ±0.05 mL, but what is the uncertainty in the computed density? And how many significant figures should be used for the density? This chapter discusses the propagation of uncertainty in lab calculations.

3-1 Significant Figures

Significant figures: minimum number of digits required to express a value in scientific notation without loss of precision

The number of **significant figures** is the minimum number of digits needed to write a given value in scientific notation without loss of precision. The number 142.7 has four significant figures, because it can be written 1.427×10^2. If you write $1.427\,0 \times 10^2$, you imply that you know the value of the digit after 7, which is not the case for the number 142.7. The number $1.427\,0 \times 10^2$ has five significant figures.

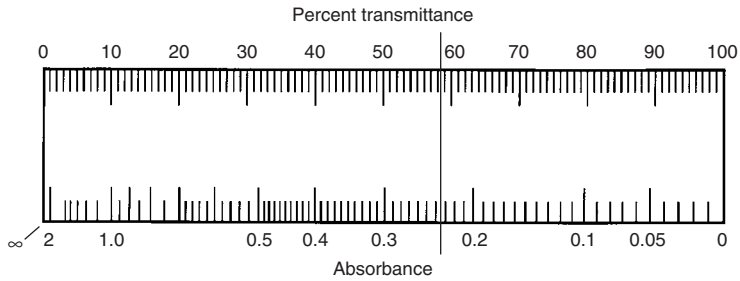


FIGURE 3-1 Analog scale of Bausch and Lomb Spectronic 20 spectrophotometer. Percent transmittance is a linear scale and absorbance is a logarithmic scale.

The number 6.302×10^{-6} has four significant figures, because all four digits are necessary. You could write the same number as 0.000 006 302, which also has just *four* significant figures. The zeros to the left of the 6 are merely holding decimal places. The number 92 500 is ambiguous. It could mean any of the following:

9.25×10^4	3 significant figures
9.250×10^4	4 significant figures
$9.250\,0 \times 10^4$	5 significant figures

You should write one of the three numbers above, instead of 92 500, to indicate how many figures are actually known.

Significant zeros below are **bold**:

1**0**6 0.01**0** 6 0.1**0**6 0.1**0**6 **0**

Zeros are significant when they occur (1) in the middle of a number or (2) at the end of a number on the right-hand side of a decimal point.

The last significant digit (farthest to the right) in a measured quantity always has some associated uncertainty. The minimum uncertainty is ± 1 in the last digit. The scale of a Spectronic 20 spectrophotometer is drawn in Figure 3-1. The needle in the figure appears to be at an absorbance of 0.234. We say that this number has three significant figures because the numbers 2 and 3 are completely certain and the number 4 is an estimate. The value might be read 0.233 or 0.235 by other people. The percent transmittance is near 58.3. Because the transmittance scale is smaller than the absorbance scale at this point, there is more uncertainty in the last digit of transmittance. A reasonable estimate of uncertainty might be 58.3 ± 0.2. There are three significant figures in the number 58.3.

Interpolation: Estimate all readings to the nearest tenth of the distance between scale divisions.

When reading the scale of any apparatus, try to estimate to the nearest tenth of a division. On a 50-mL buret, which is graduated to 0.1 mL, read the level to the nearest 0.01 mL. For a ruler calibrated in millimeters, estimate distances to the nearest 0.1 mm.

There is uncertainty in any *measured* quantity, even if the measuring instrument has a digital readout that does not fluctuate. When a digital pH meter indicates a pH of 3.51, there is uncertainty in the digit 1 (and maybe even in the digit 5). By contrast, integers are exact. To calculate the average height of four people, you would divide the sum of heights (which is a measured quantity with some uncertainty) by the integer 4. There are exactly 4 people, not 4.000 ± 0.002 people!

3-2 Significant Figures in Arithmetic

We now consider how many digits to retain in the answer after you have performed arithmetic operations with your data. Rounding should only be done on the *final answer* (not intermediate results), to avoid accumulating round-off errors.

Addition and Subtraction

If the numbers to be added or subtracted have equal numbers of digits, the answer goes to the *same decimal place* as in any of the individual numbers:

$$\begin{array}{r} 1.362 \times 10^{-4} \\ +\ 3.111 \times 10^{-4} \\ \hline 4.473 \times 10^{-4} \end{array}$$

The number of significant figures in the answer may exceed or be less than that in the original data.

$$\begin{array}{r} 5.345 \\ +\ 6.728 \\ \hline 12.073 \end{array} \qquad \begin{array}{r} 7.26 \times 10^{14} \\ -\ 6.69 \times 10^{14} \\ \hline 0.57 \times 10^{14} \end{array}$$

If the numbers being added do not have the same number of significant figures, we are limited by the least certain one. For example, the molecular mass of KrF_2 is known only to the third decimal place, because we know the atomic mass of Kr to only three decimal places:

The periodic table inside the cover of this book gives uncertainty in the last digit of atomic mass:

F: 18.998 403 2 ± 0.000 000 5

Kr: 83.798 ± 0.002

$$\begin{array}{rl} 18.998\,403\,2 & \text{(F)} \\ +\ 18.998\,403\,2 & \text{(F)} \\ +\ 83.798 & \text{(Kr)} \\ \hline 121.794\,\underbrace{806\,4}_{\text{Not significant}} & \end{array}$$

The number 121.794 806 4 should be rounded to 121.795 as the final answer.

When rounding off, look at *all* the digits *beyond* the last place desired. In the preceding example, the digits 806 4 lie beyond the last significant decimal place. Because this number is more than halfway to the next higher digit, we round the 4 up to 5 (that is, we round up to 121.795 instead of down to 121.794). If the insignificant figures were less than halfway, we would round down. For example, 121.794 3 is rounded to 121.794.

Rules for rounding off numbers

In the special case where the number is exactly halfway, round to the nearest *even* digit. Thus, 43.55 is rounded to 43.6, if we can only have three significant figures. If we are retaining only three figures, 1.425×10^{-9} becomes 1.42×10^{-9}. The number $1.425\,01 \times 10^{-9}$ would become 1.43×10^{-9}, because 501 is more than halfway to the next digit. The rationale for rounding to an even digit is to avoid systematically increasing or decreasing results through successive round-off errors. Half the round-offs will be up and half down.

In the addition or subtraction of numbers expressed in scientific notation, all numbers should first be expressed with the same exponent:

Addition and subtraction: Express all numbers with the same exponent and align all numbers with respect to the decimal point. Round off the answer according to the number of decimal places in the number with the fewest decimal places.

$$\begin{array}{r} 1.632 \times 10^5 \\ +\ 4.107 \times 10^3 \\ +\ 0.984 \times 10^6 \\ \hline \end{array} \quad \rightarrow \quad \begin{array}{rl} 1.632 & \times 10^5 \\ +\ 0.041\,07 & \times 10^5 \\ +\ 9.84 & \times 10^5 \\ \hline 11.51 & \times 10^5 \end{array}$$

The sum $11.513\,07 \times 10^5$ is rounded to 11.51×10^5 because the number 9.84×10^5 limits us to two decimal places when all numbers are expressed as multiples of 10^5.

Multiplication and Division

In multiplication and division, we are normally limited to the number of digits contained in the number with the fewest significant figures:

$$\begin{array}{r} 3.26 \times 10^{-5} \\ \times\ 1.78 \\ \hline 5.80 \times 10^{-5} \end{array} \qquad \begin{array}{rl} 4.317\,9 & \times 10^{12} \\ \times\ 3.6 & \times 10^{-19} \\ \hline 1.6 & \times 10^{-6} \end{array} \qquad \begin{array}{r} 34.60 \\ \div\ 2.462\,87 \\ \hline 14.05 \end{array}$$

The power of 10 has no influence on the number of figures that should be retained. The section on the real rule for significant figures on page 59 explains why it is reasonable to keep an extra digit when the first digit of the answer is 1. The middle product above could be expressed as 1.55×10^{-6} instead of 1.6×10^{-6} to avoid throwing away some of the precision of the factor 3.6 in the multiplication.

Logarithms and Antilogarithms

If $n = 10^a$, then we say that a is the base 10 **logarithm** of n:

Logarithm of n: $\quad n = 10^a \quad$ means that $\quad \log n = a \qquad$ **(3-1)**

For example, 2 is the logarithm of 100 because $100 = 10^2$. The logarithm of 0.001 is -3 because $0.001 = 10^{-3}$. To find the logarithm of a number with your calculator, enter the number and press the *log* function.

$$10^{-3} = \frac{1}{10^3} = \frac{1}{1\,000} = 0.001$$

In Equation 3-1, the number n is said to be the **antilogarithm** of a. That is, the antilogarithm of 2 is 100 because $10^2 = 100$, and the antilogarithm of -3 is 0.001 because $10^{-3} = 0.001$. Your calculator has either a 10^x key or an *antilog* key. To find the antilogarithm of a number, enter it in your calculator and press 10^x (or *antilog*).

A logarithm is composed of a **characteristic** and a **mantissa.** The characteristic is the integer part and the mantissa is the decimal part:

$$\log 339 = \underbrace{2}_{\substack{\text{Characteristic}\\ =2}}.\underbrace{530}_{\substack{\text{Mantissa}\\ =0.530}} \qquad \log 3.39 \times 10^{-5} = \underbrace{-4}_{\substack{\text{Characteristic}\\ =-4}}.\underbrace{470}_{\substack{\text{Mantissa}\\ =0.470}}$$

Number of digits in ***mantissa*** of log x = number of significant figures in x:

$$\log(\underbrace{5.403}_{4\text{ digits}} \times 10^{-8}) = -7.\underbrace{267\,4}_{4\text{ digits}}$$

The number 339 can be written 3.39×10^2. *The number of digits in the mantissa of log 339 should equal the number of significant figures in 339.* The logarithm of 339 is properly expressed as 2.530. The *characteristic*, 2, corresponds to the exponent in 3.39×10^2.

To see that the third decimal place is the last significant place, consider the following results:

$$10^{2.531} = 340\,(339.6)$$
$$10^{2.530} = 339\,(338.8)$$
$$10^{2.529} = 338\,(338.1)$$

The numbers in parentheses are the results prior to rounding to three figures. Changing the exponent in the third decimal place changes the answer in the third place of 339.

In the conversion of a logarithm into its antilogarithm, *the number of significant figures in the antilogarithm should equal the number of digits in the mantissa*. Thus,

Number of digits in antilog x ($= 10^x$) = number of significant figures in ***mantissa*** of x:

$$10^{\underbrace{6.142}_{3\text{ digits}}} = \underbrace{1.39}_{3\text{ digits}} \times 10^6$$

$$\text{antilog}\,(-3.\underbrace{42}_{2\text{ digits}}) = 10^{-3.\underbrace{42}_{2\text{ digits}}} = \underbrace{3.8}_{2\text{ digits}} \times 10^{-4}$$

Here are several examples showing the proper use of significant figures:

$$\log 0.001\,237 = -2.907\,6 \qquad \text{antilog } 4.37 = 2.3 \times 10^4$$
$$\log 1\,237 = 3.092\,4 \qquad 10^{4.37} = 2.3 \times 10^4$$
$$\log 3.2 = 0.51 \qquad 10^{-2.600} = 2.51 \times 10^{-3}$$

Significant Figures and Graphs

When drawing a graph on a computer, consider whether the graph is meant to display qualitative behavior of the data (Figure 3-2) or precise values that must be read with several significant figures. If someone will use the graph (such as Figure 3-3) to read points, it should at least have tick marks on both sides of the horizontal and vertical scales. Better still is a fine grid superimposed on the graph.

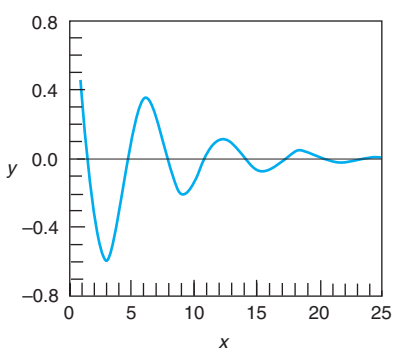


FIGURE 3-2 Example of a graph intended to show the qualitative behavior of the function $y = e^{-x/6} \cos x$. You are not expected to be able to read coordinates accurately on this graph.

Problem 3-8 shows you how to control gridlines in an Excel graph.

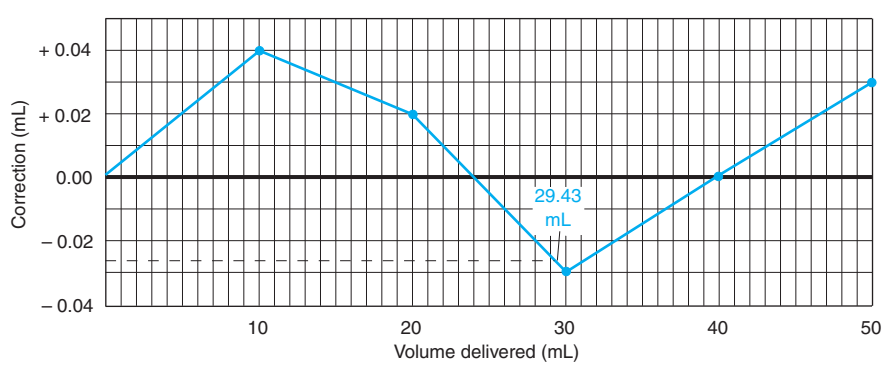


FIGURE 3-3 Calibration curve for a 50-mL buret. The volume delivered can be read to the nearest 0.1 mL. If your buret reading is 29.43 mL, you can find the correction factor accurately enough by locating 29.4 mL on the graph. The correction factor on the ordinate (y-axis) for 29.4 mL on the abscissa (x-axis) is -0.03 mL (to the nearest 0.01 mL).

3-3 Types of Error

Every measurement has some uncertainty, which is called *experimental error*. Conclusions can be expressed with a high or a low degree of confidence, but never with complete certainty. Experimental error is classified as either *systematic* or *random*.

Systematic Error

Systematic error, also called **determinate error,** arises from a flaw in equipment or the design of an experiment. If you conduct the experiment again in exactly the same manner, the error is reproducible. In principle, systematic error can be discovered and corrected, although this may not be easy.

For example, a pH meter that has been standardized incorrectly produces a systematic error. Suppose you think that the pH of the buffer used to standardize the meter is 7.00, but it is really 7.08. Then all your pH readings will be 0.08 pH unit too low. When you read a pH of 5.60, the actual pH of the sample is 5.68. This systematic error could be discovered by using a second buffer of known pH to test the meter.

Systematic error is a consistent error that can be detected and corrected. Box 3-1 provides an example from environmental analysis.

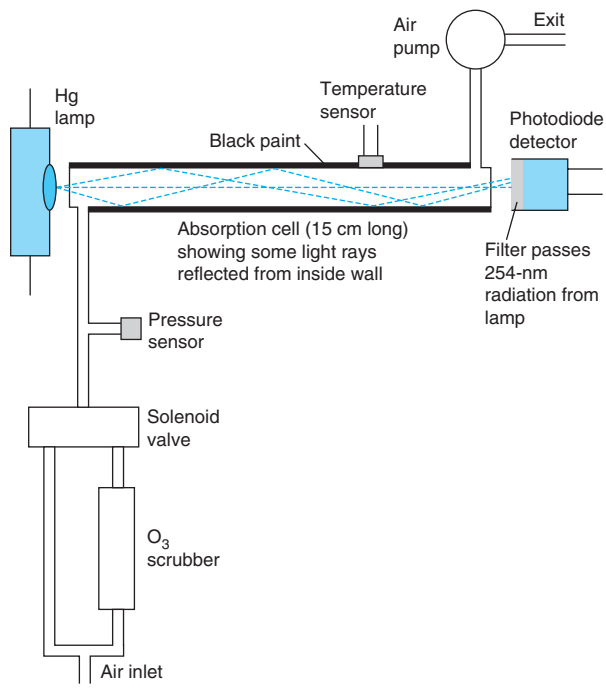
BOX 3-1 Case Study in Ethics: Systematic Error in Ozone Measurement

Ozone (O_3) is an oxidizing, corrosive gas that harms your lungs and all forms of life. It is formed near the surface of the Earth by the action of sunlight on air pollutants largely derived from automobile exhaust. The U.S. Environmental Protection Agency sets an 8-h average O_3 limit of 80 ppb (80 nL/L by volume) in air. Regions that fail to meet this standard can be required to reduce sources of pollution that contribute to O_3 formation. Error in ozone measurement can have serious consequences for the health and economy of a region.

To monitor compliance, a variety of instruments are used. The instrument in the diagram pumps air through a cell with a pathlength of 15 cm. Ultraviolet radiation from a mercury lamp is partially absorbed by O_3. The more O_3 in the air, the less radiation reaches the detector. From the measured absorbance, the instrument computes O_3 concentration. In routine use, the operator only adjusts the zero control, which sets the meter to read zero when O_3-free air is drawn through the instrument. Periodically, the instrument is recalibrated with a source of known O_3.

A study of commercial O_3 monitors found that controlled changes in humidity led to *systematic errors in the apparent O_3 concentration of tens to hundreds of ppb* (errors several times greater than the O_3 being measured). Increasing humidity produced systematic *positive* errors in some types of instruments and systematic *negative* errors in other instruments.

Water does not absorb the ultraviolet wavelength measured by the detector, so humidity is not interfering by absorbing radiation. A perceptive analysis of the problem led to the hypothesis that *adsorption* of moisture on the inside surface of the measurement cell changed the reflectivity of that surface. In one type of instrument, water adsorbed inside a quartz cell reflects less light than dry quartz and thus increases the amount of light lost by absorption in black paint on the outside of the cell. This instrument produces a false, *high* O_3 reading. Another instrument has a highly reflective aluminum cell coated on the inside with polyvinylidene fluoride. Adsorption of moisture on polyvinylidene fluoride reduces total internal reflection within the coating and increases the radiant energy reaching the detector, giving a false, *low* O_3 reading. These effects need not be large. A 0.03% change in light intensity reaching the detector corresponds to an O_3 change of 100 ppb. The solution to the problem was to install a length of water-permeable tubing just before the absorption cell to equalize the humidity in air being measured and that used to zero the instrument.



Optical path of 2B Technologies Model 202 Ozone Monitor. The solenoid alternately admits ambient air or air that has been scrubbed free of O_3. Absorbance of ultraviolet radiation from the Hg lamp is proportional to O_3 concentration. [Diagram from www.twobtech.com/manuals/model_202_new.pdf. Story from K. L. Wilson and J. W. Birks, "Mechanism and Elimination of a Water Vapor Interference in the Measurement of Ozone by UV Absorbance," *Environ. Sci. Technol.* **2006**, *40*, 6361.]

Prior to understanding the effect of humidity on O_3 measurement, it was known that O_3 monitors often exhibit erratic behavior on hot, humid days. It was conjectured by some people that half of the regions deemed to be out of compliance with the O_3 standard might actually have been under the legal limit. This error could force expensive remediation measures when none were required. Conversely, there were rumors that some unscrupulous operators of O_3 monitors were aware that zeroing their instrument at night when the humidity is higher produced lower O_3 readings the next day, thereby reducing the number of days when a region is deemed out of compliance.

Ways to detect systematic error:

1. Analyze a known sample, such as a certified reference material. Your method should reproduce the known answer. (See Box 14-1 for an example.)

2. Analyze blank samples containing no analyte being sought. If you observe a nonzero result, your method responds to more than you intend. Section 5-1 discusses different kinds of blanks.

3. Use different analytical methods to measure the same quantity. If results do not agree, there is error in one (or more) of the methods.

4. *Round robin* experiment: Different people in several laboratories analyze identical samples by the same or different methods. Disagreement beyond the estimated random error is systematic error.

Another systematic error arises from an uncalibrated buret. The manufacturer's tolerance for a Class A 50-mL buret is ±0.05 mL. When you think you have delivered 29.43 mL, the real volume could be anywhere from 29.38 to 29.48 mL and still be within tolerance. One way to correct for an error of this type is to construct a calibration curve, such as that in Figure 3-3, by the procedure on page 49. To do this, deliver distilled water from the buret into a flask and weigh it. Determine the volume of water from its mass by using Table 2-7. Figure 3-3 tells us to apply a correction factor of −0.03 mL to the measured value of 29.43 mL. The actual volume delivered is 29.43 − 0.03 = 29.40 mL.

A key feature of systematic error is that it is reproducible. For the buret just discussed, the error is always −0.03 mL when the buret reading is 29.43 mL. Systematic error may always be positive in some regions and always negative in others. With care and cleverness, you can detect and correct a systematic error.

Random Error

Random error cannot be eliminated, but it might be reduced by a better experiment.

Random error, also called **indeterminate error,** arises from uncontrolled (and maybe uncontrollable) variables in the measurement. Random error has an equal chance of being positive or negative. It is always present and cannot be corrected. There is random error associated with reading a scale. Different people reading the scale in Figure 3-1 report a range of values representing their subjective interpolation between the markings. One person reading the same instrument several times might report several different readings. Another random error results from electrical noise in an instrument. Positive and negative fluctuations occur with approximately equal frequency and cannot be completely eliminated.

Precision and Accuracy

Precision: reproducibility

Accuracy: nearness to the "truth"

Precision describes the reproducibility of a result. If you measure a quantity several times and the values agree closely with one another, your measurement is precise. If the values vary widely, your measurement is not precise. **Accuracy** describes how close a measured value is to the "true" value. If a known standard is available, accuracy is how close your value is to the known value.

The U.S. National Institute of Standards and Technology and national standards laboratories in other countries sell **certified reference materials** (called *Standard Reference Materials* in the U.S.), such as clinical and environmental standards and engineering materials that you can use to test the accuracy of your analytical procedures.[1] The quantity of analyte in a reference material is certified—with painstaking care—to lie in a stated range.

A measurement might be reproducible, but wrong. If you made a mistake preparing a solution for a titration, you might do a series of reproducible titrations but report an incorrect result because the concentration of the titrating solution was not what you intended. In this case, precision is good but accuracy is poor. Conversely, it is possible to make poorly reproducible measurements clustered around the correct value. For this case, precision is poor but accuracy is good. An ideal procedure is both precise and accurate.

Accuracy is defined as nearness to the "true" value. *True* is in quotes because somebody must *measure* the "true" value, and there is error associated with *every* measurement. The "true" value is best obtained by an experienced person using a well-tested procedure. It is desirable to test the result by using different procedures, because systematic error could lead to poor agreement between methods. Good agreement among several methods affords us confidence, but never proof, that results are accurate.

Absolute and Relative Uncertainty

An uncertainty of ±0.02 mL means that, when the reading is 13.33 mL, the true value could be anywhere in the range 13.31 to 13.35 mL.

Absolute uncertainty expresses the margin of uncertainty associated with a measurement. If the estimated uncertainty in reading a calibrated buret is ±0.02 mL, we say that ±0.02 mL is the absolute uncertainty associated with the reading.

Relative uncertainty compares the size of the absolute uncertainty with the size of its associated measurement. The relative uncertainty of a buret reading of 12.35 ± 0.02 mL is a dimensionless quotient:

Relative uncertainty:

$$\text{Relative uncertainty} = \frac{\text{absolute uncertainty}}{\text{magnitude of measurement}} \tag{3-2}$$

$$= \frac{0.02\ \text{mL}}{12.35\ \text{mL}} = 0.002$$

The percent relative uncertainty is simply

Percent relative uncertainty:

$$\text{Percent relative uncertainty} = 100 \times \text{relative uncertainty} \tag{3-3}$$

$$= 100 \times 0.002 = 0.2\%$$

If the absolute uncertainty in reading a buret is constant at ±0.02 mL, the percent relative uncertainty is 0.2% for a volume of 10 mL and 0.1% for a volume of 20 mL.

If you use a 50-mL buret, design your titration to require 20–40 mL of reagent to produce a small relative uncertainty of 0.1–0.05%.

In a gravimetric analysis, plan to have enough precipitate for a low relative uncertainty. If weighing precision is ±0.3 mg, a 100-mg precipitate has a relative weighing error of 0.3% and a 300-mg precipitate has an uncertainty of 0.1%.

3-4 Propagation of Uncertainty from Random Error[2]

We can usually estimate or measure the random error associated with a measurement, such as the length of an object or the temperature of a solution. Uncertainty might be based on how well we can read an instrument or on our experience with a particular method. If possible, uncertainty will be expressed as the *standard deviation of the mean* or a *confidence interval*, which we discuss in Chapter 4. This section applies only to random error. We assume that systematic error has been detected and corrected.

For most experiments, we need to perform arithmetic operations on several numbers, each of which has a random error. The most likely uncertainty in the result is not the sum of individual errors, because some of them are likely to be positive and some negative. We expect some cancellation of errors.

Most propagation of uncertainty computations that you will encounter deal with random error, not systematic error. Our goal is always to eliminate systematic error.

Addition and Subtraction

Suppose you wish to perform the following arithmetic, in which the experimental uncertainties, designated e_1, e_2, and e_3, are given in parentheses.

$$\begin{array}{rl} 1.76\ (\pm 0.03) & \leftarrow e_1 \\ +\ 1.89\ (\pm 0.02) & \leftarrow e_2 \\ -\ 0.59\ (\pm 0.02) & \leftarrow e_3 \\ \hline 3.06\ (\pm e_4) & \end{array} \tag{3-4}$$

The arithmetic answer is 3.06. But what is the uncertainty associated with this result?

For addition and subtraction, the uncertainty in the answer is obtained from the *absolute uncertainties* of the individual terms as follows:

Uncertainty in addition and subtraction:

$$e_4 = \sqrt{e_1^2 + e_2^2 + e_3^2} \tag{3-5}$$

For addition and subtraction, use *absolute* uncertainty.

For the sum in Equation 3-4, we can write

$$e_4 = \sqrt{(0.03)^2 + (0.02)^2 + (0.02)^2} = 0.04_1$$

The absolute uncertainty e_4 is ±0.04, and we express the answer as 3.06 ± 0.04. Although there is only one significant figure in the uncertainty, we wrote it initially as 0.04_1, with the first insignificant figure subscripted. We retain one or more insignificant figures to avoid introducing round-off errors into later calculations through the number 0.04_1. The insignificant figure was subscripted to remind us where the last significant figure should be when we conclude the calculations.

To find the percent relative uncertainty in the sum of Equation 3-4, we write

$$\text{Percent relative uncertainty} = \frac{0.04_1}{3.06} \times 100 = 1._3\%$$

The uncertainty, 0.04_1, is $1._3\%$ of the result, 3.06. The subscript 3 in $1._3\%$ is not significant. It is sensible to drop the insignificant figures now and express the final result as

$$\begin{array}{ll} 3.06\ (\pm 0.04) & \text{(absolute uncertainty)} \\ 3.06\ (\pm 1\%) & \text{(relative uncertainty)} \end{array}$$

For addition and subtraction, use absolute uncertainty. Relative uncertainty can be found at the end of the calculation.

EXAMPLE **Uncertainty in a Buret Reading**

The volume delivered by a buret is the difference between final and initial readings. If the uncertainty in each reading is ±0.02 mL, what is the uncertainty in the volume delivered?

Solution Suppose that the initial reading is 0.05 (±0.02) mL and the final reading is 17.88 (±0.02) mL. The volume delivered is the difference:

$$\begin{array}{r} 17.88\ (\pm 0.02) \\ -\ 0.05\ (\pm 0.02) \\ \hline 17.83\ (\pm e) \end{array} \qquad e = \sqrt{0.02^2 + 0.02^2} = 0.02_8 \approx 0.03$$

Regardless of the initial and final readings, if the uncertainty in each one is ±0.02 mL, the uncertainty in volume delivered is ±0.03 mL.

Test Yourself What would be the uncertainty in volume delivered if the uncertainty in each reading were 0.03 mL? (***Answer:*** ±0.04 mL)

Multiplication and Division

For multiplication and division, first convert all uncertainties into percent relative uncertainties. Then calculate the error of the product or quotient as follows:

For multiplication and division, use percent relative uncertainty.

Uncertainty in multiplication and division:

$$\%e_4 = \sqrt{(\%e_1)^2 + (\%e_2)^2 + (\%e_3)^2} \qquad \textbf{(3-6)}$$

For example, consider the following operations:

$$\frac{1.76\ (\pm 0.03) \times 1.89\ (\pm 0.02)}{0.59\ (\pm 0.02)} = 5.64\ \pm\ e_4$$

First convert absolute uncertainties into percent relative uncertainties.

$$\frac{1.76\ (\pm 1._7\%) \times 1.89\ (\pm 1._1\%)}{0.59\ (\pm 3._4\%)} = 5.64\ \pm\ e_4$$

Advice Retain one or more extra insignificant figures until you have finished your entire calculation. Then round to the correct number of digits. When storing intermediate results in a calculator, keep all digits without rounding.

Then find the percent relative uncertainty of the answer by using Equation 3-6.

$$\%e_4 = \sqrt{(1._7)^2 + (1._1)^2 + (3._4)^2} = 4._0\%$$

The answer is $5.6_4\ (\pm 4._0\%)$.

To convert relative uncertainty into absolute uncertainty, find $4._0\%$ of the answer.

$$4._0\% \times 5.6_4 = 0.04_0 \times 5.6_4 = 0.2_3$$

The answer is $5.6_4\ (\pm 0.2_3)$. Finally, drop the insignificant digits.

For multiplication and division, use percent relative uncertainty. Absolute uncertainty can be found at the end of the calculation.

$$\begin{array}{ll} 5.6\ (\pm 0.2) & \text{(absolute uncertainty)} \\ 5.6\ (\pm 4\%) & \text{(relative uncertainty)} \end{array}$$

The denominator of the original problem, 0.59, limits the answer to two digits.

Mixed Operations

Now consider a computation containing subtraction and division:

$$\frac{[1.76\ (\pm 0.03) - 0.59\ (\pm 0.02)]}{1.89\ (\pm 0.02)} = 0.619_0\ \pm\ ?$$

First work out the difference in the numerator, using absolute uncertainties. Thus,

$$1.76\ (\pm 0.03) - 0.59\ (\pm 0.02) = 1.17\ (\pm 0.03_6)$$

because $\sqrt{(0.03)^2 + (0.02)^2} = 0.03_6$.

Then convert into percent relative uncertainties. Thus,

$$\frac{1.17\ (\pm 0.03_6)}{1.89\ (\pm 0.02)} = \frac{1.17\ (\pm 3._1\%)}{1.89\ (\pm 1._1\%)} = 0.619_0\ (\pm 3._3\%)$$

because $\sqrt{(3._1\%)^2 + (1._1\%)^2} = 3._3\%$.

The percent relative uncertainty is $3._3\%$, so the absolute uncertainty is $0.03_3 \times 0.619_0 = 0.02_0$. The final answer can be written as

$$0.619\ (\pm 0.02_0) \qquad \text{(absolute uncertainty)}$$
$$0.619\ (\pm 3._3\%) \qquad \text{(relative uncertainty)}$$

Because the uncertainty begins in the 0.01 decimal place, it is reasonable to round the result to the 0.01 decimal place:

The result of a calculation ought to be written in a manner consistent with its uncertainty.

$$0.62\ (\pm 0.02) \qquad \text{(absolute uncertainty)}$$
$$0.62\ (\pm 3\%) \qquad \text{(relative uncertainty)}$$

The *Real* Rule for Significant Figures

The first digit of the absolute uncertainty is the last significant digit in the answer. For example, in the quotient

The real rule: The first uncertain figure is the last significant figure.

$$\frac{0.002\,364\ (\pm 0.000\,003)}{0.025\,00\ (\pm 0.000\,05)} = 0.094\,6\ (\pm 0.000\,2)$$

the uncertainty ($\pm 0.000\,2$) occurs in the fourth decimal place. Therefore, the answer 0.094 6 is properly expressed with *three* significant figures, even though the original data have four figures. The first uncertain figure of the answer is the last significant figure. The quotient

$$\frac{0.002\,664\ (\pm 0.000\,003)}{0.025\,00\ (\pm 0.000\,05)} = 0.106\,6\ (\pm 0.000\,2)$$

is expressed with *four* significant figures because the uncertainty occurs in the fourth place. The quotient

$$\frac{0.821\ (\pm 0.002)}{0.803\ (\pm 0.002)} = 1.022\ (\pm 0.004)$$

is expressed with *four* figures even though the dividend and divisor each have *three* figures.

Now you can appreciate why *it is alright to keep one extra digit when the first digit of an answer lies between 1 and 2*. The quotient 82/80 is better written as 1.02 than 1.0. If the uncertainties in 82 and 80 are in the ones place, the uncertainty is of the order of 1%, which is in the second decimal place of 1.02. If I write 1.0, you can surmise that the uncertainty is at least $1.0 \pm 0.1 = \pm 10\%$, which is much larger than the actual uncertainty.

In multiplication and division, keep an extra digit when the answer lies between 1 and 2.

EXAMPLE Significant Figures in Laboratory Work

You prepared a 0.250 M NH_3 solution by diluting 8.45 ($\pm$0.04) mL of 28.0 ($\pm$0.5) wt% NH_3 [density = 0.899 ($\pm$0.003) g/mL] up to 500.0 ($\pm$0.2) mL. Find the uncertainty in 0.250 M. The molecular mass of NH_3, 17.030 5 g/mol, has negligible uncertainty relative to other uncertainties in this problem.

Solution To find the uncertainty in molarity, we need to find the uncertainty in moles delivered to the 500-mL flask. The concentrated reagent contains 0.899 ($\pm$0.003) g of solution per milliliter. Weight percent tells us that the reagent contains 0.280 ($\pm$0.005) g of NH_3 per gram of solution. In our calculations, we retain extra insignificant digits and round off only at the end.

$$\begin{aligned}
\text{Grams of } NH_3 \text{ per mL in concentrated reagent} &= 0.899\ (\pm 0.003)\ \frac{\text{g solution}}{\text{mL}} \times 0.280\ (\pm 0.005)\ \frac{\text{g } NH_3}{\text{g solution}} \\
&= 0.899\ (\pm 0.334\%)\ \frac{\text{g solution}}{\text{mL}} \times 0.280\ (\pm 1.79\%)\ \frac{\text{g } NH_3}{\text{g solution}} \\
&= 0.251\,7\ (\pm 1.82\%)\ \frac{\text{g } NH_3}{\text{mL}}
\end{aligned}$$

Convert absolute uncertainty into percent relative uncertainty for multiplication.

because $\sqrt{(0.334\%)^2 + (1.79\%)^2} = 1.82\%$.

BOX 3-2 Keeling's Exquisitely Precise Measurement of CO_2

Atmospheric CO_2 measurements on Mauna Loa, introduced in Section 0-1, are made several times per hour by infrared absorption (Box 19-3). Accuracy depends on calibration gases consisting of CO_2 in dry N_2 or dry air. Calibration gas is measured at Scripps Institution of Oceanography by extremely careful manometry in which temperature, pressure, and volume of CO_2 in the gas are measured to find the number of moles of gas.

The diagram depicts the principle of the measurement. Calibration gas, passed through Dry Ice traps to freeze out traces of H_2O, goes to a chamber in panel *a* whose volume is $5.013\ 8_2 \pm 0.000\ 5$ L and whose temperature and pressure are measured. Pressure is measured within ± 0.02 mm Hg by the difference in the level of Hg on either side of a U-tube. Mercury height is read with a *cathetometer*, which is a telescope mounted on a precision threaded shaft. The shaft is rotated to move the telescope up or down until the top of the Hg meniscus is centered in the cross hairs. Height is indicated by the number of turns of the shaft.

In panel *a*, CO_2 from the 5-L volume of calibration gas is *quantitatively* (completely) collected by freezing onto the inside wall of the manometer with liquid N_2 (77 K). Gas that does not freeze is pumped out through stopcocks 1 and 2. With CO_2 frozen in the evacuated chamber, N_2 is admitted through stopcock 3 so that Hg rises and seals off port 1.

In panel *b*, CO_2 has warmed to room temperature. Pressure in the Hg reservoir is adjusted to bring the level of Hg exactly to the tip of the glass pointer in the inset. The previously measured volume above the tip of the pointer is $3.793\ 0 \pm 0.000\ 9$ mL. Pressure inside this volume is the difference in height between the Hg columns, labeled ΔP in panel *b*. From pressure, temperature, and volume, moles of CO_2 can be calculated.

The *ideal gas law* does not provide enough accuracy, so the *virial equation* is used:

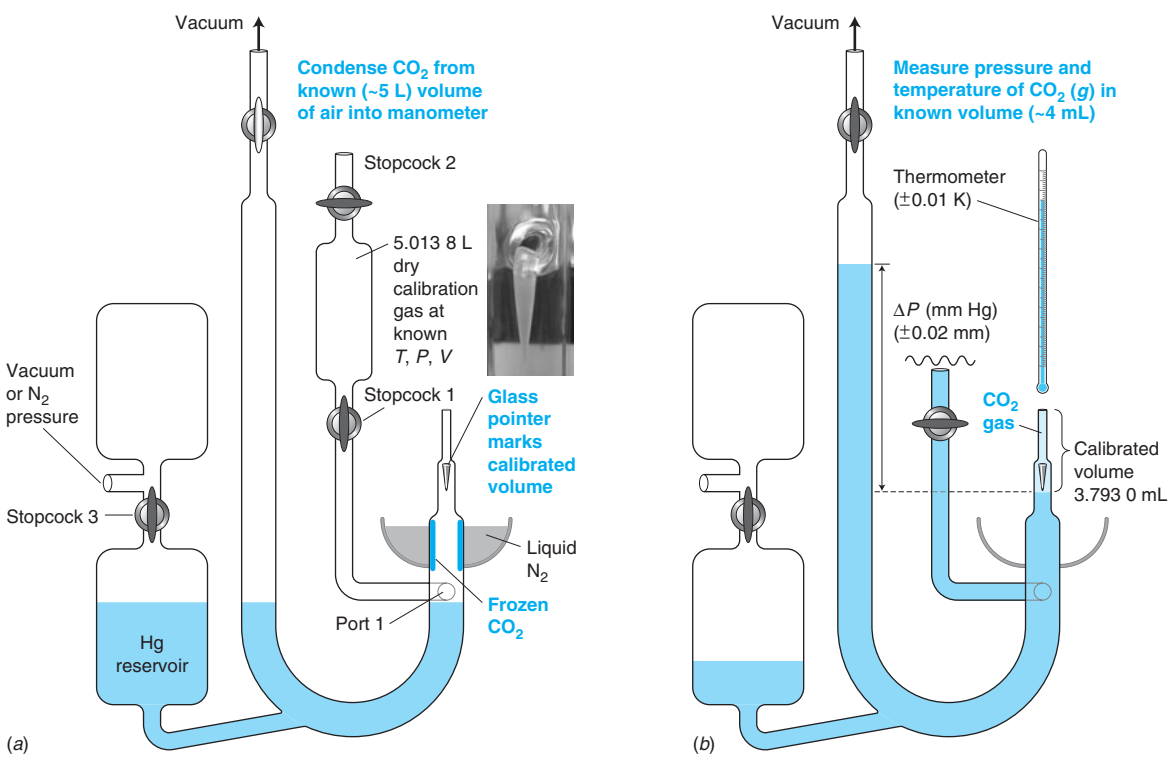
Virial equation of state: $$PV_m = RT\left(1 + \frac{B}{V_m} + \frac{C}{V_m^2} + \ldots\right)$$

where P is pressure, R is the gas constant, T is temperature (K), and V_m is the volume of 1 mol of gas. B is the *second virial coefficient* and C is the *third virial coefficient*. If the coefficients were zero, the virial equation would be identical to the ideal gas law. Virial coefficients are known as a function of temperature. The coefficient B alone provides sufficient accuracy for measuring CO_2 in air.

Air contains 0.3 ppm of N_2O, which condenses with CO_2 and interferes with the measurement. The ratio N_2O/CO_2 in air is measured by gas chromatography and the N_2O is subtracted from the sum of $CO_2 + N_2O$ measured in the manometer.

To measure the $5.013\ 8_2$-L volume in panel *a*, a 4-L flask that can be closed with a vacuum stopcock is weighed empty and weighed again filled with water. Both weights are corrected for buoyancy. From the mass of water and the temperature, the flask's volume is computed. The calibrated 4-L flask is then filled with CO_2 at known pressure and temperature. The CO_2 is quantitatively transferred to the 5-L compartment and pressure and temperature are measured. From the pressure and temperature of this known quantity of gas, the volume of the 5-L compartment is calculated. By a similar procedure, the volume of the 3.793 0-mL compartment is measured by transferring CO_2 from an external 2-mL volume. The volume of the 2-mL vessel is measured by weighing it empty and weighing it filled with mercury. Measurements conducted over many years have a standard deviation of 0.010% for the 5-L volume and 0.025% for the 4-mL volume.

The 0.025% random error in measuring the 4-mL volume limits the precision of measuring CO_2 in air to 0.025%, or about 0.1 ppm for CO_2 levels of 400 ppm. To estimate systematic error, CO_2 in a calibration standard was measured by two different methods at Scripps and, independently, at the National Oceanographic and Atmospheric Administration. The three measurements agreed within 0.2 ppm CO_2.



Next, we find the moles of ammonia contained in 8.45 (±0.04) mL of concentrated reagent. The relative uncertainty in volume is 0.04/8.45 = 0.473%.

$$\text{mol NH}_3 = \frac{0.251\,7\ (\pm 1.82\%)\ \dfrac{\text{g NH}_3}{\text{mL}} \times 8.45\ (\pm 0.473\%)\ \text{mL}}{17.030\,5\ (\pm 0\%)\ \dfrac{\text{g NH}_3}{\text{mol}}}$$

$$= 0.124\,9\ (\pm 1.88\%)\ \text{mol}$$

because $\sqrt{(1.82\%)^2 + (0.473\%)^2 + (0\%)^2} = 1.88\%$.

This much ammonia was diluted to 0.500 0 (±0.000 2) L. The relative uncertainty in the final volume is 0.000 2/0.500 0 = 0.04%. The molarity is

$$\frac{\text{mol NH}_3}{\text{L}} = \frac{0.124\,9\ (\pm 1.88\%)\ \text{mol}}{0.500\,0\ (\pm 0.04\%)\ \text{L}}$$

$$= 0.249\,8\ (\pm 1.88\%)\ \text{M}$$

because $\sqrt{(1.88\%)^2 + (0.04\%)^2} = 1.88\%$. The absolute uncertainty is 1.88% of 0.249 8 M = 0.004 7 M. The uncertainty in molarity is in the third decimal place, so our final, rounded answer is

$$[\text{NH}_3] = 0.250\ (\pm 0.005)\ \text{M}$$

Test Yourself Find the uncertainty in $[NH_3]$ if the starting reagent is 28.0 (±0.7) wt% NH_3. (***Answer:*** 0.250 (±0.006) M)

Box 3-2 describes measurements of CO_2 standards by Charles David Keeling for atmospheric CO_2 measurements. You should appreciate how precisely pressure, volume, and temperature had to be measured for an overall precision of 1 part in 4 000 (0.025%).

Exponents and Logarithms

For the function $y = x^a$, the percent relative uncertainty in y ($\%e_y$) is equal to a times the percent relative uncertainty in x ($\%e_x$):

To calculate a power or root on your calculator, use the y^x button. For example, to find a cube root ($y^{1/3}$), raise y to the 0.333 333 333 . . . power with the y^x button. In Excel, y^x is y^x. The cube root is y^(1/3).

Uncertainty for powers and roots:

$$y = x^a \quad \Rightarrow \quad \%e_y = a(\%e_x) \tag{3-7}$$

For example, if $y = \sqrt{x} = x^{1/2}$, a 2% uncertainty in x will yield a $\left(\frac{1}{2}\right)(2\%) = 1\%$ uncertainty in y. If $y = x^2$, a 3% uncertainty in x leads to a (2)(3%) = 6% uncertainty in y.

If y is the base 10 logarithm of x, then the absolute uncertainty in y (e_y) is proportional to the relative uncertainty in x, which is e_x/x:

Uncertainty for logarithm:

$$y = \log x \quad \Rightarrow \quad e_y = \frac{1}{\ln 10}\frac{e_x}{x} \approx 0.434\,29\,\frac{e_x}{x} \tag{3-8}$$

You should not work with percent relative uncertainty [100 × (e_x/x)] in calculations with logs and antilogs, because one side of Equation 3-8 has relative uncertainty and the other has absolute uncertainty.

Use relative uncertainty (e_x/x), not percent relative uncertainty [100 × (e_x/x)], in calculations involving log x, ln x, 10^x, and e^x.

The **natural logarithm** (ln) of x is the number y, whose value is such that $x = e^y$, where e (= 2.718 28 . . .) is called the base of the natural logarithm. The absolute uncertainty in y is equal to the relative uncertainty in x.

In Excel, the base 10 logarithm is log(x). The natural logarithm is ln(x). The expression 10^x is 10^x and the expression e^x is exp(x).

Uncertainty for natural logarithm:

$$y = \ln x \quad \Rightarrow \quad e_y = \frac{e_x}{x} \tag{3-9}$$

Now consider y = antilog x, which is the same as saying $y = 10^x$. In this case, the relative uncertainty in y is proportional to the absolute uncertainty in x.

Uncertainty for 10^x:

$$y = 10^x \quad \Rightarrow \quad \frac{e_y}{y} = (\ln 10)e_x \approx 2.302\,6\,e_x \tag{3-10}$$

If $y = e^x$, the relative uncertainty in y equals the absolute uncertainty in x.

Uncertainty for e^x:

$$y = e^x \quad \Rightarrow \quad \frac{e_y}{y} = e_x \tag{3-11}$$

Table 3-1 summarizes rules for propagation of uncertainty. You need not memorize the rules for exponents, logs, and antilogs, but you should be able to use them.

Appendix C gives a general rule for propagation of random uncertainty for any function.

TABLE 3-1 Summary of rules for propagation of uncertainty

Function	Uncertainty	Function[a]	Uncertainty[b]
$y = x_1 + x_2$	$e_y = \sqrt{e_{x_1}^2 + e_{x_2}^2}$	$y = x^a$	$\%e_y = a\%e_x$
$y = x_1 - x_2$	$e_y = \sqrt{e_{x_1}^2 + e_{x_2}^2}$	$y = \log x$	$e_y = \frac{1}{\ln 10}\frac{e_x}{x} \approx 0.434\,29\frac{e_x}{x}$
$y = x_1 \cdot x_2$	$\%e_y = \sqrt{\%e_{x_1}^2 + \%e_{x_2}^2}$	$y = \ln x$	$e_y = \frac{e_x}{x}$
$y = \frac{x_1}{x_2}$	$\%e_y = \sqrt{\%e_{x_1}^2 + \%e_{x_2}^2}$	$y = 10^x$	$\frac{e_y}{y} = (\ln 10)e_x \approx 2.302\,6\,e_x$
		$y = e^x$	$\frac{e_y}{y} = e_x$

a. x represents a variable and a represents a constant that has no uncertainty.
b. e_x/x is the relative error in x and $\%e_x$ is $100 \times e_x/x$.

EXAMPLE Uncertainty in H^+ Concentration

Consider the function $pH = -\log[H^+]$, where $[H^+]$ is the molarity of H^+. For $pH = 5.21 \pm 0.03$, find $[H^+]$ and its uncertainty.

$$-\log[H^+] = pH$$
$$\log[H^+] = -pH$$
$$10^{\log[H^+]} = 10^{-pH}$$
$$[H^+] = 10^{-pH}$$

Solution First solve the equation $pH = -\log[H^+]$ for $[H^+]$: Whenever $a = b$, then $10^a = 10^b$. If $pH = -\log[H^+]$, then $\log[H^+] = -pH$ and $10^{\log[H^+]} = 10^{-pH}$. But $10^{\log[H^+]} = [H^+]$. We therefore need to find the uncertainty in the equation

$$[H^+] = 10^{-pH} = 10^{-(5.21 \pm 0.03)}$$

In Table 3-1, the relevant function is $y = 10^x$, in which $y = [H^+]$ and $x = -(5.21 \pm 0.03)$. For $y = 10^x$, the table tells us that $e_y/y = 2.302\,6\,e_x$.

$$\frac{e_y}{y} = 2.302\,6\,e_x = (2.302\,6)(0.03) = 0.069\,1 \qquad (3\text{-}12)$$

The relative uncertainty in y ($= e_y/y$) is 0.069 1. Inserting the value $y = 10^{-5.21} = 6.17 \times 10^{-6}$ into Equation 3-12 gives the answer:

$$\frac{e_y}{y} = \frac{e_y}{6.17 \times 10^{-6}} = 0.069\,1 \quad \Rightarrow \quad e_y = 4.26 \times 10^{-7}$$

The concentration of H^+ is $6.17\,(\pm 0.426) \times 10^{-6} = 6.2\,(\pm 0.4) \times 10^{-6}$ M. An uncertainty of 0.03 in pH gives an uncertainty of 7% in $[H^+]$. Notice that extra digits were retained in the intermediate results and were not rounded off until the final answer.

Test Yourself If uncertainty in pH is doubled to ± 0.06, what is the relative uncertainty in $[H^+]$? (***Answer:*** 14%)

3-5 Propagation of Uncertainty from Systematic Error

Systematic error occurs in some common situations and is treated differently from random error in arithmetic operations. We will look at examples of systematic error in molecular mass and volumetric glassware.[3]

Uncertainty in Atomic Mass: The Rectangular Distribution

The periodic table inside the cover of this book gives the atomic mass of oxygen as $15.999\,4 \pm 0.000\,3$ g/mol. The uncertainty is *not* mainly from random error in measuring the atomic mass. The uncertainty is predominantly from isotopic variation in samples of oxygen from different sources. That is, oxygen from one source could have a mean atomic mass of 15.999 1 and oxygen from another source could have an atomic mass of 15.999 7. The atomic mass of oxygen in a particular lot of reagent has a *systematic* uncertainty. It could be relatively constant at 15.999 7 or 15.999 1, or any value in between, with only a small random variation around the mean value.

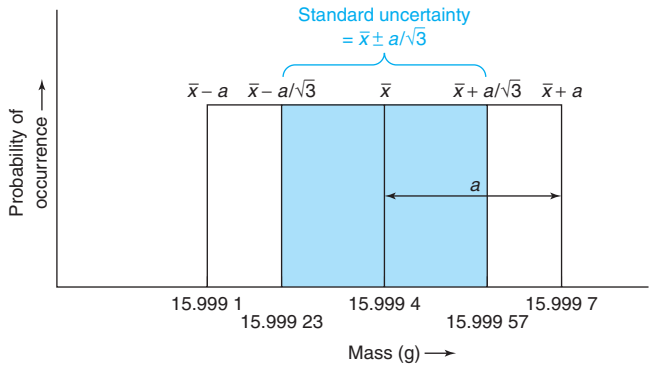


FIGURE 3-4 *Rectangular distribution* for atomic mass. The standard uncertainty interval (standard deviation) shown in color is equal to the uncertainty given in the periodic table divided by $\sqrt{3}$. The atomic mass of oxygen in the periodic table is 15.999 4 ± 0.000 3. The standard uncertainty is $\pm 0.000\,3/\sqrt{3} = \pm 0.000\,17$.

Oxygen atomic mass from different sources approximates a *rectangular distribution* (Figure 3-4). There is approximately equal probability of finding any atomic mass between 15.999 1 and 15.999 7 and negligible probability of finding an atomic mass outside of this range. We call the mean value $\bar{x}$ (= 15.999 4) and the range on either side of the mean a (= 0.000 3). The *standard deviation* (defined in Section 4-1) for this distribution, also called the *standard uncertainty*, is $\pm a/\sqrt{3} = \pm 0.000\,3/\sqrt{3} = \pm 0.000\,17$. The standard deviation is used as a measure of the uncertainty in atomic mass.

Uncertainty in Molecular Mass

What is the uncertainty in molecular mass of O_2? If the mass of each oxygen atom were at the upper limit of the standard uncertainty range in Figure 3-4 (15.999 57), the mass of O_2 is $2 \times 15.999\,57 = 31.999\,14$ g/mol. If the mass of each oxygen atom were at the lower limit of the standard uncertainty range (15.999 23), the mass of O_2 is $2 \times 15.999\,23 = 31.998\,46$ g/mol. The mass of O_2 is somewhere in the range 31.998 8 ± 0.000 34. The uncertainty of the mass of n atoms is $n \times$ (standard uncertainty of one atom) $= 2 \times (\pm 0.000\,17) = \pm 0.000\,34$. The uncertainty is not $\pm\sqrt{0.000\,17^2 + 0.000\,17^2} = \pm 0.000\,24$. *For systematic uncertainty, we add the uncertainties of each term in a sum or difference.*

Now let's find the standard uncertainty in molecular mass of C_2H_4. Uncertainties in the periodic table are 0.000 8 g/mol for carbon and 0.000 07 g/mol for hydrogen. To find the standard uncertainties, divide these uncertainties by $\sqrt{3}$:

$$\text{Atomic mass of C} = 12.010\,7 \pm 0.000\,8/\sqrt{3} = 12.010\,7 \pm 0.000\,46$$

$$\text{Atomic mass of H} = 1.007\,94 \pm 0.000\,07/\sqrt{3} = 1.007\,94 \pm 0.000\,040$$

Uncertainties in the masses of the atoms in C_2H_4 are obtained by multiplying the standard uncertainties by the number of atoms of each type:

$$\begin{aligned} 2\text{C:}\quad & 2(12.010\,7 \pm 0.000\,46) = 24.021\,4 \pm 0.000\,92 \leftarrow 2 \times 0.000\,46 \\ 4\text{H:}\quad & 4(1.007\,94 \pm 0.000\,040) = \underline{\;\;4.031\,76 \pm 0.000\,16} \leftarrow 4 \times 0.000\,040 \\ & \qquad\qquad\qquad\qquad\quad 28.053\,16 \pm ? \end{aligned} \tag{3-13}$$

Propagation of systematic uncertainty:
Uncertainty in mass of n identical atoms
$= n \times$ (standard uncertainty in atomic mass)
$= n \times$ (uncertainty listed in periodic table)$/\sqrt{3}$

For the uncertainty in the sum of the masses of 2C + 4H, we use Equation 3-5, which applies to random error, because the uncertainties in the masses of C and H are independent of each other. One might be positive and one might be negative. So the molecular mass of C_2H_4 is

$$28.053\,16 \pm \sqrt{0.000\,92^2 + 0.000\,16^2}$$

$$28.053\,16 \pm 0.000\,93$$

$$28.053\,2 \pm 0.000\,9 \text{ g/mol}$$

Use the rule for propagation of random uncertainty for the sum of atomic masses of different elements because uncertainties for different elements are independent.

In the last step, we rounded off so that the last significant digit is the first uncertain digit.

Multiple Deliveries from One Pipet: The Triangular Distribution

A 25-mL Class A volumetric pipet is certified by the manufacturer to deliver 25.00 ± 0.03 mL. The volume delivered by a given pipet is reproducible but can be in the range 24.97 to 25.03 mL. However, the pipet manufacturer works hard to make the volume close to 25.00 mL. In such case, we approximate the volumes of a large number of pipets by the *triangular distribution* in Figure 3-5. There is highest probability that the pipet will deliver

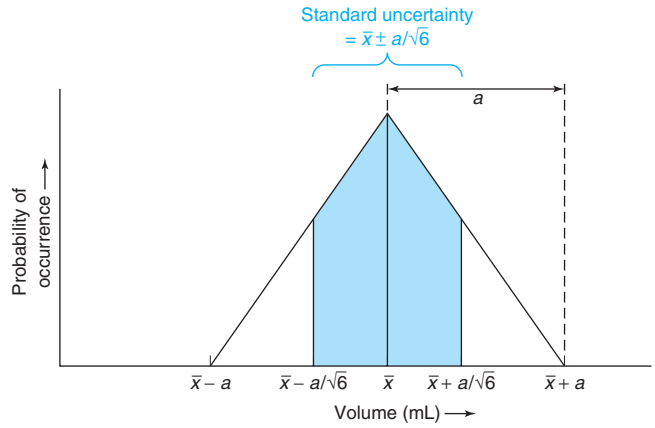


FIGURE 3-5 *Triangular distribution* for volumetric glassware including volumetric flasks and transfer pipets. The standard uncertainty interval (standard deviation) shown in color is $a/\sqrt{6}$.

25.00 mL. The probability falls off approximately in a linear manner as the volume deviates from 25.00 mL. There is negligible probability that a volume outside of 25.00 ± 0.03 mL will be delivered. The *standard uncertainty* (standard deviation) in the triangular distribution is $\pm a/\sqrt{6} = \pm 0.03/\sqrt{6} = \pm 0.012$ mL.

If you use an uncalibrated 25-mL Class A volumetric pipet four times to deliver a total of 100 mL, what is the uncertainty in 100 mL? The uncertainty is a systematic error, so the uncertainty in four pipet volumes is like the uncertainty in the mass of 4 mol of oxygen: The standard uncertainty is $\pm 4 \times 0.012 = \pm 0.048$ mL, not $\pm\sqrt{0.012^2 + 0.012^2 + 0.012^2 + 0.012^2} = \pm 0.024$ mL.

The difference between 25.00 mL and the actual volume delivered by a particular pipet is a *systematic* error. It is always the same, within a small random error. You could calibrate a pipet by weighing the water it delivers, as in Section 2-9. Calibration eliminates systematic error, because we would know that the pipet always delivers, say, 24.991 ± 0.006 mL. The uncertainty (±0.006 mL) is random error.

0.006 mL is the standard deviation (defined in Chapter 4) measured for multiple deliveries of water.

Calibration improves certainty by removing systematic error. If a calibrated pipet delivers a mean volume of 24.991 mL with a standard uncertainty of ±0.006 mL, and you deliver four aliquots, the volume delivered is $4 \times 24.991 = 99.964$ mL and the uncertainty is $\pm\sqrt{0.006^2 + 0.006^2 + 0.006^2 + 0.006^2} = \pm 0.012$ mL. For an uncalibrated pipet, the uncertainty is ±0.048 mL.

$$\text{Calibrated pipet volume} = 99.964 \pm 0.012 \text{ mL}$$
$$\text{Uncalibrated pipet volume} = 100.00 \pm 0.05 \text{ mL}$$

Terms to Understand

absolute uncertainty
accuracy
antilogarithm
certified reference material
characteristic
determinate error
indeterminate error
logarithm
mantissa
natural logarithm
precision
random error
relative uncertainty
significant figure
systematic error

Summary

The number of significant digits in a number is the minimum required to write the number in scientific notation. The first uncertain digit is the last significant figure. In addition and subtraction, the last significant figure is determined by the number with the fewest decimal places (when all exponents are equal). In multiplication and division, the number of figures is usually limited by the factor with the smallest number of digits. The number of figures in the mantissa of the logarithm of a quantity should equal the number of significant figures in the quantity. Random (indeterminate) error affects the precision (reproducibility) of a result, whereas systematic (determinate) error affects the accuracy (nearness to the "true" value). Systematic error can be discovered and eliminated by a clever person, but some random error is always present. We must strive to eliminate systematic errors in all measurements. For random errors, propagation of uncertainty in addition and subtraction requires absolute uncertainties ($e_3 = \sqrt{e_1^2 + e_2^2}$), whereas multiplication and division utilize relative uncertainties ($\%e_3 = \sqrt{\%e_1^2 + \%e_2^2}$). Other rules for propagation of random error are found in Table 3-1. Always retain more digits than necessary during a calculation and round off to the appropriate number of digits at the end. Systematic error in the mass on n atoms of one element is n times the standard uncertainty in mass of that element. For a rectangular distribution of atomic mass, standard uncertainty in atomic mass is the uncertainty listed in the periodic table divided by $\sqrt{3}$. Uncertainty in the mass of a molecule with several elements is computed from the sum of squares of the systematic uncertainty for each element.

Exercises

3-A. Write each answer with a reasonable number of figures. Find the absolute and percent relative uncertainty for each answer.

(a) $[12.41\ (\pm 0.09) \div 4.16\ (\pm 0.01)] \times 7.068\ 2\ (\pm 0.000\ 4) = ?$

(b) $[3.26\ (\pm 0.10) \times 8.47\ (\pm 0.05)] - 0.18\ (\pm 0.06) = ?$

(c) $6.843\ (\pm 0.008) \times 10^4 \div [2.09\ (\pm 0.04) - 1.63\ (\pm 0.01)] = ?$

(d) $\sqrt{3.24 \pm 0.08} = ?$

(e) $(3.24 \pm 0.08)^4 = ?$

(f) $\log (3.24 \pm 0.08) = ?$

(g) $10^{3.24 \pm 0.08} = ?$

3-B. (a) How many milliliters of 53.4 (±0.4) wt% NaOH with a density of 1.52 (±0.01) g/mL will you need to prepare 2.000 L of 0.169 M NaOH?

(b) If the uncertainty in delivering NaOH is ±0.01 mL, calculate the absolute uncertainty in the molarity (0.169 M). Assume there is negligible uncertainty in the formula mass of NaOH and in the final volume (2.000 L).

3-C. We have a 37.0 (±0.5) wt% HCl solution with a density of 1.18 (±0.01) g/mL. To deliver 0.050 0 mol of HCl requires 4.18 mL of solution. If the uncertainty that can be tolerated in 0.050 0 mol is ±2%, how big can the absolute uncertainty in 4.18 mL be? (*Caution:* In this problem, you have to work backward. You would normally compute the uncertainty in mol HCl from the uncertainty in volume:

$$\text{mol HCl} = \frac{\text{mL solution} \times \dfrac{\text{g solution}}{\text{mL solution}} \times \dfrac{\text{g HCl}}{\text{g solution}}}{\dfrac{\text{g HCl}}{\text{mol HCl}}}$$

But, in this case, we know the uncertainty in mol HCl (2%) and we need to find what uncertainty in mL solution leads to that 2% uncertainty. The arithmetic has the form $a = b \times c \times d$, for which $\%e_a^2 = \%e_b^2 + \%e_c^2 + \%e_d^2$. If we know $\%e_a$, $\%e_c$, and $\%e_d$, we can find $\%e_b$ by subtraction: $\%e_b^2 = \%e_a^2 - \%e_c^2 - \%e_d^2$.)

3-D. Compute the molecular mass and its standard uncertainty for NH_3. What is the percent relative uncertainty in molecular mass?

Problems

Significant Figures

3-1. How many significant figures are there in the following numbers?

(a) 1.903 0 **(b)** 0.039 10 **(c)** 1.40×10^4

3-2. Round each number as indicated:

(a) 1.236 7 to 4 significant figures

(b) 1.238 4 to 4 significant figures

(c) 0.135 2 to 3 significant figures

(d) 2.051 to 2 significant figures

(e) 2.005 0 to 3 significant figures

3-3. Round each number to three significant figures:

(a) 0.216 74 **(b)** 0.216 5 **(c)** 0.216 500 3

3-4. *Vernier scale*. The figure below shows a scale found on instruments such as a micrometer caliper used for accurately measuring dimensions of objects. The lower scale slides along the upper scale and is used to interpolate between the markings on the upper scale. In (*a*), the reading (at the left-hand 0 of the lower scale) is between 1.4 and 1.5 on the upper scale. To find the exact reading, observe which mark on the lower scale is aligned with a mark on the upper scale. Because the 6 on the lower scale is aligned with the upper scale, the correct reading is 1.46. Write the correct readings in (*b*) and (*c*) and indicate how many significant figures are in each reading.

3-5. Write each answer with the correct number of digits.

(a) $1.021 + 2.69 = 3.711$

(b) $12.3 - 1.63 = 10.67$

(c) $4.34 \times 9.2 = 39.928$

(d) $0.060\ 2 \div (2.113 \times 10^4) = 2.849\ 03 \times 10^{-6}$

(e) $\log(4.218 \times 10^{12}) = ?$

(f) $\text{antilog}\ (-3.22) = ?$

(g) $10^{2.384} = ?$

3-6. Write the formula mass of **(a)** BaF_2 and **(b)** $C_6H_4O_4$ with a reasonable number of digits. Use the periodic table inside the cover of this book to find atomic masses.

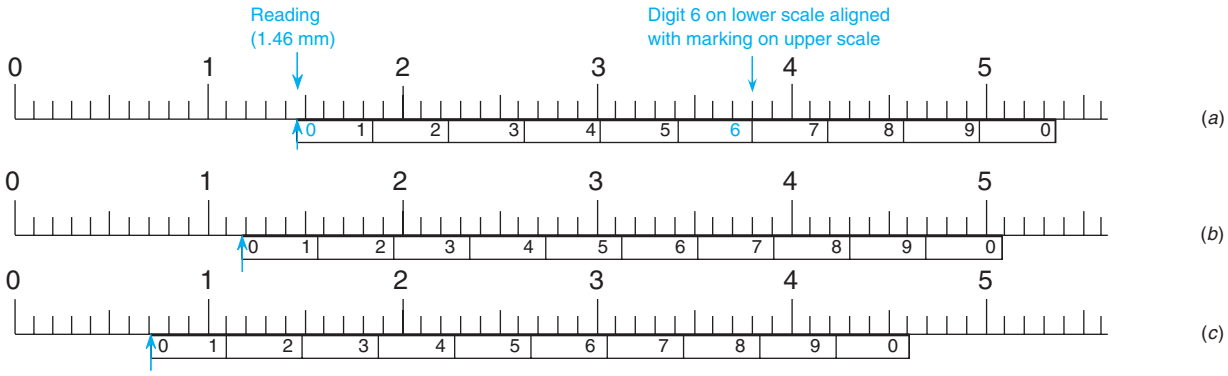


Figure for Problem 3-4.

3-7. Write each answer with the correct number of significant figures.

(a) $1.0 + 2.1 + 3.4 + 5.8 = 12.300\,0$

(b) $106.9 - 31.4 = 75.500\,0$

(c) $107.868 - (2.113 \times 10^2) + (5.623 \times 10^3) = 5\,519.568$

(d) $(26.14/37.62) \times 4.38 = 3.043\,413$

(e) $(26.14/(37.62 \times 10^8)) \times (4.38 \times 10^{-2}) = 3.043\,413 \times 10^{-10}$

(f) $(26.14/3.38) + 4.2 = 11.933\,7$

(g) $\log(3.98 \times 10^4) = 4.599\,9$

(h) $10^{-6.31} = 4.897\,79 \times 10^{-7}$

3-8. *Controlling the appearance of a graph.* Figure 3-3 requires gridlines to read buret corrections. In this exercise, you will format a graph so that it looks like Figure 3-3. Follow the procedure in Section 2-11 to graph the data in the following table. For Excel 2007, insert a Chart of the type Scatter with data points connected by straight lines. Delete the legend and title. With Chart Tools, Layout, Axis Titles, add labels for both axes. Click any number on the abscissa (*x*-axis) and go to Chart Tools, Format. In Format Selection, Axis Options, choose Minimum = 0, Maximum = 50, Major unit = 10, and Minor unit = 1. In Format Selection, Number, choose Number and set Decimal places = 0. In a similar manner, set the ordinate (*y*-axis) to run from −0.04 to +0.05 with a Major unit of 0.02 and a Minor unit of 0.01. To display gridlines, go to Chart Tools, Layout, and Gridlines. For Primary Horizontal Gridlines, select Major & Minor Gridlines. For Primary Vertical Gridlines, select Major & Minor Gridlines. To move *x*-axis labels from the middle of the chart to the bottom, click a number on the *y*-axis (not the *x*-axis) and select Chart Tools, Layout, Format Selection. In Axis Options, choose Horizontal axis crosses Axis value and type in −0.04. Close the Format Axis window and your graph should look like Figure 3-3.

For earlier versions of Excel, select Chart Type XY (Scatter) showing data points connected by straight lines. Double click the *x*-axis and select the Scale tab. Set Minimum = 0, Maximum = 50, Major unit = 10, and Minor unit = 1. Select the Number tab and highlight Number. Set Decimal places = 0. In a similar manner, set the ordinate to run from −0.04 to +0.05 with a Major unit of 0.02 and a Minor unit of 0.01, as in Figure 3-3. The spreadsheet might overrule you. Continue to reset the limits you want and click OK each time until the graph looks the way you intend. To add gridlines, click inside the graph, go to the Chart menu and select Chart Options. Select the Gridlines tab and check both sets of Major gridlines and Minor gridlines and click OK. In Chart Options, select the Legend tab and deselect Show legend. To move *x*-axis numbers to the bottom of the chart, double click the *y*-axis (not the *x*-axis) and select the Scale tab. Set "Value (x) axis crosses at" to −0.04. Click OK and your graph should look like Figure 3-3.

Volume (mL)	Correction (mL)
0.03	0.00
10.04	0.04
20.03	0.02
29.98	−0.03
40.00	0.00
49.97	0.03

Types of Error

3-9. Why do we use quotation marks around the word *true* in the statement that accuracy refers to how close a measured value is to the "true" value?

3-10. Explain the difference between systematic and random error.

3-11. Suppose that in a gravimetric analysis, you forget to dry the filter crucibles before collecting precipitate. After filtering the product, you dry the product and crucible thoroughly before weighing them. Is the apparent mass of product always high or always low? Is the error in mass systematic or random?

3-12. State whether the errors in **(a)–(d)** are random or systematic:

(a) A 25-mL transfer pipet consistently delivers 25.031 ± 0.009 mL.

(b) A 10-mL buret consistently delivers 1.98 ± 0.01 mL when drained from exactly 0 to exactly 2 mL and consistently delivers 2.03 mL ± 0.02 mL when drained from 2 to 4 mL.

(c) A 10-mL buret delivered 1.983 9 g of water when drained from exactly 0.00 to 2.00 mL. The next time I delivered water from the 0.00 to the 2.00 mL mark, the delivered mass was 1.990 0 g.

(d) Four consecutive 20.0-μL injections of a solution into a chromatograph were made and the area of a particular peak was 4 383, 4 410, 4 401, and 4 390 units.

3-13. Cheryl, Cynthia, Carmen, and Chastity shot the targets below at Girl Scout camp. Match each target with the proper description.

(a) accurate and precise

(b) accurate but not precise

(c) precise but not accurate

(d) neither precise nor accurate

3-14. Rewrite the number 3.123 56 (±0.167 89%) in the forms **(a)** number (± absolute uncertainty) and **(b)** number (± percent relative uncertainty) with an appropriate number of digits.

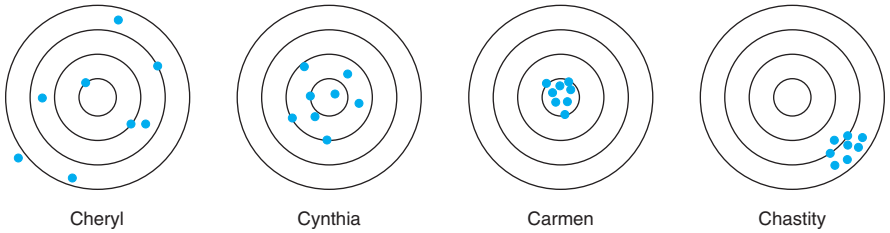


Figure for Problem 3-13.

Propagation of Uncertainty

3-15. Find the absolute and percent relative uncertainty and express each answer with a reasonable number of significant figures.

(a) 6.2 (±0.2) − 4.1 (±0.1) = ?

(b) 9.43 (±0.05) × 0.016 (±0.001) = ?

(c) [6.2 (±0.2) − 4.1 (±0.1)] ÷ 9.43 (±0.05) = ?

(d) 9.43 (±0.05) × {[6.2 (±0.2) × 10^{-3}] + [4.1 (±0.1) × 10^{-3}]} = ?

3-16. Find the absolute and percent relative uncertainty and express each answer with a reasonable number of significant figures.

(a) 9.23 (±0.03) + 4.21 (±0.02) − 3.26 (±0.06) = ?

(b) 91.3 (±1.0) × 40.3 (±0.2)/21.1 (±0.2) = ?

(c) [4.97 (±0.05) − 1.86 (±0.01)]/21.1 (±0.2) = ?

(d) 2.016 4 (±0.000 8) + 1.233 (±0.002) + 4.61 (±0.01) = ?

(e) 2.016 4 (±0.000 8) × 10^3 + 1.233 (±0.002) × 10^2 + 4.61 (±0.01) × 10^1 = ?

(f) [3.14 (±0.05)]$^{1/3}$ = ?

(g) log[3.14 (±0.05)] = ?

3-17. Verify the following calculations:

(a) $\sqrt{3.141\,5(\pm 0.001\,1)} = 1.772\,4_3\ (\pm 0.000\,3_1)$

(b) log[3.141 5 (±0.001 1)] = 0.497 1_4 (±0.000 1_5)

(c) antilog[3.141 5 (±0.001 1)] = 1.385$_2$ (±0.003$_5$) × 10^3

(d) ln[3.141 5 (±0.001 1)] = 1.144 7_0 (±0.000 3_5)

(e) $\log\left(\dfrac{\sqrt{0.104(\pm 0.006)}}{0.051\,1(\pm 0.000\,9)}\right) = 0.80_0\ (\pm 0.01_5)$

3-18. (a) Show that the formula mass of NaCl is 58.443 (±0.001$_2$) g/mol.

(b) To prepare a solution of NaCl, you weigh out 2.634 (±0.002) g and dissolve it in a volumetric flask whose volume is 100.00 (±0.08) mL. Express the molarity of the solution, along with its uncertainty, with an appropriate number of digits.

3-19. What is the true mass of water weighed at 24°C in the air if the apparent mass is 1.034 6 ± 0.000 2 g? The density of air is 0.001 2 ± 0.000 1 g/mL and the density of balance weights is 8.0 ± 0.5 g/mL. The uncertainty in the density of water in Table 2-7 is negligible in comparison to the uncertainty in the density of air.

3-20. Twelve dietary iron tablets were analyzed by the gravimetric procedure in Section 1-4 and the final mass of Fe_2O_3 (FM 159.688) was 0.277$_4$ ± 0.001$_8$ g. Find the average mass of Fe per tablet. (Relative uncertainties in atomic masses are small compared with relative uncertainty in the mass of Fe_2O_3. Neglect uncertainties in atomic masses in this problem.)

3-21. We can measure the concentration of HCl solution by reaction with pure sodium carbonate: $2H^+ + Na_2CO_3 \rightarrow 2Na^+ + H_2O + CO_2$. Complete reaction with 0.967 4 ± 0.000 9 g of Na_2CO_3 (FM 105.988 4 ± 0.000 7) required 27.35 ± 0.04 mL of HCl. Find the molarity of the HCl and its absolute uncertainty.

3-22. Avogadro's number can be computed from the following measured properties of pure crystalline silicon:[4] (1) atomic mass (obtained from the mass and abundance of each isotope), (2) density of the crystal, (3) size of the unit cell (the smallest repeating unit in the crystal), and (4) number of atoms in the unit cell. For silicon, the mass is m_{Si} = 28.085 384 2 (35) g/mol, where 35 is the uncertainty (standard deviation) in the last two digits. The density is ρ = 2.329 031 9 (18) g/cm^3, the size of the cubic unit cell is c_0 = 5.431 020 36 (33) × 10^{-8} cm, and there are 8 atoms per unit cell. Avogadro's number is computed from the equation

$$N_A = \frac{m_{Si}}{(\rho c_0^3)/8}$$

From the measured properties and their uncertainties, compute Avogadro's number and its uncertainty. To find the uncertainty of c_0^3, use the function $y = x^a$ in Table 3-1.

3-23. Express the molecular mass (±uncertainty) of $C_9H_9O_6N_3$ with the correct number of significant figures.

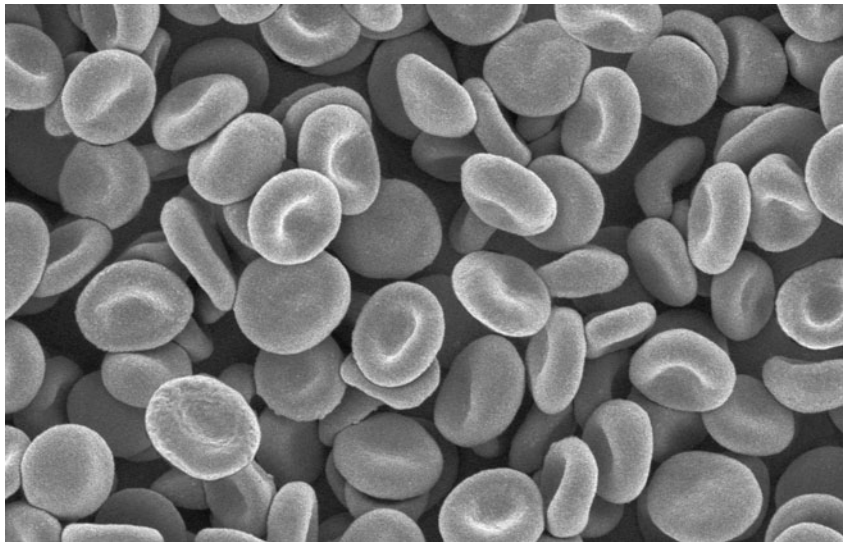
3-24. *Estimating uncertainty in Keeling's CO_2 measurements.* The manometer in Box 3-2 has the following key uncertainties:

Volume of large vessel: 5.013 8_2 ± 0.000 5 L
Volume of small vessel: 3.793 0 ± 0.000 9 mL
Pressure: ±0.03 mm Hg in ~400 mm Hg
Temperature: ±0.03 K in ~300 K

Which factor has the largest percent relative uncertainty? If one uncertainty is sufficiently larger than the others, then the uncertainty in measuring CO_2 is governed by that factor. Considering just the most uncertain factor, estimate the uncertainty in 400 ppm CO_2 in air.

4 Statistics

IS MY RED BLOOD CELL COUNT HIGH TODAY?



Red blood cells, also called erythrocytes, transport oxygen bound to the protein hemoglobin. [Susumu Nishinaga/Photo Researchers.]

All measurements contain experimental error, so it is never possible to be completely certain of a result. Nevertheless, we often seek the answers to questions such as "Is my red blood cell count today higher than usual?" If today's count is twice as high as usual, it is probably truly higher than normal. But what if the "high" count is not excessively above "normal" counts?

Count on "normal" days	Today's count
5.1 5.3 4.8 5.4 5.2 } $\times 10^6$ cells/μL	5.6×10^6 cells/μL
Average = 5.16	

The number 5.6 is higher than the five normal values, but the random variation in normal values might lead us to expect that 5.6 will be observed on some "normal" days.

We will learn in Section 4-3 that there is only a 1.3% random chance of observing a value as far from the average as 5.6 on a "normal" day. It is still up to you to decide what to do with this information.

Experimental measurements always contain some variability, so no conclusion can be drawn with certainty. Statistics gives us tools to accept conclusions that have a high probability of being correct and to reject conclusions that do not.[1]

4-1 Gaussian Distribution

We say that the variation in experimental data is *normally distributed* when replicate measurements exhibit the bell-shaped distribution in Figure 4-1. It is equally probable that a measurement will be higher or lower than the mean. The probability of observing any value decreases as its distance from the mean increases.

If an experiment is repeated a great many times and if the errors are purely random, then the results tend to cluster symmetrically about the average value (Figure 4-1). The more times the experiment is repeated, the more closely the results approach an ideal smooth curve called the **Gaussian distribution.** In general, we cannot make so many measurements in a lab experiment. We are more likely to repeat an experiment 3 to 5 times than 2 000 times. However, from the small set of results, we can estimate parameters that describe the large set. We can then make estimates of statistical behavior from the small number of measurements.

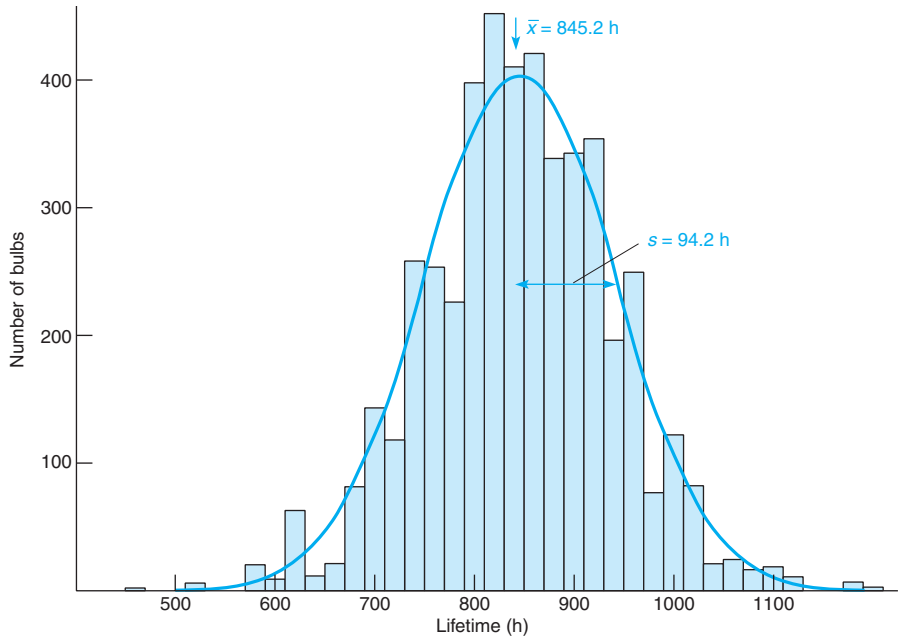


FIGURE 4-1 Bar graph and Gaussian curve describing the lifetimes of a hypothetical set of incandescent light bulbs. The smooth curve has the same mean, standard deviation, and area as the bar graph. Any finite set of data, however, will differ from the bell-shaped curve. The more measurements we make, the closer the results will come to the smooth curve.

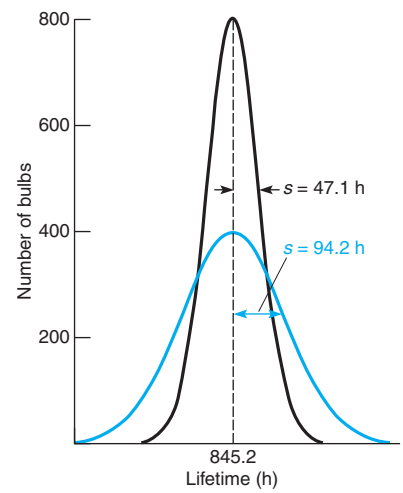


FIGURE 4-2 Gaussian curves for two sets of light bulbs, one having a standard deviation half as great as the other. The number of bulbs described by each curve is the same.

Mean Value and Standard Deviation

In the hypothetical case in Figure 4-1, a manufacturer tested the lifetimes of 4 768 electric light bulbs. The bar graph shows the number of bulbs with a lifetime in each 20-h interval. Lifetimes approximate a Gaussian distribution because variations in the construction of light bulbs, such as filament thickness and quality of attachments, are random. The smooth curve is the Gaussian distribution that best fits the data. Any finite set of data will vary somewhat from the Gaussian curve.

Light bulb lifetimes, and the corresponding Gaussian curve, are characterized by two parameters. The arithmetic **mean,** $\bar{x}$—also called the **average**—is the sum of the measured values divided by n, the number of measurements:

Mean:

$$\bar{x} = \frac{\sum_i x_i}{n} \tag{4-1}$$

The mean gives the center of the distribution. The standard deviation measures the width of the distribution.

where x_i is the lifetime of an individual bulb. The Greek capital sigma, Σ, means summation: $\Sigma_i x_i = x_1 + x_2 + x_3 + \cdots + x_n$. In Figure 4-1, the mean value is 845.2 h.

The **standard deviation,** s, measures how closely the data are clustered about the mean. *The smaller the standard deviation, the more closely the data are clustered about the mean* (Figure 4-2).

An experiment that produces a small standard deviation is more *precise* than one that produces a large standard deviation. Greater precision does not necessarily imply greater *accuracy*, which is nearness to the "truth."

Standard deviation:

$$s = \sqrt{\frac{\sum_i (x_i - \bar{x})^2}{n - 1}} \tag{4-2}$$

In Figure 4-1, $s = 94.2$ h. A set of light bulbs having a small standard deviation in lifetime is more uniformly manufactured than a set with a large standard deviation.

For an *infinite* set of data, the mean is designated by the lowercase Greek letter mu, μ (the population mean), and the standard deviation is written as a lowercase Greek sigma, σ (the population standard deviation). We can never measure μ and σ, but the values of $\bar{x}$ and s approach μ and σ as the number of measurements increases.

As the number of measurements increases, $\bar{x}$ approaches μ, *if there is no systematic error.*

The quantity $n - 1$ in Equation 4-2 is called the **degrees of freedom.** The square of the standard deviation is called the **variance.** The standard deviation expressed as a percentage of the mean value ($= 100 \times s/\bar{x}$) is called the *relative standard deviation* or the *coefficient of variation*.

Coefficient of variation $= 100 \times \frac{s}{\bar{x}}$

EXAMPLE **Mean and Standard Deviation**

Find the average, standard deviation, and coefficient of variation for 821, 783, 834, and 855.

Solution The average is

$$\bar{x} = \frac{821 + 783 + 834 + 855}{4} = 823._2$$

To avoid accumulating round-off errors, retain one more digit than was present in the original data. The standard deviation is

$$s = \sqrt{\frac{(821 - 823.2)^2 + (783 - 823.2)^2 + (834 - 823.2)^2 + (855 - 823.2)^2}{(4 - 1)}} = 30._3$$

Learn to use the standard deviation function on your calculator and see that you get $s = 30.269\,6\ldots$.

The average and the standard deviation should both end at the *same decimal place*. For $\bar{x} = 823._2$, we will write $s = 30._3$. The coefficient of variation is the percent relative uncertainty:

$$\text{Coefficient of variation} = 100 \times \frac{s}{\bar{x}} = 100 \times \frac{30._3}{823._2} = 3.7\%$$

Test Yourself If each of the four numbers 821, 783, 834, and 855 in the example is divided by 2, how will the mean, standard deviation, and coefficient of variation be affected? (***Answer:*** $\bar{x}$ and s will be divided by 2, but the coefficient of variation is unchanged)

	A	B
1		821
2		783
3		834
4		855
5	Average =	823.25
6	Std dev =	30.27
7	B5 = AVERAGE(B1:B4)	
8	B6 = STDEV(B1:B4)	

Spreadsheets have built-in functions for the average and standard deviation. In the adjacent spreadsheet, data points are entered in cells B1 through B4. The average in cell B5 is computed with the statement "= AVERAGE(B1:B4)". B1:B4 means cells B1, B2, B3, and B4. The standard deviation in cell B6 is computed with "= STDEV(B1:B4)".

For ease of reading, cells B5 and B6 were set to display two decimal places. A heavy line was placed beneath cell B4 in Excel 2007 by highlighting the cell, going to Home, Font, and selecting the Border icon. In earlier versions of Excel, highlight cell B4, go to Format, Cells, and select Border.

Significant Figures in Mean and Standard Deviation

Do not round off during a calculation. Retain all the extra digits in your calculator.

We commonly express experimental results in the form $\bar{x} \pm s(n = _)$, where n is the number of data points. It is sensible to write the preceding result as 823 ± 30 ($n = 4$) or even $8.2\ (\pm 0.3) \times 10^2$ ($n = 4$) to indicate that the mean has just two significant figures. The expressions 823 ± 30 and $8.2\ (\pm 0.3) \times 10^2$ are not suitable for continued calculations in which $\bar{x}$ and s are intermediate results. Retain one or more insignificant digits to avoid introducing round-off errors into subsequent work. Try not to go into cardiac arrest over significant figures when you see $823._2 \pm 30._3$ as the answer to a problem in this book.

Standard Deviation and Probability

The formula for a Gaussian curve is

Gaussian curve:

$$y = \frac{1}{\sigma\sqrt{2\pi}}\, e^{-(x-\mu)^2/2\sigma^2} \tag{4-3}$$

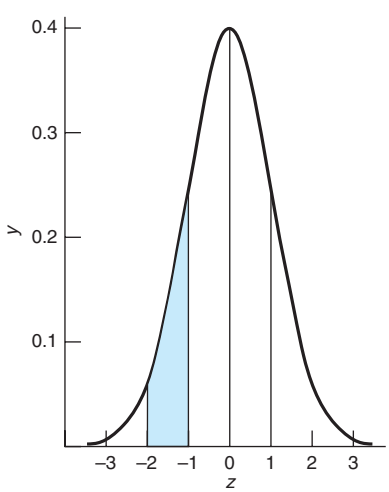


FIGURE 4-3 A Gaussian curve in which $\mu = 0$ and $\sigma = 1$. A Gaussian curve whose area is unity is called a normal error curve. The abscissa $z = (x - \mu)/\sigma$ is the distance away from the mean, measured in units of the standard deviation. When $z = 2$, we are two standard deviations away from the mean.

where e (= 2.718 28 . . .) is the base of the natural logarithm. For a finite set of data, we approximate μ by $\bar{x}$ and σ by s. A graph of Equation 4-3 is shown in Figure 4-3, in which the values $\sigma = 1$ and $\mu = 0$ are used for simplicity. The maximum value of y is at $x = \mu$ and the curve is symmetric about $x = \mu$.

It is useful to express deviations from the mean value in multiples, z, of the standard deviation. That is, we transform x into z, given by

$$z = \frac{x - \mu}{\sigma} \approx \frac{x - \bar{x}}{s} \tag{4-4}$$

TABLE 4–1 Ordinate and area for the normal (Gaussian) error curve, $y = \frac{1}{\sqrt{2\pi}} e^{-z^2/2}$

$\lvert z\rvert$[a]	y	Area[b]	$\lvert z\rvert$	y	Area	$\lvert z\rvert$	y	Area
0.0	0.398 9	0.000 0	1.4	0.149 7	0.419 2	2.8	0.007 9	0.497 4
0.1	0.397 0	0.039 8	1.5	0.129 5	0.433 2	2.9	0.006 0	0.498 1
0.2	0.391 0	0.079 3	1.6	0.110 9	0.445 2	3.0	0.004 4	0.498 650
0.3	0.381 4	0.117 9	1.7	0.094 1	0.455 4	3.1	0.003 3	0.499 032
0.4	0.368 3	0.155 4	1.8	0.079 0	0.464 1	3.2	0.002 4	0.499 313
0.5	0.352 1	0.191 5	1.9	0.065 6	0.471 3	3.3	0.001 7	0.499 517
0.6	0.333 2	0.225 8	2.0	0.054 0	0.477 3	3.4	0.001 2	0.499 663
0.7	0.312 3	0.258 0	2.1	0.044 0	0.482 1	3.5	0.000 9	0.499 767
0.8	0.289 7	0.288 1	2.2	0.035 5	0.486 1	3.6	0.000 6	0.499 841
0.9	0.266 1	0.315 9	2.3	0.028 3	0.489 3	3.7	0.000 4	0.499 904
1.0	0.242 0	0.341 3	2.4	0.022 4	0.491 8	3.8	0.000 3	0.499 928
1.1	0.217 9	0.364 3	2.5	0.017 5	0.493 8	3.9	0.000 2	0.499 952
1.2	0.194 2	0.384 9	2.6	0.013 6	0.495 3	4.0	0.000 1	0.499 968
1.3	0.171 4	0.403 2	2.7	0.010 4	0.496 5	∞	0	0.5

a. $z = (x - \mu)/\sigma$.

b. The area refers to the area between $z = 0$ and $z =$ the value in the table. Thus the area from $z = 0$ to $z = 1.4$ is 0.419 2. The area from $z = -0.7$ to $z = 0$ is the same as from $z = 0$ to $z = 0.7$. The area from $z = -0.5$ to $z = +0.3$ is $(0.191\ 5 + 0.117\ 9) = 0.309\ 4$. The total area between $z = -\infty$ and $z = +\infty$ is unity.

The probability of measuring z in a certain *range* is equal to the *area* of that range. For example, the probability of observing z between –2 and –1 is 0.136. This probability corresponds to the shaded area in Figure 4-3. The area under each portion of the Gaussian curve is given in Table 4-1. Because the sum of the probabilities of all the measurements must be unity, the area under the whole curve from $z = -\infty$ to $z = +\infty$ must be unity. The number $1/(\sigma\sqrt{2\pi})$ in Equation 4-3 is called the *normalization factor*. It guarantees that the area under the entire curve is unity. A Gaussian curve with unit area is called a *normal error curve*.

When $z = +1$, x is one standard deviation above the mean. When $z = -2$, x is two standard deviations below the mean.

EXAMPLE Area Under a Gaussian Curve

Suppose the manufacturer of the bulbs used for Figure 4-1 offers to replace free of charge any bulb that burns out in less than 600 hours. If she plans to sell a million bulbs, how many extra bulbs should she keep available as replacements?

Solution We need to express the desired interval in multiples of the standard deviation and then find the area of the interval in Table 4-1. Because $\bar{x} = 845.2$ and $s = 94.2$, $z = (600 - 845.2)/94.2 = -2.60$. The area under the curve between the mean value and $z = -2.60$ is 0.495 3 in Table 4-1. The entire area from $-\infty$ to the mean value is 0.500 0, so the area from $-\infty$ to –2.60 must be 0.500 0 – 0.495 3 = 0.004 7. The area to the left of 600 hours in Figure 4-1 is only 0.47% of the entire area under the curve. Only 0.47% of the bulbs are expected to fail in fewer than 600 h. If the manufacturer sells 1 million bulbs a year, she should make 4 700 extra bulbs to meet the replacement demand.

Test Yourself If the manufacturer will replace bulbs that burn out in less than 620 hours, how many extras should she make? (***Answer:*** $z \approx -2.4$, area $\approx 0.008\ 2 = 8\ 200$ bulbs)

EXAMPLE Using a Spreadsheet to Find Area Under a Gaussian Curve

What fraction of bulbs is expected to have a lifetime between 900 and 1 000 h?

Solution *We need to find the fraction of the area of the Gaussian curve between $x = 900$ and $x = 1\ 000$ h.* The function NORMDIST in Excel gives the area of the curve from $-\infty$ up to a specified point, x. Here is the strategy: We will find the area from $-\infty$ to 900 h, which is the shaded area to the left of 900 h in Figure 4-4. Then we will find the area from $-\infty$ to 1 000 h, which is all the shaded area to the left of 1 000 h in Figure 4-4. The difference between the two is the area from 900 to 1 000 h:

$$\text{Area from 900 to 1 000} = (\text{area from } -\infty \text{ to 1 000}) - (\text{area from } -\infty \text{ to 900})$$

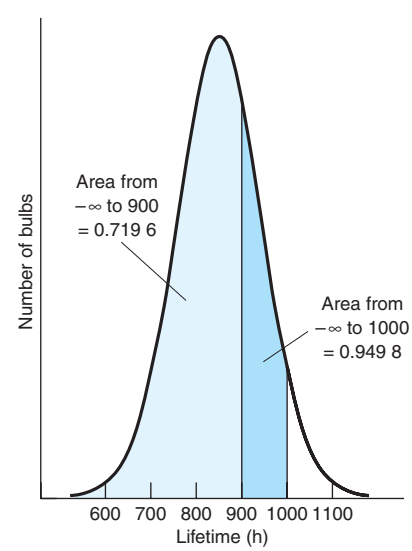


FIGURE 4-4 Use of the Gaussian curve to find the fraction of bulbs with a lifetime between 900 and 1 000 h. We find the area between $-\infty$ and 1 000 h and subtract the area between $-\infty$ and 900 h.

In a spreadsheet, enter the mean in cell A2 and the standard deviation in cell B2. To find the area under the Gaussian curve from $-\infty$ to 900 h in cell C4, select cell C4 and, in Excel 2007, go to Formulas, Insert Function. In earlier versions of Excel, go to the Insert menu and choose Function. In the window that appears, select Statistical functions and find NORMDIST from the list of possibilities. Double click on NORMDIST and another window appears asking for four values that will be used by NORMDIST. (If you click on Help, you will find a cryptic explanation of how to use NORMDIST.)

	A	B	C
1	Mean =	Std dev =	
2	845.2	94.2	
3			
4	Area from $-\infty$ to 900 =		0.7196
5	Area from $-\infty$ to 1000 =		0.9498
6	Area from 900 to 1000		0.2302
7			
8	C4 = NORMDIST(900,$A$2,$B$2,TRUE)		
9	C5 = NORMDIST(1000,$A$2,$B$2,TRUE)		
10	C6 = C5-C4		

Values provided to the function NORMDIST(x,mean,standard_dev,cumulative) are called *arguments* of the function. The first argument is x, which is 900. The second argument is the mean, which is 845.2. You can enter 845.2 for the mean or enter A2, which is the cell containing 845.2. We will enter $A$2 so that we can move the entry to other cells and still always refer to cell A2. The third argument is the standard deviation, for which we enter $B$2. The last argument is called "cumulative." When it has the value TRUE, NORMDIST gives the area under the Gaussian curve. When cumulative is FALSE, NORMDIST gives the ordinate (the y-value) of the Gaussian curve. We want area, so enter TRUE. The formula "= NORMDIST(900,$A$2,$B$2,TRUE)" in cell C4 returns 0.719 6. This is the area under the Gaussian curve from $-\infty$ to 900 h. To get the area from $-\infty$ to 1 000 h, write "= NORMDIST(1000,$A$2,$B$2,TRUE)" in cell C5. The value returned is 0.949 8. Then subtract the areas (C5 – C4) to obtain 0.230 2, which is the area from 900 to 1 000. That is, 23.02% of the area lies in the range 900 to 1 000 h. We expect 23% of the bulbs to have a lifetime of 900 to 1 000 h.

Test Yourself Find the area from 800 to 1 000 hours. (***Answer:*** 0.634 2)

The standard deviation measures the width of the Gaussian curve. The larger the value of σ, the broader the curve. In any Gaussian curve, 68.3% of the area is in the range from $\mu - 1\sigma$ to $\mu + 1\sigma$. That is, more than two-thirds of the measurements are expected to lie within one standard deviation of the mean. Also, 95.5% of the area lies within $\mu \pm 2\sigma$, and 99.7% of the area lies within $\mu \pm 3\sigma$. Suppose that you use two different techniques to measure sulfur in coal: Method A has a standard deviation of 0.4%, and method B has a standard deviation of 1.1%. You can expect that approximately two-thirds of measurements from method A will lie within 0.4% of the mean. For method B, two-thirds will lie within 1.1% of the mean.

Range	Percentage of measurements
$\mu \pm 1\sigma$	68.3
$\mu \pm 2\sigma$	95.5
$\mu \pm 3\sigma$	99.7

Standard Deviation of the Mean

To measure the mean lifetime of a large number of light bulbs, we could select one at a time and measure its lifetime. Alternatively, we could select, say, four at a time, measure the life of each, and compute the average of the four. We repeat this process of measuring four at a time many times and compute a mean μ and a standard deviation that we label σ_4 because it is based on sets of four bulbs. The mean of many sets of four bulbs is the same as the population mean. However, the standard deviation of the means of sets of four bulbs is smaller than the population standard deviation, σ. The relation is $\sigma_4 = \sigma/\sqrt{4}$. We call σ_4 the **standard deviation of the mean** of sets of four samples. In general, the standard deviation of the mean for sets of n samples is

Standard deviation of the mean of sets of n values:

$$\sigma_n = \frac{\sigma}{\sqrt{n}} \tag{4-5}$$

The more times you measure a quantity, the more confident you can be that the average is close to the population mean. Uncertainty decreases in proportion to $1/\sqrt{n}$, where n is the number of measurements. You can decrease uncertainty by a factor of $2(=\sqrt{4})$ by making 4 times as many measurements and by a factor of 10 $(=\sqrt{100})$ by making 100 times as many measurements.

Instruments with rapid data acquisition allow us to average many experiments in a short time to improve precision.

4-2 Confidence Intervals

Student's *t* is a statistical tool used most frequently to express confidence intervals and to compare results from different experiments. It is the tool you could use to evaluate the probability that your red blood cell count will be found in a certain range on "normal" days.

"Student" was the pseudonym of W. S. Gosset, whose employer, the Guinness breweries of Ireland, restricted publications for proprietary reasons. Because of the importance of Gosset's work, he was allowed to publish it (*Biometrika* **1908**, *6*, 1), but under an assumed name.

Calculating Confidence Intervals

From a limited number of measurements (n), we cannot find the true population mean, μ, or the true standard deviation, σ. What we determine are $\bar{x}$ and s, the sample mean and the sample standard deviation. The **confidence interval** is computed from the equation

$$\text{Confidence interval} = \bar{x} \pm \frac{ts}{\sqrt{n}} \tag{4-6}$$

where t is Student's t, taken from Table 4-2 for a desired level of confidence, such as 95%. The meaning of the confidence interval is this: If we were to repeat the n measurements many times to compute the mean and standard deviation, the 95% confidence interval would include the true population mean (whose value we do not know) in 95% of the sets of n measurements. We say (somewhat imprecisely) that "we are 95% confident that the true mean lies within the confidence interval."

EXAMPLE **Calculating Confidence Intervals**

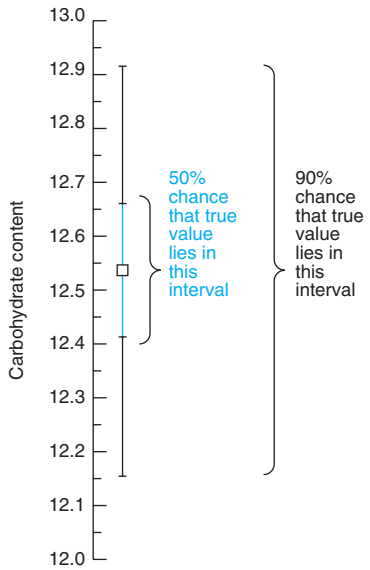
The carbohydrate content of a glycoprotein (a protein with sugars attached to it) is found to be 12.6, 11.9, 13.0, 12.7, and 12.5 wt% (g carbohydrate/100 g glycoprotein) in replicate analyses. Find the 50% and 90% confidence intervals for the carbohydrate content.

TABLE 4-2 Values of Student's *t*

Degrees of freedom	Confidence level (%)						
	50	90	95	98	99	99.5	99.9
1	1.000	6.314	12.706	31.821	63.656	127.321	636.578
2	0.816	2.920	4.303	6.965	9.925	14.089	31.598
3	0.765	2.353	3.182	4.541	5.841	7.453	12.924
4	0.741	2.132	2.776	3.747	4.604	5.598	8.610
5	0.727	2.015	2.571	3.365	4.032	4.773	6.869
6	0.718	1.943	2.447	3.143	3.707	4.317	5.959
7	0.711	1.895	2.365	2.998	3.500	4.029	5.408
8	0.706	1.860	2.306	2.896	3.355	3.832	5.041
9	0.703	1.833	2.262	2.821	3.250	3.690	4.781
10	0.700	1.812	2.228	2.764	3.169	3.581	4.587
15	0.691	1.753	2.131	2.602	2.947	3.252	4.073
20	0.687	1.725	2.086	2.528	2.845	3.153	3.850
25	0.684	1.708	2.060	2.485	2.787	3.078	3.725
30	0.683	1.697	2.042	2.457	2.750	3.030	3.646
40	0.681	1.684	2.021	2.423	2.704	2.971	3.551
60	0.679	1.671	2.000	2.390	2.660	2.915	3.460
120	0.677	1.658	1.980	2.358	2.617	2.860	3.373
∞	0.674	1.645	1.960	2.326	2.576	2.807	3.291

In calculating confidence intervals, σ may be substituted for s in Equation 4-6 if you have a great deal of experience with a particular method and have therefore determined its "true" population standard deviation. If σ is used instead of s, the value of t to use in Equation 4-6 comes from the bottom row of Table 4-2.

Values of t in this table apply to two-tailed tests illustrated in Figure 4-9a. The 95% confidence level specifies the regions containing 2.5% of the area in each wing of the curve. For a one-tailed test, we use values of t listed for 90% confidence. Each wing outside of t for 90% confidence contains 5% of the area of the curve.



Solution First calculate $\bar{x}$ ($=12.5_4$) and s ($= 0.4_0$) for the five measurements. For the 50% confidence interval, look up t in Table 4-2 under 50 and across from *four* degrees of freedom (degrees of freedom $= n - 1$). The value of t is 0.741, so the 50% confidence interval is

$$50\% \text{ confidence interval} = \bar{x} \pm \frac{ts}{\sqrt{n}} = 12.5_4 \pm \frac{(0.741)(0.4_0)}{\sqrt{5}} = 12.5_4 \pm 0.1_3 \text{ wt\%}$$

The 90% confidence interval is

$$90\% \text{ confidence interval} = \bar{x} \pm \frac{ts}{\sqrt{n}} = 12.5_4 \pm \frac{(2.132)(0.4_0)}{\sqrt{5}} = 12.5_4 \pm 0.3_8 \text{ wt\%}$$

If we repeated sets of five measurements many times, half of 50% confidence intervals are expected to include the true mean, μ. Nine-tenths of the 90% confidence intervals are expected to include the true mean, μ.

Test Yourself Carbohydrate measured on one more sample was 12.3 wt%. Using six results, find the 90% confidence interval. (***Answer:*** $12.5_0 \pm (2.015)(0.3_7)/\sqrt{6} = 12.5_0 \pm 0.3_1$ wt%)

The Meaning of a Confidence Interval

Figure 4-5 illustrates the meaning of confidence intervals. A computer chose numbers at random from a Gaussian population with a population mean (μ) of 10 000 and a population standard deviation (σ) of 1 000 in Equation 4-3. In trial 1, four numbers were chosen, and their mean and standard deviation were calculated with Equations 4-1 and 4-2. The 50% confidence interval was then calculated with Equation 4-6, using $t = 0.765$ from Table 4-2 (50% confidence, 3 degrees of freedom). This trial is plotted as the first point at the left in Figure 4-5a; the square is centered at the mean value of 9 526, and the error bar extends from the lower limit to the upper limit of the 50% confidence interval (± 290). The experiment was repeated 100 times to produce the points in Figure 4-5a.

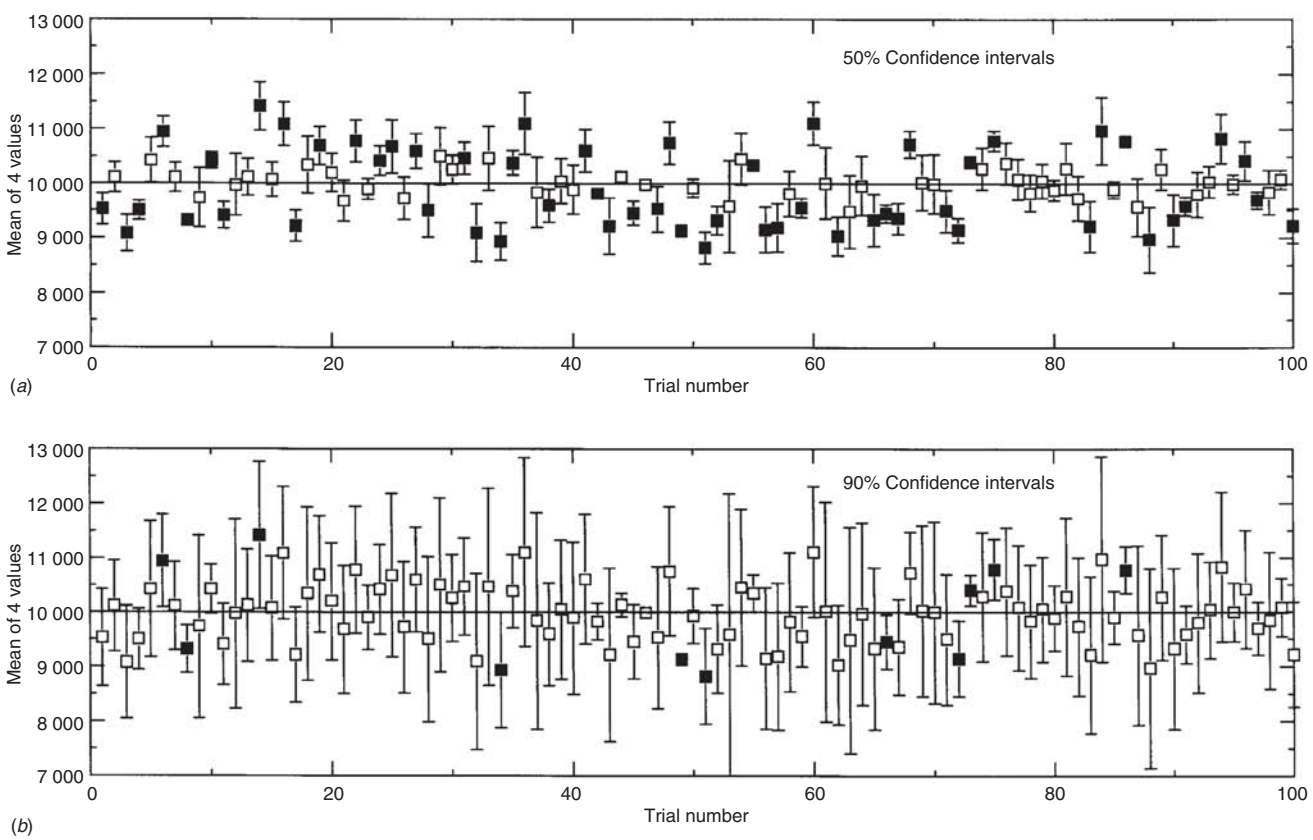


FIGURE 4-5 50% and 90% confidence intervals for the same set of random data. Filled squares are the data points whose confidence interval does not include the true population mean of 10 000.

The 50% confidence interval is defined such that, if we repeated this experiment an infinite number of times, 50% of the error bars in Figure 4-5a would include the true population mean of 10 000. In fact, I did the experiment 100 times, and 45 of the error bars in Figure 4-5a pass through the horizontal line at 10 000.

Figure 4-5b shows the same experiment with the same set of random numbers, but this time the 90% confidence interval was calculated. For an infinite number of experiments, we would expect 90% of the confidence intervals to include the population mean of 10 000. In Figure 4-5b, 89 of the 100 error bars cross the horizontal line at 10 000.

Standard Deviation and Confidence Interval as Estimates of Experimental Uncertainty

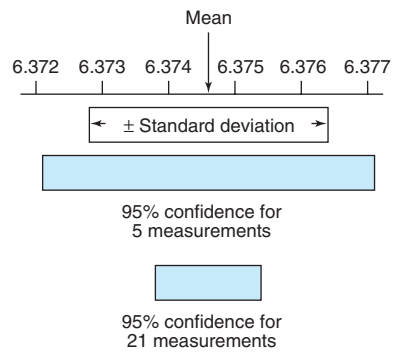
Chapter 3 gave rules for propagation of uncertainty in calculations. For example, if we were dividing a mass by a volume to find density, the uncertainty in density is derived from the uncertainties in mass and volume. Common estimates of uncertainty are the standard deviation and the confidence interval.

"Analytical chemists must always emphasize to the public that the single most important characteristic of any result obtained from one or more analytical measurements is an adequate statement of its uncertainty interval."[2]

Suppose you measure the volume of a vessel five times and observe values of 6.375, 6.372, 6.374, 6.377, and 6.375 mL. The average is $\bar{x} = 6.374_6$ mL and the standard deviation is $s = 0.001_8$ mL. We could report a volume of $6.374_6 \pm 0.001_8$ mL ($n = 5$), where n is the number of measurements.

You could choose a confidence interval (such as 95%) for the estimate of uncertainty. Using Equation 4-6 with 4 degrees of freedom, you find that the 95% confidence interval is $\pm ts/\sqrt{n} = \pm(2.776)(0.001_8)/\sqrt{5} = \pm 0.002_5$. By this criterion, the uncertainty in volume is $\pm 0.002_5$ mL. *It is critical to specify what kind of uncertainty you are reporting*, such as the standard deviation for n measurements or the 95% confidence interval for n measurements.

We reduce uncertainty by making more measurements. If we make 21 measurements and have the same mean and standard deviation, the 95% confidence interval is reduced from $\pm 0.002_5$ to $\pm(2.086)(0.001_8)/\sqrt{21} = \pm 0.000\,8$ mL.



Finding Confidence Intervals with Excel

Excel has a built-in function to compute Student's t. In Figure 4-6, we enter data in the block of cells A4:A13. We reserved 10 cells for data, but you could modify a spreadsheet to accept more data. For the five data points entered in Figure 4-6, the mean is computed in cell C3 with the statement "=AVERAGE(A4:A13)" even though some of the cells in the range A4:A13 are empty. Excel ignores empty cells and does not consider them to be 0, which would produce an incorrect average. Standard deviation is computed in cell C4. We find the number of data points, n, with the statement in cell C5 "=COUNT(A4:A13)". Degrees of freedom are computed as $n - 1$ in cell C7. Cell C9 has the desired confidence level (0.95), which is our only input other than the data.

The function for finding Student's t in cell C11 is "=TINV(probability,deg_freedom). Probability in this function is 1 – confidence level = 1 – 0.95 = 0.05. So, the statement in cell C11 is "=TINV(1-C9,C7)", which returns Student's t for 95% confidence and 4 degrees of freedom. Cell C13 gives the confidence interval computed with Equation 4-6.

Verify that Student's t in cell C11 is the same as the value in Table 4-2.

	A	B	C	D	E	F
1	Confidence Inverval					
2						
3	Data	mean =	6.3746		= AVERAGE (A4:A13)	
4	6.375	stdev =	0.0018		= STDEV (A4:A13)	
5	6.372	n =	5		= COUNT (A4:A13)	
6	6.374	degrees of				
7	6.377	freedom =	4		= C5-1	
8	6.375	confidence				
9		level =	0.95			
10		Student's				
11		t =	2.776		= TINV (1-C9,C7)	
12		confidence				
13		interval =	0.0023		= C11*C4/SQRT(C5)	

FIGURE 4-6 Spreadsheet for finding confidence interval.

4-3 Comparison of Means with Student's *t*

Confidence limits and the *t* test (and, later in this chapter, the Grubbs test) assume that data follow a Gaussian distribution.

If you make two sets of measurements of the same quantity, the mean value from one set will generally not be equal to the mean value from the other set because of small, random variations in the measurements. We use a ***t* test** to compare one mean value with another to decide whether there is a statistically significant difference between the two. That is, do the two means agree "within experimental error"? The *null hypothesis* in statistics states that the mean values from two sets of measurements are *not* different. Statistics gives us a probability that the observed difference between two means arises from random measurement error. *We customarily reject the null hypothesis if there is less than a 5% chance that the observed difference arises from random variations*. With this criterion, we have a 95% chance that our conclusion is correct. One time out of 20 when we conclude that two means are not different we will be wrong.

Here are three cases that are handled in slightly different manners:

Case 1 We measure a quantity several times, obtaining an average value and standard deviation. We need to compare our answer with an accepted answer. The average is not exactly the same as the accepted answer. Does our measured answer agree with the accepted answer "within experimental error"?

Case 2 We measure a quantity multiple times by two different methods that give two different answers, each with its own standard deviation. Do the two results agree with each other "within experimental error"?

Case 3 Sample A is measured once by method 1 and once by method 2; the two measurements do not give exactly the same result. Then a different sample, designated B, is measured once by method 1 and once by method 2; and, again, the results are not exactly equal. The procedure is repeated for n different samples. Do the two methods agree with each other "within experimental error"?

Case 1. Comparing a Measured Result with a "Known" Value

If the "known" answer does not lie within the 95% confidence interval, then the two methods give "different" results.

You purchased a Standard Reference Material coal sample certified by the National Institute of Standards and Technology to contain 3.19 wt% sulfur. You are testing a new analytical method to see whether it can reproduce the known value. The measured values are 3.29, 3.22, 3.30, and 3.23 wt% sulfur, giving a mean of $\bar{x} = 3.26_0$ and a standard deviation of $s = 0.04_1$. Does your answer agree with the known answer? To find out, *compute the 95% confidence interval for your answer and see if that range includes the known answer*. If the known answer is not within your 95% confidence interval, then the results do not agree.

So here we go. For four measurements, there are 3 degrees of freedom and $t_{95\%} = 3.182$ in Table 4-2. The 95% confidence interval is

Retain many digits in this calculation.

$$95\% \text{ confidence interval} = \bar{x} \pm \frac{ts}{\sqrt{n}} = 3.26_0 \pm \frac{(3.182)(0.04_1)}{\sqrt{4}} = 3.26_0 \pm 0.06_5 \quad \textbf{(4-7)}$$

$$95\% \text{ confidence interval} = 3.19_5 \text{ to } 3.32_5 \text{ wt\%}$$

The known answer (3.19 wt%) is just outside the 95% confidence interval. Therefore we conclude that there is less than a 5% chance that our method agrees with the known answer.

We conclude that our method gives a "different" result from the known result. However, in this case, the 95% confidence interval is so close to including the known result that it would be prudent to make more measurements before concluding that our new method is not accurate.

Case 2. Comparing Replicate Measurements

Do the results of two different sets of measurements agree "within experimental error"?[3] An example comes from the work of Lord Rayleigh (John W. Strutt), who is remembered today for landmark investigations of light scattering, blackbody radiation, and elastic waves in solids. His Nobel Prize in 1904 was received for discovering the inert gas argon. This discovery occurred when he noticed a small discrepancy between two sets of measurements of the density of nitrogen gas.

In Rayleigh's time, it was known that dry air was composed of about one-fifth oxygen and four-fifths nitrogen. Rayleigh removed all O_2 from air by passing the air through red-hot copper (to make solid CuO). He then measured the density of the remaining gas by collecting it in a fixed volume at constant temperature and pressure. He also prepared the same volume

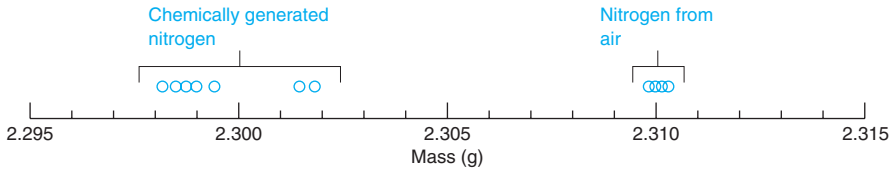


FIGURE 4-7 Lord Rayleigh's measurements of the mass of constant volumes of gas (at constant temperature and pressure) isolated by removing oxygen from air or generated by decomposition of nitrogen compounds. Rayleigh recognized that the difference between the two clusters was outside of his experimental error and deduced that a heavier component, which turned out to be argon, was present in gas isolated from air.

of pure N_2 by chemical decomposition of nitrous oxide (N_2O), nitric oxide (NO), or ammonium nitrite ($NH_4^+NO_2^-$). Table 4-3 and Figure 4-7 show the mass of gas collected in each experiment. The average mass collected from air (2.310 11 g) is 0.46% greater than the average mass of the same volume of gas from chemical sources (2.299 47 g).

If Rayleigh's measurements had not been performed with care, this difference might have been attributed to experimental error. Instead, Rayleigh understood that the discrepancy was outside his margin of error, and he postulated that gas collected from the air was a mixture of nitrogen with a small amount of a heavier gas, which turned out to be argon.

Let's see how to use a t test to decide whether gas isolated from air is "significantly" heavier than nitrogen isolated from chemical sources. In this case, we have two sets of measurements, each with its own uncertainty and no "known" value. We assume that the population standard deviation (σ) for each method is essentially the same.

For two sets of data consisting of n_1 and n_2 measurements (with averages $\bar{x}_1$ and $\bar{x}_2$), we calculate a value of t with the formula

$$t_{\text{calculated}} = \frac{|\bar{x}_1 - \bar{x}_2|}{s_{\text{pooled}}}\sqrt{\frac{n_1 n_2}{n_1 + n_2}} \tag{4-8}$$

where $|\bar{x}_1 - \bar{x}_2|$ is the absolute value of the difference (a positive number) and s_{pooled} is a *pooled* standard deviation making use of both sets of data:

$$s_{\text{pooled}} = \sqrt{\frac{\sum_{\text{set 1}}(x_i - \bar{x}_1)^2 + \sum_{\text{set 2}}(x_j - \bar{x}_2)^2}{n_1 + n_2 - 2}} = \sqrt{\frac{s_1^2(n_1 - 1) + s_2^2(n_2 - 1)}{n_1 + n_2 - 2}} \tag{4-9}$$

$t_{\text{calculated}}$ from Equation 4-8 is compared with t in Table 4-2 for $n_1 + n_2 - 2$ degrees of freedom. *If $t_{calculated}$ is greater than t_{table} at the 95% confidence level, the two results are considered to be different.* There is less than a 5% chance that the two sets of data were drawn from populations with the same population mean.

If $t_{\text{calculated}} > t_{\text{table}}$ (95%), the difference is significant.

TABLE 4-3 Masses of gas isolated by Lord Rayleigh

From air (g)	From chemical decomposition (g)
2.310 17	2.301 43
2.309 86	2.298 90
2.310 10	2.298 16
2.310 01	2.301 82
2.310 24	2.298 69
2.310 10	2.299 40
2.310 28	2.298 49
—	2.298 89
Average	
2.310 11	2.299 47
Standard deviation	
$0.000\ 14_3$	0.001 38

SOURCE: R. D. Larsen, J. Chem. Ed. ***1990****, 67, 925; see also C. J. Giunta, J. Chem. Ed.* ***1998****, 75, 1322.*

EXAMPLE **Is Lord Rayleigh's Gas from Air Denser Than N_2 from Chemicals?**

The average mass of gas from air in Table 4-3 is $\bar{x}_1 = 2.310\ 11$ g, with a standard deviation of $s_1 = 0.000\ 14_3$ (for $n_1 = 7$ measurements). The mass of gas from chemical sources is $\bar{x}_2 = 2.299\ 47$ g, with $s_2 = 0.001\ 38$ ($n_2 = 8$ measurements).

Solution To answer the question, we calculate s_{pooled} with Equation 4-9,

$$s_{\text{pooled}} = \sqrt{\frac{(0.000\ 14_3)^2(7 - 1) + (0.001\ 38)^2(8 - 1)}{7 + 8 - 2}} = 0.001\ 02$$

and $t_{\text{calculated}}$ with Equation 4-8:

$$t_{\text{calculated}} = \frac{|2.310\ 11 - 2.299\ 47|}{0.001\ 02}\sqrt{\frac{7 \cdot 8}{7 + 8}} = 20.2$$

For $7 + 8 - 2 = 13$ degrees of freedom in Table 4-2, t_{table} lies between 2.228 and 2.131 for 95% confidence. Because $t_{\text{calculated}} > t_{\text{table}}$, the difference is significant. In fact, t_{table} for

99.9% confidence is ~4.3. The difference is significant beyond the 99.9% confidence level. Our eyes were not lying to us in Figure 4-7: Gas from the air is undoubtedly denser than N_2 from chemical sources. This observation led Rayleigh to discover a heavy constituent of air.

Test Yourself If $|\bar{x}_1 - \bar{x}_2|$ is only half as great, but s_{pooled} is unchanged, are the two means significantly different? (***Answer:*** $t_{calculated} = 10.1$ and the difference is still significant)

Section 4-4 uses for *F* test to see if two standard deviations are significantly different.

Equations 4-8 and 4-9 assume that the population standard deviation is the same for both sets of measurements. If this is not true, then we use the equations[4]

$$t_{calculated} = \frac{|\bar{x}_1 - \bar{x}_2|}{\sqrt{s_1^2/n_1 + s_2^2/n_2}} \tag{4-8a}$$

Equation 4-9a is slightly different from its ancestor in previous editions of this book. The new and old equations are both approximations.

$$\text{Degrees of freedom} = \frac{(s_1^2/n_1 + s_2^2/n_2)^2}{\dfrac{(s_1^2/n_1)^2}{n_1 - 1} + \dfrac{(s_2^2/n_2)^2}{n_2 - 1}} \tag{4-9a}$$

For Rayleigh's data in Figure 4-7, we suspect that the population standard deviation from air is smaller than that from chemical sources. Using Equations 4-8a and 4-9a, we find that $t_{calculated} = 21.7$ and degrees of freedom $= 7.17 \approx 7$. This value of $t_{calculated}$ still far exceeds values in Table 4-2 for 7 degrees of freedom at 95% or 99.9% confidence.

Case 3. Paired *t* Test for Comparing Individual Differences

In this case, we use two methods to make single measurements on several different samples. No measurement has been duplicated. Do the two methods give the same answer "within experimental error"? Figure 4-8 shows measurements of aluminum in 11 samples of drinking water. Results for Method 1 are in column B and results for Method 2 are in column C. For each sample, the two results are similar, but not identical.

To see if there is a significant difference between the methods, we use the paired *t* test. First, column D computes the difference (d_i) between the two results for each sample. The mean of the 11 differences ($\bar{d} = -2.4_{91}$) is computed in cell D16 and the standard deviation of the 11 differences (s_d) is computed in cell D17.

	A	B	C	D
1	Comparison of two methods for measuring Al			
2				
3	Sample	Method 1	Method 2	Difference
4	number	(μg/L)	(μg/L)	(d_i)
5	1	17.2	14.2	−3.0
6	2	23.1	27.9	4.8
7	3	28.5	21.2	−7.3
8	4	15.3	15.9	0.6
9	5	23.1	32.1	9.0
10	6	32.5	22.0	−10.5
11	7	39.5	37.0	−2.5
12	8	38.7	41.5	2.8
13	9	52.5	42.6	−9.9
14	10	42.6	42.8	0.2
15	11	52.7	41.1	−11.6
16			mean =	−2.491
17			std dev =	6.748
18			$t_{calculated}$ =	1.224
19	D5 = C5-B5			
20	D16 = AVERAGE(D5:D15)			
21	D17 = STDEV(D5:D15)			
22	D18 = ABS(D16)*SQRT(A15)/D17			
23		ABS = absolute value		

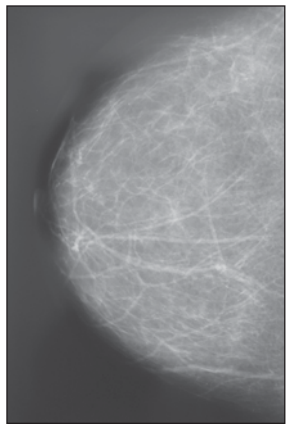
FIGURE 4-8 Measurement of Al by two methods. [Data from P. T. Srinivasan, T. Viraraghavan, and K. S. Subramanian, "Method Development for Drinking Water Aluminum Measurement Using a Graphite Furnace Atomic Absorption Spectrophotometer," *Am. Lab.*, February 2000, p. 76.]

BOX 4-1 Choosing the Null Hypothesis in Epidemiology

One fine morning, I found myself seated on a cross-country flight next to Malcolm Pike, an epidemiologist at the University of Southern California. Epidemiologists employ methods of statistics to guide practices in medicine. Pike was studying the relation between menopausal oestrogen–progestin hormone therapy and breast cancer in women. His study concluded that there was a 7.6% increase in breast cancer risk per year of oestrogen–progestin hormone therapy.[5]

How could such therapy have been approved? Pike explained that tests required by the U.S. Food and Drug Administration are designed to test the null hypothesis that "the treatment does no harm." Instead, he said, the null hypothesis should be "the treatment increases the likelihood of causing breast cancer."

What did he mean? In the field of statistics, the null hypothesis is assumed to be true. Unless you find strong evidence that it is not true, you continue to believe that it is true. In the U.S. legal system, the null hypothesis is that the accused person is innocent. It is up to the prosecution to produce compelling evidence that the accused person is not innocent; failing that, the jury must acquit the defendant. In the hormone therapy example, the null hypothesis is that the treatment does not cause cancer. The burden of the test is to provide compelling evidence that the treatment *does cause* cancer. Pike is saying that if you believe a treatment causes cancer, the null hypothesis should be that the treatment causes cancer. Then it is up to the proponent of the treatment to provide compelling evidence that the treatment *does not* cause cancer. In Pike's words, test the hypothesis that "the obvious is likely to be true!"



White regions of mammogram are denser tissue than dark regions. [allOver photography/Alamy.]

$$s_d = \sqrt{\frac{\sum(d_i - \bar{d})^2}{n - 1}}$$

$$s_d = \sqrt{\frac{(-3.0 - \bar{d})^2 + (4.8 - \bar{d})^2 + \ldots + (0.2 - \bar{d})^2 + (-11.6 - \bar{d})^2}{11 - 1}} = 6.7_{48} \qquad \textbf{(4-10)}$$

Once you have the mean and standard deviation, compute $t_{\text{calculated}}$ with the formula

$$t_{\text{calculated}} = \frac{|\bar{d}|}{s_d}\sqrt{n} \qquad \textbf{(4-11)}$$

where $|\bar{d}|$ is the absolute value of the mean difference, so that $t_{\text{calculated}}$ is always positive. Inserting numbers into Equation 4-11 gives

$$t_{\text{calculated}} = \frac{2.4_{91}}{6.7_{48}}\sqrt{11} = 1.2_{24}$$

We find that $t_{\text{calculated}}$ (1.2_{24}) is less than t_{table} (2.228) listed in Table 4-2 for 95% confidence and 10 degrees of freedom. *There is more than a 5% chance that the two sets of results lie "within experimental error" of each other, so we conclude that the results are not significantly different.* You have now read enough to appreciate Box 4-1.

One-Tailed and Two-Tailed Significance Tests

In Equation 4-7, we sought to compare the mean from four replicate measurements with a certified value. The curve in Figure 4-9a is the t distribution for 3 degrees of freedom. If the certified value lies in the outer 5% of the area under the curve, we reject the null hypothesis and conclude with 95% confidence that the measured mean is not equivalent to the certified value. The critical value of t for rejecting the null hypothesis is 3.182 for 3 degrees of freedom in Table 4-2. In Figure 4-9a, *2.5% of the area* beneath the curve lies above $t = 3.182$ and *2.5% of the area* lies below $t = -3.182$. We call this a *two-tailed test* because we reject the null hypothesis if the certified value lies in the low-probability region on either side of the mean.

If we have a preconceived reason to believe that our method gives systematically low values, we could use the *one-tailed t test* in Figure 4-9b. In this case, we reject the null hypothesis (which states that there is no significant difference between the measured and certified values) if $t_{\text{calculated}}$ is greater than 2.353. Figure 4-9b shows that *5% of the area* beneath the curve lies above $t = 2.353$. We did not consider area at the left side of the curve because we had a reason to believe that our method produces low results, not high results.

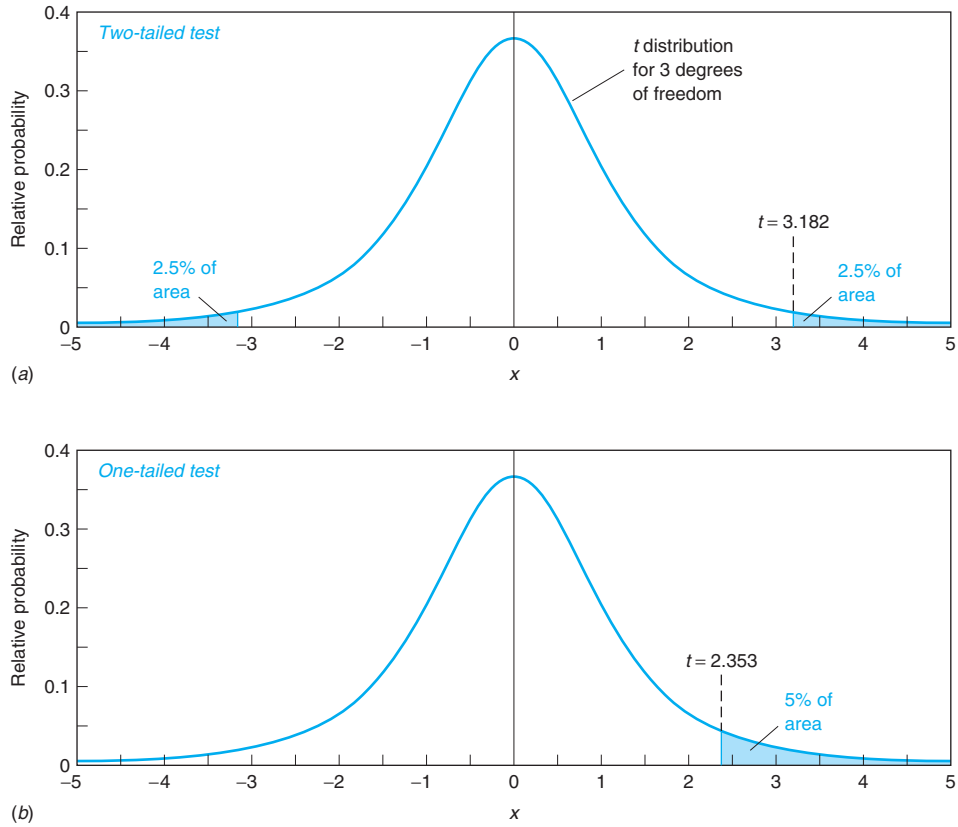


FIGURE 4-9 Student's t distribution for 3 degrees of freedom. In panel *a*, each shaded tail contains 2.5% of the area under the curve. In panel *b*, the single shaded tail contains 5% of the area. The fewer the degrees of freedom, the broader the distribution. As the degrees of freedom increase, the curve approaches a Gaussian curve.

How can you find the value of t that bounds the upper 5% of the area of the curve? Because the t distribution is symmetric, the two-tailed value $t = 2.353$ for 90% confidence in Table 4-2 must be the value we seek, because 5% of the area lies above $t = 2.353$ and 5% of the area lies below $t = -2.353$.

The purpose of this discussion was to inform you of the distinction between one- and two-tailed tests. All t tests in this book will be two-tailed.

Is My Red Blood Cell Count High Today?

At the opening of this chapter, red cell counts on five "normal" days were 5.1, 5.3, 4.8, 5.4, and 5.2×10^6 cells/μL. The question was whether today's count of 5.6×10^6 cells/μL is "significantly" higher than normal? Disregarding the factor of 10^6, the mean of the normal values is $\bar{x} = 5.16$ and the standard deviation is $s = 0.23$. For today's value of 5.6,

$$t_{\text{calculated}} = \frac{|\text{today's count} - \bar{x}|}{s}\sqrt{n} = \frac{|5.16 - 5.6|}{0.23}\sqrt{5} = 4.28$$

What is the probability of finding $t = 4.28$ for 4 degrees of freedom?

In Table 4-2, looking across the row for 4 degrees of freedom, we see that 4.28 lies between the 98% ($t = 3.747$) and 99% ($t = 4.604$) confidence levels. Today's red cell count lies in the upper tail of the curve containing less than 2% of the area of the curve. There is less than a 2% probability of observing a count of 5.6×10^6 cells/μL on "normal" days. It is reasonable to conclude that today's count is elevated.

Find probability with Excel: TDIST(*x*,deg_freedom,tails)

Table 4-2 places the probability of today's red cell count between 1 and 2%. Excel provides a probability with the function TDIST(x,deg_freedom,tails), where x is $t_{\text{calculated}}$, deg_freedom = 4, and tails = 2. The function TDIST(4.28,4,2) returns the value 0.013. Today's red cell count lies in the upper 1.3% of the area of the t-distribution.

4-4 Comparison of Standard Deviations with the *F* Test

To decide whether Rayleigh's two sets of nitrogen masses in Figure 4-7 are "significantly" different from each other, we used the t test. If the standard deviations of two data sets are not significantly different from each other, then we use Equation 4-8 for the t test. If the standard deviations are significantly different, then we use Equation 4-8a instead.

TABLE 4-4 Critical values of $F = s_1^2/s_2^2$ at 95% confidence level

Degrees of freedom for s_2	Degrees of freedom for s_1													
	2	3	4	5	6	7	8	9	10	12	15	20	30	∞
2	19.0	19.2	19.2	19.3	19.3	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.5	19.5
3	9.55	9.28	9.12	9.01	8.94	8.89	8.84	8.81	8.79	8.74	8.70	8.66	8.62	8.53
4	6.94	6.59	6.39	6.26	6.16	6.09	6.04	6.00	5.96	5.91	5.86	5.80	5.75	5.63
5	5.79	5.41	5.19	5.05	4.95	4.88	4.82	4.77	4.74	4.68	4.62	4.56	4.50	4.36
6	5.14	4.76	4.53	4.39	4.28	4.21	4.15	4.10	4.06	4.00	3.94	3.87	3.81	3.67
7	4.74	4.35	4.12	3.97	3.87	3.79	3.73	3.68	3.64	3.58	3.51	3.44	3.38	3.23
8	4.46	4.07	3.84	3.69	3.58	3.50	3.44	3.39	3.35	3.28	3.22	3.15	3.08	2.93
9	4.26	3.86	3.63	3.48	3.37	3.29	3.23	3.18	3.14	3.07	3.01	2.94	2.86	2.71
10	4.10	3.71	3.48	3.33	3.22	3.14	3.07	3.02	2.98	2.91	2.84	2.77	2.70	2.54
11	3.98	3.59	3.36	3.20	3.10	3.01	2.95	2.90	2.85	2.79	2.72	2.65	2.57	2.40
12	3.88	3.49	3.26	3.11	3.00	2.91	2.85	2.80	2.75	2.69	2.62	2.54	2.47	2.30
13	3.81	3.41	3.18	3.02	2.92	2.83	2.77	2.71	2.67	2.60	2.53	2.46	2.38	2.21
14	3.74	3.34	3.11	2.96	2.85	2.76	2.70	2.65	2.60	2.53	2.46	2.39	2.31	2.13
15	3.68	3.29	3.06	2.90	2.79	2.71	2.64	2.59	2.54	2.48	2.40	2.33	2.25	2.07
16	3.63	3.24	3.01	2.85	2.74	2.66	2.59	2.54	2.49	2.42	2.35	2.28	2.19	2.01
17	3.59	3.20	2.96	2.81	2.70	2.61	2.55	2.49	2.45	2.38	2.31	2.23	2.15	1.96
18	3.56	3.16	2.93	2.77	2.66	2.58	2.51	2.46	2.41	2.34	2.27	2.19	2.11	1.92
19	3.52	3.13	2.90	2.74	2.63	2.54	2.48	2.42	2.38	2.31	2.23	2.16	2.07	1.88
20	3.49	3.10	2.87	2.71	2.60	2.51	2.45	2.39	2.35	2.28	2.20	2.12	2.04	1.84
30	3.32	2.92	2.69	2.53	2.42	2.33	2.27	2.21	2.16	2.09	2.01	1.93	1.84	1.62
∞	3.00	2.60	2.37	2.21	2.10	2.01	1.94	1.88	1.83	1.75	1.67	1.57	1.46	1.00

Critical values of F for a one-tailed test of the hypothesis that $s_1 > s_2$. There is a 5% probability of observing F above the tabulated value.

You can compute F for a chosen level of confidence with the Excel function FINV(probability,deg_freedom1,deg_freedom2). The statement "=FINV(0.05,7,6)" reproduces the value F = 4.21 in this table. The statement "=FINV(0.1,7,6)" gives F = 3.01 for 90% confidence.

The ***F* test** tells us whether two standard deviations are "significantly" different from each other. F is the quotient of the squares of the standard deviations:

$$F_{\text{calculated}} = \frac{s_1^2}{s_2^2} \tag{4-12}$$

We always put the larger standard deviation in the numerator so that $F \geq 1$. We test the hypothesis that $s_1 > s_2$ by using the one-tailed F test in Table 4-4. If $F_{\text{calculated}} > F_{\text{table}}$, then the difference is significant.

Use the F test for Case 2 in comparison of means in Section 4-3.

If $F_{\text{calculated}} < F_{\text{table}}$, use Equation 4-8.
If $F_{\text{calculated}} > F_{\text{table}}$, use Equation 4-8a.

The square of the standard deviation is called the *variance*.

EXAMPLE **Is the Standard Deviation from Chemical Decomposition Significantly Greater Than the Standard Deviation from Air in Rayleigh's Data?**

In Table 4-3, the standard deviation from chemical decomposition is $s_1 = 0.001\,38$ ($n_1 = 8$ measurements) and the standard deviation from air is $s_2 = 0.000\,14_3$ ($n_2 = 7$ measurements).

Solution To answer the question, find F with Equation 4-12:

$$F_{\text{calculated}} = \frac{s_1^2}{s_2^2} = \frac{(0.001\,38)^2}{(0.000\,14_3)^2} = 93._1$$

In Table 4-4, look for F_{table} in the column with 7 degrees of freedom for s_1 (because degrees of freedom $= n - 1$) and the row with 6 degrees of freedom for s_2. *Because $F_{calculated}$ (= 93.1) > F_{table} (= 4.21), we accept the hypothesis that $s_1 > s_2$ above the 95% confidence level*. The obvious difference in scatter of the two data sets in Figure 4-7 is highly significant.

Test Yourself If two variances were $s_1^2 = (0.002\,00)^2$ (7 degrees of freedom) and $s_2^2 = (0.001\,00)^2$ (6 degrees of freedom), is the difference significant? (***Answer:*** No. $F_{\text{calculated}} = 4.00 < F_{\text{table}} = 4.21$)

4-5 *t* Tests with a Spreadsheet

To compare Rayleigh's two sets of results in Table 4-3, enter his data in columns B and C of a spreadsheet (Figure 4-10). In rows 13 and 14, we computed the averages and standard deviations, but we did not need to do this.

In Excel 2007, in the Data ribbon, you might find Data Analysis as an option. If not, click the Microsoft Office Button at the upper left of the Excel window. Click Excel Options and Add-Ins. Select Analysis ToolPak and click OK to load the Analysis ToolPak. For future use, follow the same steps to load Solver Add-In. In earlier versions of Excel, you might find Data Analysis in the Tools Menu. If not, go to Tools, Add-Ins, and check both Analysis ToolPak and Solver Add-In. Click OK to load the applications.

Returning to Figure 4-10, we want to test the null hypothesis that the two sets of data are not statistically different. In Excel 2007, in the Data ribbon, select Data Analysis. In earlier versions of Excel, go to the Tools Menu and select Data Analysis. In the window that appears, select t-Test: Two-Sample Assuming Equal Variances. Click OK. The next window asks you in which cells the data are located. Write B5:B12 for Variable 1 and C5:C12 for Variable 2. The routine ignores the blank space in cell B12. For the Hypothesized Mean Difference enter 0 and for Alpha enter 0.05. Alpha is the level of probability to which we are testing the difference in the means. With Alpha = 0.05, we are at the 95% confidence level. For Output Range, select cell E1 and click OK.

Excel goes to work and prints results in cells E1 to G13 of Figure 4-10. Mean values are in cells F3 and G3. Cells F4 and G4 give *variance*, which is the square of the standard deviation. Cell F6 gives *pooled variance* computed with Equation 4-9. That equation was painful to use by hand. Cell F8 shows degrees of freedom (df) = 13 and $t_{\text{calculated}}$ (t Stat) = 20.2 from Equation 4-8 appears in cell F9.

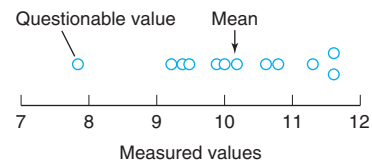
At this point in Section 4-3, we consulted Table 4-2 to find that t_{table} lies between 2.228 and 2.131 for 95% confidence and 13 degrees of freedom. Excel gives us the critical value of t (2.160) in cell F13 of Figure 4-10. Because $t_{\text{calculated}}$ (= 20.2) > t_{table} (= 2.160), we conclude that the two means are not the same. The difference is significant. Cell F12 states that the probability of observing these two mean values and standard deviations by random chance if the mean values were really the same is 3×10^{-11}. The difference is *highly* significant. For any value of $P \leq 0.05$ in cell F12, we reject the *null hypothesis* and conclude that the means *are different*.

	A	B	C	D	E	F	G
1	Analysis of Rayleigh's Data				t-Test: Two-Sample Assuming Equal Variances		
2						*Variable 1*	*Variable 2*
3		Mass of gas (g) collected from			Mean	2.310109	2.299473
4		air	chemical		Variance	2.03E-08	1.9E-06
5		2.31017	2.30143		Observations	7	8
6		2.30986	2.29890		Pooled Variance	1.03E-06	
7		2.31010	2.29816		Hypothesized Mean Diff	0	
8		2.31001	2.30182		df	13	
9		2.31024	2.29869		t Stat	20.21372	
10		2.31010	2.29940		P(T<=t) one-tail	1.66E-11	
11		2.31028	2.29849		t Critical one-tail	1.770932	
12			2.29889		P(T<=t) two-tail	3.32E-11	
13	Average	2.31011	2.29947		t Critical two-tail	2.160368	
14	Std Dev	0.00014	0.00138				
15					t-Test: Two-Sample Assuming Unequal Variances		
16	B13 = AVERAGE(B5:B12)					*Variable 1*	*Variable 2*
17	B14 = STDEV(B5:B12)				Mean	2.310109	2.299473
18					Variance	2.03E-08	1.9E-06
19					Observations	7	8
20					Hypothesized Mean Diff	0	
21					df	7	
22					t Stat	21.68022	
23					P(T<=t) one-tail	5.6E-08	
24					t Critical one-tail	1.894578	
25					P(T<=t) two-tail	1.12E-07	
26					t Critical two-tail	2.364623	

FIGURE 4-10 Spreadsheet for comparing mean values of Rayleigh's measurements in Table 4-3.

The F test in Equation 4-12 told us that the standard deviations of Rayleigh's two experiments are different. Therefore, we can select the other t test found in the Analysis ToolPak. Select t-Test: Two-Sample Assuming Unequal Variances and fill in the blanks as before. Results based on Equations 4-8a and 4-9a are displayed in cells E15 to G26 of Figure 4-10. Just as we found in Section 4-3, the degrees of freedom are 7 (cell F21) and $t_{\text{calculated}} = 21.7$ (cell F22). Because $t_{\text{calculated}}$ is greater than the critical value of t (2.36 in cell F26), we reject the null hypothesis and conclude that the two means *are* significantly different.

4-6 Grubbs Test for an Outlier



Students dissolved zinc from a galvanized nail and measured the mass lost by the nail to tell how much of the nail was zinc. Here are 12 results:

Mass loss (%): 10.2, 10.8, 11.6, 9.9, 9.4, 7.8, 10.0, 9.2, 11.3, 9.5, 10.6, 11.6

The value 7.8 appears out of line. A datum that is far from other points is called an **outlier.** Should 7.8 be discarded before averaging the rest of the data or should 7.8 be retained?

We answer this question with the **Grubbs test.** First compute the average ($\bar{x} = 10.16$) and the standard deviation ($s = 1.11$) of the complete data set (all 12 points in this example). Then compute the Grubbs statistic G, defined as

The Grubbs test is recommended by the International Standards Organization and the American Society for Testing and Materials in place of the Q test, which was formerly used in this book.

Grubbs test:

$$G_{\text{calculated}} = \frac{|\text{questionable value} - \bar{x}|}{s} \tag{4-13}$$

where the numerator is the absolute value of the difference between the suspected outlier and the mean value. *If $G_{\text{calculated}}$ is greater than G in Table 4-5, the questionable point should be discarded.*

In our example, $G_{\text{calculated}} = |7.8 - 10.16| / 1.11 = 2.13$. In Table 4-5, $G_{\text{table}} = 2.285$ for 12 observations. *Because $G_{\text{calculated}} < G_{\text{table}}$, the questionable point should be retained.* There is more than a 5% chance that the value 7.8 is a member of the same population as the other measurements.

Common sense must prevail. If you know that a result is low because you spilled part of a solution, then the probability that the result is wrong is 100% and the datum should be discarded. Any datum based on a faulty procedure should be discarded, no matter how well it fits the rest of the data.

TABLE 4-5 Critical values of G for rejection of outlier

Number of observations	G (95% confidence)
4	1.463
5	1.672
6	1.822
7	1.938
8	2.032
9	2.110
10	2.176
11	2.234
12	2.285
15	2.409
20	2.557

$G_{calculated} = |\text{questionable value} - \text{mean}|/s$. *If* $G_{calculated} > G_{table}$, *the value in question can be rejected with 95% confidence. Values in this table are for a one-tailed test, as recommended by ASTM.*

SOURCE: *ASTM E 178-02 Standard Practice for Dealing with Outlying Observations, http://webstore.ansi.org; F. E. Grubbs and G. Beck, Technometrics* ***1972,*** *14, 847.*

4-7 The Method of Least Squares

For most chemical analyses, the response of the procedure must be evaluated for known quantities of analyte (called *standards*) so that the response to an unknown quantity can be interpreted. For this purpose, we commonly prepare a **calibration curve,** such as the one for caffeine in Figure 0-13. Most often, we work in a region where the calibration curve is a straight line.

We use the **method of least squares** to draw the "best" straight line through experimental data points that have some scatter and do not lie perfectly on a straight line.[6] The best line will be such that some of the points lie above and some lie below the line. We will learn to estimate the uncertainty in a chemical analysis from the uncertainties in the calibration curve and in the measured response to replicate samples of unknown.

Finding the Equation of the Line

The procedure we use assumes that the errors in the y values are substantially greater than the errors in the x values.[7] This condition is often true in a calibration curve in which the experimental response (y values) is less certain than the quantity of analyte (x values). A second assumption is that uncertainties (standard deviations) in all y values are similar.

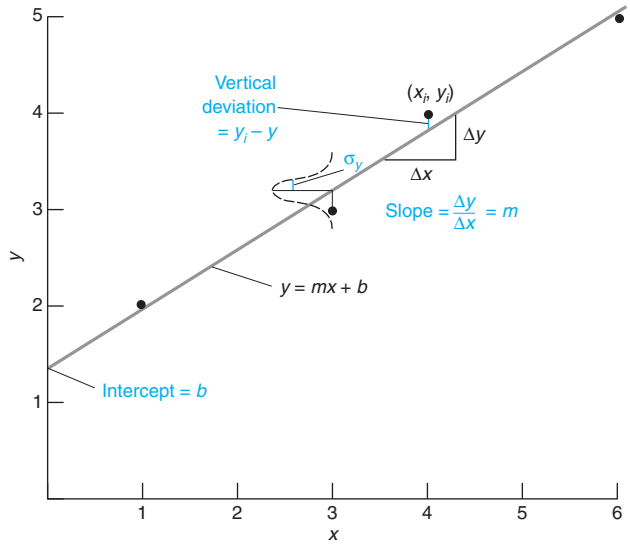
Suppose we seek to draw the best straight line through the points in Figure 4-11 by minimizing the vertical deviations between the points and the line. We minimize only the vertical deviations because we assume that uncertainties in y values are much greater than uncertainties in x values.

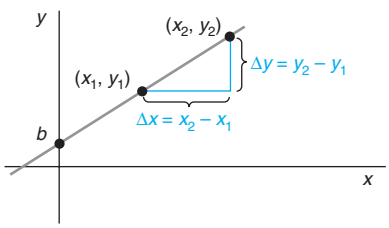
Let the equation of the line be

Equation of straight line:

$$y = mx + b \tag{4-14}$$

FIGURE 4-11 Least-squares curve fitting. The Gaussian curve drawn over the point (3,3) is a schematic indication of the fact that each value of y_i is normally distributed about the straight line. That is, the most probable value of y will fall on the line, but there is a finite probability of measuring y some distance from the line.





Equation for a straight line: $y = mx + b$

Slope $(m) = \dfrac{\Delta y}{\Delta x} = \dfrac{y_2 - y_1}{x_2 - x_1}$

y-Intercept (b) = crossing point on y-axis

in which m is the **slope** and b is the ***y*-intercept.** The vertical deviation for the point (x_i, y_i) in Figure 4-11 is $y_i - y$, where y is the ordinate of the straight line when $x = x_i$.

$$\text{Vertical deviation} = d_i = y_i - y = y_i - (mx_i + b) \tag{4-15}$$

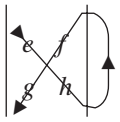
Some of the deviations are positive and some are negative. Because we wish to minimize the magnitude of the deviations irrespective of their signs, we square all the deviations so that we are dealing only with positive numbers:

$$d_i^2 = (y_i - y)^2 = (y_i - mx_i - b)^2$$

Because we minimize the squares of the deviations, this is called the *method of least squares*. It can be shown that minimizing the squares of the deviations (rather than simply their magnitudes) corresponds to assuming that the set of y values is the most probable set.

Finding values of m and b that minimize the sum of the squares of the vertical deviations involves some calculus, which we omit. We express the final solution for slope and intercept in terms of *determinants*, which summarize certain arithmetic operations. The **determinant** $\begin{vmatrix} e & f \\ g & h \end{vmatrix}$ represents the value $eh - fg$. So, for example,

To evaluate the determinant, multiply the diagonal elements $e \times h$ and then subtract the product of the other diagonal elements $f \times g$.



$$\begin{vmatrix} 6 & 5 \\ 4 & 3 \end{vmatrix} = (6 \times 3) - (5 \times 4) = -2$$

The slope and the intercept of the "best" straight line are found to be

$$\text{Least-squares "best" line} \begin{cases} \text{Slope:} \quad m = \begin{vmatrix} \Sigma(x_i y_i) & \Sigma x_i \\ \Sigma y_i & n \end{vmatrix} \div D & \textbf{(4-16)} \\ \text{Intercept:} \quad b = \begin{vmatrix} \Sigma(x_i^2) & \Sigma(x_i y_i) \\ \Sigma x_i & \Sigma y_i \end{vmatrix} \div D & \textbf{(4-17)} \end{cases}$$

Translation of least-squares equations:

$$m = \frac{n\Sigma(x_i y_i) - \Sigma x_i \Sigma y_i}{n\Sigma(x_i^2) - (\Sigma x_i)^2}$$

$$b = \frac{\Sigma(x_i^2)\Sigma y_i - \Sigma(x_i y_i)\Sigma x_i}{n\Sigma(x_i^2) - (\Sigma x_i)^2}$$

where D is

$$D = \begin{vmatrix} \Sigma(x_i^2) & \Sigma x_i \\ \Sigma x_i & n \end{vmatrix} \tag{4-18}$$

and n is the number of points.

Let's use these equations to find the slope and intercept of the best straight line through the four points in Figure 4-11. The work is set out in Table 4-6. Noting that $n = 4$ and putting the various sums into the determinants in Equations 4-16, 4-17, and 4-18 gives

$$m = \begin{vmatrix} 57 & 14 \\ 14 & 4 \end{vmatrix} \div \begin{vmatrix} 62 & 14 \\ 14 & 4 \end{vmatrix} = \frac{(57 \times 4) - (14 \times 14)}{(62 \times 4) - (14 \times 14)} = \frac{32}{52} = 0.615\,38$$

$$b = \begin{vmatrix} 62 & 57 \\ 14 & 14 \end{vmatrix} \div \begin{vmatrix} 62 & 14 \\ 14 & 4 \end{vmatrix} = \frac{(62 \times 14) - (57 \times 14)}{(62 \times 4) - (14 \times 14)} = \frac{70}{52} = 1.346\,15$$

TABLE 4-6 Calculations for least-squares analysis

x_i	y_i	x_iy_i	x_i^2	$d_i(= y_i - mx_i - b)$	d_i^2
1	2	2	1	0.038 46	0.001 479 3
3	3	9	9	−0.192 31	0.036 982
4	4	16	16	0.192 31	0.036 982
6	5	30	36	−0.038 46	0.001 479 3
$\Sigma x_i = 14$	$\Sigma y_i = 14$	$\Sigma(x_iy_i) = 57$	$\Sigma(x_i^2) = 62$		$\Sigma(d_i^2) = 0.076\,923$

The equation of the best straight line through the points in Figure 4-11 is therefore

$$y = 0.615\,38x + 1.346\,15$$

We tackle the question of significant figures for m and b in the next section.

EXAMPLE **Finding Slope and Intercept with a Spreadsheet**

Excel has functions called SLOPE and INTERCEPT whose use is illustrated here:

	A	B	C	D	E	F
1	x	y			Formulas:	
2	1	2		slope =		
3	3	3		0.61538	D3 = SLOPE(B2:B5,A2:A5)	
4	4	4		intercept =		
5	6	5		1.34615	D5 = INTERCEPT(B2:B5,A2:A5)	

The slope in cell D3 is computed with the formula "=SLOPE(B2:B5,A2:A5)", where B2:B5 is the range containing the y values and A2:A5 is the range containing x values.

Test Yourself Change the second value of x from 3 to 3.5 and find the slope and intercept. (***Answer:*** 0.610 84, 1.285 71)

How Reliable Are Least-Squares Parameters?

To estimate the uncertainties (expressed as standard deviations) in the slope and intercept, an uncertainty analysis must be performed on Equations 4-16 and 4-17. Because the uncertainties in m and b are related to the uncertainty in measuring each value of y, we first estimate the standard deviation that describes the population of y values. This standard deviation, σ_y, characterizes the little Gaussian curve inscribed in Figure 4-11.

We estimate σ_y, the population standard deviation of all y values, by calculating s_y, the standard deviation, for the four measured values of y. The deviation of each value of y_i from the center of its Gaussian curve is $d_i = y_i - y = y_i - (mx_i + b)$. The standard deviation of these vertical deviations is

$$\sigma_y \approx s_y = \sqrt{\frac{\sum(d_i - \bar{d})^2}{(\text{degrees of freedom})}} \qquad \textbf{(4-19)}$$

Equation 4-19 is analogous to Equation 4-2.

But the average deviation, $\bar{d}$, is 0 for the best straight line, so the numerator of Equation 4-19 reduces to $\Sigma(d_i^2)$.

The *degrees of freedom* is the number of independent pieces of information available. For n data points, there are n degrees of freedom. If you were calculating the standard deviation of n points, you would first find the average to use in Equation 4-2. This calculation leaves $n - 1$ degrees of freedom in Equation 4-2 because only $n - 1$ pieces of information are available in addition to the average. If you know $n - 1$ values and you also know their average, then the nth value is fixed and you can calculate it.

For Equation 4-19, we began with n points. Two degrees of freedom were lost in determining the slope and the intercept. Therefore, $n - 2$ degrees of freedom remain. Equation 4-19 becomes

$$s_y = \sqrt{\frac{\sum(d_i^2)}{n - 2}} \qquad \textbf{(4-20)}$$

where d_i is given by Equation 4-15.

Uncertainty analysis for Equations 4-16 and 4-17 leads to the following results:

$$\text{Standard deviation of slope and intercept} \begin{cases} s_m^2 = \dfrac{s_y^2 n}{D} & \textbf{(4-21)} \\[2ex] s_b^2 = \dfrac{s_y^2 \sum (x_i^2)}{D} & \textbf{(4-22)} \end{cases}$$

where s_m is an estimate of the standard deviation of the slope, s_b is an estimate of the standard deviation of the intercept, s_y is given by Equation 4-20, and D is given by Equation 4-18.

At last, we can assign significant figures to the slope and the intercept in Figure 4-11. In Table 4-6, we see that $\Sigma(d_i^2) = 0.076\,923$. Putting this number into Equation 4-20 gives

$$s_y^2 = \frac{0.076\,923}{4 - 2} = 0.038\,462$$

Now, we can plug numbers into Equations 4-21 and 4-22 to find

$$s_m^2 = \frac{s_y^2 n}{D} = \frac{(0.038\,462)(4)}{52} = 0.002\,958\,6 \Rightarrow s_m = 0.054\,39$$

$$s_b^2 = \frac{s_y^2 \sum (x_i^2)}{D} = \frac{(0.038\,462)(62)}{52} = 0.045\,859 \Rightarrow s_b = 0.214\,15$$

Combining the results for m, s_m, b, and s_b, we write

The first digit of the uncertainty is the last significant figure. We often retain extra, insignificant digits to prevent round-off errors in further calculations.

$$\text{Slope:} \quad \begin{matrix} 0.615\,38 \\ \pm 0.054\,39 \end{matrix} = 0.62 \pm 0.05 \quad \text{or} \quad 0.61_5 \pm 0.05_4 \qquad \textbf{(4-23)}$$

$$\text{Intercept:} \quad \begin{matrix} 1.346\,15 \\ \pm 0.214\,15 \end{matrix} = 1.3 \pm 0.2 \quad \text{or} \quad 1.3_5 \pm 0.2_1 \qquad \textbf{(4-24)}$$

where the uncertainties represent one standard deviation. *The first decimal place of the standard deviation is the last significant figure of the slope or intercept*. Many scientists write results such as 1.35 ± 0.21 to avoid excessive round-off.

If you want to express the uncertainty as a confidence interval instead of one standard deviation, multiply the uncertainties in Equations 4-23 and 4-24 by the appropriate value of Student's t from Table 4-2 for $n - 2$ degrees of freedom.

The 95% confidence interval for the slope is

$$\pm t s_m = \pm(4.303)(0.054) = \pm 0.23$$

based on degrees of freedom $= n - 2 = 2$. The confidence interval is $\pm t s_m$, not $\pm t s_m/\sqrt{n}$, because $\sqrt{n}$ is already implicit in s_m.

EXAMPLE Finding s_y, s_m, and s_b with a Spreadsheet

The Excel function LINEST returns the slope and intercept and their uncertainties in a table (a *matrix*). As an example, enter x and y values in columns A and B. Then highlight the 3-row × 2-column region E3:F5 with your mouse. This block of cells is selected to contain the output of the LINEST function. In the Insert Function window, go to Statistical and double click on LINEST. The new window asks for four inputs to the function. For y values, enter B2:B5. Then enter A2:A5 for x values. The next two entries are both "TRUE". The first TRUE tells Excel that we want to compute the y-intercept of the least-squares line and not force the intercept to be 0. The second TRUE tells Excel to print out the standard deviations as well as the slope and intercept. The formula you have just entered is "=LINEST(B2:B5,A2:A5,TRUE,TRUE)". Click OK and the slope appears in cell E3.

	A	B	C	D	E	F	G
1	x	y			Output from LINEST		
2	1	2			Slope	Intercept	
3	3	3		Parameter	0.61538	1.34615	
4	4	4		Std Dev	0.05439	0.21414	
5	6	5		R^2	0.98462	0.19612	Std Dev (y)
6							
7	Highlight cells E3:F5						
8	Type "= LINEST(B2:B5,A2:A5,TRUE,TRUE)"						
9	Press CTRL+SHIFT+ENTER (on PC)						
10	Press COMMAND+RETURN (on Mac)						

The output of LINEST should be a matrix, not a single number. What went wrong? To tell the computer that you want a matrix, go back and highlight cells E3:F5. "=LINEST(B2:B5,A2:A5,TRUE,TRUE)" appears once again in the formula line. Now press CONTROL+SHIFT+ENTER on a PC or COMMAND(⌘)+RETURN on a Mac. Excel dutifully prints out a matrix in cells E3:F5. Write labels around the block to indicate what is in each cell. The slope and intercept are on the top line. The second line contains s_m and s_b. Cell F5 contains s_y and cell E5 contains a quantity called R^2, which is defined in Equation 5-2 and is a measure of the goodness of fit of the data to the line. The closer R^2 is to unity, the better the fit.

Test Yourself Change the second value of x from 3 to 3.5 and apply LINEST. What is the value of s_y from LINEST? (***Answer:*** 0.364 70)

4-8 Calibration Curves

A *calibration curve* shows the response of an analytical method to known quantities of analyte.[8] Table 4-7 gives real data from a protein analysis that produces a colored product. A *spectrophotometer* measures the absorbance of light, which is proportional to the quantity of protein analyzed. Solutions containing known concentrations of analyte are called **standard solutions.** Solutions containing all reagents and solvents used in the analysis, but no deliberately added analyte, are called **blank solutions.** Blanks measure the response of the analytical procedure to impurities or interfering species in the reagents.

Sections 17-1 and 17-2 discuss absorption of light and define the term *absorbance*. We will use concepts from these two sections throughout this book. You may want to read these sections for background.

When we scan across the three absorbance values in each row of Table 4-7, the number 0.392 seems out of line: It is inconsistent with the other values for 15.0 μg, and the range of values for the 15.0-μg samples is much bigger than the range for the other samples. The linear relation between the average values of absorbance up to the 20.0-μg sample also indicates that the value 0.392 is in error (Figure 4-12). We choose to omit 0.392 from subsequent calculations.

It is reasonable to ask whether all three absorbances for the 25.0-μg samples are low for some unknown reason, because this point falls below the straight line in Figure 4-12. Repetition of this analysis shows that the 25.0-μg point is consistently below the straight line and there is nothing "wrong" with the data in Table 4-7.

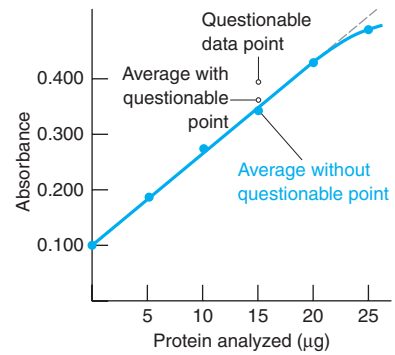


FIGURE 4-12 Average absorbance values in Table 4-7 versus micrograms of protein analyzed. Averages for 0 to 20 μg of protein lie on a straight line if the questionable datum 0.392 at 15 μg is omitted.

Constructing a Calibration Curve

We adopt the following procedure for constructing a calibration curve:

Step 1 Prepare known samples of analyte covering a range of concentrations expected for unknowns. Measure the response of the analytical procedure to these standards to generate data like the left half of Table 4-7.

Step 2 Subtract the average absorbance (0.099_3) of the *blank* samples from each measured absorbance to obtain *corrected absorbance*. The blank measures the response of the procedure when no protein is present.

Absorbance of the blank can arise from the color of starting reagents, reactions of impurities, and reactions of interfering species. Blank values can vary from one set of reagents to another, but corrected absorbance should not.

Step 3 Make a graph of corrected absorbance versus quantity of protein analyzed (Figure 4-13). Use the least-squares procedure to find the best straight line through the linear portion of the data, up to and including 20.0 μg of protein (14 points, including the 3 corrected blanks, in the shaded portion of Table 4-7). Find the slope and intercept and uncertainties with Equations 4-16, 4-17, 4-20, 4-21, and 4-22. The results are

$$m = 0.016\,3_0 \qquad s_m = 0.000\,2_2 \qquad s_y = 0.005_9$$
$$b = 0.004_7 \qquad s_b = 0.002_6$$

TABLE 4-7 Spectrophotometer data used to construct calibration curve

Amount of protein (μg)	Absorbance of independent samples			Range	Corrected absorbance		
0	0.099	0.099	0.100	0.001	-0.000_3	-0.000_3	0.000_7
5.0	0.185	0.187	0.188	0.003	0.085_7	0.087_7	0.088_7
10.0	0.282	0.272	0.272	0.010	0.182_7	0.172_7	0.172_7
15.0	0.345	0.347	(0.392)	0.047	0.245_7	0.247_7	—
20.0	0.425	0.425	0.430	0.005	0.325_7	0.325_7	0.330_7
25.0	0.483	0.488	0.496	0.013	0.383_7	0.388_7	0.396_7

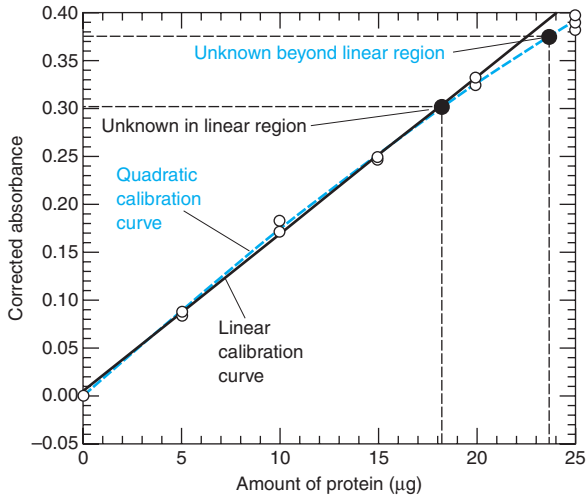


FIGURE 4-13 Calibration curve for protein analysis in Table 4-7. The equation of the solid straight line fitting the 14 data points (open circles) from 0 to 20 μg, derived by the method of least squares, is $y = 0.016\,3_0\ (\pm 0.000\,2_2)x + 0.004_7\ (\pm 0.002_6)$ with $s_y = 0.005_9$. The equation of the dashed quadratic curve that fits all 17 data points from 0 to 25 μg, determined by a nonlinear least squares procedure[6] is $y = -1.1_7(\pm 0.2_1) \times 10^{-4}\,x^2 + 0.018\,5_8\ (\pm 0.000\,4_6)x - 0.000\,7\ (\pm 0.001\,0)$ with $s_y = 0.004_6$.

The equation of the linear calibration line is

Equation of calibration line:

$$y(\pm s_y) = [m(\pm s_m)]x + [b(\pm s_b)]$$

$$\underbrace{\text{absorbance}}_{y} = m \times \underbrace{(\mu\text{g of protein})}_{x} + b$$

$$= (0.016\,3_0)(\mu\text{g of protein}) + 0.004_7 \qquad \textbf{(4-25)}$$

where y is the corrected absorbance (= observed absorbance – blank absorbance).

Step 4 If you analyze an unknown at a future time, run a blank at the same time. Subtract the new blank absorbance from the unknown absorbance to obtain corrected absorbance.

EXAMPLE Using a Linear Calibration Curve

An unknown protein sample gave an absorbance of 0.406 and a blank had an absorbance of 0.104. How many micrograms of protein are in the unknown?

Solution The corrected absorbance is 0.406 – 0.104 = 0.302, which lies on the linear portion of the calibration curve in Figure 4-13. Equation 4-25 therefore becomes

$$\mu\text{g of protein} = \frac{\text{absorbance} - 0.004_7}{0.016\,3_0} = \frac{0.302 - 0.004_7}{0.016\,3_0} = 18.2_4\ \mu\text{g} \qquad \textbf{(4-26)}$$

Test Yourself What mass of protein gives a corrected absorbance of 0.250? (***Answer:*** 15.0_5 μg)

We prefer calibration procedures with a **linear response,** in which the corrected analytical signal (= signal from sample – signal from blank) is proportional to the quantity of analyte. Although we try to work in the linear range, you can obtain valid results beyond the linear region (>20 μg) in Figure 4-13. The dashed curve that goes up to 25 μg of protein comes from a least-squares fit of the data to the equation $y = ax^2 + bx + c$ (Box 4-2).

BOX 4-2 Using a Nonlinear Calibration Curve

Consider an unknown whose corrected absorbance of 0.375 lies beyond the linear region in Figure 4-13. We can fit all the data points with the quadratic equation[6]

$$y = -1.17 \times 10^{-4}x^2 + 0.018\,58x - 0.000\,7 \qquad \textbf{(a)}$$

To find the quantity of protein, substitute the corrected absorbance into Equation a:

$$0.375 = -1.17 \times 10^{-4}x^2 + 0.018\,58x - 0.000\,7$$

This equation can be rearranged to

$$1.17 \times 10^{-4}x^2 - 0.018\,58x + 0.375\,7 = 0$$

which is a quadratic equation of the form

$$ax^2 + bx + c = 0$$

whose two possible solutions are

$$x = \frac{-b + \sqrt{b^2 - 4ac}}{2a} \qquad x = \frac{-b - \sqrt{b^2 - 4ac}}{2a}$$

Substituting $a = 1.17 \times 10^{-4}$, $b = -0.018\,58$, and $c = 0.375\,7$ into these equations gives

$$x = 135\ \mu\text{g} \qquad x = 23.8\ \mu\text{g}$$

Figure 4-13 tells us that the correct choice is 23.8 μg, not 135 μg.

The **linear range** of an analytical method is the analyte concentration range over which response is proportional to concentration. A related quantity in Figure 4-14 is **dynamic range**—the concentration range over which there is a measurable response to analyte, even if the response is not linear.

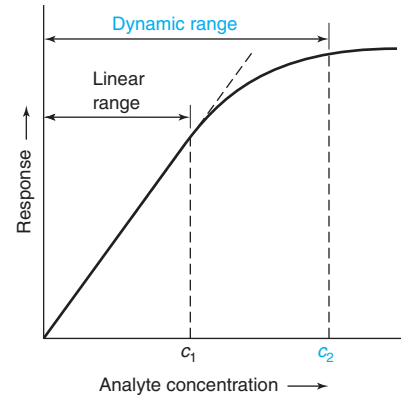


FIGURE 4-14 Calibration curve illustrating linear and dynamic ranges.

Good Practice

Always make a graph of your data. The graph gives you an opportunity to reject bad data or the stimulus to repeat a measurement or decide that a straight line is not an appropriate function.

It is not reliable to extrapolate any calibration curve, linear or nonlinear, beyond the measured range of standards. Measure standards in the entire concentration range of interest.

At least six calibration concentrations and two replicate measurements of unknown are recommended. The most rigorous procedure is to make each calibration solution independently from a certified material. Avoid serial dilution of a single stock solution. Serial dilution propagates any systematic error in the stock solution. Measure calibration solutions in random order, not in consecutive order by increasing concentration.

Propagation of Uncertainty with a Calibration Curve

In the preceding example, an unknown with a corrected absorbance of $y = 0.302$ had a protein content of $x = 18.2_4$ μg. What is the uncertainty in the number 18.2_4? Propagation of uncertainty for fitting the equation $y = mx + b$ (but not $y = mx$) gives the following result:[1,9]

$$\text{Uncertainty in } x\ (= s_x) = \frac{s_y}{|m|}\sqrt{\frac{1}{k} + \frac{1}{n} + \frac{(y - \bar{y})^2}{m^2 \sum (x_i - \bar{x})^2}} \qquad \textbf{(4-27)}$$

y = corrected absorbance of unknown = 0.302
x_i = μg of protein in standards in Table 4-7
= (0, 0, 0, 5.0, 5.0, 5.0, 10.0, 10.0, 10.0, 15.0, 15.0, 20.0, 20.0, 20.0)
$\bar{y}$ = average of 14 y values = 0.161_8
$\bar{x}$ = average of 14 x values = 9.64_3 μg

where s_y is the standard deviation of y (Equation 4-20), $|m|$ is the absolute value of the slope, k is the number of replicate measurements of the unknown, n is the number of data points for the calibration line (14 in Table 4-7), $\bar{y}$ is the mean value of y for the points on the calibration line, x_i are the individual values of x for the points on the calibration line, and $\bar{x}$ is the mean value of x for the points on the calibration line. For a single measurement of the unknown, $k = 1$ and Equation 4-27 gives $s_x = \pm 0.3_9$ μg. Four replicate unknowns ($k = 4$) with an average corrected absorbance of 0.302 reduce the uncertainty to $\pm 0.2_3$ μg.

The confidence interval for x is $\pm ts_x$, where t is Student's t (Table 4-2) for $n - 2$ degrees of freedom. If $s_x = 0.2_3$ μg and $n = 14$ points (12 degrees of freedom), the 95% confidence interval for x is $\pm ts_x = \pm(2.179)(0.2_3) = \pm 0.5_0$ μg.

To find values of t that are not in Table 4-2, use the Excel function TINV. For 12 degrees of freedom and 95% confidence, the function TINV(0.05,12) returns $t = 2.179$.

4-9 A Spreadsheet for Least Squares

Figure 4-15 implements least-squares analysis, including propagation of error with Equation 4-27. Enter values of x and y in columns B and C. Then select cells B10:C12. Enter the formula "=LINEST(C4:C7,B4:B7,TRUE,TRUE)" and press CONTROL+SHIFT+ENTER on a PC or COMMAND(⌘)+RETURN on a Mac. LINEST returns m, b, s_m, s_b, R^2, and s_y in cells B10:C12. Write labels in cells A10:A12 and D10:D12 so that you know what the numbers in cells B10:C12 mean.

Cell B14 gives the number of data points with the formula "=COUNT(B4:B7)". Cell B15 computes the mean value of y. Cell B16 computes the sum $\Sigma(x_i - \bar{x})^2$ that we need for Equation 4-27. This sum is common enough that Excel has a built-in function called DEVSQ that you can find in the Statistics menu of the Insert Function window.

Enter the measured mean value of y for replicate measurements of the unknown in cell B18. In cell B19, enter the number of replicate measurements of the unknown. Cell B20 computes the value of x corresponding to the measured mean value of y. Cell B21 uses Equation 4-27 to find the uncertainty (the standard deviation) in the value of x for the unknown. If you want a confidence interval for x, multiply s_x times Student's t from Table 4-2 for $n - 2$ degrees of freedom and the desired confidence level.

95% confidence interval for x in Figure 4-15:
$x \pm ts_x = 2.232\,5 \pm (4.303)(0.373\,5)$
$= 2.2 \pm 1.6$
(degrees of freedom = $n - 2 = 2$)

We always want a graph to see if the calibration points lie on a straight line. Follow the instructions in Section 2-11 to plot the calibration data as a scatter plot with only markers (no line yet). To add a straight line in Excel 2007, click on the chart to obtain the Chart Tools ribbon. Select Layout, then Trendline and Choose More Trendline Options. Select Linear and Display Equation on chart. The least-squares straight line and its equation appear on the

	A	B	C	D
1	Least-Squares Spreadsheet			
2				
3	Highlight cells B10:C12	x	y	
4	Type "= LINEST(C4:C7,	1	2	
5	B4:B7,TRUE,TRUE)	3	3	
6	For PC, press	4	4	
7	CTRL+SHIFT+ENTER	6	5	
8	For Mac, press			
9	COMMAND+RETURN	LINEST output:		
10	m	0.6154	1.3462	b
11	s_m	0.0544	0.2141	s_b
12	R^2	0.9846	0.1961	s_y
13				
14	n =	4	B14 = COUNT(B4:B7)	
15	Mean y =	3.5	B15 = AVERAGE(C4:C7)	
16	$\Sigma(x_i - \text{mean } x)^2$ =	13	B16 = DEVSQ(B4:B7)	
17				
18	Measured y =	2.72	Input	
19	k = Number of replicate measurements of y =	1	Input	
20	Derived x =	2.2325	B20 = (B18-C10)/B10	
21	s_x =	0.3735	B21 = (C12/B10)*SQRT((1/B19)+(1/B14)+((B18-B15)^2)/(B10^2*B16))	

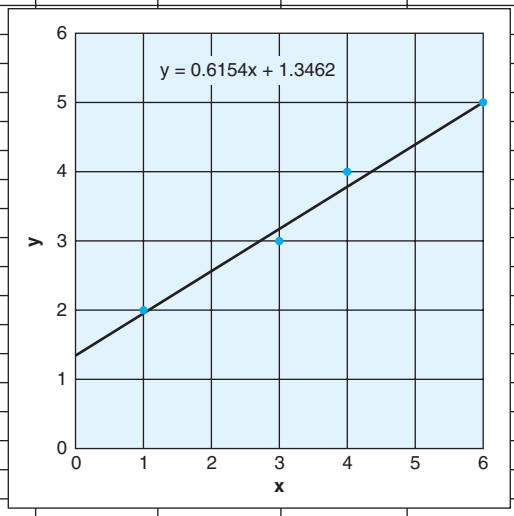


FIGURE 4-15 Spreadsheet for linear least-squares analysis.

graph. Use the Forecast section of the Format Trendline box to extend the line forward or backward beyond the range of data. The Format Trendline box also allows you to select the color and style of the line.

In earlier versions of Excel, click on one data point and they will all be highlighted. In the Chart menu, select Add Trendline. In the window that appears, select Linear. Go to Options in the Trendline box and select Display Equation on Chart. Double click on the line and you can adjust its thickness and appearance. Double clicking on the equation allows you to modify its format. Double click on the straight line and select Options. In the Forecast box, you can extend the trendline Forward and Backward as far as you like.

Adding Error Bars to a Graph

Error bars on a graph help us judge the quality of the data and the fit of a curve to the data. Consider the data in Table 4-7. Let's plot the mean absorbance of columns 2 to 4 versus sample mass in column 1. Then we will add error bars corresponding to the 95% confidence interval for each point. Figure 4-16 lists mass in column A and mean absorbance in column B. The standard deviation of absorbance is given in column C. The 95% confidence interval for absorbance is computed in column D with the formula in the margin. Student's $t = 4.303$ can be found for 95% confidence and $3 - 1 = 2$ degrees of freedom in Table 4-2. Alternatively, compute Student's t with the function TINV(0.05,2) in cell B11. The parameters for TINV are 0.05 for 95% confidence and 2 for degrees of freedom. The 95% confidence interval in cell D4 is computed with "=$B$11*C4/SQRT(3)". You should be able to plot mean absorbance (y) in column B versus protein mass (x) in column A.

Confidence interval $= \pm ts/\sqrt{n}$
t = Student's t for 95% confidence and $n - 1 = 2$ degrees of freedom
s = standard deviation
n = number of values in average = 3

To add error bars in Excel 2007, click on one of the points to highlight all points on the graph. In Chart Tools, Layout, select Error Bars and choose More Error Bars Options. For Error Amount, choose Custom and Specify Value. For both Positive Value and Negative Value, enter D4:D9. You just told the spreadsheet to use 95% confidence intervals for error bars. When you click OK, the graph has both x and y error bars. Click on any x error bar and press Delete to remove all x error bars.

To add error bars in earlier versions of Excel, click on one of the points to highlight all points on the graph. In the Format menu, choose Selected Data Series. Select Y Error Bars and a window appears. Click Custom. Click in the positive error bars box and select cells D4:D9. Click the negative error bars box and select cells D4:D9 again. You just told Excel to use values in cells D4:D9 for the lengths of the error bars. Click OK and error bars appear in the graph.

	A	B	C	D	E	F	G	H
1	Adding error bars to a graph							
2	Protein	Mean	Std dev	95%				
3	(μg)	absorbance	absorbance	confidence				
4	0	0.0993	0.00058	0.0014				
5	5	0.1867	0.00153	0.0038				
6	10	0.2753	0.00577	0.0143				
7	15	0.3613	0.02658	0.0660				
8	20	0.4267	0.00289	0.0072				
9	25	0.4890	0.00656	0.0163				
10								
11	TINV(0.05,2) =	4.303						
12	Student's t (95% conf, 2 deg freedom)							
13	95% confidence interval: D4 = $B$11*C4/SQRT(3)							
14	Excel 2007 instructions:							
15	To insert y error bars for data in column D:							
16	Click one point on the graph to highlight all points							
17	In Chart Tools, Layout, select Error Bars							
18	Choose More Error Bars Options							
19	Click Custom and click Specify Value							
20	For Positive Error Value, highlight D4:D9							
21	For Negative Error Value, highlight D4:D9							
22	Click OK and error bars will appear on the chart							
23	Click on one x error bar and press Delete to remove all x error bars							

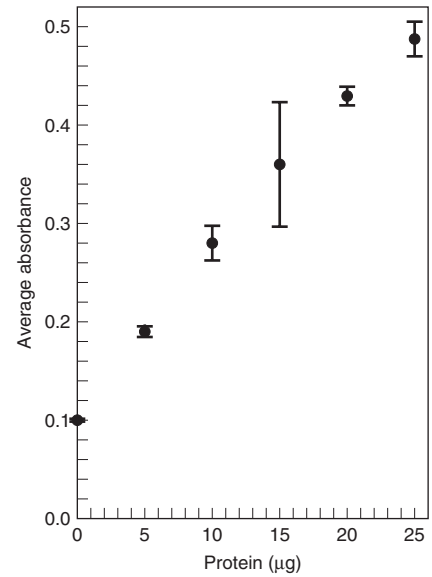


FIGURE 4-16 Adding 95% confidence error bars to a graph.

Terms to Understand

average
blank solution
calibration curve
confidence interval
degrees of freedom
determinant
dynamic range
F test
Gaussian distribution
Grubbs test
intercept
linear range
linear response
mean
method of least squares
outlier
slope
standard deviation
standard deviation of the mean
standard solution
Student's *t*
t test
variance

Summary

The results of many measurements of an experimental quantity follow a Gaussian distribution. The measured mean, $\bar{x}$, approaches the true mean, μ, as the number of measurements becomes very large. The broader the distribution, the greater is σ, the standard deviation. For *n* measurements, an estimate of the standard deviation is given by $s = \sqrt{[\Sigma(x_i + \bar{x})^2]/(n - 1)}$. About two-thirds of all measurements lie within $\pm 1\sigma$, and 95% lie within 2σ. The probability of observing a value within a certain interval is proportional to the area of that interval.

Student's *t* is used to find confidence intervals ($\mu = \bar{x} \pm ts/\sqrt{n}$) and to compare mean values measured by different methods. The *F* test is used to decide whether two standard deviations are significantly different from each other. The Grubbs test helps you to decide whether or not a questionable datum should be discarded. It is best to repeat the measurement several times to increase the probability that your decision to accept or reject a datum is correct.

A calibration curve shows the response of a chemical analysis to known quantities (standard solutions) of analyte. When there is a linear response, the corrected analytical signal (= signal from sample – signal from blank) is proportional to the quantity of analyte. Blank solutions are prepared from the same reagents and solvents used to prepare standards and unknowns, but blanks have no intentionally added analyte. The blank tells us the response of the procedure to impurities or interfering species in the reagents. The blank value is subtracted from measured values of standards prior to constructing the calibration curve. The blank value is subtracted from the response of an unknown prior to computing the quantity of analyte in the unknown.

The method of least squares is used to determine the equation of the "best" straight line through experimental data points. Equations 4-16 to 4-18 and 4-20 to 4-22 provide the least-squares slope and intercept and their standard deviations. Equation 4-27 estimates the uncertainty in *x* from a measured value of *y* with a calibration curve. A spreadsheet simplifies least-squares calculations and graphical display of the results.

Exercises

4-A. For the numbers 116.0, 97.9, 114.2, 106.8, and 108.3, find the mean, standard deviation, range, and 90% confidence interval for the mean. Using the Grubbs test, decide whether the number 97.9 should be discarded.

4-B. *Spreadsheet for standard deviation*. Let's create a spreadsheet to compute the mean and standard deviation of a column of numbers in two different ways. The spreadsheet here is a template for this exercise.

	A	B	C	D
1	Computing standard deviation			
2				
3		Data = x	x-mean	(x-mean)^2
4		17.4		
5		18.1		
6		18.2		
7		17.9		
8		17.6		
9	sum =			
10	mean =			
11	std dev =			
12				
13	Formulas:	B9 =		
14		B10 =		
15		B11 =		
16		C4 =		
17		D4 =		
18		D9 =		
19				
20	Calculations using built-in functions:			
21	sum =			
22	mean =			
23	std dev =			

(a) Reproduce the template on your spreadsheet. Cells B4 to B8 contain the data (x values) whose mean and standard deviation we will compute.

(b) Write a formula in cell B9 to compute the sum of numbers in B4 to B8.

(c) Write a formula in cell B10 to compute the mean value.

(d) Write a formula in cell C4 to compute (x – mean), where x is in cell B4 and the mean is in cell B10. Use Fill Down to compute values in cells C5 to C8.

(e) Write a formula in cell D4 to compute the square of the value in cell C4. Use Fill Down to compute values in cells D5 to D8.

(f) Write a formula in cell D9 to compute the sum of the numbers in cells D4 to D8.

(g) Write a formula in cell B11 to compute the standard deviation.

(h) Use cells B13 to B18 to document your formulas.

(i) Now we are going to simplify life by using formulas built into the spreadsheet. In cell B21 type "=SUM(B4:B8)", which means find the sum of numbers in cells B4 to B8. Cell B21 should display the same number as cell B9. In general, you will not know what functions are available and how to write them. In Excel 2007, use the Formulas ribbon and Insert Function to find SUM. In earlier versions of Excel, find the Function menu under Insert.

(j) Select cell B22. Go to Insert Function and find AVERAGE. When you type "=AVERAGE(B4:B8)" in cell B22, its value should be the same as B10.

(k) For cell B23, find the standard deviation function ("=STDEV(B4:B8)") and check that the value agrees with cell B11.

4-C. Use Table 4-1 for this exercise. Suppose that the mileage at which 10 000 sets of automobile brakes had been 80% worn through was recorded. The average was 62 700, and the standard deviation was 10 400 miles.

(a) What fraction of brakes is expected to be 80% worn in less than 40 860 miles?

(b) What fraction is expected to be 80% worn at a mileage between 57 500 and 71 020 miles?

4-D. Use the NORMDIST spreadsheet function to answer these questions about the brakes described in Exercise 4-C:

(a) What fraction of brakes is expected to be 80% worn in less than 45 800 miles?

(b) What fraction is expected to be 80% worn at a mileage between 60 000 and 70 000 miles?

4-E. A reliable assay shows that the ATP (adenosine triphosphate) content of a certain cell type is 111 μmol/100 mL. You developed a new assay, which gave the following values for replicate analyses: 117, 119, 111, 115, 120 μmol/100 mL (average = $116._4$). Does your result agree with the known value at the 95% confidence level?

4-F. Traces of toxic, man-made hexachlorohexanes in North Sea sediments were extracted by a known process and by two new procedures, and measured by chromatography.

Method	Concentration found (pg/g)	Standard deviation (pg/g)	Number of replications
Conventional	34.4	3.6	6
Procedure A	42.9	1.2	6
Procedure B	51.1	4.6	6

SOURCE: *D. Sterzenbach, B. W. Wenclawiak, and V. Weigelt, Anal. Chem.* ***1997***, *69, 831.*

(a) Are the concentrations parts per million, parts per billion, or something else?

(b) Is the standard deviation for procedure B significantly different from that of the conventional procedure?

(c) Is the mean concentration found by procedure B significantly different from that of the conventional procedure?

(d) Answer the same two questions as parts **(b)** and **(c)** to compare procedure A to the conventional procedure.

4-G. *Calibration curve*. (You can do this exercise with your calculator, but it is more easily done by the spreadsheet in Figure 4-15.) In the Bradford protein determination, the color of a dye changes from brown to blue when it binds to protein. Absorbance of light is measured.

Protein (μg):	0.00	9.36	18.72	28.08	37.44
Absorbance at 595 nm:	0.466	0.676	0.883	1.086	1.280

(a) Find the equation of the least-squares straight line through these points in the form $y = [m(\pm s_m)]x + [b(\pm s_b)]$ with a reasonable number of significant figures.

(b) Make a graph showing the experimental data and the calculated straight line.

(c) An unknown protein sample gave an absorbance of 0.973. Calculate the number of micrograms of protein in the unknown and estimate its uncertainty.

Problems

Gaussian Distribution

4-1. What is the relation between the standard deviation and the precision of a procedure? What is the relation between standard deviation and accuracy?

4-2. Use Table 4-1 to state what fraction of a Gaussian population lies within the following intervals:

(a) $\mu \pm \sigma$ **(c)** μ to $+\sigma$ **(e)** $-\sigma$ to -0.5σ
(b) $\mu \pm 2\sigma$ **(d)** μ to $+0.5\sigma$

4-3. The ratio of the number of atoms of the isotopes ^{69}Ga and ^{71}Ga in eight samples from different sources was measured in an effort to understand differences in reported values of the atomic mass of gallium:

Sample	^{69}Ga/^{71}Ga	Sample	^{69}Ga/^{71}Ga
1	1.526 60	5	1.528 94
2	1.529 74	6	1.528 04
3	1.525 92	7	1.526 85
4	1.527 31	8	1.527 93

SOURCE: *J. W. Gramlich and L. A. Machlan, Anal. Chem.* ***1985***, *57, 1788.*

Find the **(a)** mean, **(b)** standard deviation, and **(c)** variance. **(d)** Write the mean and standard deviation together with an appropriate number of significant digits.

4-4. (a) Calculate the fraction of bulbs in Figure 4-1 expected to have a lifetime greater than 1 005.3 h.

(b) What fraction of bulbs is expected to have a lifetime between 798.1 and 901.7 h?

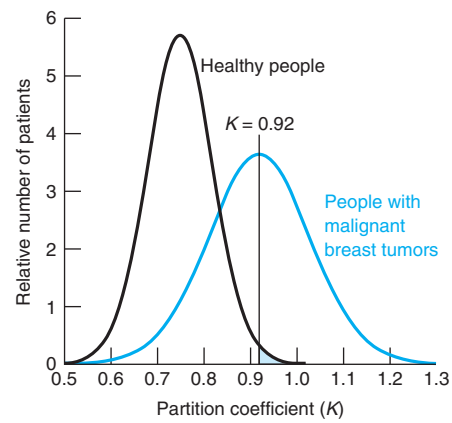
(c) Use the Excel NORMDIST function to find the fraction of bulbs expected to have a lifetime between 800 and 900 h.

4-5. Blood plasma proteins of patients with malignant breast tumors differ from proteins of healthy people in their solubility in the presence of various polymers. When the polymers dextran and poly(ethylene glycol) are mixed with water, a two-phase mixture is formed. When plasma proteins of tumor patients are added, the distribution of proteins between the two phases is different from that of plasma proteins of a healthy person. The distribution coefficient (K) for any substance is defined as K = [concentration of the substance in phase A] / [concentration of the substance in phase B]. Proteins of healthy people have a mean distribution coefficient of 0.75 with a standard deviation of 0.07. For the proteins of people with cancer, the mean is 0.92 with a standard deviation of 0.11.

(a) Suppose that K were used as a diagnostic tool and that a positive indication of cancer is taken as $K \geq 0.92$. What fraction of people with tumors would have a false negative indication of cancer because $K < 0.92$?

(b) What fraction of healthy people would have a false positive indication of cancer? This number is the fraction of healthy people with $K \geq 0.92$, shown by the shaded area in the adjoining graph. Estimate an answer with Table 4-1 and obtain a more exact result with the NORMDIST function in Excel.

(c) Vary the first argument of the NORMDIST function to select a distribution coefficient that would identify 75% of people with tumors. That is, 75% of patients with tumors would have K above the selected distribution coefficient. With this value of K, what fraction of healthy people would have a false positive result indicating they have a tumor?



Distribution coefficients of plasma proteins from healthy people and from people with malignant breast tumors. [Data from B. Y. Zaslavsky, "Bioanalytical Applications of Partitioning in Aqueous Polymer Two-Phase Systems," *Anal. Chem.* ***1992***, *64, 765A.*]

4-6. The equation for the Gaussian curve in Figure 4-1 is

$$y = \frac{(\text{total bulbs})(\text{hours per bar})}{s\sqrt{2\pi}} e^{-(x-\bar{x})^2/2s^2}$$

where $\bar{x}$ is the mean value (845.2 h), s is the standard deviation (94.2 h), total bulbs = 4 768, and hours per bar (= 20) is the width of each bar in Figure 4-1. Set up a spreadsheet like the one on the next page to calculate the coordinates of the Gaussian curve in Figure 4-1 from 500 to 1 200 h in 25-h intervals. Note the heavy use of parentheses in the formula at the bottom of the spreadsheet to force the computer to do the arithmetic as intended. Use Excel to graph your results.

4-7. Repeat Problem 4-6 but use the values 50, 100, and 150 for the standard deviation. Superimpose all three curves on a single graph.

Confidence Intervals, *t* Test, *F* Test, and Grubbs Test

4-8. What is the meaning of a confidence interval?

4-9. What fraction of vertical bars in Figure 4-5a is expected to include the population mean (10 000) if many experiments are carried out? Why are the 90% confidence interval bars longer than the 50% bars in Figure 4-5?

	A	B	C
1	Gaussian curve for light bulbs (Fig 4-1)		
2			
3	mean =	x (hours)	y (bulbs)
4	845.2	500	0.49
5	std dev =	525	1.25
6	94.2	550	2.98
7	total bulbs =	600	13.64
8	4768	700	123.11
9	hours per bar =	800	359.94
10	20	845.2	403.85
11	sqrt(2 pi) =	900	340.99
12	2.506628	1000	104.67
13		1100	10.41
14		1200	0.34
15	Formula for cell C4 =		
16	($A$8*$A$10/($A$6*$A$12))*		
17	EXP(-((B4-$A$4)^2)/(2*$A$6^2))		

Spreadsheet for Problem 4-6

4-10. List the three different cases that we studied for comparison of means, and write the equations used in each case.

4-11. The percentage of an additive in gasoline was measured six times with the following results: 0.13, 0.12, 0.16, 0.17, 0.20, 0.11%. Find the 90% and 99% confidence intervals for the percentage of the additive.

4-12. Sample 8 of Problem 4-3 was analyzed seven times, with $\bar{x} = 1.527\,93$ and $s = 0.000\,07$. Find the 99% confidence interval for sample 8.

4-13. A trainee in a medical lab will be released to work on her own when her results agree with those of an experienced worker at the 95% confidence level. Results for a blood urea nitrogen analysis are shown below.

Trainee: $\bar{x} = 14.5_7$ mg/dL $s = 0.5_3$ mg/dL $n = 6$ samples

Experienced worker: $\bar{x} = 13.9_5$ mg/dL $s = 0.4_2$ mg/dL $n = 5$ samples

(a) What does the abbreviation dL stand for?

(b) Should the trainee be released to work alone?

4-14. The CdSe content (g/L) of nanocrystals was measured by two methods for six different samples. Do the two methods differ significantly at the 95% confidence level?

Sample	Method 1 Anodic stripping	Method 2 Atomic absorption
A	0.88	0.83
B	1.15	1.04
C	1.22	1.39
D	0.93	0.91
E	1.17	1.08
F	1.51	1.31

SOURCE: *E. Kuçur, F. M. Boldt, S. Cavaliere-Jaricont, J. Ziegler, and T. Nann, Anal. Chem.* ***2007****, 79, 8987.*

4-15. Now we use a built-in routine in Excel for the paired t test to see if the two methods in Problem 4-14 produce significantly different results. Enter the data for Methods 1 and 2 into two columns of a spreadsheet. For Excel 2007, find Data Analysis in the Data ribbon. In earlier versions of Excel, find Data Analysis in the Tools menu. If Data Analysis does not appear, follow the instructions at the beginning of Section 4-5 to load this software. Select Data Analysis and then select t-Test: Paired Two Sample for Means. Follow the instructions of Section 4-5, and the routine will print out information including $t_{\text{calculated}}$ (labeled t Stat) and t_{table} (labeled t Critical two-tail). You should reproduce the results of Problem 4-14.

4-16. Two methods were used to measure fluorescence lifetime of a dye. Are the standard deviations significantly different? Are the means significantly different?

Quantity	Method 1	Method 2
Mean lifetime (ns)	1.382	1.346
Standard deviation (ns)	0.025	0.039
Number of measurements	4	4

SOURCE: *N. Boens et al., Anal. Chem.* ***2007****, 79, 2137.*

4-17. Do the following two sets of measurements of $^6Li/^7Li$ in a Standard Reference Material give statistically equivalent results?

Method 1	Method 2
0.082 601	0.081 83
0.082 621	0.081 86
0.082 589	0.082 05
0.082 617	0.082 06
0.082 598	0.082 15
	0.082 08

SOURCE: *S. Ahmed, N. Jabeen, and E. ur Rehman, Anal. Chem.* ***2002****, 74, 4133; L. W. Green, J. J. Leppinen, and N. L. Elliot, Anal. Chem.* ***1988****, 60, 34.*

4-18. If you measure a quantity four times and the standard deviation is 1.0% of the average, can you be 90% confident that the true value is within 1.2% of the measured average?

4-19. Students measured the concentration of HCl in a solution by titrating with different indicators to find the end point.

Indicator	Mean HCl concentration (M) (± standard deviation)	Number of measurements
1. Bromothymol blue	0.095 65 ± 0.002 25	28
2. Methyl red	0.086 86 ± 0.000 98	18
3. Bromocresol green	0.086 41 ± 0.001 13	29

SOURCE: *D. T. Harvey, J. Chem. Ed.* ***1991****, 68, 329.*

Is the difference between indicators 1 and 2 significant at the 95% confidence level? Answer the same question for indicators 2 and 3.

4-20. Hydrocarbons in the cab of an automobile were measured during trips on the New Jersey Turnpike and trips through the Lincoln Tunnel connecting New York and New Jersey.[10] The concentrations (± standard deviations) of *m*- and *p*-xylene were

Turnpike: $31.4 \pm 30.0\ \mu g/m^3$ (32 measurements)

Tunnel: $52.9 \pm 29.8\ \mu g/m^3$ (32 measurements)

Do these results differ at the 95% confidence level? At the 99% confidence level?

4-21. A Standard Reference Material is certified to contain 94.6 ppm of an organic contaminant in soil. Your analysis gives values of 98.6, 98.4, 97.2, 94.6, and 96.2 ppm. Do your results differ from the expected result at the 95% confidence level? If you made one more measurement and found 94.5, would your conclusion change?

4-22. Nitrite (NO_2^-) was measured by two methods in rainwater and unchlorinated drinking water. The results ± standard deviation (number of samples) are

Sample source	Gas chromatography	Spectrophotometry
Rainwater	0.069 ± 0.005 mg/L (n = 7)	0.063 ± 0.008 mg/L (n = 5)
Drinking water	0.078 ± 0.007 mg/L (n = 5)	0.087 ± 0.008 mg/L (n = 5)

SOURCE: *I. Sarudi and I. Nagy, Talanta* ***1995****, 42, 1099.*

(a) Do the two methods agree with each other at the 95% confidence level for both rainwater and drinking water?

(b) For each method, does the drinking water contain significantly more nitrite than the rainwater (at the 95% confidence level)?

4-23. Should the value 216 be rejected from the set of results 192, 216, 202, 195, and 204?

Linear Least Squares

4-24. A straight line is drawn through the points (3.0, -3.87×10^4), (10.0, -12.99×10^4), (20.0, -25.93×10^4), (30.0, -38.89×10^4), and (40.0, -51.96×10^4) to give $m = -1.298\ 72 \times 10^4$, $b = 256.695$, $s_m = 13.190$, $s_b = 323.57$, and $s_y = 392.9$. Express the slope and intercept and their uncertainties with reasonable significant figures.

4-25. Here is a least-squares problem that you can do by hand with a calculator. Find the slope and intercept and their standard deviations for the straight line drawn through the points $(x,y) = (0,1)$, (2,2), and (3,3). Make a graph showing the three points and the line. Place error bars ($\pm s_y$) on the points.

4-26. Set up a spreadsheet to reproduce Figure 4-15. *Add error bars:* Follow the procedure on page 90. Use s_y for the + and – error.

4-27. *Excel LINEST function*. Enter the following data in a spreadsheet and use LINEST to find slope, intercept, and standard deviations. Use Excel to draw a graph of the data and add a trendline. Draw error bars of $\pm s_y$ on the points.

x:	3.0	10.0	20.0	30.0	40.0
y:	–0.074	–1.411	–2.584	–3.750	–5.407

Calibration Curves

4-28. Explain the following statement: "The validity of a chemical analysis ultimately depends on measuring the response of the analytical procedure to known standards."

4-29. Suppose that you carry out an analytical procedure to generate a linear calibration curve like that shown in Figure 4-13. Then you analyze an unknown and find an absorbance that gives a negative concentration for the analyte. What does this mean?

4-30. Using the linear calibration curve in Figure 4-13, find the quantity of unknown protein that gives a measured absorbance of 0.264 when a blank has an absorbance of 0.095.

4-31. Consider the least-squares problem in Figure 4-11.

(a) Suppose that a single new measurement produces a y value of 2.58. Find the corresponding x value and its uncertainty.

(b) Suppose you measure y four times and the average is 2.58. Calculate the uncertainty based on four measurements, not one.

4-32. Consider the linear calibration curve in Figure 4-13, which is derived from the 14 corrected absorbances in the shaded region at the right side of Table 4-7. Create a least-squares spreadsheet like Figure 4-15 to compute the equation of the line and the standard deviations of the parameters. Suppose that you find absorbance values of 0.265, 0.269, 0.272, and 0.258 for four identical samples of unknown and absorbances of 0.099, 0.091, 0.101, and 0.097 for four blanks. Find the corrected absorbance by subtracting the average blank from the average absorbance of the unknown. Calculate the amount of protein and its uncertainty in the unknown.

4-33. Here are mass spectrometric signals for methane in H_2:

CH_4 (vol%):	0	0.062	0.122	0.245	0.486	0.971	1.921
Signal (mV):	9.1	47.5	95.6	193.8	387.5	812.5	1 671.9

(a) Subtract the blank value (9.1) from all other values. Then use the method of least squares to find the slope and intercept and their uncertainties. Construct a calibration curve.

(b) Replicate measurements of an unknown gave 152.1, 154.9, 153.9, and 155.1 mV, and a blank gave 8.2, 9.4, 10.6, and 7.8 mV. Subtract the average blank from the average unknown to find the average corrected signal for the unknown.

(c) Find the concentration of the unknown and its uncertainty.

4-34. *Nonlinear calibration curve.* Following the procedure in Box 4-2, find how many micrograms (μg) of protein are contained in a sample with a corrected absorbance of 0.350 in Figure 4-13.

4-35. *Logarithmic calibration curve.* Calibration data spanning five orders of magnitude for an electrochemical determination of *p*-nitrophenol are given in the table. (The blank has already been subtracted from the measured current.) If you try to plot these data on a linear graph extending from 0 to 310 μg/mL and from 0 to 5 260 nA, most of the points will be bunched up near the origin. To handle data with such a large range, a logarithmic plot is helpful.

p-Nitrophenol (μg/mL)	Current (nA)	*p*-Nitrophenol (μg/mL)	Current (nA)
0.010 0	0.215	3.00	66.7
0.029 9	0.846	10.4	224
0.117	2.65	31.2	621
0.311	7.41	107	2 020
1.02	20.8	310	5 260

SOURCE: *Data from Figure 4 of L. R. Taylor, Am. Lab., February 1993, p. 44.*

(a) Make a graph of log(current) versus log(concentration). Over what range is the log-log calibration linear?

(b) Find the equation of the line in the form log (current) = $m \times$ log (concentration) + b.

(c) Find the concentration of *p*-nitrophenol corresponding to a signal of 99.9 nA.

4-36. *Confidence interval for calibration curve*. To use a calibration curve based on n points, we measure a new value of y and calculate the corresponding value of x. The one-standard-deviation uncertainty in x, s_x, is given by Equation 4-27. We express a *confidence interval* for x, using Student's t:

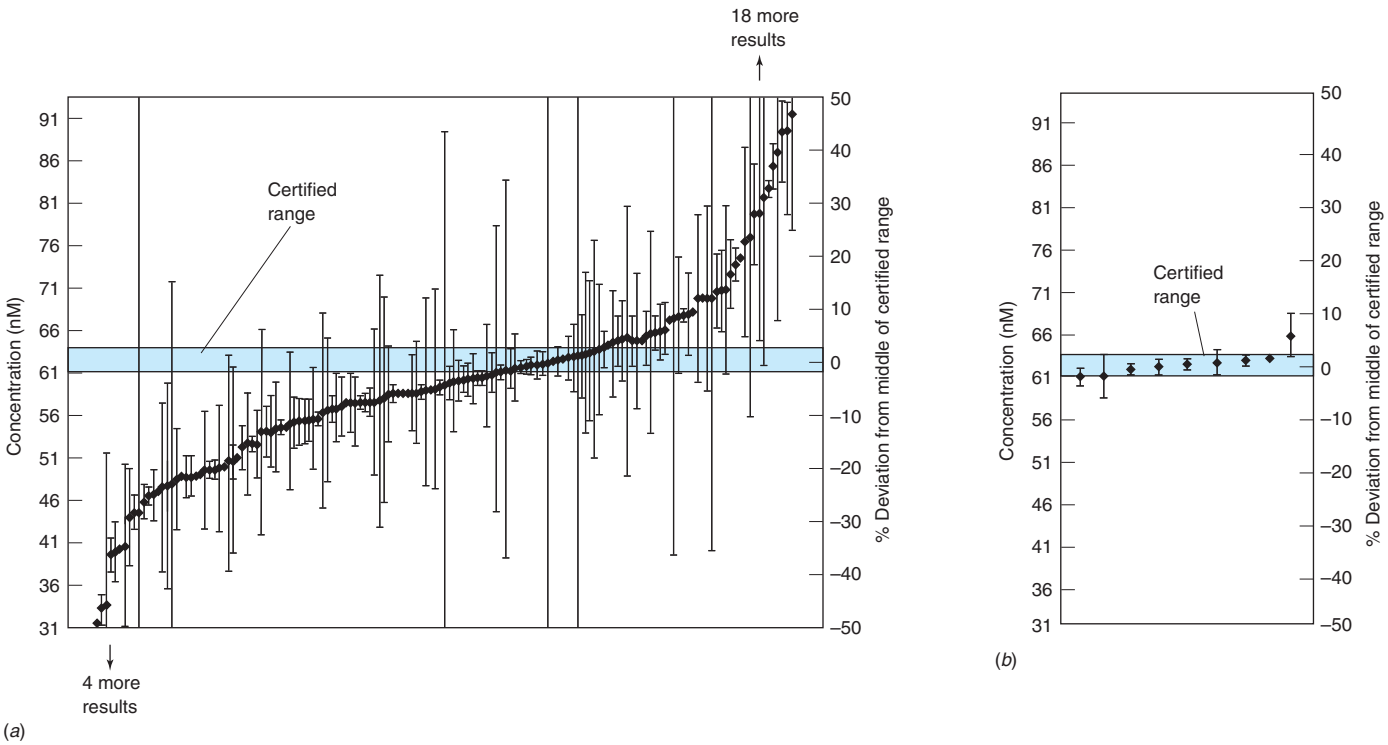
$$\text{Confidence interval} = x \pm ts_x$$

where t is taken from Table 4-2 for $n - 2$ degrees of freedom.

A calibration curve based on $n = 10$ known points was used to measure the protein in an unknown. The results were protein = 15.2_2 ($\pm 0.4_6$) μg, where $s_x = 0.4_6$ μg. Find the 90% and 99% confidence intervals for protein in the unknown.

5 Quality Assurance and Calibration Methods

THE NEED FOR QUALITY ASSURANCE



(*a*) Scattered measurements of lead in river water by different laboratories, each of which employed a recognized quality management system. (*b*) Reproducible results from national measurement institutes. [From P. De Bièvre and P. D. P. Taylor, "'Demonstration' vs. 'Designation' of Measurement Competence: The Need to Link Accreditation to Metrology," *Fresenius J. Anal. Chem.* **2000**, *368*, 567.]

The Institute for Reference Materials and Measurements in Belgium conducts an International Measurement Evaluation Program to allow laboratories to assess the reliability of their analyses. Panel *a* shows results for lead in river water. Of 181 labs, 18 reported results more than 50% above and 4 reported results more than 50% below the certified level of 62.3 ± 1.3 nM. Even though most labs in the study employed recognized quality management procedures, a large fraction of results did not include the certified range. Panel *b* shows that when this same river water was analyzed by nine different national measurement institutes, where the most care is taken, all results were close to the certified range.

This example illustrates that there is no guarantee that results are reliable, even if they are obtained by "accredited" laboratories using accepted procedures. A good way to assess the reliability of a lab working for you is to provide the lab with "blind" samples—similar to your unknowns—for which you know the "right" answer but the analyst does not. If the lab does not find the known result, there is a problem. Periodic blind check samples are required to demonstrate continuing reliability.

Data quality standards:
- Get the right data
- Get the data right
- Keep the data right

[Nancy W. Wentworth, U.S. Environmental Protection Agency.[1]]

Quality assurance is what we do to get the right answer for our purpose. The answer should have sufficient accuracy and precision to support subsequent decisions. There is no point in spending extra money to obtain a more accurate or more precise answer if it is not necessary. This chapter describes basic issues and procedures in quality assurance[2] and introduces two more calibration methods. In Chapter 4, we discussed how to make a calibration curve. In this chapter, we describe *standard addition* and *internal standards*.

5-1 Basics of Quality Assurance

"Suppose you are cooking for some friends. While making spaghetti sauce, you taste it, season it, taste it some more. Each tasting is a sampling event with a quality control test. You can taste the whole batch because there is only one batch. Now suppose you run a spaghetti sauce plant that makes 1 000 jars a day. You can't taste each one, so you decide to taste three a day, one each at 11 A.M., 2 P.M., and 5 P.M. If the three jars all taste OK, you conclude all 1 000 are OK. Unfortunately, that may not be true, but the relative risk—that a jar has too much or too little seasoning—is not very important because you agree to refund the money of any customer who is dissatisfied. If the number of refunds is small, say, 100 a year, there is no apparent benefit in tasting 4 jars a day." There would be 365 additional tests to avoid refunds on 100 jars, giving a net loss of 265 jars worth of profit.

Quotation from Ed Urbansky. Section 5-1 is adapted from a description written by Ed Urbansky.

In analytical chemistry, the product is not spaghetti sauce but, rather, raw data, treated data, and results. *Raw data* are individual values of a measured quantity, such as peak areas from a chromatogram or volumes from a buret. *Treated data* are concentrations or amounts found by applying a calibration procedure to the raw data. *Results* are what we ultimately report, such as the mean, standard deviation, and confidence interval, after applying statistics to treated data.

Raw data: individual measurements

Treated data: concentrations derived from raw data by use of calibration method

Results: quantities reported after statistical analysis of treated data

Use Objectives

An important goal of quality assurance is making sure that results meet the customer's needs. If you manufacture a drug whose therapeutic dose is just a little less than the lethal dose, you should be more careful than if you make spaghetti sauce. The kind of data that you collect and the way in which you collect them depend on how you plan to use those data. A bathroom scale does not have to measure mass to the nearest milligram, but a drug tablet required to contain 2 mg of active ingredient probably cannot contain 2 ± 1 mg. Writing clear, concise **use objectives** for data and results is a critical step in quality assurance and helps prevent misuse of data and results.

Use objective: states purpose for which results will be used

Here is an example of a use objective. Drinking water is usually disinfected with chlorine, which kills microorganisms. Unfortunately, chlorine also reacts with organic matter in water to produce "disinfection by-products"—compounds that might harm humans. A disinfection facility was planning to introduce a new chlorination process and wrote the following analytical use objective:

> Analytical data and results shall be used to determine whether the modified chlorination process results in at least a 10% reduction of formation of selected disinfection by-products.

The new process was expected to decrease the disinfection by-products. The use objective says that uncertainty in the analysis must be small enough that a 10% decrease in selected by-products is clearly distinguishable from experimental error. In other words, is an observed decrease of 10% real?

Specifications

Once you have use objectives, you are ready to write **specifications** stating how good the numbers need to be and what precautions are required in the analytical procedure. How shall samples be taken and how many are needed? Are special precautions required to protect samples and ensure that they are not degraded? Within practical restraints, such as cost, time, and limited amounts of material available for analysis, what level of accuracy and precision will satisfy the use objectives? What rate of false positives or false negatives is acceptable? These questions need to be answered in detailed specifications.

Specifications might include

- sampling requirements
- accuracy and precision
- rate of false results
- selectivity
- sensitivity
- acceptable blank values
- recovery of fortification
- calibration checks
- quality control samples

Quality assurance begins with sampling. We must collect representative samples, and analyte must be preserved after sample is collected. If our sample is not representative or if analyte is lost after collection, then even the most accurate analysis is meaningless.

What do we mean by *false positives* and *false negatives*? Suppose you must certify that a contaminant in drinking water is below a legal limit. A **false positive** says that the concentration exceeds the legal limit when, in fact, the concentration is below the limit. A **false negative** says that the concentration is below the limit when it is actually above the limit. Even well-executed procedures produce some false conclusions because of the statistical nature of sampling and measurement. For drinking water, it is more important to have a low rate of false negatives than a low rate of false positives. It would be worse to certify that contaminated water is safe than to certify that safe water is contaminated. Drug testing of

athletes is designed to minimize false positives so that an innocent athlete is not falsely accused of doping. In Section 5-2, we will see that there is a tradeoff between false positives, false negatives, and the *detection limit* of an analytical method.

In choosing a method, we also consider selectivity and sensitivity. **Selectivity** (also called *specificity*) means being able to distinguish analyte from other species in the sample (avoiding interference). **Sensitivity** is the capability of responding reliably and measurably to changes in analyte concentration. The *detection limit* of an analytical method must be lower than the concentrations to be measured.

Sensitivity

$$= \text{slope of calibration curve} = \frac{\text{change in signal}}{\text{change in analyte concentration}}$$

Specifications could include required accuracy and precision, reagent purity, tolerances for apparatus, the use of certified reference materials, and acceptable values for blanks. *Certified reference materials* contain certified levels of analyte in realistic materials that you might be analyzing, such as blood or coal or metal alloys. Your analytical method should produce an answer acceptably close to the certified level or there is something wrong with the accuracy of your method.

Blanks account for interference by other species in the sample and for traces of analyte found in reagents used for sample preservation, preparation, and analysis. Frequent measurements of blanks detect whether analyte from previous samples is carried into subsequent analyses by adhering to vessels or instruments.

A **method blank** is a sample containing all components except analyte, and it is taken through all steps of the analytical procedure. We subtract the response of the method blank from the response of a real sample prior to calculating the quantity of analyte in the sample. A **reagent blank** is similar to a method blank, but it has not been subjected to all sample preparation procedures. The method blank is a more complete estimate of the blank contribution to the analytical response.

A **field blank** is similar to a method blank, but it has been exposed to the site of sampling. For example, to analyze particulates in air, a certain volume of air could be sucked through a filter, which is then dissolved and analyzed. A field blank would be a filter carried to the collection site in the same package with the collection filters. The filter for the blank would be taken out of its package in the field and placed in the same kind of sealed container used for collection filters. The difference between the blank and the collection filters is that air was not sucked through the blank filter. Volatile organic compounds encountered during transportation or in the field are conceivable contaminants of a field blank.

Another performance requirement often specified is *spike recovery*. Sometimes, response to analyte can be decreased or increased by something else in the sample. **Matrix** refers to everything in the sample other than analyte. A **spike,** also called a *fortification*, is a known quantity of analyte added to a sample to test whether the response to a sample is the same as that expected from a calibration curve. Spiked samples are analyzed in the same manner as unknowns. For example, if drinking water is found to contain 10.0 μg/L of nitrate, a spike of 5.0 μg/L could be added. Ideally, the concentration in the spiked portion found by analysis will be 15.0 μg/L. If a number other than 15.0 μg/L is found, then the matrix could be interfering with the analysis.

Add a small volume of concentrated standard to avoid changing the volume of the sample significantly. For example, add 50.5 μL of 500 μg/L standard to 5.00 mL of sample to increase analyte by 5.00 μg/L.

Final concentration

$$= \text{initial concentration} \times \text{dilution factor} = \left(500\frac{\mu g}{L}\right)\left(\frac{50.5\ \mu L}{5050.5\ \mu L}\right) = 5.00\ \frac{\mu g}{L}$$

EXAMPLE **Spike Recovery**

Let C stand for concentration. One definition of spike recovery is

$$\%\ \text{recovery} = \frac{C_{\text{spiked sample}} - C_{\text{unspiked sample}}}{C_{\text{added}}} \times 100 \qquad \textbf{(5-1)}$$

An unknown was found to contain 10.0 μg of analyte per liter. A spike of 5.0 μg/L was added to a replicate portion of unknown. Analysis of the spiked sample gave a concentration of 14.6 μg/L. Find the percent recovery of the spike.

Solution The percent of the spike found by analysis is

$$\%\ \text{recovery} = \frac{14.6\ \mu g/L - 10.0\ \mu g/L}{5.0\ \mu g/L} \times 100 = 92\%$$

If the acceptable recovery is specified to be in the range from 96% to 104%, then 92% is unacceptable. Something in your method or techniques needs improvement.

Matrix effects can decrease (Figure 5-4 and Problem 5-26) or increase (Problem 5-33) response to analyte.

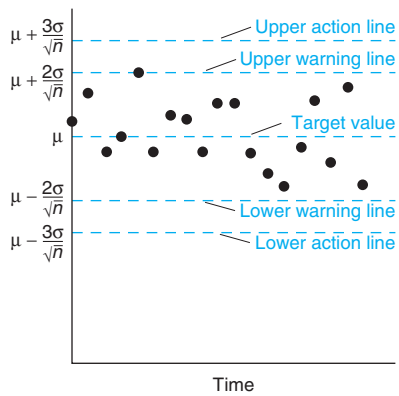
Test Yourself Find % recovery if the spiked sample gave a concentration of 15.3 μg/L. (***Answer:*** 106%)

BOX 5-1 Control Charts

A **control chart** is a visual representation of confidence intervals for a Gaussian distribution. The chart warns us when a monitored property strays dangerously far from an intended *target value*.

Consider a manufacturer making vitamin C tablets intended to have a target value of μ milligrams of vitamin C per tablet. Many analyses over a long time tell us the population standard deviation, σ, associated with the manufacturing process.

For quality control, 25 tablets are removed at random from the manufacturing line each hour and analyzed. The mean value of vitamin C in the 25 tablets is shown by a data point on the control chart.



For a Gaussian distribution, 95.5% of all observations are within $\pm 2\sigma/\sqrt{n}$ from the mean and 99.7% are within $\pm 3\sigma/\sqrt{n}$, where n is the number of tablets (= 25) that are averaged each hour. Recall that $\sigma/\sqrt{n}$ is the standard deviation of the mean discussed in Section 4-1. The $\pm 2\sigma/\sqrt{n}$ limits are *warning lines* and the $\pm 3\sigma/\sqrt{n}$ limits are *action lines*. We expect ~4.5% of measurements to be outside the warning lines and ~0.3% to be outside the action lines. It is unlikely that we would observe two consecutive measurements at the warning line (probability = 0.045 × 0.045 = 0.002 0).

The following conditions are considered to be so unlikely that, if they occur, the process should be shut down for troubleshooting:

- 1 observation outside the action lines
- 2 out of 3 consecutive measurements between the warning and action lines
- 7 consecutive measurements all above or all below the center line
- 6 consecutive measurements all increasing or all decreasing, wherever they are located
- 14 consecutive points alternating up and down, regardless of where they are located
- an obvious nonrandom pattern

For quality assessment of an analytical process, a control chart could show the relative deviation of measured values of calibration check samples or quality control samples from their known values. Another control chart could display the precision of replicate analyses of unknowns or standards as a function of time.

When dealing with large numbers of samples and replicates, we perform periodic calibration checks to make sure that our instrument continues to work properly and the calibration remains valid. In a **calibration check,** we analyze solutions formulated to contain known concentrations of analyte. A specification might, for example, call for one calibration check for every 10 samples. Solutions for calibration checks should be different from the ones used to prepare the original calibration curve. This practice helps verify that the initial calibration standards were made properly.

Performance test samples (also called *quality control samples* or *blind samples*) are a quality control measure to help eliminate bias introduced by an analyst who knows the concentration of the calibration check sample. These samples of known composition are provided to the analyst as unknowns. Results are then compared with the known values, usually by a quality assurance manager. For example, the U.S. Department of Agriculture maintains a bank of quality control homogenized food samples for distribution as blind samples to test laboratories that measure nutrients in foods.[3]

To gauge accuracy:
- calibration checks
- fortification recoveries
- quality control samples
- blanks

To gauge precision:
- replicate samples
- replicate portions of same sample

Together, raw data and results from calibration checks, spike recoveries, quality control samples, and blanks are used to gauge accuracy. Analytical performance on replicate samples and replicate portions of the same sample measures precision. Fortification also helps ensure that qualitative identification of analyte is correct. If you spike the unknown in Figure 0-11 with extra caffeine and the area of a chromatographic peak not thought to be caffeine increases, then you have misidentified the caffeine peak.

Standard operating procedures stating what steps will be taken and how they will be carried out are the bulwark of quality assurance. For example, if a reagent has "gone bad" for some reason, control experiments built into your normal procedures should detect that something is wrong and your results should not be reported. It is implicit that everyone follows the standard operating procedures. Adhering to these procedures guards against the normal human desire to take shortcuts based on assumptions that could be false.

A meaningful analysis requires a meaningful sample that represents what is to be analyzed. It must be stored in containers and under conditions that do not allow relevant chemical characteristics to change. Protection might be needed to prevent oxidation, photodecomposition, or growth of organisms. The *chain of custody* is the trail followed by a sample from the time

In drug testing of athletes, the chain of custody necessarily uses different people to collect samples and to analyze samples. The identity of the athlete is known to the collector, but not to the analyst, so that the analyst will not deliberately falsify a result to favor or incriminate a particular person or team.

it is collected to the time it is analyzed and, possibly, archived. Documents are signed each time the material changes hands to indicate who is responsible for the sample. Each person in the chain of custody follows a written procedure telling how the sample is to be handled and stored. Each person receiving a sample should inspect it to see that it is in the expected condition in an appropriate container. If the original sample was a homogeneous liquid, but it contains a precipitate when you receive it, the standard operating procedure may dictate that you reject that sample.

Standard operating procedures specify how instruments are to be maintained and calibrated to ensure their reliability. Many labs have their own standard practices, such as recording temperatures of refrigerators, calibrating balances, conducting routine instrument maintenance, or replacing reagents. These practices are part of the overall quality management plan. The rationale behind standard practices is that some equipment is used by many people for different analyses. We save money by having one program to ensure that the most rigorous needs are met.

Assessment

Assessment is the process of (1) collecting data to show that analytical procedures are operating within specified limits and (2) verifying that final results meet use objectives.

Documentation is critical for assessment. Standard *protocols* provide directions for what must be documented and how the documentation is to be done, including how to record information in notebooks. For labs that rely on manuals of standard practices, it is imperative that tasks done to comply with the manuals be monitored and recorded. *Control charts* (Box 5-1) can be used to monitor performance on blanks, calibration checks, and spiked samples to see if results are stable over time or to compare the work of different employees. Control charts can also monitor sensitivity or selectivity, especially if a laboratory encounters a wide variety of matrixes.

Government agencies such as the U.S. Environmental Protection Agency set requirements for quality assurance for their own labs and for certification of other labs. Published standard methods specify precision, accuracy, numbers of blanks, replicates, and calibration checks. To monitor drinking water, regulations state how often and how many samples are to be taken. Documentation is necessary to demonstrate that all requirements have been met. Table 5-1 summarizes the quality assurance process.

TABLE 5-1 Quality assurance process

Question	Actions
Use Objectives Why do you want the data and results and how will you use the results?	• Write use objectives
Specifications How good do the numbers have to be?	• Write specifications • Pick methods to meet specifications • Consider sampling, precision, accuracy, selectivity, sensitivity, detection limit, robustness, rate of false results • Employ blanks, fortification, calibration checks, quality control samples, and control charts to monitor performance • Write and follow standard operating procedures
Assessment Were the specifications achieved?	• Compare data and results with specifications • Document procedures and keep records suitable to meet use objectives • Verify that use objectives were met

5-2 Method Validation

Method validation is the process of proving that an analytical method is acceptable for its intended purpose.[4] In pharmaceutical chemistry, method validation requirements for regulatory submission include studies of *method specificity*, *linearity*, *accuracy*, *precision*, *range*, *limit of detection*, *limit of quantitation*, and *robustness*.

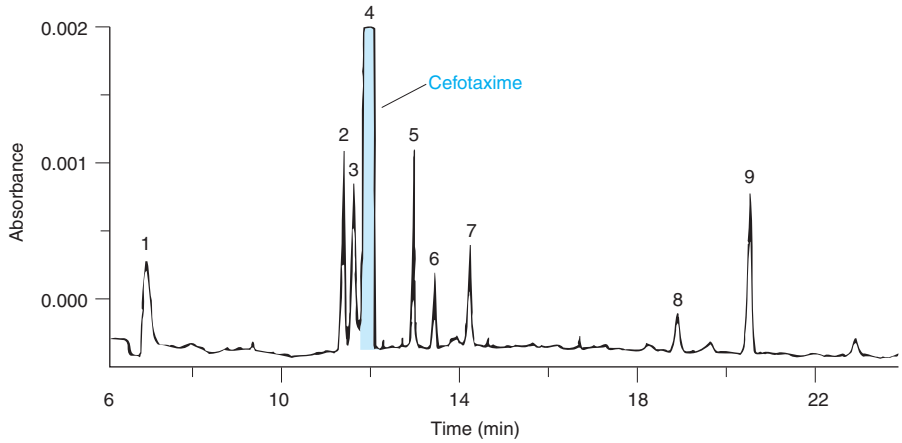


FIGURE 5-1 Electropherogram of the drug cefotaxime (peak 4) spiked with known impurities (peaks 2, 3, 5–9) from synthesis of the drug. Peak 1 is a marker for electroosmotic flow. Smaller peaks from unknown impurities are also observed. Separation was performed by micellar electrophoretic capillary chromatography (Section 25-7). [From H. Fabre and K. D. Altria, "Key Points for Validating CE Methods, Particularly in Pharmaceutical Analysis," *LCGC* **2001**, *19*, 498.]

Specificity

Specificity is the ability of an analytical method to distinguish analyte from everything else that might be in the sample. *Electrophoresis* is an analytical method in which substances are separated from one another by their differing rates of migration in a strong electric field. An *electropherogram* is a graph of detector response versus time in an electrophoretic separation. Figure 5-1 shows an electropherogram of the drug cefotaxime (peak 4) spiked with 0.2 wt% of known impurities normally present from the synthesis. A reasonable requirement for specificity might be that there is baseline separation of analyte (cefotaxime) from all impurities that might be present. *Baseline separation* means that the detector signal returns to its baseline before the next compound reaches the detector.

In Figure 5-1, impurity peak 3 is not completely resolved from the cefotaxime. In this case, another reasonable criterion for specificity might be that unresolved impurities at their maximum expected concentration do not affect the assay of cefotaxime by more than 0.5%. If we were trying to measure impurities, as opposed to assaying cefotaxime, a reasonable criterion for specificity is that all impurities having $>0.1\%$ of the area in the electropherogram are baseline separated from cefotaxime. Figure 5-1 does not meet this criterion.

When developing an assay, we need to decide what impurities to deliberately add to test for specificity. For analysis of a drug formulation, we would want to compare the pure drug with one containing additions of all possible synthetic by-products and intermediates, degradation products, and *excipients* (substances added to give desirable form or consistency). Degradation products might be introduced by exposing pure material to heat, light, humidity, acid, base, and oxidants to decompose ~20% of the original material.

Linearity

Linearity measures how well a calibration curve follows a straight line, showing that response is proportional to the quantity of analyte. If you know the target concentration of analyte in a drug preparation, for example, test the calibration curve for linearity with five standard solutions spanning the range from 0.5 to 1.5 times the expected analyte concentration. Each standard should be prepared and analyzed three times. (This procedure requires $3 \times 5 = 15$ standards plus three blanks.) To prepare a calibration curve for an impurity that might be present at, say, 0.1 to 1 wt%, you might prepare a calibration curve with five standards spanning the range 0.05 to 2 wt%.

A superficial, but common, measure of linearity is the *square of the correlation coefficient*, R^2:

Square of correlation coefficient:

$$R^2 = \frac{[\sum(x_i - \bar{x})(y_i - \bar{y})]^2}{\sum(x_i - \bar{x})^2 \sum(y_i - \bar{y})^2} \qquad \textbf{(5-2)}$$

where $\bar{x}$ is the mean of all the x values and $\bar{y}$ is the mean of all the y values. An easy way to find R^2 is with the LINEST function in Excel. In the example on page 86, values of x and y are entered in columns A and B. LINEST produces a table in cells E3:F5 that contains R^2 in cell E5. R^2 must be very close to 1 to represent a linear fit. For a major component of an unknown, a value of R^2 above 0.995 or, perhaps, 0.999, is deemed a good fit for many purposes.[5] For data in Figure 4-11, which do not lie very close to the straight line, $R^2 = 0.985$.

R^2 can be used as a diagnostic. If R^2 decreases after a method is established, something has gone wrong with the procedure.

Another criterion for linearity is that the y-intercept of the calibration curve (after the response of the blank has been subtracted from each standard) should be close to 0. An acceptable degree of "closeness to 0" might be 2% of the response for the target value of analyte. For the assay of impurities, which are present at concentrations lower than that of the major component, an acceptable value of R^2 might be ≥ 0.98 for the range 0.1 to 2 wt% and the y-intercept should be $\leq 10\%$ of the response for the 2 wt% standard.

Accuracy

Accuracy is "nearness to the truth." Ways to demonstrate accuracy include

1. Analyze a *certified reference material* in a matrix similar to that of your unknown. Your method should find the certified value for analyte in the reference material, within the precision (random uncertainty) of your method.
2. Compare results from two or more different analytical methods. They should agree within their expected precision.
3. Analyze a blank sample spiked with a known addition of analyte. The matrix must be the same as your unknown. When assaying a major component, three replicate samples at each of three levels ranging from 0.5 to 1.5 times the expected sample concentration are customary. For impurities, spikes could cover three levels spanning an expected range of concentrations, such as 0.1 to 2 wt%.
4. If you cannot prepare a blank with the same matrix as the unknown, then it is appropriate to make *standard additions* (Section 5-3) of analyte to the unknown. An accurate assay will find the known amount of analyte that was added.

Spiking is the most common method to evaluate accuracy because reference materials are not usually available and a second analytical method may not be readily available. Spiking ensures that the matrix remains nearly constant.

An example of a specification for accuracy is that the analysis will recover 100 ± 2% of the spike of a major constituent. For an impurity, the specification might be that recovery is within 0.1 wt% absolute or ±10% relative.

Precision

Precision is how well replicate measurements agree with one another, usually expressed as a standard deviation. Many types of precision are distinguished.

Autosamplers in chromatography and graphite furnace atomic spectroscopy, for example, have improved injection precision by a factor of 3–10 compared with that attained by humans.

Instrument precision, also called *injection precision*, is the reproducibility observed when the same quantity of one sample is repeatedly introduced ($\geq$10 times) into an instrument. Variability could arise from variation in the injected quantity and variation of instrument response.

Intra-assay precision is evaluated by analyzing aliquots of a homogeneous material several times by one person on one day with the same equipment. Each analysis is independent, so the intra-assay precision is telling us how reproducible the analytical method can be. Intra-assay variability is greater than instrument variability, because more steps are involved. Examples of specifications might be that instrument precision is $\leq 1\%$ and intra-assay precision is $\leq 2\%$.

Intermediate precision, formerly called *ruggedness*, is the variation observed when an assay is performed by different people on different instruments on different days in the same lab. Each analysis might incorporate fresh reagents and different chromatography columns.

Interlaboratory precision, also called *reproducibility*, is the most general measure of reproducibility observed when aliquots of the same sample are analyzed by different people in different laboratories. Interlaboratory precision becomes poorer as the level of analyte decreases (Box 5-2).

Range

Confusing terms:

Linear range: concentration range over which calibration curve is linear (Figure 4-14)

Dynamic range: concentration range over which there is measurable response

Range: concentration range over which linearity, accuracy, and precision meet specifications for analytical method

Range is the concentration interval over which linearity, accuracy, and precision are all acceptable. An example of a specification for range for a major component of a mixture is the concentration interval providing a correlation coefficient of $R^2 \geq 0.995$ (a measure of linearity), spike recovery of 100 ± 2% (a measure of accuracy), and interlaboratory precision of ±3%. For an impurity, an acceptable range might provide a correlation coefficient of $R^2 \geq 0.98$, spike recovery of 100 ± 10%, and interlaboratory precision of ±15%.

BOX 5-2 The Horwitz Trumpet: Variation In Interlaboratory Precision

Interlaboratory tests are routinely used to validate new analytical procedures—especially those intended for regulatory use. Typically, 5 to 10 laboratories are given identical samples and the same written procedure. If all results are "similar," and there is no serious systematic error, then the method is considered "reliable."

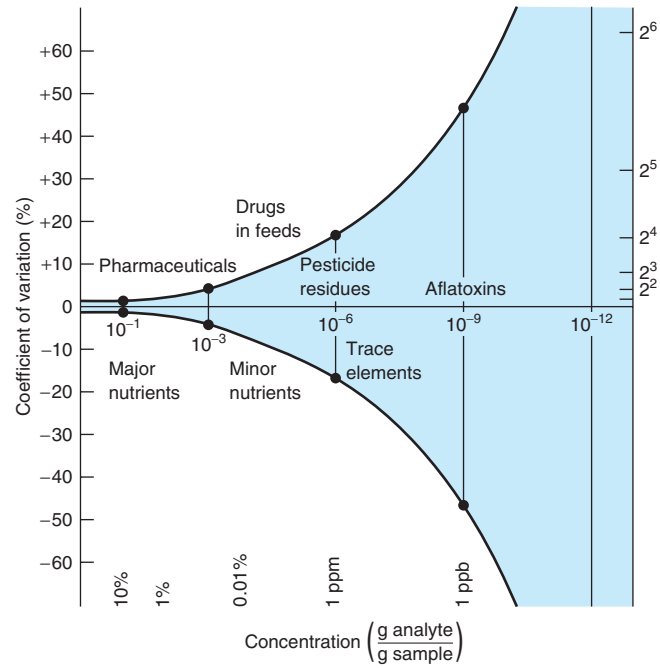
The **coefficient of variation** is the standard deviation divided by the mean, usually expressed as a percentage: $\text{CV}(\%) = 100 \times s/\bar{x}$. The smaller the coefficient of variation, the more precise is a set of measurements.

In reviewing more than 150 interlaboratory studies with different analytes measured by different techniques, it was observed that the coefficient of variation of mean values reported by different laboratories increased as analyte concentration decreased. At best, the coefficient of variation never seemed to be better than[6]

Horwitz curve: $\text{CV}(\%) \approx 2^{(1-0.5 \log C)}$

where C is the fraction of analyte in the sample (C = g analyte/g sample). The coefficient of variation within a laboratory is about one-half to two-thirds of the between-laboratory variation. Experimental results varied from the idealized curve by about a factor of 2 in the vertical direction and a factor of 10 in the horizontal direction. About 5–15% of all interlaboratory results were "outliers"—clearly outside the cluster of other results. This incidence of outliers is above the statistical expectation.

The Horwitz curve predicts that when the concentration of analyte is 1 ppm, the coefficient of variation between laboratories is ~16%. When the concentration is 1 ppb, the coefficient of variation is ~45%. If, perchance, you become a regulation writer one day, acceptable analyte levels should allow for variation among laboratories. The Gaussian distribution tells us that ~5% of measurements lie above $\bar{x} + 1.65s$ (Section 4-1). If the target allowable level of analyte is 1.0 ppb, the allowed observed amount might be set at $1 + 1.65 \times 0.45$ ppb, or about 1.7 ppb. This level gives a 5% rate of false positives that exceed the allowed value even though the true value is below 1.0 ppb.



Coefficient of variation of interlaboratory results as a function of sample concentration (expressed as g analyte/g sample). The shaded region has been referred to as the "Horwitz trumpet" because of the way it flares open. [From W. Horwitz, "Evaluation of Analytical Methods Used for Regulation of Foods and Drugs," *Anal. Chem.* **1982**, *54*, 67A.]

Limits of Detection and Quantitation

The **detection limit** (also called the *lower limit of detection*) is the smallest quantity of analyte that is "significantly different" from the blank.[7] Here is a procedure that produces a detection limit with ~99% chance of being greater than the blank. That is, only ~1% of samples containing no analyte will give a signal greater than the detection limit (Figure 5-2). We say that there is a ~1% rate of *false positives* in Figure 5-2. We assume that the standard deviation of the signal from samples near the detection limit is similar to the standard deviation from blanks.

1. After estimating the detection limit from previous experience with the method, prepare a sample whose concentration is ~1 to 5 times the detection limit.
2. Measure the signal from n replicate samples ($n \geq 7$).
3. Compute the standard deviation (s) of the n measurements.
4. Measure the signal from n blanks (containing no analyte) and find the mean value, y_{blank}.
5. The minimum detectable signal, y_{dl}, is defined as

   Signal detection limit: $$y_{\text{dl}} = y_{\text{blank}} + 3s \quad \textbf{(5-3)}$$

6. The corrected signal, $y_{\text{sample}} - y_{\text{blank}}$, is proportional to sample concentration:

   Calibration line: $$y_{\text{sample}} - y_{\text{blank}} = m \times \text{sample concentration} \quad \textbf{(5-4)}$$

   where y_{sample} is the signal observed for the sample and m is the slope of the linear calibration curve. The *minimum detectable concentration*, also called the detection limit, is obtained by substituting y_{dl} from Equation 5-3 for y_{sample} in Equation 5-4:

   Detection limit: $$\text{Minimum detectable concentration} = \frac{3s}{m} \quad \textbf{(5-5)}$$

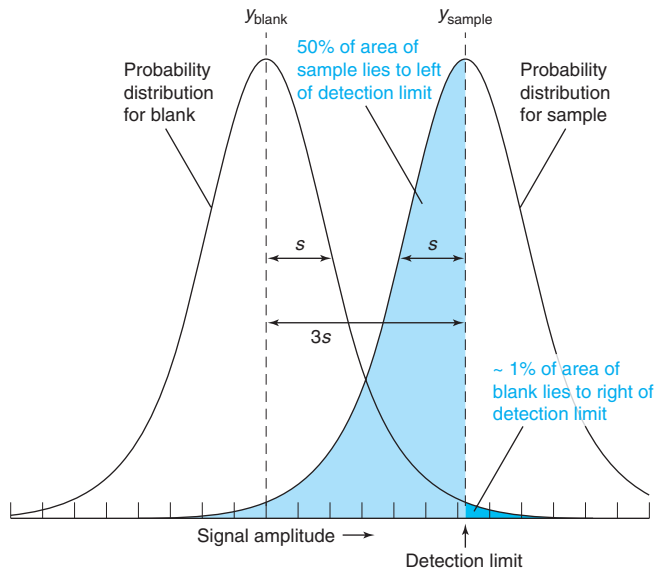
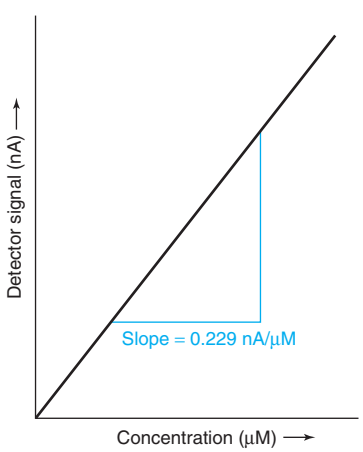


FIGURE 5-2 Detection limit. Distribution of measurements for a blank and a sample whose concentration is at the detection limit. The area of any region is proportional to the number of measurements in that region. Only ~1% of measurements for a blank are expected to exceed the detection limit. However, 50% of measurements for a sample containing analyte at the detection limit will be below the detection limit. There is a 1% chance of concluding that a blank has analyte above the detection limit (*false positive*). If a sample contains analyte at the detection limit, there is a 50% chance of concluding that analyte is *absent* because its signal is below the detection limit (*false negative*). Curves are Student's *t* distributions for 6 degrees of freedom and are broader than the corresponding Gaussian distributions.



EXAMPLE Detection Limit

From previous measurements of a low concentration of analyte, the signal detection limit was estimated to be in the low nanoampere range. Signals from seven replicate samples with a concentration about three times the detection limit were 5.0, 5.0, 5.2, 4.2, 4.6, 6.0, and 4.9 nA. Reagent blanks gave values of 1.4, 2.2, 1.7, 0.9, 0.4, 1.5, and 0.7 nA. The slope of the calibration curve for higher concentrations is $m = 0.229$ nA/μM. **(a)** Find the signal detection limit and the minimum detectable concentration. **(b)** What is the concentration of analyte in a sample that gave a signal of 7.0 nA?

Solution **(a)** First compute the mean for the blanks and the standard deviation of the samples. Retain extra, insignificant digits to reduce round-off errors.

Blank: Average $= y_{blank} = 1.2_6$ nA
Sample: Standard deviation $= s = 0.5_6$ nA

The signal detection limit from Equation 5-3 is

$$y_{dl} = y_{blank} + 3s = 1.2_6\,\text{nA} + (3)(0.5_6\,\text{nA}) = 2.9_4\,\text{nA}$$

The minimum detectable concentration is obtained from Equation 5-5:

$$\text{Detection limit} = \frac{3s}{m} = \frac{(3)(0.5_6\,\text{nA})}{0.229\,\text{nA}/\mu\text{M}} = 7._3\,\mu\text{M}$$

(b) To find the concentration of a sample whose signal is 7.0 nA, use Equation 5-4:

$$y_{sample} - y_{blank} = m \times \text{concentration}$$

$$\Rightarrow \quad \text{Concentration} = \frac{y_{sample} - y_{blank}}{m} = \frac{7.0\,\text{nA} - 1.2_6\,\text{nA}}{0.229\,\text{nA}/\mu\text{M}} = 25._1\,\mu\text{M}$$

Test Yourself Find the minimum detectable concentration if the average of the blanks is 1.0_5 nA and $s = 0.6_3$ nA. (***Answer:*** $8._3$ μM)

Another common way to define detection limit is from the least-squares equation of a calibration curve: signal detection limit $= b + 3s_y$, where b is the y-intercept and s_y is given by Equation 4-20. A more rigorous procedure is described in the notes for this chapter.[8]

The lower limit of detection in Equation 5-5 is $3s/m$, where s is the standard deviation of a low-concentration sample and m is the slope of the calibration curve. The standard deviation is a measure of the *noise* (random variation) in a blank or a small signal. When the signal is 3 times greater than the noise, it is detectable, but still too small for accurate measurement. A signal that is 10 times greater than the noise is defined as the **lower limit of quantitation,** or the smallest amount that can be measured with reasonable accuracy.

$$\text{Lower limit of quantitation} \equiv \frac{10s}{m} \tag{5-6}$$

Detection limit $\equiv \dfrac{3s}{m}$

Quantitation limit $\equiv \dfrac{10s}{m}$

The symbol $\equiv$ means "is defined as."

The *instrument detection limit* is obtained by replicate measurements ($n \geq 7$) of aliquots from one sample. The *method detection limit*, which is greater than the instrument detection limit, is obtained by preparing $n \geq 7$ individual samples and analyzing each one once.

The **reporting limit** is the concentration below which regulations say that a given analyte is reported as "not detected," which does not mean that analyte is not observed. It means that analyte is below a prescribed level. Reporting limits are set at least 5 to 10 times higher than the detection limit, so that detecting analyte at the reporting limit is not ambiguous.

Labels on U.S. packaged foods must state how much *trans* fat is present. This type of fat is derived mainly from partial hydrogenation of vegetable oil and is a major component of margarine and shortening. *Trans* fat is thought to increase risk of heart disease, stroke, and some cancers. However, the *reporting limit* for *trans* fat is 0.5 g per serving. If the concentration is <0.5 g/serving, it is reported as 0, as in Figure 5-3. By reducing the serving size, a manufacturer can state that *trans* fat content is 0. If your favorite snack food is made with partially hydrogenated oil, it contains *trans* fat even if the label says otherwise.

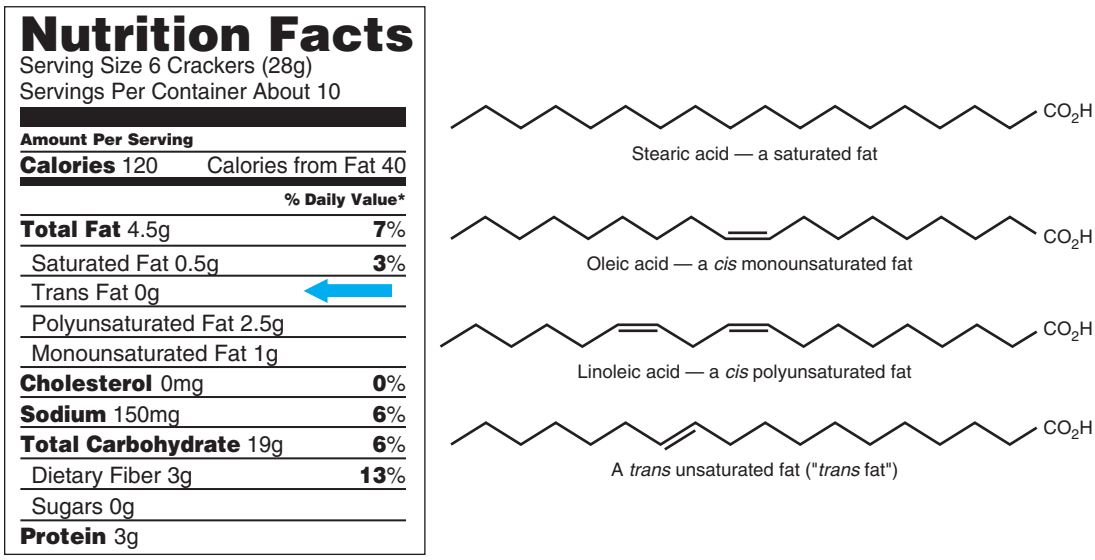


FIGURE 5-3 Nutritional label from a package of crackers. The *reporting limit* for *trans* fat is 0.5 g/serving. Any amount less than this is reported as 0. The end of Chapter 6 explains the shorthand used to draw these 18-carbon compounds.

Robustness

Robustness is the ability of an analytical method to be unaffected by small, deliberate changes in operating parameters. For example, a chromatographic method is robust if it gives acceptable results when small changes are made in solvent composition, pH, buffer concentration, temperature, injection volume, and detector wavelength. In tests for robustness, the organic solvent content in the mobile phase could be varied by, say, ±2%, the eluent pH varied by ±0.1, and column temperature varied by ±5°C. If acceptable results are obtained, the written procedure should state that these variations are tolerable. Capillary electrophoresis requires such small volumes that a given solution could conceivably be used for months before it is used up. Therefore, solution stability (shelf life) should be evaluated for robustness.

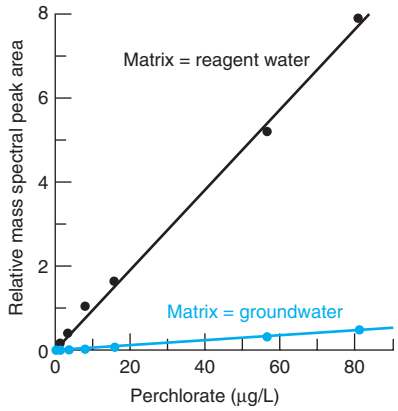


FIGURE 5-4 Calibration curves for perchlorate in pure water and in groundwater. [Data from C. J. Koester, H. R. Beller, and R. U. Halden, "Analysis of Perchlorate in Groundwater by Electrospray Ionization Mass Spectrometry/Mass Spectrometry," *Environ. Sci. Technol.* **2000**, *34*, 1862.]

The matrix affects the magnitude of the analytical signal. In standard addition, all samples are in the same matrix.

5-3 Standard Addition[9]

In **standard addition**, known quantities of analyte are added to the unknown. From the increase in signal, we deduce how much analyte was in the original unknown. This method requires a linear response to analyte. As in titrations, higher precision can be achieved when standards are added by mass instead of volume.[10]

Standard addition is especially appropriate when the sample composition is unknown or complex and affects the analytical signal. The *matrix* is everything in the unknown, other than analyte. A **matrix effect** is a change in the analytical signal caused by anything in the sample other than analyte.

Figure 5-4 shows a strong matrix effect in the analysis of perchlorate (ClO_4^-) by mass spectrometry. Perchlorate at a level above 18 μg/L in drinking water is of concern because it can reduce thyroid hormone production. Standard solutions of ClO_4^- in pure water gave the upper calibration curve in Figure 5-4. The slope in the lower curve for standard solutions in groundwater was 15 times less. Reduction of the ClO_4^- signal is a *matrix effect* attributed to other anions present in the groundwater.

Different groundwaters have different concentrations of many anions, so there is no way to construct a calibration curve for this analysis that would apply to more than one specific groundwater. Hence, the method of standard addition is required. When we add a small volume of concentrated standard to an existing unknown, we do not change the concentration of the matrix very much.

Consider a standard addition in which a sample with unknown initial concentration of analyte $[X]_i$ gives a signal intensity I_X. Then a known concentration of standard, S, is added to an aliquot of the sample and a signal I_{S+X} is observed for this second solution. Addition of standard to the unknown changes the concentration of the original analyte because of dilution. Let's call the diluted concentration of analyte $[X]_f$, where "f" stands for "final." We designate the concentration of standard in the final solution as $[S]_f$. (Bear in mind that the chemical species X and S are the same.)

Signal is directly proportional to analyte concentration, so

$$\frac{\text{Concentration of analyte in initial solution}}{\text{Concentration of analyte plus standard in final solution}} = \frac{\text{signal from initial solution}}{\text{signal from final solution}}$$

Derivation of Equation 5-7:

$I_X = k[X]_i$, where k is a constant of proportionality

$I_{S+X} = k([S]_f + [X]_f)$, where k is the same constant

Dividing one equation by the other gives

$$\frac{I_X}{I_{S+X}} = \frac{k[X]_i}{k([S]_f + [X]_f)} = \frac{[X]_i}{[S]_f + [X]_f}$$

Standard addition equation:

$$\frac{[X]_i}{[S]_f + [X]_f} = \frac{I_X}{I_{S+X}} \qquad (5\text{-}7)$$

For an initial volume V_o of unknown and added volume V_S of standard with concentration $[S]_i$, the total volume is $V = V_o + V_S$ and the concentrations in Equation 5-7 are

$$[X]_f = [X]_i\left(\frac{V_o}{V}\right) \qquad [S]_f = [S]_i\left(\frac{V_S}{V}\right) \qquad (5\text{-}8)$$

The quotient (initial volume/final volume), which relates final concentration to initial concentration, is called the **dilution factor.** It comes directly from Equation 1-3.

By expressing the diluted concentration of analyte, $[X]_f$, in terms of the initial concentration of analyte, $[X]_i$, we can solve for $[X]_i$, because everything else in Equation 5-7 is known.

EXAMPLE Standard Addition

Serum containing Na^+ gave a signal of 4.27 mV in an atomic emission analysis. Then 5.00 mL of 2.08 M NaCl were added to 95.0 mL of serum. This spiked serum gave a signal of 7.98 mV. Find the original concentration of Na^+ in the serum.

Solution From Equation 5-8, the final concentration of Na^+ after dilution with the standard is $[X]_f = [X]_i(V_o/V) = [X]_i(95.0\text{ mL}/100.0\text{ mL})$. The final concentration of added standard is $[S]_f = [S]_i(V_S/V) = (2.08\text{ M})(5.00\text{ mL}/100.0\text{ mL}) = 0.104\text{ M}$. Equation 5-7 becomes

$$\frac{[Na^+]_i}{[0.104\text{ M}] + 0.950[Na^+]_i} = \frac{4.27\text{ mV}}{7.98\text{ mV}} \Rightarrow [Na^+]_i = 0.113\text{ M}$$

Test Yourself If spiked serum gave a signal of 6.50 mV, what was the original concentration of Na^+? (***Answer:*** 0.182 M)

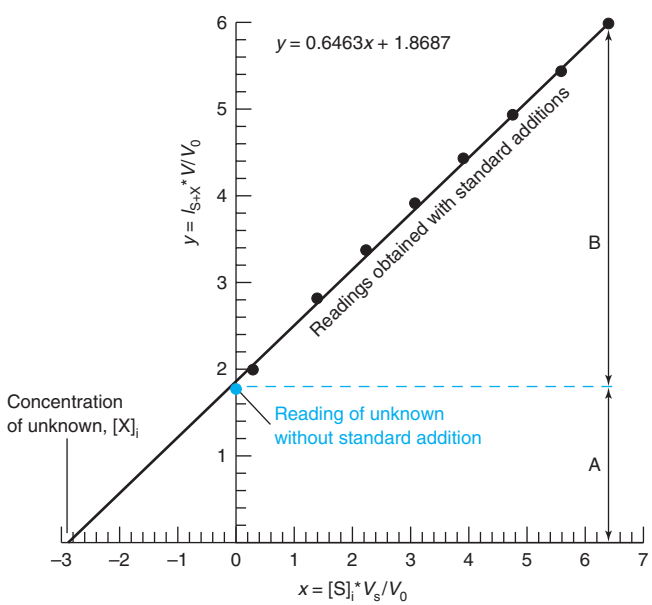
Graphical Procedure for Standard Addition to a Single Solution

There are two common methods to perform standard addition. If the analysis does not consume solution, we begin with an unknown solution and measure the analytical signal. Then we add a small volume of concentrated standard and measure the signal again. We add several more small volumes of standard and measure the signal after each addition. Standard should be concentrated so that only small volumes are added and the sample matrix is not appreciably altered. Added standards should increase the analytical signal by a factor of 1.5 to 3. The other common procedure is described in the next section.

	A	B	C	D	E
1	Vitamin C standard addition experiment				
2	Add 0.279 M ascorbic acid to 50.0 mL orange juice				
3					
4		Vs =			
5	Vo (mL) =	mL ascorbic	I(s+x) =	x-axis function	y-axis function
6	50	acid added	signal (μA)	Si*Vs/Vo	I(s+x)*V/Vo
7	[S]i (mM) =	0.000	1.78	0.000	1.780
8	279	0.050	2.00	0.279	2.002
9		0.250	2.81	1.395	2.824
10		0.400	3.35	2.232	3.377
11		0.550	3.88	3.069	3.923
12		0.700	4.37	3.906	4.431
13		0.850	4.86	4.743	4.943
14		1.000	5.33	5.580	5.437
15		1.150	5.82	6.417	5.954
16					
17	D7 = $A$8*B7/$A$6		E7 = C7*($A$6+B7)/$A$6		

FIGURE 5-5 Data for standard addition experiment with *variable total volume*.

Figure 5-5 shows data for an experiment in which ascorbic acid (vitamin C) was measured in orange juice by an electrochemical method. The current between a pair of electrodes immersed in the juice is proportional to the concentration of ascorbic acid. Eight standard additions increased current from 1.78 to 5.82 μA (column C), which is at the upper end of the desired range of 1.5- to 3-fold increase in analytical signal.



The equation of a line is $y = mx + b$. The x-intercept is obtained by setting $y = 0$:

$$0 = mx + b$$
$$x = -b/m$$

FIGURE 5-6 Graphical treatment of standard additions to a single solution *with variable total volume*. Data from Figure 5-5. Standard additions should increase the analytical signal to between 1.5 and 3 times its original value (that is, B = 0.5A to 2A).

Figure 5-6 allows us to find the original concentration of unknown. The theoretical response is derived by substituting expressions for $[X]_f$ and $[S]_f$ from Equations 5-8 into Equation 5-7. Following a little rearrangement, we find

For successive standard additions to one solution:

$$\underbrace{I_{S+X}\left(\frac{V}{V_o}\right)}_{\text{Function to plot on } y\text{-axis}} = I_X + \frac{I_X}{[X]_i}\underbrace{[S]_i\left(\frac{V_s}{V_o}\right)}_{\text{Function to plot on } x\text{-axis}} \qquad (5\text{-}9)$$

Successive standard additions to one solution:

Plot $I_{S+X}\left(\frac{V}{V_o}\right)$ versus $[S]_i\left(\frac{V_S}{V_o}\right)$

x-intercept is $[X]_i$

A graph of $I_{S+X}(V/V_o)$ (the *corrected response*) on the y-axis versus $[S]_i(V_S/V_o)$ on the x-axis should be a straight line. The data plotted in Figure 5-6 are computed in columns D and E of Figure 5-5. The right side of Equation 5-9 is 0 when $[S]_i(V_S/V_o) = -[X]_i$. The magnitude of the intercept on the x-axis is the *original* concentration of unknown, $[X]_i = 2.89$ mM in Figure 5-6.

The uncertainty in the x-intercept is[11]

$$\text{Standard deviation of } x\text{-intercept} = \frac{s_y}{|m|}\sqrt{\frac{1}{n} + \frac{\bar{y}^2}{m^2 \sum (x_i - \bar{x})^2}} \qquad \textbf{(5-10)}$$

where s_y is the standard deviation of y (Equation 4-20), $|m|$ is the absolute value of the slope of the least-squares line (Equation 4-16), n is the number of data points (nine in Figure 5-6), $\bar{y}$ is the mean value of y for the nine points, x_i are the individual values of x for the nine points, and $\bar{x}$ is the mean value of x for the nine points. For the points in Figure 5-6, the uncertainty in the x-intercept is 0.09_8 mM.

The confidence interval is $\pm t \times$ (standard deviation of x-intercept) where t is Student's t (Table 4-2) for $n - 2$ degrees of freedom. The 95% confidence interval for the intercept in Figure 5-6 is $\pm(2.365)(0.09_8 \text{ mM}) = \pm 0.23$ mM. The value $t = 2.365$ was taken from Table 4-2 for $9 - 2 = 7$ degrees of freedom.

Graphical Procedure for Multiple Solutions with Constant Volume

The second common standard addition procedure is shown in Figure 5-7. Equal volumes of unknown are pipetted into several volumetric flasks. Increasing volumes of standard are added to each flask and each is diluted to the *same final volum*e. Every flask contains the same concentration of unknown and differing concentrations of standard. For each flask, a measurement of analytical signal, I_{S+X}, is then made. The method in Figure 5-7 is necessary when the analysis consumes some of the solution.

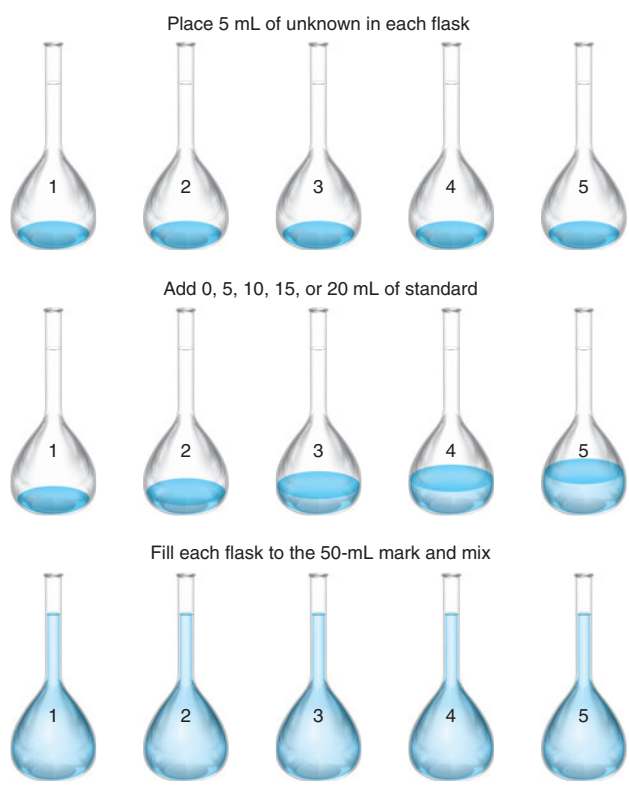


FIGURE 5-7 Standard addition experiment with *constant total volume*.

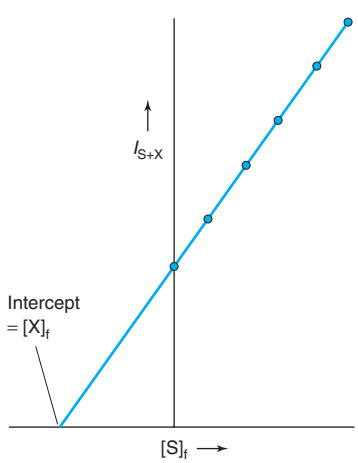


FIGURE 5-8 Graphical treatment of standard addition with *constant total volume*. Plot I_{S+X} versus $[S]_f$, and the x-intercept is $[X]_f$. The lines in Figures 5-6 and 5-8 are both derived from Equation 5-9.

If all standard additions are made to a constant final volume, plot the signal I_{S+X} versus the concentration of diluted standard, $[S]_f$ (Figure 5-8). In this case, the x-intercept is the *final* concentration of unknown, $[X]_f$, after dilution to the final sample volume. Equation 5-10 still applies to the uncertainty. The initial concentration of unknown, $[X]_i$, is calculated from the dilution that was applied to make the final sample.

5-4 Internal Standards

An **internal standard** is a known amount of a compound, different from analyte, that is added to the unknown. Signal from analyte is compared with signal from the internal standard to find out how much analyte is present.

In *standard addition*, the standard is the same substance as the analyte. An *internal standard* is different from the analyte.

Internal standards are especially useful for analyses in which the quantity of sample analyzed or the instrument response varies slightly from run to run. For example, gas or liquid flow rates that vary by a few percent in a chromatography experiment (Figure 0-10) could change the detector response. A calibration curve is accurate only for the one set of conditions under which it was obtained. However, the *relative* response of the detector to the analyte and standard is usually constant over a range of conditions. If signal from the standard increases by 8.4% because of a change in flow rate, signal from the analyte usually increases by 8.4% also. As long as the concentration of standard is known, the correct concentration of analyte can be derived. Internal standards are used in chromatography because the small quantity of sample injected into the chromatograph is not reproducible.

The assumption that relative response to analyte and standard remains constant over a range of concentrations must be verified.

Internal standards are desirable when sample loss can occur during sample preparation steps prior to analysis. If a known quantity of standard is added to the unknown prior to any manipulations, the ratio of standard to analyte remains constant because the same fraction of each is lost in any operation.

To use an internal standard, we prepare a known mixture of standard and analyte to measure the relative response of the detector to the two species. In the chromatogram in Figure 5-9, the area, A, under each peak is proportional to the concentration of the species injected into the column. However, the detector generally has a different response to each component. For example, if both analyte (X) and internal standard (S) have concentrations of 10.0 mM, the area under the analyte peak might be 2.30 times greater than the area under the standard peak. We say that the **response factor,** F, is 2.30 times greater for X than for S.

Response factor:

$$\frac{\text{Area of analyte signal}}{\text{Concentration of analyte}} = F\left(\frac{\text{area of standard signal}}{\text{concentration of standard}}\right) \qquad \textbf{(5-11)}$$

If the detector responds equally to standard and analyte, $F = 1$. If the detector responds twice as much to analyte as to standard, $F = 2$. If the detector responds half as much to analyte as to standard, $F = 0.5$.

$$\frac{A_X}{[X]} = F\left(\frac{A_S}{[S]}\right)$$

[X] and [S] are the concentrations of analyte and standard *after they have been mixed together*. Equation 5-11 is predicated on linear response to analyte and standard.

EXAMPLE Using an Internal Standard

In a preliminary experiment, a solution containing 0.083 7 M X and 0.066 6 M S gave peak areas of $A_X = 423$ and $A_S = 347$. (Areas are measured in arbitrary units by the instrument's computer.) To analyze the unknown, 10.0 mL of 0.146 M S were added to 10.0 mL of unknown, and the mixture was diluted to 25.0 mL in a volumetric flask. This mixture gave the chromatogram in Figure 5-9, for which $A_X = 553$ and $A_S = 582$. Find the concentration of X in the unknown.

Solution First use the standard mixture to find the response factor in Equation 5-11:

Standard mixture:

$$\frac{A_X}{[X]} = F\left(\frac{A_S}{[S]}\right)$$

$$\frac{423}{0.083\,7} = F\left(\frac{347}{0.066\,6}\right) \Rightarrow F = 0.970_0$$

In the mixture of unknown plus standard, the concentration of S is

$$[S] = \underbrace{(0.146\text{ M})}_{\text{Initial concentration}}\underbrace{\left(\frac{10.0}{25.0}\right)}_{\text{Dilution factor}} = 0.058\,4\text{ M}$$

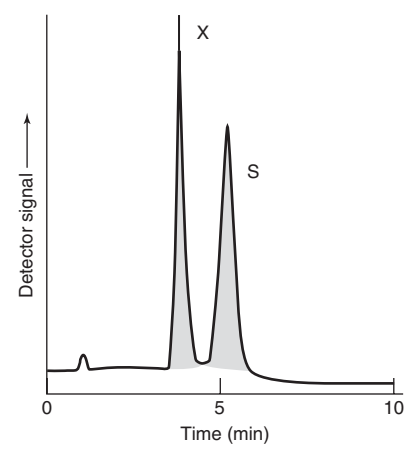


FIGURE 5-9 Chromatographic separation of unknown (X) and internal standard (S). A known amount of S was added to the unknown. The relative areas of the signals from X and S allow us to find out how much X is in the mixture. It is necessary first to measure the relative response of the detector to each compound.

The dilution factor $\frac{\text{initial volume}}{\text{final volume}}$ converts initial concentration into final concentration.

Using the known response factor, substitute back into Equation 5-11 to find the concentration of unknown in the mixture:

Unknown mixture:

$$\frac{A_X}{[X]} = F\left(\frac{A_S}{[S]}\right)$$

$$\frac{553}{[X]} = 0.970_0\left(\frac{582}{0.058\,4}\right) \Rightarrow [X] = 0.057\,2_1\ \text{M}$$

Because X was diluted from 10.0 to 25.0 mL when the mixture with S was prepared, the original concentration of X in the unknown was (25.0 mL/10.0 mL)(0.057 2_1 M) = 0.143 M.

Test Yourself Suppose that peak areas for the known mixture were $A_X = 423$ and $A_S = 447$. Find [X] in the unknown. (***Answer:*** $F = 0.753_0$, [X] = 0.184 M)

5-5 Efficiency In Experimental Design

Operating parameters usually need to be optimized when we develop an analytical method. The least efficient way to do this is to vary one parameter at a time while keeping everything else constant. More efficient procedures are called *fractional factorial experimental design*[12] and *simplex optimization*.[13] We now discuss one example of experimental design intended to provide maximum information in the fewest number of trials.

Suppose we have three different unknown solutions of acid, designated A, B, and C. If we titrate each one once with base, we find its concentration, but have no estimate of uncertainty. If we titrate each solution three times, for a total of nine measurements, we would find each concentration and its standard deviation.

Acids could be delivered by transfer pipets whose tolerances are given in Table 2-4. So 2 mL means 2.000 mL with uncertainty in the third decimal place.

A more efficient experimental design provides concentrations and standard deviations in fewer than nine experiments.[14] One of many efficient designs is shown in Figure 5-10. Instead of titrating each acid by itself, we titrate mixtures of the acids. For example, in row 5 of the spreadsheet, a mixture containing 2 mL A, 2 mL B, and 2 mL C required 23.29 mL of 0.120 4 M NaOH, which amounts to 2.804 mmol of OH^-. In row 6, the acid mixture contained 2 mL A, 3 mL B, and 1 mL C. Other permutations are titrated in rows 7 and 8. Then row 5 is repeated independently in row 9. Column E gives mmol of base for each run.

	A	B	C	D	E
1	Experimental Design				
2					
3	Volumes of unknown acids (mL)			mL NaOH	mmol
4	A	B	C	(0.1204 M)	NaOH
5	2	2	2	23.29	2.804
6	2	3	1	20.01	2.409
7	3	1	2	21.72	2.615
8	1	2	3	28.51	3.433
9	2	2	2	23.26	2.801
10					
11			[C]	[B]	[A]
12		Molarity	0.8099	0.4001	0.1962
13		Std. dev.	0.0062	0.0062	0.0062
14			0.9994	0.0130	#N/A
15			R^2	S_y	
16	Highlight cells C12:E14				
17	Type "= LINEST(E5:E9,A5:C9,FALSE,TRUE)"				
18	Press CTRL +SHIFT+ENTER (on PC)				
19	Press COMMAND+RETURN (on Mac)				

FIGURE 5-10 Spreadsheet for efficient experimental design uses Excel LINEST routine to fit the function $y = m_A x_A + m_B x_B + m_C x_C$ to experimental data by a least-squares procedure.

For each experiment, mmol of base consumed equals mmol of acid in the mixture:

$$\underbrace{\text{mmol OH}^-}_{y} = \underbrace{[\text{A}]V_\text{A}}_{m_\text{A}x_\text{A}} + \underbrace{[\text{B}]V_\text{B}}_{m_\text{B}x_\text{B}} + \underbrace{[\text{C}]V_\text{C}}_{m_\text{C}x_\text{C}} \qquad \textbf{(5-12)}$$

$\left(\frac{\text{mol}}{\text{L}}\right) \cdot \text{mL} = \text{mmol}$

where [A] is the concentration of acid A (mol/L) and V_A is the volume of A in mL. Rows 5 through 9 of the spreadsheet are equivalent to the following equalities:

$$\left.\begin{aligned} 2.804 &= [\text{A}] \cdot 2 + [\text{B}] \cdot 2 + [\text{C}] \cdot 2 \\ 2.409 &= [\text{A}] \cdot 2 + [\text{B}] \cdot 3 + [\text{C}] \cdot 1 \\ 2.615 &= [\text{A}] \cdot 3 + [\text{B}] \cdot 1 + [\text{C}] \cdot 2 \\ 3.433 &= [\text{A}] \cdot 1 + [\text{B}] \cdot 2 + [\text{C}] \cdot 3 \\ 2.801 &= [\text{A}] \cdot 2 + [\text{B}] \cdot 2 + [\text{C}] \cdot 2 \end{aligned}\right\} \qquad \textbf{(5-13)}$$

Our problem is to find the best values for the molarities [A], [B], and [C].

As luck would have it, Excel will find these values for us by the least-squares procedure LINEST. On page 86, we used LINEST to find the slope and intercept in the equation $y = mx + b$. In Figure 5-10, we use LINEST to find the slopes for $y = m_\text{A}x_\text{A} + m_\text{B}x_\text{B} + m_\text{C}x_\text{C} + b$ (where the intercept, b, is 0). To execute LINEST, highlight cells C12:E14 and type "=LINEST(E5:E9,A5:C9,FALSE,TRUE)". Then press CTRL+SHIFT+ENTER on a PC or COMMAND(⌘)+RETURN on a Mac. The first argument of LINEST, E5:E9, contains values of y (= mmol OH^-). The second argument, A5:C9, contains values of x (= volumes of acid). The third argument (FALSE) tells the computer to set the intercept (b) to zero, and the fourth argument (TRUE) says that we want statistics to be computed.

Excel finds the least-squares slopes in row 12 and their uncertainties in row 13. These slopes are the molarites [C], [B], and [A], in reverse order. So, for example, cells C12 and C13 tell us that the molarity of acid C is $0.809_9 \pm 0.006_2$ M. Uncertainty is derived from the quality of the least-squares fit to Equations 5-13, which is related to uncertainties in volumes and estimation of the equivalence point of the titrations.

We require at least n equations to solve for n unknowns. In this example, we have five equations (5-13), but just three unknowns ([A], [B], [C]). The two extra equations allow us to estimate uncertainty in the unknowns. If you do more experiments, you will generally decrease the uncertainty in concentration. An efficient experimental design with five experiments leaves us with more uncertainty than if we had done nine experiments. However, we have cut our effort nearly in half with the efficient design.

For five equations and three unknowns, there are 5 − 3 = 2 *degrees of freedom*. With no degrees of freedom, there is no information with which to estimate uncertainty.

Terms to Understand

assessment
calibration check
coefficient of variation
control chart
detection limit
dilution factor
false negative
false positive
field blank
internal standard
linearity
lower limit of quantitation
matrix
matrix effect
method blank
method validation
performance test sample
quality assurance
range
reagent blank
reporting limit
response factor
robustness
selectivity
sensitivity
specifications
specificity
spike
standard addition
standard operating procedure
use objectives

Summary

Quality assurance is what we do to get the right answer for our purpose. We begin by writing use objectives, from which specifications for data quality can be derived. Specifications could include requirements for sampling, accuracy, precision, specificity, detection limit, standards, and blank values. For any meaningful analysis, we must first collect a representative sample. A method blank containing all components except analyte is taken through all steps of the analytical procedure. We subtract the response of the method blank from the response of a real sample prior to calculating the quantity of analyte in the sample. A field blank tells us if analyte is inadvertently picked up by exposure to field conditions. Accuracy can be assessed by analyzing certified standards, by calibration checks performed by the analyst, with spikes made by the analyst, and by analyzing blind quality control samples. Written standard operating procedures must be followed rigorously to avoid inadvertent changes in procedure that could affect the outcome. Assessment is the process of (1) collecting data to show that analytical procedures are operating within specified limits and (2) verifying that final results meet use objectives. Control charts can be used to monitor accuracy, precision, or instrument performance as a function of time.

Method validation is the process of proving that an analytical method is acceptable for its intended purpose. In validating a

method, we typically demonstrate that requirements are met for specificity, linearity, accuracy, precision, range, limit of detection, limit of quantitation, and robustness. Specificity is the ability to distinguish analyte from anything else. Linearity is usually measured by the square of the correlation coefficient for the calibration curve. Types of precision include instrument precision, intra-assay precision, intermediate precision, and, most generally, interlaboratory precision. The "Horwitz trumpet" is an empirical statement that precision becomes poorer as analyte concentration decreases. Range is the concentration interval over which linearity, accuracy, and precision are acceptable. The detection limit is usually taken as 3 times the standard deviation of the blank. The lower limit of quantitation is 10 times the standard deviation of the blank. The reporting limit is the concentration below which regulations say that analyte is reported as "not detected," even when it is observed. Robustness is the ability of an analytical method to be unaffected by small changes in operating parameters.

A standard addition is a known quantity of analyte added to an unknown to increase the concentration of analyte. Standard additions are especially useful when matrix effects are important. A matrix effect is a change in the analytical signal caused by anything in the sample other than analyte. Use Equation 5-7 to compute the quantity of analyte after a single standard addition. For multiple standard additions to a single solution, use Equation 5-9 to construct the graph in Figure 5-6, in which the x-intercept gives us the concentration of analyte. For multiple solutions made up to the same final volume, the slightly different graph in Figure 5-8 is used. Equation 5-10 gives the x-intercept uncertainty in either graph.

An internal standard is a known amount of a compound, different from analyte, that is added to the unknown. Signal from analyte is compared with signal from the internal standard to find out how much analyte is present. Internal standards are useful when the quantity of sample analyzed is not reproducible, when instrument response varies from run to run, or when sample losses occur in sample preparation. The response factor in Equation 5-11 is the relative response to analyte and standard.

Efficient experimental design decreases the number of experiments needed to obtain required information and an estimate of uncertainty in that information. A tradeoff is that the fewer experiments we do, the greater the uncertainty in the results.

Exercises

5-A. *Detection limit.* In spectrophotometry, we measure the concentration of analyte by its absorbance of light. A low-concentration sample was prepared, and nine replicate measurements gave absorbances of 0.004 7, 0.005 4, 0.006 2, 0.006 0, 0.004 6, 0.005 6, 0.005 2, 0.004 4, and 0.005 8. Nine reagent blanks gave values of 0.000 6, 0.001 2, 0.002 2, 0.000 5, 0.001 6, 0.000 8, 0.001 7, 0.001 0, and 0.001 1.

(a) Find the absorbance detection limit with Equation 5-3.

(b) The calibration curve is a graph of absorbance versus concentration. Absorbance is a dimensionless quantity. The slope of the calibration curve is $m = 2.24 \times 10^4\ \mathrm{M}^{-1}$. Find the concentration detection limit with Equation 5-5.

(c) Find the lower limit of quantitation with Equation 5-6.

5-B. *Standard addition.* An unknown sample of Ni^{2+} gave a current of 2.36 μA in an electrochemical analysis. When 0.500 mL of solution containing 0.028 7 M Ni^{2+} was added to 25.0 mL of unknown, the current increased to 3.79 μA.

(a) Denoting the initial, unknown concentration as $[Ni^{2+}]_i$, write an expression for the final concentration, $[Ni^{2+}]_f$, after 25.0 mL of unknown were mixed with 0.500 mL of standard. Use the dilution factor for this calculation.

(b) In a similar manner, write the final concentration of added standard Ni^{2+}, designated as $[S]_f$.

(c) Find $[Ni^{2+}]_i$ in the unknown.

5-C. *Internal standard.* A solution was prepared by mixing 5.00 mL of unknown element X with 2.00 mL of solution containing 4.13 μg of standard element S per milliliter, and diluting to 10.0 mL. The signal ratio in atomic absorption spectrometry was (signal from X)/(signal from S) = 0.808. In a separate experiment, with equal concentrations of X and S, (signal from X)/(signal from S) = 1.31. Find the concentration of X in the unknown.

5-D. In Figure 5-6, the x-intercept is –2.89 mM and its standard deviation is 0.09_8 mM. Find the 90% and 99% confidence intervals for the intercept.

5-E. *Control chart.* Volatile compounds in human blood serum were measured by purge and trap gas chromatography/mass spectrometry. For quality control, serum was periodically spiked with a constant amount of 1,2-dichlorobenzene and the concentration (ng/g = ppb) was measured. Find the mean and standard deviation for the following spike data and prepare a control chart. State whether or not the observations (Obs.) meet each criterion for stability in a control chart.

Day	Obs. (ppb)	Day	Obs. (ppb)	Day	Obs. (ppb)	Day	Obs. (ppb)	Day	Obs. (ppb)
0	1.05	91	1.13	147	0.83	212	1.03	290	1.04
1	0.70	101	1.64	149	0.88	218	0.90	294	0.85
3	0.42	104	0.79	154	0.89	220	0.86	296	0.59
6	0.95	106	0.66	156	0.72	237	1.05	300	0.83
7	0.55	112	0.88	161	1.18	251	0.79	302	0.67
30	0.68	113	0.79	167	0.75	259	0.94	304	0.66
70	0.83	115	1.07	175	0.76	262	0.77	308	1.04
72	0.97	119	0.60	182	0.93	277	0.85	311	0.86
76	0.60	125	0.80	185	0.72	282	0.72	317	0.88
80	0.87	128	0.81	189	0.87	286	0.68	321	0.67
84	1.03	134	0.84	199	0.85	288	0.86	323	0.68

SOURCE: *D. L. Ashley, M. A. Bonin, F. L. Cardinali, J. M. McCraw, J. S. Holler, L. L. Needham, and D. G. Patterson, Jr., "Determining Volatile Organic Compounds in Blood by Using Purge and Trap Gas Chromatography/Mass Spectrometry," Anal. Chem.* ***1992****, 64, 1021.*

Problems

Quality Assurance and Method Validation

5-1. Explain the meaning of the quotation at the beginning of this chapter: "Get the right data. Get the data right. Keep the data right."

5-2. What are the three parts of quality assurance? What questions are asked in each part and what actions are taken in each part?

5-3. How can you validate precision and accuracy?

5-4. Distinguish *raw data*, *treated data*, and *results*.

5-5. What is the difference between a *calibration check* and a *performance test sample*?

5-6. What is the purpose of a blank? Distinguish *method blank*, *reagent blank,* and *field blank*.

5-7. Distinguish *linear range*, *dynamic range*, and *range*.

5-8. What is the difference between a *false positive* and a *false negative*?

5-9. Consider a sample that contains analyte at the detection limit defined in Figure 5-2. Explain the following statements: There is approximately a 1% chance of falsely concluding that a sample containing no analyte contains analyte above the detection limit. There is a 50% chance of concluding that a sample that really contains analyte at the detection limit does not contain analyte above the detection limit.

5-10. How is a control chart used? State six indications that a process is going out of control.

5-11. Here is a use objective for a chemical analysis to be performed at a drinking water purification plant: "Data and results collected quarterly shall be used to determine whether the concentrations of haloacetates in the treated water demonstrate compliance with the levels set by the Stage 1 Disinfection By-products Rule using Method 552.2" (a specification that sets precision, accuracy, and other requirements). Which one of the following questions best summarizes the meaning of the use objective?

(a) Are haloacetate concentrations known within specified precision and accuracy?

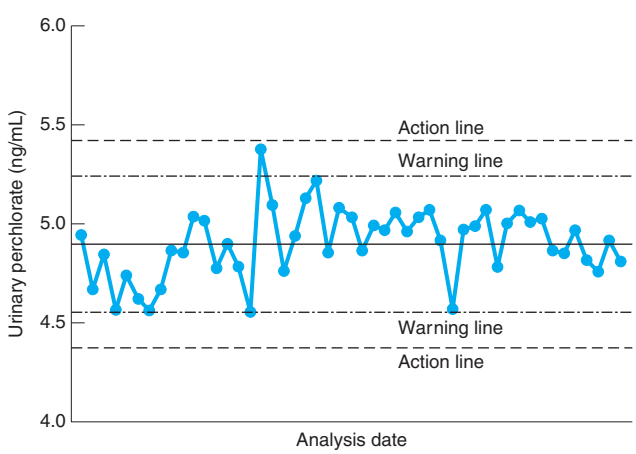
(b) Are any haloacetates detectable in the water?

(c) Do any haloacetate concentrations exceed the regulatory limit?

5-12. What is the difference between an instrument detection limit and a method detection limit? What is the difference between robustness and intermediate precision?

5-13. Define the following terms: instrument precision, injection precision, intra-assay precision, intermediate precision, and interlaboratory precision.

5-14. *Control chart*. A laboratory monitoring perchlorate (ClO_4^-) in urine measured quality control samples made from synthetic urine spiked with (ClO_4^-). The graph shows consecutive quality control measurements. Are any troubleshooting conditions from Box 5-1 observed in these data?



Control chart for ClO_4^- in urine. [Data from L. Valentin-Blasini, J. P. Mauldin, D. Maple, and B. C. Blount, "Analysis of Perchlorate in Human Urine Using Ion Chromatography and Electrospray Tandem Mass Spectrometry," *Anal. Chem.* **2005**, *77*, 2475.]

5-15. *Correlation coefficient and Excel graphing*. Synthetic data are given below for a calibration curve in which random Gaussian noise with a magnitude of 80 was superimposed on y values that follow the equation $y = 26.4x + 1.37$. This exercise shows that a high value of R^2 does not guarantee that data quality is excellent.

(a) Enter concentration in column A and signal in column B of a spreadsheet. Prepare an XY (Scatter) chart of signal versus concentration without a line as described in Section 2-11. Use LINEST (Section 4-7) to find the least-squares parameters including R^2.

(b) Now insert the Trendline by following instructions in Section 4-9. In the Options window used to select the Trendline, select Display Equation and Display R-Squared. Verify that Trendline and LINEST give identical results.

(c) Add 95% confidence interval y error bars following the instructions at the end of Section 4-9. The 95% confidence interval is $\pm ts_y$, where s_y comes from LINEST and Student's t comes from Table 4-2 for 95% confidence and $11 - 2 = 9$ degrees of freedom. Also, compute t with the statement "=TINV(0.05,9)".

Concentration (x)	Signal (y)	Concentration (x)	Signal (y)
0	14	60	1 573
10	350	70	1 732
20	566	80	2 180
30	957	90	2 330
40	1 067	100	2 508
50	1 354		

5-16. In a murder trial in the 1990s, the defendant's blood was found at the crime scene. The prosecutor argued that blood was left by the defendant during the crime. The defense argued that police "planted" the defendant's blood from a sample collected later. Blood is normally collected in a vial containing the metal-binding compound EDTA as an anticoagulant with a concentration of ~4.5 mM after the vial has been filled with blood. At the time of the trial, procedures to measure EDTA in blood were not well established. Even though the amount of EDTA found in the crime-scene blood was orders of magnitude below 4.5 mM, the jury acquitted the defendant. This trial motivated the development of a new method to measure EDTA in blood.

(a) *Precision and accuracy*. To measure accuracy and precision of the method, blood was fortified with EDTA to known levels.

$$\text{Accuracy} = 100 \times \frac{\text{mean value found} - \text{known value}}{\text{known value}}$$

$$\text{Precision} = 100 \times \frac{\text{standard deviation}}{\text{mean}} \equiv \textit{coefficient of variation}$$

For each of the three spike levels in the table, find the precision and accuracy of the quality control samples.

EDTA measurements (ng/mL) at three fortification levels

Spike:	22.2 ng/mL	88.2 ng/mL	314 ng/mL
Found:	33.3	83.6	322
	19.5	69.0	305
	23.9	83.4	282
	20.8	100.0	329
	20.8	76.4	276

SOURCE: *R. L. Sheppard and J. Henion, Anal. Chem.* ***1997,*** *69, 477A, 2901.*

(b) *Detection and quantitation limits*. Low concentrations of EDTA near the detection limit gave the following dimensionless instrument

readings: 175, 104, 164, 193, 131, 189, 155, 133, 151, and 176. Ten blanks had a mean reading of $45._0$. The slope of the calibration curve is $1.75 \times 10^9\ M^{-1}$. Estimate the signal and concentration detection limits and the lower limit of quantitation for EDTA.

5-17. (a) From Box 5-2, estimate the minimum expected coefficient of variation, CV(%), for interlaboratory results when the analyte concentration is (i) 1 wt% or (ii) 1 part per trillion.

(b) The coefficient of variation within a laboratory is typically ~0.5–0.7 of the between-laboratory variation. If your class analyzes an unknown containing 10 wt% NH_3, what is the minimum expected coefficient of variation for the class?

5-18. *Spike recovery and detection limit*. Species of arsenic found in drinking water include AsO_3^{3-} (arsenite), AsO_4^{3-} (arsenate), $(CH_3)_2AsO_2^-$ (dimethylarsinate), and $(CH_3)AsO_3^{2-}$ (methylarsonate). Pure water containing no arsenic was spiked with 0.40 μg arsenate/L. Seven replicate determinations gave 0.39, 0.40, 0.38, 0.41, 0.36, 0.35, and 0.39 μg/L.[15] Find the mean percent recovery of the spike and the concentration detection limit (μg/L).

5-19. *Detection limit*. Low concentrations of Ni^{2+}-EDTA near the detection limit gave the following counts in a mass spectral measurement: 175, 104, 164, 193, 131, 189, 155, 133, 151, 176. Ten measurements of a blank had a mean of 45 counts. A sample containing 1.00 μM Ni^{2+}-EDTA gave 1 797 counts. Estimate the detection limit for Ni-EDTA.

5-20. *Detection limit*. A sensitive chromatographic method was developed to measure sub-part-per-billion levels of the disinfectant by-products iodate (IO_3^-), chlorite (ClO_2^-), and bromate (BrO_3^-) in drinking water. As the oxyhalides emerge from the column, they react with Br^- to make Br_3^-, which is measured by its strong absorption at 267 nm. For example, each mole of bromate makes 3 mol of Br_3^- by the reaction

$$BrO_3^- + 8Br^- + 6H^+ \rightarrow 3Br_3^- + 3H_2O$$

Bromate near its detection limit gave the following chromatographic peak heights and standard deviations (s). For each concentration, estimate the detection limit. Find the mean detection limit. The blank is 0 because chromatographic peak height is measured from the baseline adjacent to the peak. Because blank = 0, relative standard deviation applies to both peak height and concentration, which are proportional to each other. Detection limit is $3s$ for peak height or concentration.

Bromate concentration (μg/L)	Peak height (arbitrary units)	Relative standard deviation (%)	Number of measurements
0.2	17	14.4	8
0.5	31	6.8	7
1.0	56	3.2	7
2.0	111	1.9	7

SOURCE: *H. S. Weinberg and H. Yamada, "Post-Ion-Chromatography Derivatization for the Determination of Oxyhalides at Sub-PPB Levels in Drinking Water," Anal. Chem.* ***1998,*** *70, 1.*

5-21. Olympic athletes are tested to see if they are using illegal performance-enhancing drugs. Suppose that urine samples are taken and analyzed and the rate of false positive results is 1%. Suppose also that it is too expensive to refine the method to reduce the rate of false positive results. We do not want to accuse innocent people of using illegal drugs. What can you do to reduce the rate of false accusations even though the test always has a false positive rate of 1%?

5-22. *Blind samples*. The U.S. Department of Agriculture provided homogenized baby food samples to three labs for analysis.[3] Results agreed well for protein, fat, zinc, riboflavin, and palmitic acid. Results for iron were questionable: Lab A, 1.59 ± 0.14 (13); Lab B, 1.65 ± 0.56 (8); Lab C, 2.68 ± 0.78 (3) mg/100 g. Uncertainty is the standard deviation, with the number of replicate analyses in parentheses. Use two separate t tests to compare results from Lab C with those from Lab A and Lab B at the 95% confidence level. Comment on the sensibility of the t test results. Offer your own conclusions.

Standard Addition

5-23. Why is it desirable in the method of standard addition to add a small volume of concentrated standard rather than a large volume of dilute standard?

5-24. An unknown sample of Cu^{2+} gave an absorbance of 0.262 in an atomic absorption analysis. Then 1.00 mL of solution containing 100.0 ppm (= μg/mL) Cu^{2+} was mixed with 95.0 mL of unknown, and the mixture was diluted to 100.0 mL in a volumetric flask. The absorbance of the new solution was 0.500.

(a) Denoting the initial, unknown concentration as $[Cu^{2+}]_i$, write an expression for the final concentration, $[Cu^{2+}]_f$, after dilution. Units of concentration are ppm.

(b) In a similar manner, write the final concentration of added standard Cu^{2+}, designated as $[S]_f$.

(c) Find $[Cu^{2+}]_i$ in the unknown.

5-25. *Standard addition graph.* Tooth enamel consists mainly of the mineral calcium hydroxyapatite, $Ca_{10}(PO_4)_6(OH)_2$. Trace elements in teeth of archeological specimens provide anthropologists with clues about diet and diseases of ancient people. Students at Hamline University measured strontium in enamel from extracted wisdom teeth by atomic absorption spectroscopy. Solutions were prepared with a constant total volume of 10.0 mL containing 0.750 mg of dissolved tooth enamel plus variable concentrations of added Sr.

Added Sr (ng/mL = ppb)	Signal (arbitrary units)
0	28.0
2.50	34.3
5.00	42.8
7.50	51.5
10.00	58.6

SOURCE: *V. J. Porter, P. M. Sanft, J. C. Dempich, D. D. Dettmer, A. E. Erickson, N. A. Dubauskie, S. T. Myster, E. H. Matts, and E. T. Smith, "Elemental Analysis of Wisdom Teeth by Atomic Spectroscopy Using Standard Addition," J. Chem. Ed.* ***2002,*** *79, 1114.*

(a) Find the concentration of Sr and its uncertainty in the 10-mL sample solution in parts per billion = ng/mL.

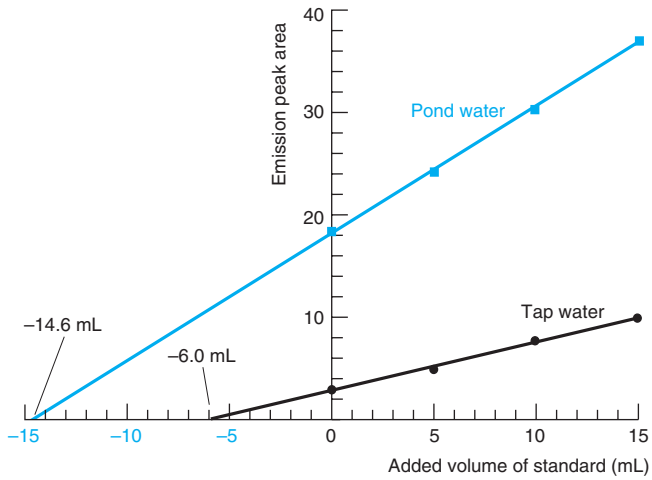
(b) Find the concentration of Sr in tooth enamel in parts per million = μg/g.

(c) If the standard addition intercept is the major source of uncertainty, find the uncertainty in the concentration of Sr in tooth enamel in parts per million.

(d) Find the 95% confidence interval for Sr in tooth enamel.

5-26. Europium is a lanthanide element found in parts per billion levels in natural waters. It can be measured from the intensity of orange light emitted when a solution is illuminated with ultraviolet radiation. Certain organic compounds that bind Eu(III) are required

to enhance the emission. The figure shows standard addition experiments in which 10.00 mL of sample and 20.00 mL containing a large excess of organic additive were placed in 50-mL volumetric flasks. Then Eu(III) standards (0, 5.00, 10.00, or 15.00 mL) were added and the flasks were diluted to 50.0 mL with H_2O. Standards added to tap water contained 0.152 ng/mL (ppb) of Eu(III), but those added to pond water were 100 times more concentrated (15.2 ng/mL).



Standard addition of Eu(III) to pond water or tap water. [Data from A. L. Jenkins and G. M. Murray, "Enhanced Luminescence of Lanthanides," *J. Chem. Ed.* **1998**, *75*, 227.]

(a) Calculate the concentration of Eu(III) (ng/mL) in pond water and tap water.

(b) For tap water, emission peak area increases by 4.61 units when 10.00 mL of 0.152 ng/mL standard are added. This response is 4.61 units/1.52 ng = 3.03 units per ng of Eu(III). For pond water, the response is 12.5 units when 10.00 mL of 15.2 ng/mL standard are added, or 0.082 2 units per ng. How would you explain these observations? Why was standard addition necessary for this analysis?

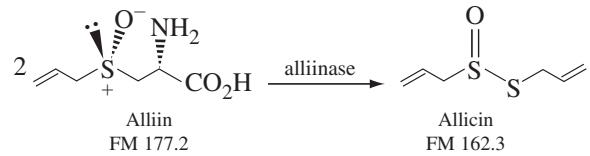
5-27. *Standard addition graph*. Students performed an experiment like that in Figure 5-7 in which each flask contained 25.00 mL of serum, varying additions of 2.640 M NaCl standard, and a total volume of 50.00 mL.

Flask	Volume of standard (mL)	Na^+ atomic emission signal (mV)
1	0	3.13
2	1.000	5.40
3	2.000	7.89
4	3.000	10.30
5	4.000	12.48

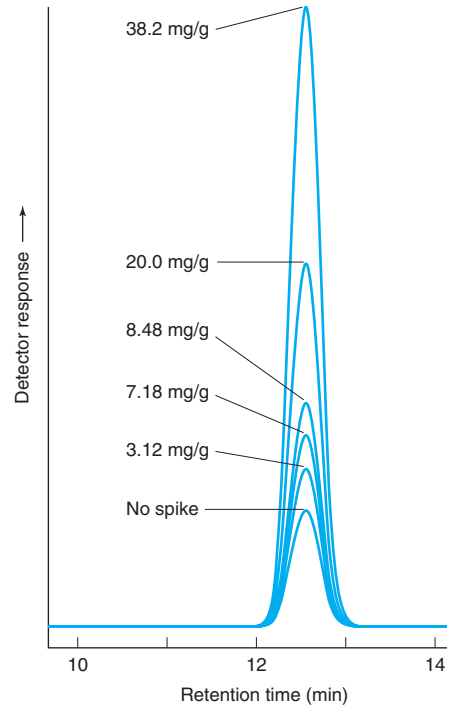
(a) Prepare a standard addition graph and find $[Na^+]$ in the serum.

(b) Find the standard deviation and 95% confidence interval for $[Na^+]$.

5-28. *Standard addition graph*. Allicin is a major component in garlic (0.4 wt% in fresh garlic) with antimicrobial and possibly anticancer and antioxidant activity. It is unstable and therefore difficult to measure. An assay was developed in which the stable precursor alliin is added to freshly crushed garlic and rapidly converted to allicin by the enzyme alliinase found in garlic. Components of the crushed garlic are extracted and measured by liquid chromatography. The graph shows standard additions reported as mg alliin added per gram of garlic. The chromatographic peak is allicin from the conversion of alliin.



(a) The standard addition procedure has a constant total volume. Prepare a graph to find how much alliin equivalent was in the unspiked garlic. The units of your answer will be mg alliin/g garlic. Include the standard deviation in your answer.



Chromatographic measurement of alliin after standard addition to garlic. [From M. E. Rybak, E. M. Calvey, and J. M. Harnly, "Quantitative Determination of Allicin in Garlic: Supercritical Fluid Extraction and Standard Addition of Alliin," *J. Agric. Food Chem.* **2004**, *52*, 682.]

(b) Given that 2 mol of alliin are converted to 1 mol of allicin in the assay, find the allicin content of garlic expressed as mg allicin/g garlic, including the standard deviation.

Internal Standards

5-29. State when standard additions and internal standards, instead of a calibration curve, are desirable, and why.

5-30. A solution containing 3.47 mM X (analyte) and 1.72 mM S (standard) gave peak areas of 3 473 and 10 222, respectively, in a chromatographic analysis. Then 1.00 mL of 8.47 mM S was added to 5.00 mL of unknown X, and the mixture was diluted to 10.0 mL. This solution gave peak areas of 5 428 and 4 431 for X and S, respectively.

(a) Calculate the response factor for the analyte.

(b) Find the concentration of S (mM) in the 10.0 mL of mixed solution.

(c) Find the concentration of X (mM) in the 10.0 mL of mixed solution.

(d) Find the concentration of X in the original unknown.

5-31. Chloroform is an internal standard in the determination of the pesticide DDT in a polarographic analysis in which each compound is reduced at an electrode surface. A mixture containing 0.500 mM chloroform and 0.800 mM DDT gave signals of 15.3 μA for chloroform and 10.1 μA for DDT. An unknown solution (10.0 mL) containing DDT was placed in a 100-mL volumetric flask and 10.2 μL of chloroform (FM 119.39, density = 1.484 g/mL) were added. After dilution to the mark with solvent, polarographic signals of 29.4 and 8.7 μA were observed for the chloroform and DDT, respectively. Find the concentration of DDT in the unknown.

5-32. *Verifying constant response for an internal standard.* When we develop a method using an internal standard, it is important to verify that the response factor is constant over the calibration range. Data are shown below for a chromatographic analysis of naphthalene ($C_{10}H_8$), using deuterated naphthalene ($C_{10}D_8$ in which D is the isotope ^2H) as an internal standard. The two compounds emerge from the column at almost identical times and are measured by a mass spectrometer, which distinguishes them by molecular mass. From the definition of response factor in Equation 5-11, we can write

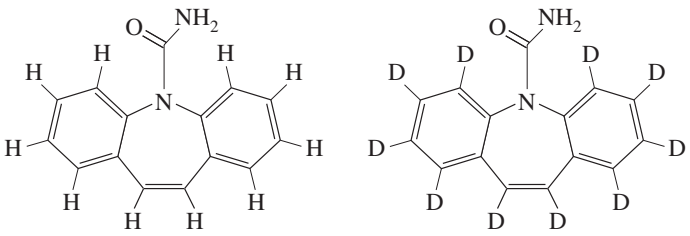
$$\frac{\text{Area of analyte signal}}{\text{Area of standard signal}} = F\left(\frac{\text{concentration of analyte}}{\text{concentration of standard}}\right)$$

Prepare a graph of peak area ratio ($C_{10}H_8/C_{10}D_8$) versus concentration ratio ($[C_{10}H_8]/[C_{10}D_8]$) and find the slope, which is the response factor. Evaluate F for each of the three samples and find the standard deviation of F to see how "constant" it is.

Sample	$C_{10}H_8$ (ppm)	$C_{10}D_8$ (ppm)	$C_{10}H_8$ peak area	$C_{10}D_8$ peak area
1	1.0	10.0	303	2 992
2	5.0	10.0	3 519	6 141
3	10.0	10.0	3 023	2 819

The volume of solution injected into the column was different in all three runs.

5-33. *Correcting for matrix effects with an internal standard.* The appearance of pharmaceuticals in municipal wastewater (sewage) is an increasing problem that is likely to have adverse effects on our drinking water supply. Sewage is a complex matrix. When the drug carbamazepine was spiked into sewage at a concentration of 5 ppb, chromatographic analysis gave an apparent spike recovery of 154%.[16] When deuterated carbamazepine was used as an internal standard for the analysis, the apparent recovery was 98%. Explain how the internal standard is used in this analysis and rationalize why it works so well to correct for matrix effects.



Carbamazepine Carbamazepine-d_{10}

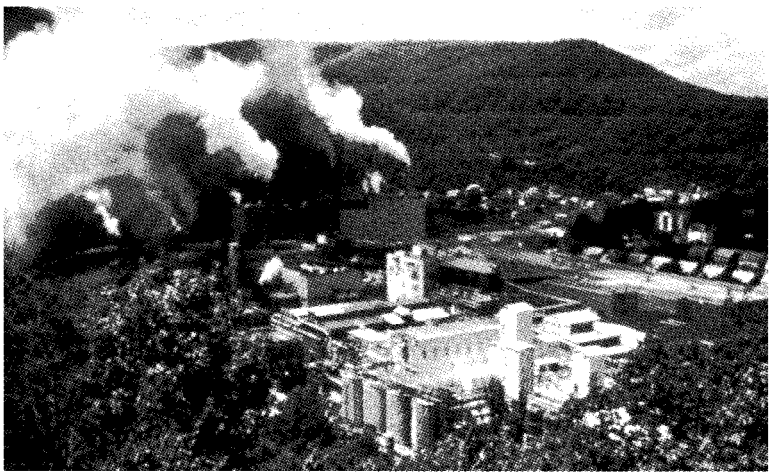
Experimental Design

5-34. Acid-base titrations similar to those in Section 5-5 had volumes and results shown in the table.[14] Use Excel LINEST to find the concentrations of acids A, B, and C and estimate their uncertainty.

Acid volume (mL)			mmol of OH^-
A	B	C	required
2	2	2	3.015
0	2	2	1.385
2	0	2	2.180
2	2	0	2.548
2	2	2	3.140

6 Chemical Equilibrium

CHEMICAL EQUILIBRIUM IN THE ENVIRONMENT



Paper mill on the Potomac River near Westernport, Maryland, neutralizes acid mine drainage in the water. Upstream of the mill, the river is acidic and lifeless; below the mill, the river teems with life. [Photo courtesy C. Dalpra, Potomac River Basin Commission.]

Great Barrier Reef and other coral reefs are threatened with extinction by rising atmospheric CO_2. [Copyright Jon Arnold Images/Almay.]

Part of the North Branch of the Potomac River runs crystal clear through the scenic Appalachian Mountains, but it is lifeless—a victim of acid drainage from abandoned coal mines. As the river passes a paper mill and a wastewater treatment plant near Westernport, Maryland, the pH rises from an acidic, lethal value of 4.5 to a neutral value of 7.2, at which fish and plants thrive. This happy "accident" comes about because calcium carbonate exiting the paper mill equilibrates with massive quantities of carbon dioxide from bacterial respiration at the sewage treatment plant. The resulting soluble bicarbonate neutralizes the acidic river and restores life downstream of the plant.[1] In the absence of CO_2, solid $CaCO_3$ would be trapped at the treatment plant and would never enter the river.

$$\underset{\text{Calcium carbonate trapped at treatment plant}}{CaCO_3(s)} + CO_2(aq) + H_2O(l) \rightleftharpoons \underset{\text{Dissolved calcium bicarbonate enters river and neutralizes acid}}{Ca^{2+}(aq) + 2HCO_3^-(aq)}$$

$$\underset{\text{Bicarbonate}}{HCO_3^-(aq)} + \underset{\text{Acid in river}}{H^+(aq)} \xrightarrow{\text{neutralization}} CO_2(g) + H_2O(l)$$

The chemistry that helps the Potomac River endangers coral reefs, which are largely $CaCO_3$. Burning of fossil fuel has increased CO_2 in the atmosphere from 280 ppm when Captain Cook first sighted the Great Barrier Reef in 1770 to 380 ppm today (Figure 0-6). CO_2 in the atmosphere adds CO_2 to the ocean, dissolving $CaCO_3$ from coral. Rising CO_2 and, perhaps, rising atmospheric temperature from the greenhouse effect threaten coral reefs with extinction.[2] CO_2 has lowered the average pH of the ocean from its preindustrial value of 8.16 to 8.04 today.[3] Without changes in man's activities, the pH could be 7.7 by 2100.

Chemical equilibrium provides a foundation not only for chemical analysis, but also for other subjects such as biochemistry, geology, and oceanography. This chapter introduces equilibria for the solubility of ionic compounds, complex formation, and acid-base reactions.

6-1 The Equilibrium Constant

For the reaction

$$aA + bB \rightleftharpoons cC + dD \tag{6-1}$$

we write the **equilibrium constant,** K, in the form

Equation 6-2, the *law of mass action*, was formulated by the Norwegians C. M. Guldenberg and P. Waage in 1864. Their derivation was based on the idea that the forward and reverse rates of a reaction at equilibrium must be equal.[4]

Equilibrium constant:

$$K = \frac{[C]^c[D]^d}{[A]^a[B]^b} \tag{6-2}$$

where the lowercase superscript letters denote stoichiometry coefficients and each capital letter stands for a chemical species. The symbol [A] stands for the concentration of A relative to its standard state (defined next). By definition, *a reaction is favored whenever* $K > 1$.

The equilibrium constant is more correctly expressed as a ratio of *activities* rather than of concentrations. We reserve the discussion of activity for Chapter 7.

In the thermodynamic derivation of the equilibrium constant, each quantity in Equation 6-2 is expressed as the *ratio* of the concentration of a species to its concentration in its **standard state.** For solutes, the standard state is 1 M. For gases, the standard state is 1 bar ($\equiv 10^5$ Pa; 1 atm $\equiv$ 1.013 25 bar), and for solids and liquids, the standard states are the pure solid or liquid. It is understood that [A] in Equation 6-2 really means [A]/(1 M) if A is a solute. If D is a gas, [D] really means (pressure of D in bars)/(1 bar). To emphasize that [D] means pressure of D, we usually write P_D in place of [D]. The terms in Equation 6-2 are actually dimensionless; therefore, all equilibrium constants are dimensionless.

Equilibrium constants are dimensionless.

For the ratios [A]/(1 M) and [D]/(1 bar) to be dimensionless, [A] *must* be expressed in moles per liter (M), and [D] *must* be expressed in bars. If C were a pure liquid or solid, the ratio [C]/(concentration of C in its standard state) would be unity (1) because the standard state is the pure liquid or solid. If C is a solvent, the concentration is so close to that of pure liquid C that the value of [C] is still essentially 1.

The take-home lesson is this: When you evaluate an equilibrium constant,

1. Concentrations of solutes should be expressed as moles per liter.
2. Concentrations of gases should be expressed in bars.
3. Concentrations of pure solids, pure liquids, and solvents are omitted because they are unity.

Equilibrium constants are dimensionless but, when specifying concentrations, you must use units of molarity (M) for solutes and bars for gases.

These conventions are arbitrary, but you must use them if you wish to use tabulated values of equilibrium constants, standard reduction potentials, and free energies.

Manipulating Equilibrium Constants

Consider the reaction

Throughout this book, assume that all species in chemical equations are in aqueous solution, unless otherwise specified.

$$HA \rightleftharpoons H^+ + A^- \qquad K_1 = \frac{[H^+][A^-]}{[HA]}$$

If the direction of a reaction is reversed, the new value of K is simply the reciprocal of the original value of K.

Equilibrium constant for reverse reaction:

$$H^+ + A^- \rightleftharpoons HA \qquad K_1' = \frac{[HA]}{[H^+][A^-]} = 1/K_1$$

If two reactions are added, the new K is the product of the two individual values:

$$\begin{array}{lll} HA & \rightleftharpoons \cancel{[H^+]} + A^- & K_1 \\ \cancel{[H^+]} + C & \rightleftharpoons CH^+ & K_2 \\ \hline HA + C & \rightleftharpoons A^- + CH^+ & K_3 \end{array}$$

If a reaction is reversed, then $K' = 1/K$. If two reactions are added, then $K_3 = K_1K_2$.

Equilibrium constant for sum of reactions:

$$K_3 = K_1K_2 = \frac{\cancel{[H^+]}[A^-]}{[HA]} \cdot \frac{[CH^+]}{\cancel{[H^+]}[C]} = \frac{[A^-][CH^+]}{[HA][C]}$$

If n reactions are added, the overall equilibrium constant is the product of n individual equilibrium constants.

EXAMPLE **Combining Equilibrium Constants**

The equilibrium constant for the reaction $H_2O \rightleftharpoons H^+ + OH^-$ is called K_w ($= [H^+][OH^-]$) and has the value 1.0×10^{-14} at 25°C. Given that $K_{NH_3} = 1.8 \times 10^{-5}$ for the reaction $NH_3(aq) + H_2O \rightleftharpoons NH_4^+ + OH^-$, find K for the reaction $NH_4^+ \rightleftharpoons NH_3(aq) + H^+$.

Solution The third reaction can be obtained by reversing the second reaction and adding it to the first reaction:

$$\begin{array}{rcl} \cancel{H_2O} \rightleftharpoons H^+ + \cancel{OH^-} & & K = K_w \\ NH_4^+ + \cancel{OH^-} \rightleftharpoons NH_3(aq) + \cancel{H_2O} & & K = 1/K_{NH_3} \\ \hline NH_4^+ \rightleftharpoons H^+ + NH_3(aq) & & K = K_w \cdot \dfrac{1}{K_{NH_3}} = 5.6 \times 10^{-10} \end{array}$$

Test Yourself For the reaction $Li^+ + H_2O \rightleftharpoons Li(OH)(aq) + H^+$, $K_{Li} = 2.3 \times 10^{-14}$. Combine this reaction with the K_w reaction to find the equilibrium constant for the reaction $Li^+ + OH^- \rightleftharpoons Li(OH)(aq)$. (***Answer:*** 2.3)

6-2 Equilibrium and Thermodynamics

Equilibrium is controlled by the thermodynamics of a chemical reaction. The heat absorbed or released (*enthalpy*) and the degree of disorder of reactants and products (*entropy*) independently contribute to the degree to which the reaction is favored or disfavored.

Enthalpy

The **enthalpy change,** ΔH, for a reaction is the heat absorbed or released when the reaction takes place under constant applied pressure.[5] The *standard enthalpy change*, $\Delta H°$, refers to the heat absorbed when all reactants and products are in their standard states:[†]

$$HCl(g) \rightleftharpoons H^+(aq) + Cl^-(aq) \qquad \Delta H° = -74.85 \text{ kJ/mol at } 25°C \qquad \textbf{(6-3)}$$

$\Delta H = (+)$
Heat is absorbed
Endothermic

$\Delta H = (-)$
Heat is liberated
Exothermic

The negative sign of $\Delta H°$ indicates that heat is released by Reaction 6-3—the solution becomes warmer. For other reactions, ΔH is positive, which means that heat is absorbed. Consequently, the solution gets colder during the reaction. A reaction for which ΔH is positive is said to be **endothermic.** Whenever ΔH is negative, the reaction is **exothermic.**

Entropy

The **entropy,** S, of a substance is a measure of its "disorder," which we will not attempt to define in a quantitative way. The greater the disorder, the greater the entropy. In general, a gas is more disordered (has higher entropy) than a liquid, which is more disordered than a solid. Ions in aqueous solution are normally more disordered than in their solid salt:

$$KCl(s) \rightleftharpoons K^+(aq) + Cl^-(aq) \qquad \Delta S° = +76.4 \text{ J/(K·mol) at } 25°C \qquad \textbf{(6-4)}$$

$\Delta S = (+)$
Products more disordered than reactants

$\Delta S = (-)$
Products less disordered than reactants

$\Delta S°$ is the change in entropy (entropy of products minus entropy of reactants) when all species are in their standard states. The positive value of $\Delta S°$ indicates that a mole of $K^+(aq)$ plus a mole of $Cl^-(aq)$ is more disordered than a mole of $KCl(s)$. For Reaction 6-3, $\Delta S° = -130.4$ J/(K·mol) at 25°C. The aqueous ions are less disordered than gaseous HCl.

Free Energy

Systems at constant temperature and pressure, which are common laboratory conditions, have a tendency toward lower enthalpy and higher entropy. A chemical reaction is driven toward the formation of products by a *negative* value of ΔH (heat given off) or a *positive* value of ΔS (more disorder) or both. When ΔH is negative and ΔS is positive, the reaction is clearly favored. When ΔH is positive and ΔS is negative, the reaction is clearly disfavored.

[†]The definition of the standard state contains subtleties beyond the scope of this book. For Reaction 6-3, the standard state of H^+ or Cl^- is the hypothetical state in which each ion is present at a concentration of 1 M but behaves as if it were in an infinitely dilute solution. That is, the standard concentration is 1 M, but the standard behavior is what would be observed in a very dilute solution in which each ion is unaffected by surrounding ions.

When ΔH and ΔS are both positive or both negative, what decides whether a reaction will be favored? The change in **Gibbs free energy,** ΔG, is the arbiter between opposing tendencies of ΔH and ΔS. At constant temperature, T,

Free energy: $$\Delta G = \Delta H - T\Delta S \tag{6-5}$$

A *reaction is favored if* ΔG *is negative*.

For the dissociation of HCl (Reaction 6-3) when all species are in their standard states, $\Delta H°$ favors the reaction and $\Delta S°$ disfavors it. To find the net result, we evaluate $\Delta G°$:

Note that 25.00°C = 298.15 K.

$$\begin{aligned}\Delta G° &= \Delta H° - T\Delta S° \\ &= (-74.85 \times 10^3 \text{ J/mol}) - (298.15 \text{ K})(-130.4 \text{ J/K·mol}) \\ &= -35.97 \text{ kJ/mol}\end{aligned}$$

$\Delta G°$ is negative, so the reaction is favored when all species are in their standard states. The favorable influence of $\Delta H°$ is greater than the unfavorable influence of $\Delta S°$ in this case.

The point of discussing free energy is to relate the equilibrium constant to the energetics ($\Delta H°$ and $\Delta S°$) of a reaction. The equilibrium constant depends on $\Delta G°$ in the following manner:

Challenge Satisfy yourself that K > 1 if $\Delta G°$ is negative.

Free energy and equilibrium: $$K = e^{-\Delta G°/RT} \tag{6-6}$$

where R is the gas constant [= 8.314 472 J/(K·mol)] and T is temperature (Kelvin). The more negative the value of $\Delta G°$, the larger is the equilibrium constant. For Reaction 6-3,

$$K = e^{-(-35.97\times 10^3 \text{ J/mol})/[8.314\,472 \text{ J/(K·mol)}](298.15 \text{ K})} = 2.00 \times 10^6$$

Because the equilibrium constant is large, HCl(g) is very soluble in water and is nearly completely ionized to H^+ and Cl^- when it dissolves.

$\Delta G = (+)$
Reaction is disfavored

$\Delta G = (-)$
Reaction is favored

To summarize, a chemical reaction is favored by the liberation of heat (ΔH negative) and by an increase in disorder (ΔS positive). ΔG takes both effects into account to determine whether or not a reaction is favorable. We say that a reaction is *spontaneous* under standard conditions if $\Delta G°$ is negative or, equivalently, if $K > 1$. The reaction is not spontaneous if $\Delta G°$ is positive ($K < 1$). You should be able to calculate K from $\Delta G°$ and vice versa.

Le Châtelier's Principle

Suppose that a system at equilibrium is subjected to a change that disturbs the system. **Le Châtelier's principle** states that the direction in which the system proceeds back to equilibrium is such that the change is partially offset.

To see what this statement means, let's see what happens when we attempt to change the concentration of one species in the reaction

$$\underset{\text{Bromate}}{BrO_3^-} + \underset{\text{Chromium(III)}}{2Cr^{3+}} + 4H_2O \rightleftharpoons Br^- + \underset{\text{Dichromate}}{Cr_2O_7^{2-}} + 8H^+ \tag{6-7}$$

Notice that H_2O is omitted from K because it is the solvent.

$$K = \frac{[Br^-][Cr_2O_7^{2-}][H^+]^8}{[BrO_3^-][Cr^{3+}]^2} = 1 \times 10^{11} \text{ at } 25°C$$

In one particular equilibrium state of this system, the following concentrations exist: $[H^+] = 5.0$ M, $[Cr_2O_7^{2-}] = 0.10$ M, $[Cr^{3+}] = 0.003\,0$ M, $[Br^-] = 1.0$ M, and $[BrO_3^-] = 0.043$ M. Suppose that the equilibrium is disturbed by adding dichromate to the solution to increase the concentration of $[Cr_2O_7^{2-}]$ from 0.10 to 0.20 M. In what direction will the reaction proceed to reach equilibrium?

According to the principle of Le Châtelier, the reaction should go back to the left to partially offset the increase in dichromate, which appears on the right side of Reaction 6-7. We can verify this algebraically by setting up the **reaction quotient,** Q, which has the same form as the equilibrium constant. The only difference is that Q is evaluated with whatever concentrations happen to exist, even though the solution is not at equilibrium. When the system reaches equilibrium, $Q = K$. For Reaction 6-7,

The reaction quotient has the same form as the equilibrium constant, but the concentrations are generally not the equilibrium concentrations.

$$Q = \frac{(1.0)\,(0.20)(5.0)^8}{(0.043)(0.003\,0)^2} = 2 \times 10^{11} > K$$

Because $Q > K$, the reaction must go to the left to decrease the numerator and increase the denominator, until $Q = K$.

If $Q < K$, then the reaction must proceed to the right to reach equilibrium. If $Q > K$, then the reaction must proceed to the left to reach equilibrium.

1. If a reaction is at equilibrium and products are added (or reactants are removed), the reaction goes to the left.
2. If a reaction is at equilibrium and reactants are added (or products are removed), the reaction goes to the right.

When the temperature of a system is changed, so is the equilibrium constant. Equations 6-5 and 6-6 can be combined to predict the effect of temperature on K:

$$K = e^{-\Delta G^\circ/RT} = e^{-(\Delta H^\circ - T\Delta S^\circ)/RT} = e^{(-\Delta H^\circ/RT + \Delta S^\circ/R)}$$
$$= e^{-\Delta H^\circ/RT} \cdot e^{\Delta S^\circ/R} \qquad \textbf{(6-8)}$$

$e^{(a+b)} = e^a \cdot e^b$

The term $e^{\Delta S^\circ/R}$ is independent of T (at least over a limited temperature range in which ΔS° is constant). The term $e^{-\Delta H^\circ/RT}$ increases with increasing temperature if ΔH° is positive and decreases if ΔH° is negative. Therefore,

1. The equilibrium constant of an endothermic reaction ($\Delta H^\circ = +$) increases if the temperature is raised.
2. The equilibrium constant of an exothermic reaction ($\Delta H^\circ = -$) decreases if the temperature is raised.

These statements can be understood in terms of Le Châtelier's principle as follows. Consider an endothermic reaction:

$$\text{Heat} + \text{reactants} \rightleftharpoons \text{products}$$

Heat can be treated as if it were a reactant in an endothermic reaction and a product in an exothermic reaction.

If the temperature is raised, then heat is added to the system. The reaction proceeds to the right to partially offset this change.[6]

In dealing with equilibrium problems, we are making *thermodynamic* predictions, not *kinetic* predictions. We are calculating what must happen for a system to reach equilibrium, but not how long it will take. Some reactions are over in an instant; others will not reach equilibrium in a million years. For example, dynamite remains unchanged indefinitely, until a spark sets off the spontaneous, explosive decomposition. The size of an equilibrium constant tells us nothing about the rate (the kinetics) of the reaction. A large equilibrium constant does not imply that a reaction is fast.

6-3 Solubility Product

In chemical analysis, we encounter solubility in precipitation titrations, electrochemical reference cells, and gravimetric analysis. The effect of acid on the solubility of minerals and the effect of atmospheric CO_2 on the solubility (and death) of coral reefs are important in environmental science.

The **solubility product** is the equilibrium constant for the reaction in which a solid salt dissolves to give its constituent ions in solution. Solid is omitted from the equilibrium constant because it is in its standard state. Appendix F lists solubility products.

As an example, consider the dissolution of mercury(I) chloride (Hg_2Cl_2, also called mercurous chloride) in water. The reaction is

$$Hg_2Cl_2(s) \rightleftharpoons Hg_2^{2+} + 2Cl^- \qquad \textbf{(6-9)}$$

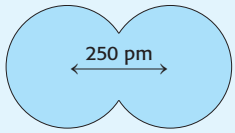
for which the solubility product, K_{sp}, is

$$K_{sp} = [Hg_2^{2+}][Cl^-]^2 = 1.2 \times 10^{-18} \qquad \textbf{(6-10)}$$

A solution containing excess, undissolved solid is said to be **saturated** with that solid. The solution contains all the solid capable of being dissolved under the prevailing conditions.

The physical meaning of the solubility product is this: If an aqueous solution is left in contact with excess solid Hg_2Cl_2, the solid will dissolve until the condition $[Hg_2^{2+}][Cl^-]^2 = K_{sp}$ is satisfied. Thereafter, the amount of undissolved solid remains constant. Unless excess solid remains, there is no guarantee that $[Hg_2^{2+}][Cl^-]^2 = K_{sp}$. If Hg_2^{2+} and Cl^- are mixed together (with appropriate counterions) such that the product $[Hg_2^{2+}][Cl^-]^2$ exceeds K_{sp}, then Hg_2Cl_2 will precipitate.

Mercurous ion, Hg_2^{2+}, is a *dimer* (pronounced DIE mer), which means that it consists of two identical units bound together:



$[Hg{-}Hg]^{2+}$
+1 oxidation state of mercury

OH^-, S^{2-}, and CN^- stabilize Hg(II), thereby converting Hg(I) into Hg(0) and Hg(II):

$$\underset{\text{Hg(I)}}{Hg_2^{2+}} + 2CN^- \rightarrow \underset{\text{Hg(II)}}{Hg(CN)_2(aq)} + \underset{\text{Hg(0)}}{Hg(l)}$$

Disproportionation is the process in which an element in an intermediate oxidation state gives products in both higher and lower oxidation states.

BOX 6-1 Solubility Is Governed by More Than the Solubility Product

If we want to know how much Hg_2^{2+} is dissolved in a saturated solution of Hg_2Cl_2, we are tempted to look at Reaction 6-9 and to note that two Cl^- are created for each Hg_2^{2+}. If we let x be the concentration of Hg_2^{2+}, we could say that the concentration of Cl^- is $2x$. Substituting these values into the solubility product expression 6-10, we could write $K_{sp} = [Hg_2^{2+}][Cl^-]^2 = (x)(2x)^2$, and we would find $[Hg_2^{2+}] = x = 6.7 \times 10^{-7}$ M.

However, this answer is incorrect because we have not accounted for other reactions, such as

Hydrolysis: $Hg_2^{2+} + H_2O \rightleftharpoons Hg_2OH^+ + H^+ \quad K = 10^{-5.3}$

Disproportionation: $2Hg_2^{2+} \rightleftharpoons Hg^{2+} + Hg(l) \quad K = 10^{-2.1}$

Both reactions consume Hg_2^{2+}. By Le Chatelier's principle, if Hg_2^{2+} is consumed, more Hg_2Cl_2 will dissolve. We need to know all significant chemical reactions to compute the solubility of a compound.

We most commonly use the solubility product to find the concentration of one ion when the concentration of the other is known or fixed by some means. For example, what is the concentration of Hg_2^{2+} in equilibrium with 0.10 M Cl^- in a solution of KCl containing excess, undissolved $Hg_2Cl_2(s)$? To answer this question, we rearrange Equation 6-10 to find

$$[Hg_2^{2+}] = \frac{K_{sp}}{[Cl^-]^2} = \frac{1.2 \times 10^{-18}}{0.10^2} = 1.2 \times 10^{-16}\ \text{M}$$

Because Hg_2Cl_2 is so slightly soluble, additional Cl^- obtained from Hg_2Cl_2 is negligible compared with 0.10 M Cl^-.

A *salt* is any ionic solid, such as Hg_2Cl_2 or $CaSO_4$.

The solubility product does not tell the entire story of solubility. In addition to complications described in Box 6-1, most salts form soluble *ion pairs* to some extent. That is, $MX(s)$ can give $MX(aq)$ as well as $M^+(aq)$ and $X^-(aq)$. In a saturated solution of $CaSO_4$, for example, two-thirds of the dissolved calcium is Ca^{2+} and one third is $CaSO_4(aq)$.[7] The $CaSO_4(aq)$ **ion pair** is a closely associated pair of ions that behaves as one species in solution. Appendix J and Box 7-1 provide information on ion pairs.[8]

Common Ion Effect

For the ionic solubility reaction

$$CaSO_4(s) \rightleftharpoons Ca^{2+} + SO_4^{2-} \qquad K_{sp} = 2.4 \times 10^{-5}$$

the product $[Ca^{2+}][SO_4^{2-}]$ is constant at equilibrium in the presence of excess solid $CaSO_4$. If the concentration of Ca^{2+} were increased by adding another source of Ca^{2+}, such as $CaCl_2$, then the concentration of SO_4^{2-} must decrease so that the product $[Ca^{2+}][SO_4^{2-}]$ remains constant. In other words, less $CaSO_4(s)$ will dissolve if Ca^{2+} or SO_4^{2-} is already present from some other source. Figure 6-1 shows how the solubility of $CaSO_4$ decreases in the presence of dissolved $CaCl_2$.

Common ion effect: A salt is less soluble if one of its ions is already present in the solution. Demonstration 6-1 illustrates the common ion effect.

This application of Le Chatelier's principle is called the **common ion effect.** *A salt will be less soluble if one of its constituent ions is already present in the solution.*

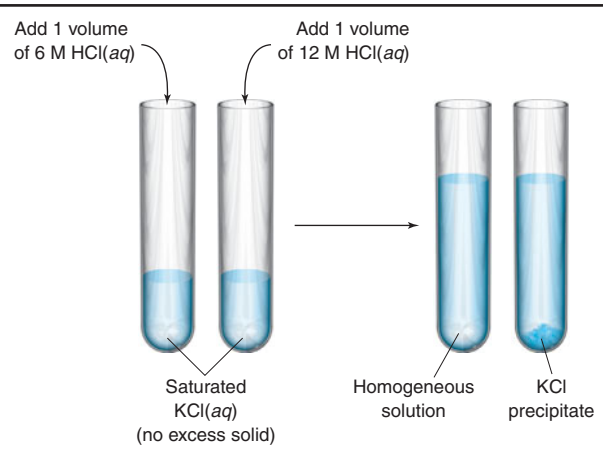
DEMONSTRATION 6-1 Common Ion Effect[9,10]

Fill two large test tubes about one-third full with saturated aqueous KCl containing no excess solid. The solubility of KCl is approximately 3.7 M, so the solubility product (ignoring activity effects introduced later) is

$$K_{sp} \approx [K^+][Cl^-] = (3.7)(3.7) = 13.7$$

Now add one-third of a test tube of 6 M HCl to one test tube and an equal volume of 12 M HCl to the other. Even though a common ion, Cl^-, is added in each case, KCl precipitates only in one tube.

To understand your observations, calculate the concentrations of K^+ and Cl^- in each tube after HCl addition. Then evaluate the reaction quotient, $Q = [K^+][Cl^-]$, for each tube. Explain your observations.



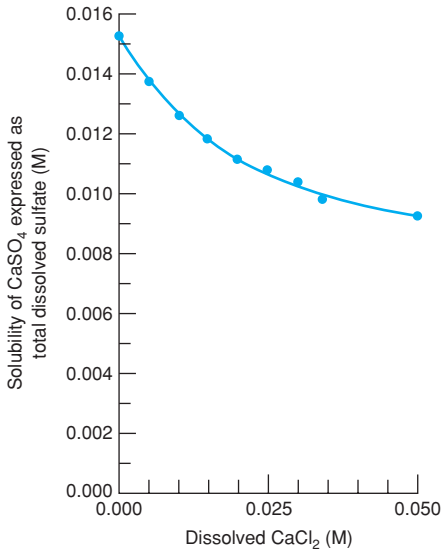


FIGURE 6-1 Solubility of $CaSO_4$ in solutions containing dissolved $CaCl_2$. Solubility is expressed as total dissolved sulfate, which is present as free SO_4^{2-} and as the ion pair, $CaSO_4(aq)$. [Data from reference 8.]

FIGURE 6-2 A yellow solid, lead(II) iodide (PbI_2), precipitates when a colorless solution of lead nitrate ($Pb(NO_3)_2$) is added to a colorless solution of potassium iodide (KI). [Photo by Chip Clark.]

Separation by Precipitation

Precipitation can sometimes be used to separate ions from each other.[11] For example, consider a solution containing lead(II) (Pb^{2+}) and mercury(I) (Hg_2^{2+}) ions, each at a concentration of 0.010 M. Each forms an insoluble iodide (Figure 6-2), but the mercury(I) iodide is considerably less soluble, as indicated by the smaller value of K_{sp}:

$$PbI_2(s) \rightleftharpoons Pb^{2+} + 2I^- \qquad K_{sp} = 7.9 \times 10^{-9}$$

$$Hg_2I_2(s) \rightleftharpoons Hg_2^{2+} + 2I^- \qquad K_{sp} = 4.6 \times 10^{-29}$$

The smaller K_{sp} implies a lower solubility for Hg_2I_2 because the stoichiometries of the two reactions are the same. If the stoichiometries were different, it does not follow that the smaller K_{sp} would imply lower solubility.

Is it possible to lower the concentration of Hg_2^{2+} by 99.990% by selective precipitation with I^-, without precipitating Pb^{2+}?

We are asking whether we can lower $[Hg_2^{2+}]$ to 0.010% of 0.010 M $= 1.0 \times 10^{-6}$ M without precipitating Pb^{2+}. Here is the experiment: We add enough I^- to precipitate 99.990% of Hg_2^{2+} if all the I^- reacts with Hg_2^{2+} and none reacts with Pb^{2+}. To see if any Pb^{2+} should precipitate, we need to know the concentration of I^- in equilibrium with precipitated $Hg_2I_2(s)$ plus the remaining 1.0×10^{-6} M Hg_2^{2+}.

$$Hg_2I_2(s) \overset{K_{sp}}{\rightleftharpoons} Hg_2^{2+} + 2I^-$$

$$[Hg_2^{2+}][I^-]^2 = K_{sp}$$

$$(1.0 \times 10^{-6})[I^-]^2 = 4.6 \times 10^{-29}$$

$$[I^-] = \sqrt{\frac{4.6 \times 10^{-29}}{1.0 \times 10^{-6}}} = 6.8 \times 10^{-12}\ \text{M}$$

Will this concentration of I^- cause 0.010 M Pb^{2+} to precipitate? That is, is the solubility product of PbI_2 exceeded?

$$Q = [Pb^{2+}][I^-]^2 = (0.010)(6.8 \times 10^{-12})^2$$

$$= 4.6 \times 10^{-25} < K_{sp} \quad (\text{for } PbI_2)$$

The reaction quotient, $Q = 4.6 \times 10^{-25}$ is less than K_{sp} for $PbI_2 = 7.9 \times 10^{-9}$. Therefore, Pb^{2+} will not precipitate and separation of Pb^{2+} and Hg_2^{2+} is feasible. We predict that adding I^- to a solution of Pb^{2+} and Hg_2^{2+} will precipitate virtually all the mercury(I) before any lead(II) precipitates.

Life should be so easy! We have just made a thermodynamic prediction. If the system comes to equilibrium, we can achieve the desired separation. However, occasionally one substance *coprecipitates* with the other. In **coprecipitation,** a substance whose solubility is not

Question If you want to know whether a small amount of Pb^{2+} coprecipitates with Hg_2I_2, should you measure the Pb^{2+} concentration in the mother liquor (the solution) or the Pb^{2+} concentration in the precipitate? Which measurement is more sensitive? By "sensitive," we mean responsive to a small amount of coprecipitation. (Answer: Measure Pb^{2+} in precipitate.)

exceeded precipitates along with another substance whose solubility is exceeded. For example, some Pb^{2+} might become adsorbed on the surface of the Hg_2I_2 crystal or might even occupy sites within the crystal. Our calculation says that the separation is worth trying. *Only an experiment can show whether the separation actually works.*

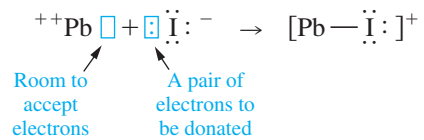
6-4 Complex Formation

If anion X^- precipitates metal M^+, it is often observed that a high concentration of X^- causes solid MX to redissolve. The increased solubility arises from formation of **complex ions,** such as MX_2^-, which consist of two or more simple ions bonded to one another.

Lewis Acids and Bases

In complex ions such as PbI^+, PbI_3^-, and PbI_4^{2-}, iodide is said to be the *ligand* of Pb^{2+}. A **ligand** is any atom or group of atoms attached to the species of interest. We say that Pb^{2+} acts as a *Lewis acid* and I^- acts as a *Lewis base* in these complexes. A **Lewis acid** accepts a pair of electrons from a **Lewis base** when the two form a bond:

Lewis acid + Lewis base ⇌ adduct
Electron pair acceptor — Electron pair donor



The product of the reaction between a Lewis acid and a Lewis base is called an *adduct*. The bond between a Lewis acid and a Lewis base is called a *dative* or *coordinate covalent* bond.

Effect of Complex Ion Formation on Solubility[12]

If Pb^{2+} and I^- only reacted to form solid PbI_2, then the solubility of Pb^{2+} would always be very low in the presence of excess I^-:

$$PbI_2(s) \overset{K_{sp}}{\rightleftharpoons} Pb^{2+} + 2I^- \qquad K_{sp} = [Pb^{2+}][I^-]^2 = 7.9 \times 10^{-9} \tag{6-11}$$

We observe, however, that high concentrations of I^- cause solid PbI_2 to dissolve. We explain this by the formation of a series of complex ions:

Notation for these equilibrium constants is discussed in Box 6-2.

$$Pb^{2+} + I^- \overset{K_1}{\rightleftharpoons} PbI^+ \qquad K_1 = [PbI^+]/[Pb^{2+}][I^-] = 1.0 \times 10^2 \tag{6-12}$$

$$Pb^{2+} + 2I^- \overset{\beta_2}{\rightleftharpoons} PbI_2(aq) \qquad \beta_2 = [PbI_2(aq)]/[Pb^{2+}][I^-]^2 = 1.4 \times 10^3 \tag{6-13}$$

$$Pb^{2+} + 3I^- \overset{\beta_3}{\rightleftharpoons} PbI_3^- \qquad \beta_3 = [PbI_3^-]/[Pb^{2+}][I^-]^3 = 8.3 \times 10^3 \tag{6-14}$$

$$Pb^{2+} + 4I^- \overset{\beta_4}{\rightleftharpoons} PbI_4^{2-} \qquad \beta_4 = [PbI_4^{2-}]/[Pb^{2+}][I^-]^4 = 3.0 \times 10^4 \tag{6-15}$$

The species $PbI_2(aq)$ in Reaction 6-13 is *dissolved* PbI_2, containing two iodine atoms bound to a lead atom. Reaction 6-13 is *not* the reverse of Reaction 6-11, in which the species is solid PbI_2.

BOX 6-2 Notation For Formation Constants

Formation constants are the equilibrium constants for complex ion formation. The **stepwise formation constants,** designated K_i, are defined as follows:

$$M + X \overset{K_1}{\rightleftharpoons} MX \qquad K_1 = [MX]/[M][X]$$

$$MX + X \overset{K_2}{\rightleftharpoons} MX_2 \qquad K_2 = [MX_2]/[MX][X]$$

$$MX_{n-1} + X \overset{K_n}{\rightleftharpoons} MX_n \qquad K_n = [MX_n]/[MX_{n-1}][X]$$

The **overall,** or **cumulative, formation constants** are denoted β_i:

$$M + 2X \overset{\beta_2}{\rightleftharpoons} MX_2 \qquad \beta_2 = [MX_2]/[M][X]^2$$

$$M + nX \overset{\beta_n}{\rightleftharpoons} MX_n \qquad \beta_n = [MX_n]/[M][X]^n$$

A useful relation is that $\beta_n = K_1K_2 \cdots K_n$. Some formation constants can be found in Appendix I.

At low I^- concentrations, the solubility of lead is governed by precipitation of $PbI_2(s)$. At high I^- concentrations, Reactions 6-12 through 6-15 are driven to the right (Le Châtelier's principle), and the total concentration of dissolved lead is considerably greater than that of Pb^{2+} alone (Figure 6-3).

A most useful characteristic of chemical equilibrium is that *all equilibria are satisfied simultaneously*. If we know $[I^-]$, we can calculate $[Pb^{2+}]$ by substituting the value of $[I^-]$ into

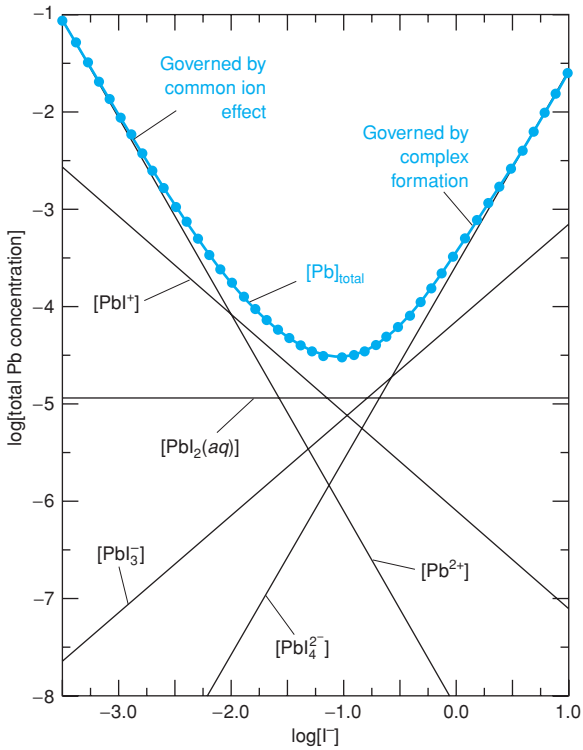


FIGURE 6-3 Total solubility of lead(II) (curve with circles) and solubilities of individual species (straight lines) as a function of the concentration of free iodide. To the left of the minimum, $[Pb]_{total}$ is governed by the solubility product for $PbI_2(s)$. As $[I^-]$ increases, $[Pb]_{total}$ decreases because of the common ion effect. At high values of $[I^-]$, $PbI_2(s)$ redissolves because it reacts with I^- to form soluble complex ions, such as PbI_4^{2-}. Note logarithmic scales. The solution is made slightly acidic so that $[PbOH^+]$ is negligible.

the equilibrium constant expression for Reaction 6-11, regardless of whether there are other reactions involving Pb^{2+}. *The concentration of Pb^{2+} that satisfies any one equilibrium must satisfy all equilibria. There can be only one concentration of Pb^{2+} in the solution.*

EXAMPLE Effect of I^- on the Solubility of Pb^{2+}

Find the concentrations of PbI^+, $PbI_2(aq)$, PbI_3^-, and PbI_4^{2-} in a solution saturated with $PbI_2(s)$ and containing dissolved I^- with a concentration of **(a)** 0.001 0 M and **(b)** 1.0 M.

Solution **(a)** From K_{sp} for Reaction 6-11, we calculate

$$[Pb^{2+}] = K_{sp}/[I^-]^2 = (7.9 \times 10^{-9})/(0.001\,0)^2 = 7.9 \times 10^{-3}\ \text{M}$$

From Reactions 6-12 through 6-15, we then calculate the concentrations of the other lead-containing species:

$$\begin{aligned}
[PbI^+] = K_1[Pb^{2+}[I^-] &= (1.0 \times 10^2)(7.9 \times 10^{-3})(1.0 \times 10^{-3}) \\
&= 7.9 \times 10^{-4}\ \text{M} \\
[PbI_2(aq)] = \beta_2[Pb^{2+}][I^-]^2 &= 1.1 \times 10^{-5}\ \text{M} \\
[PbI_3^-] = \beta_3[Pb^{2+}][I^-]^3 &= 6.6 \times 10^{-8}\ \text{M} \\
[PbI_4^{2-}] = \beta_4[Pb^{2+}][I^-]^4 &= 2.4 \times 10^{-10}\ \text{M}
\end{aligned}$$

(b) If, instead, we take $[I^-] = 1.0$ M, then analogous computations show that

$$[Pb^{2+}] = 7.9 \times 10^{-9}\ \text{M} \qquad [PbI_3^-] = 6.6 \times 10^{-5}\ \text{M}$$
$$[PbI^+] = 7.9 \times 10^{-7}\ \text{M} \qquad [PbI_4^{2-}] = 2.4 \times 10^{-4}\ \text{M}$$
$$[PbI_2(aq)] = 1.1 \times 10^{-5}\ \text{M}$$

Test Yourself Find $[Pb^{2+}]$, $[PbI_2(aq)]$, and $[PbI_3^-]$, in a saturated solution of $PbI_2(s)$ with $[I^-] = 0.10$ M. (***Answer:*** 7.9×10^{-7}, 1.1×10^{-5}, 6.6×10^{-6} M)

The total concentration of dissolved lead in the preceding example is

$$[Pb]_{total} = [Pb^{2+}] + [PbI^+] + [PbI_2(aq)] + [PbI_3^-] + [PbI_4^{2-}]$$

When $[I^-] = 10^{-3}$ M, $[Pb]_{total} = 8.7 \times 10^{-3}$ M, of which 91% is Pb^{2+}. As $[I^-]$ increases, $[Pb]_{total}$ decreases by the common ion effect operating in Reaction 6-11. However, at sufficiently high $[I^-]$, complex formation takes over and $[Pb]_{total}$ increases in Figure 6-3. When $[I^-] = 1.0$ M, $[Pb]_{total} = 3.2 \times 10^{-4}$ M, of which 76% is PbI_4^{2-}.

Tabulated Equilibrium Constants Are Usually Not "Constant"

If you look up the equilibrium constant of a chemical reaction in two different books, there is an excellent chance that the values will be different (sometimes by a factor of 10 or more).[13] This discrepancy occurs because the constant may have been determined under different conditions and, perhaps, by using different techniques.

The effect of dissolved ions on chemical equilibria is the subject of Chapter 7.

A common source of variation in the reported value of K is the ionic composition of the solution. Note whether K is reported for a particular ionic composition (for example, 1 M $NaClO_4$) or whether K has been extrapolated to zero ion concentration. If you need an equilibrium constant for your own work, choose a value of K measured under conditions as close as possible to those you will employ.

6-5 Protic Acids and Bases

Understanding the behavior of acids and bases is essential to every branch of science having anything to do with chemistry. In analytical chemistry, we almost always need to account for the effect of pH on analytical reactions involving complex formation or oxidation-reduction. pH can affect molecular charge and shape—factors that help determine which molecules can be separated from others in chromatography and electrophoresis and which molecules will be detected in some types of mass spectrometry.

In aqueous chemistry, an **acid** is a substance that increases the concentration of H_3O^+ **(hydronium ion)** when added to water. Conversely, a **base** decreases the concentration of H_3O^+. We will see that a decrease in H_3O^+ concentration necessarily requires an increase in OH^- concentration. Therefore, a base increases the concentration of OH^- in aqueous solution.

The word *protic* refers to chemistry involving transfer of H^+ from one molecule to another. The species H^+ is also called a *proton* because it is what remains when a hydrogen atom loses its electron. Hydronium ion, H_3O^+, is a combination of H^+ with H_2O. Although H_3O^+ is a more accurate representation than H^+ for the hydrogen ion in aqueous solution, we will use H_3O^+ and H^+ interchangeably in this book.

Brønsted-Lowry Acids and Bases

Brønsted-Lowry acid: proton donor

Brønsted-Lowry base: proton acceptor

J. N. Brønsted (1879–1947) of the University of Copenhagen and T. M. Lowry (1874–1936) of Cambridge University independently published their definitions of acids and bases in 1923.

Brønsted and Lowry classified *acids* as *proton donors* and *bases* as *proton acceptors*. HCl is an acid (a proton donor), and it increases the concentration of H_3O^+ in water:

$$HCl + H_2O \rightleftharpoons H_3O^+ + Cl^-$$

The Brønsted-Lowry definition does not require that H_3O^+ be formed. This definition can therefore be extended to nonaqueous solvents and to the gas phase:

$$\underset{\substack{\text{Hydrochloric acid}\\ \text{(acid)}}}{HCl(g)} + \underset{\substack{\text{Ammonia}\\ \text{(base)}}}{NH_3(g)} \rightleftharpoons \underset{\substack{\text{Ammonium chloride}\\ \text{(salt)}}}{NH_4^+Cl^-(s)}$$

For the remainder of this book, when we speak of acids and bases, we are speaking of Brønsted-Lowry acids and bases.

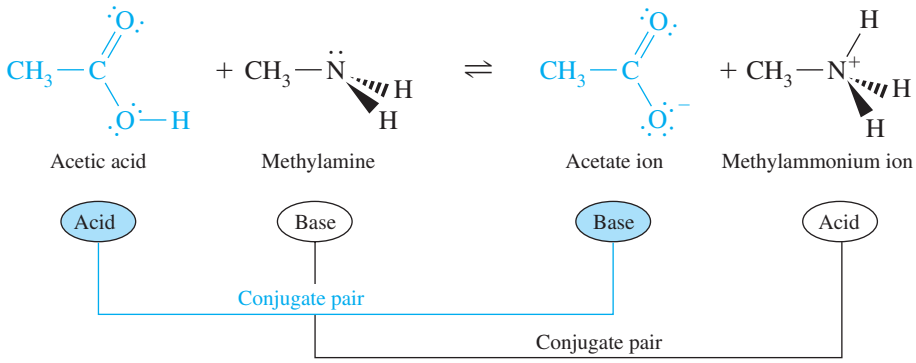
Salts

Any ionic solid, such as ammonium chloride, is called a **salt.** In a formal sense, a salt can be thought of as the product of an acid-base reaction. When an acid and a base react, they are said to **neutralize** each other. Most salts containing cations and anions with single positive and negative charges are strong electrolytes—they dissociate nearly completely into ions in dilute aqueous solution. Thus, ammonium chloride gives NH_4^+ and Cl^- in water:

$$NH_4^+Cl^-(s) \rightarrow NH_4^+(aq) + Cl^-(aq)$$

Conjugate Acids and Bases

The products of a reaction between an acid and a base are also classified as acids and bases:

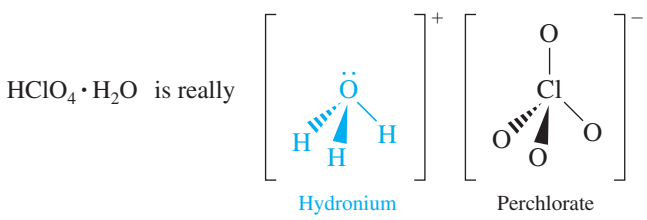


Conjugate acids and bases are related by the gain or loss of one proton. In these structures, a solid wedge is a bond coming out of the plane of the page and a dashed wedge is a bond to an atom behind the page.

Acetate is a base because it can accept a proton to make acetic acid. Methylammonium ion is an acid because it can donate a proton and become methylamine. Acetic acid and the acetate ion are said to be a **conjugate acid-base pair.** Methylamine and methylammonium ion are likewise conjugate. *Conjugate acids and bases are related to each other by the gain or loss of one* H^+.

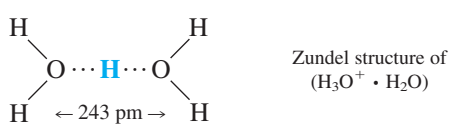
The Nature of H^+ and OH^-

The proton does not exist by itself in water. The simplest formula found in some crystalline salts is H_3O^+. For example, crystals of perchloric acid monohydrate contain pyramidal hydronium (also called *hydroxonium*) ions:



The formula $HClO_4 \cdot H_2O$ is a way of specifying the composition of the substance when we are ignorant of its structure. A more accurate formula would be $H_3O^+ClO_4^-$.

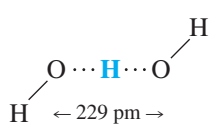
Average dimensions of the H_3O^+ cation in many crystals are shown in Figure 6-4. In aqueous solution, H_3O^+ is tightly associated with three molecules of water through exceptionally strong hydrogen bonds (Figure 6-5). The $H_5O_2^+$ cation is another simple species in which a hydrogen ion is shared by two water molecules.[16,17]

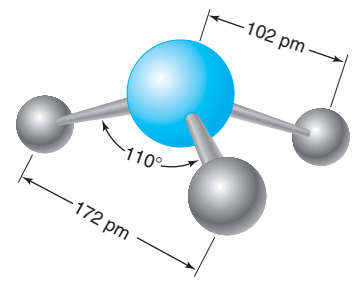


Zundel structure of ($H_3O^+ \cdot H_2O$)

In the gas phase, H_3O^+ can be surrounded by 20 molecules of H_2O in a regular dodecahedron held together by 30 hydrogen bonds.[18] In a salt containing the discrete cation $(C_6H_6)_3H_3O^+$, and in benzene solution, hydrogen atoms of the pyramidal H_3O^+ ion are each attracted toward the center of the pi electron cloud of a benzene ring (Figure 6-6).

The ion $H_3O_2^-$ ($OH^- \cdot H_2O$) has been observed by X-ray crystallography.[19] The central O···H···O linkage contains the shortest hydrogen bond involving H_2O that has ever been observed.





Eigen structure of H_3O^+

FIGURE 6-4 Structure of hydronium ion, H_3O^+, proposed by M. Eigen and found in many crystals.[14] The bond enthalpy (heat needed to break the OH bond) of H_3O^+ is 544 kJ/mol, about 84 kJ/mol greater than the bond enthalpy in H_2O.

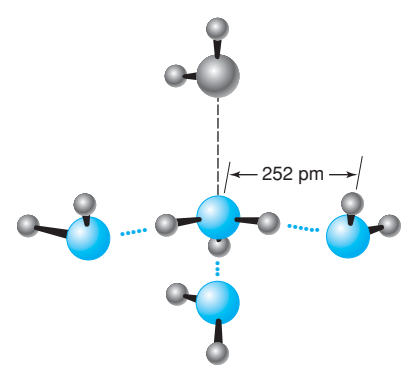


FIGURE 6-5 Environment of aqueous H_3O^+.[14] Three H_2O molecules are bound to H_3O^+ by strong hydrogen bonds (dotted lines), and one H_2O (at the top) is held by weaker ion-dipole attraction (dashed line). The O—H···O hydrogen-bonded distance of 252 pm (picometers, 10^{-12} m) compares with an O—H···O distance of 283 pm between hydrogen-bonded water molecules. The discrete cation $(H_2O)_3H_3O^+$ found in some crystals is similar in structure to $(H_2O)_4H_3O^+$, with the weakly bonded H_2O at the top removed.[15]

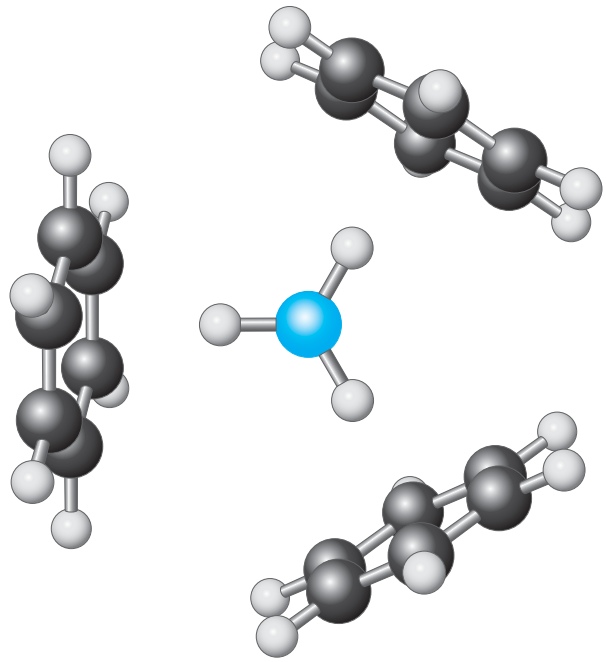


FIGURE 6-6 $H_3O^+ \cdot 3C_6H_6$ cation found in the crystal structure of $[(C_6H_6)_3H_3O^+][CHB_{11}Cl_{11}^-]$. [From E. S. Stoyanov, K.-C. Kim, and C. A. Reed, "The Nature of the H_3O^+ Hydronium Ion in Benzene and Chlorinated Hydrocarbon Solvents," *J. Am. Chem. Soc.* **2006,** *128*, 1948.]

We will ordinarily write H^+ in most chemical equations, although we really mean H_3O^+. To emphasize the chemistry of water, we will write H_3O^+. For example, water can be either an acid or a base. Water is an acid with respect to methoxide:

$$\underset{\text{Water}}{H-\ddot{\underset{\cdot\cdot}{O}}-H} + \underset{\text{Methoxide}}{CH_3-\ddot{\underset{\cdot\cdot}{O}}^-} \rightleftharpoons \underset{\text{Hydroxide}}{H-\ddot{\underset{\cdot\cdot}{O}}^-} + \underset{\text{Methanol}}{CH_3-\ddot{\underset{\cdot\cdot}{O}}-H}$$

But with respect to hydrogen bromide, water is a base:

$$\underset{\text{Water}}{H_2O} + \underset{\text{Hydrogen bromide}}{HBr} \rightleftharpoons \underset{\text{Hydronium ion}}{H_3O^+} + \underset{\text{Bromide}}{Br^-}$$

Autoprotolysis

Water undergoes self-ionization, called **autoprotolysis,** in which it acts as both an acid and a base:

$$H_2O + H_2O \rightleftharpoons H_3O^+ + OH^- \qquad \textbf{(6-16)}$$

or

We will write H^+ when we really mean H_3O^+.

$$H_2O \rightleftharpoons H^+ + OH^- \qquad \textbf{(6-17)}$$

Reactions 6-16 and 6-17 mean the same thing.

Protic solvents have a reactive H^+, and all protic solvents undergo autoprotolysis. An example is acetic acid:

Examples of protic solvents (acidic proton **bold**):

$\mathbf{H}_2O$	$CH_3CH_2O\mathbf{H}$
Water	Ethanol

$$2CH_3\overset{O}{\overset{\|}{C}}O\mathbf{H} \rightleftharpoons CH_3\overset{O\mathbf{H}}{\overset{\|}{C}}{}^+ + CH_3\overset{O}{\overset{\|}{C}}-O^- \quad \text{(in acetic acid)} \qquad \textbf{(6-18)}$$

$$\ \ \mathbf{OH}$$

Examples of **aprotic solvents** (no acidic protons):

$CH_3CH_2OCH_2CH_3$	CH_3CN
Diethyl ether	Acetonitrile

The extent of these reactions is very small. The *autoprotolysis constants* (equilibrium constants) for Reactions 6-17 and 6-18 are 1.0×10^{-14} and 3.5×10^{-15}, respectively, at 25°C.

6-6 pH

The autoprotolysis constant for H_2O has the special symbol K_w, where "w" stands for water:

Autoprotolysis of water:

$$H_2O \overset{K_w}{\rightleftharpoons} H^+ + OH^- \qquad K_w = [H^+][OH^-] \qquad \textbf{(6-19)}$$

Recall that H_2O (the solvent) is omitted from the equilibrium constant. The value $K_w = 1.0 \times 10^{-14}$ at 25°C is accurate enough for problems in this book.

Table 6-1 shows how K_w varies with temperature. Its value at 25.0°C is 1.01×10^{-14}.

TABLE 6-1 Temperature dependence of K_w[a]

Temperature (°C)	K_w	$pK_w = -\log K_w$	Temperature (°C)	K_w	$pK_w = -\log K_w$
0	1.15×10^{-15}	14.938	40	2.88×10^{-14}	13.541
5	1.88×10^{-15}	14.726	45	3.94×10^{-14}	13.405
10	2.97×10^{-15}	14.527	50	5.31×10^{-14}	13.275
15	4.57×10^{-15}	14.340	100	5.43×10^{-13}	12.265
20	6.88×10^{-15}	14.163	150	2.30×10^{-12}	11.638
25	1.01×10^{-14}	13.995	200	5.14×10^{-12}	11.289
30	1.46×10^{-14}	13.836	250	6.44×10^{-12}	11.191
35	2.07×10^{-14}	13.685	300	3.93×10^{-12}	11.406

a. Concentrations in the product $[H^+][OH^-]$ in this table are expressed in molality rather than in molarity. Accuracy of log K_w is ±0.01. To convert molality (mol/kg) into molarity (mol/L), multiply by the density of H_2O at each temperature. At 25°C, $K_w = 10^{-13.995}$ (mol/kg)^2(0.997 05 kg/L)^2 = $10^{-13.998}$(mol/L)^2.

*SOURCE: W. L. Marshall and E. U. Franck, "Ion Product of Water Substance, 0–1 000°C, 1–10,000 Bars," J. Phys. Chem. Ref. Data **1981,** 10, 295. For values of K_w over a temperature range of 0°–800°C and a density range of 0–1.2 g/cm^3, see A. V. Bandura and S. N. Lvov, "The Ionization Constant of Water over Wide Ranges of Temperature and Pressure," J. Phys. Chem. Ref. Data **2006**, 35, 15.*

EXAMPLE Concentration of H^+ and OH^- in Pure Water at 25°C

Calculate the concentrations of H^+ and OH^- in pure water at 25°C.

Solution The stoichiometry of Reaction 6-19 tells us that H^+ and OH^- are produced in a 1:1 molar ratio. Their concentrations must be equal. Calling each concentration x, we can write

$$K_w = 1.0 \times 10^{-14} = [H^+][OH^-] = [x][x] \Rightarrow x = 1.0 \times 10^{-7}\ \text{M}$$

The concentrations of H^+ and OH^- are both 1.0×10^{-7} M in pure water.

Test Yourself Use Table 6-1 to find the $[H^+]$ in water at 100°C and at 0°C. (***Answer:*** 7.4×10^{-7} and 3.4×10^{-8} M)

EXAMPLE Concentration of OH^- When $[H^+]$ Is Known

What is the concentration of OH^- if $[H^+] = 1.0 \times 10^{-3}$ M? (From now on, assume that the temperature is 25°C unless otherwise stated.)

Solution Putting $[H^+] = 1.0 \times 10^{-3}$ M into the K_w expression gives

$$K_w = 1.0 \times 10^{-14} = (1.0 \times 10^{-3})[OH^-] \Rightarrow [OH^-] = 1.0 \times 10^{-11}\ \text{M}$$

A concentration of $[H^+] = 1.0 \times 10^{-3}$ M gives $[OH^-] = 1.0 \times 10^{-11}$ M. *As the concentration of* H^+ *increases, the concentration of* OH^- *necessarily decreases, and vice versa.* A concentration of $[OH^-] = 1.0 \times 10^{-3}$ M gives $[H^+] = 1.0 \times 10^{-11}$ M.

Test Yourself Find $[OH^-]$ if $[H^+] = 1.0 \times 10^{-4}$ M. (***Answer:*** 1.0×10^{-10} M)

An approximate definition of **pH** is the negative logarithm of the H^+ concentration.

Approximate definition of pH: $$pH \approx -\log[H^+] \quad \textbf{(6-20)}$$

$pH \approx -\log[H^+]$. The term "pH" was introduced in 1909 by the Danish biochemist S. P. L. Sørensen, who called it the "hydrogen ion exponent."[20]

Chapter 7 defines pH more accurately in terms of *activities*, but, for many purposes, Equation 6-20 is a good definition. The measurement of pH with glass electrodes, and buffers used by the U.S. National Institute of Standards and Technology to define the pH scale, are described in Chapter 14.

In pure water at 25°C with $[H^+] = 1.0 \times 10^{-7}$ M, the pH is $-\log(1.0 \times 10^{-7}) = 7.00$. If $[OH^-] = 1.0 \times 10^{-3}$ M, then $[H^+] = 1.0 \times 10^{-11}$ M and the pH is 11.00. A useful relation between $[H^+]$ and $[OH^-]$ is

$$pH + pOH = -\log(K_w) = 14.00 \text{ at } 25°C \quad \textbf{(6-21)}$$

where $pOH = -\log[OH^-]$, just as $pH = -\log[H^+]$. Equation 6-21 is a fancy way of saying that if pH = 3.58, then pOH = 14.00 – 3.58 = 10.42, or $[OH^-] = 10^{-10.42} = 3.8 \times 10^{-11}$ M.

Take the log of both sides of the K_w expression to derive Equation 6-21:

$$K_w = [H^+][OH^-]$$
$$\log K_w = \log[H^+] + \log[OH^-]$$
$$-\log K_w = -\log[H^+] - \log[OH^-]$$
$$14.00 = pH + pOH \quad (\text{at } 25°C)$$

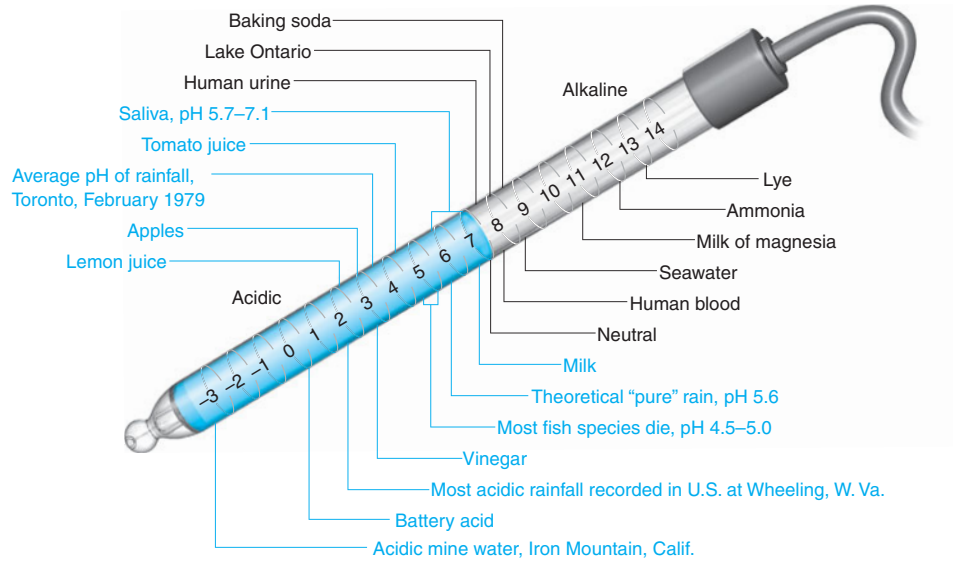
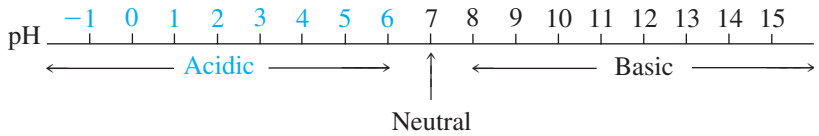


FIGURE 6-7 pH of various substances. [From *Chem. Eng. News,* 14 September 1981.] The most acidic rainfall (Box 14-1) is a stronger acid than lemon juice. The most acidic natural waters known are mine waters, with total dissolved metal concentrations of 200 g/L and sulfate concentrations of 760 g/L.[22] The pH of this water, –3.6, does not mean that $[H^+] = 10^{3.6}$ M = 4 000 M! It means that the *activity* of H^+ (discussed in Chapter 7) is $10^{3.6}$.

A solution is **acidic** if $[H^+] > [OH^-]$. A solution is **basic** if $[H^+] < [OH^-]$. At 25°C, an acidic solution has a pH below 7 and a basic solution has a pH above 7.



pH values for various common substances are shown in Figure 6-7.

Although pH generally falls in the range 0 to 14, these are not the limits of pH. A pH of –1, for example, means $-\log[H^+] = -1$; or $[H^+] = 10$ M. This concentration is attained in a concentrated solution of a strong acid such as HCl.

pH is measured with a *glass electrode* described in Chapter 14.

The surface of water or ice is ~2 pH units more acidic than the bulk because H_3O^+ is more stable on the surface. Surface acidity could be important to the chemistry of atmospheric clouds.[21]

Is There Such a Thing as Pure Water?

In most labs, the answer is "No." Pure water at 25°C should have a pH of 7.00. Distilled water from the tap in most labs is acidic because it contains CO_2 from the atmosphere. CO_2 is an acid by virtue of the reaction

$$CO_2 + H_2O \rightleftharpoons \underset{\text{Bicarbonate}}{HCO_3^-} + H^+ \qquad \textbf{(6-22)}$$

CO_2 can be largely removed by boiling water and then protecting it from the atmosphere.

More than a century ago, careful measurements of the conductivity of water were made by F. Kohlrausch and his students. To remove impurities, they found it necessary to distill water *42 consecutive times* under vacuum to reduce conductivity to a limiting value.

6-7 Strengths of Acids and Bases

Acids and bases are commonly classified as strong or weak, depending on whether they react nearly "completely" or only "partially" to produce H^+ or OH^-. Although there is no sharp distinction between weak and strong, some acids or bases react so completely that they are easily classified as strong—and, by convention, everything else is termed weak.

Strong Acids and Bases

Common strong acids and bases are listed in Table 6-2, which you need to memorize. By definition, a strong acid or base is completely dissociated in aqueous solution. That is, the equilibrium constants for the following reactions are large.

$$HCl(aq) \rightleftharpoons H^+ + Cl^-$$
$$KOH(aq) \rightleftharpoons K^+ + OH^-$$

Virtually no undissociated HCl or KOH exists in aqueous solution. Demonstration 6-2 shows a consequence of the strong-acid behavior of HCl.

TABLE 6-2 Common strong acids and bases

Formula	Name
Acids	
HCl	Hydrochloric acid (hydrogen chloride)
HBr	Hydrogen bromide
HI	Hydrogen iodide
H_2SO_4[a]	Sulfuric acid
HNO_3	Nitric acid
$HClO_4$	Perchloric acid
Bases	
LiOH	Lithium hydroxide
NaOH	Sodium hydroxide
KOH	Potassium hydroxide
RbOH	Rubidium hydroxide
CsOH	Cesium hydroxide
R_4NOH[b]	Quaternary ammonium hydroxide

a. For H_2SO_4, only the first proton ionization is complete. Dissociation of the second proton has an equilibrium constant of 1.0×10^{-2}.

b. This is a general formula for any hydroxide salt of an ammonium cation containing four organic groups. An example is tetrabutylammonium hydroxide: $(CH_3CH_2CH_2CH_2)_4N^+OH^-$.

DEMONSTRATION 6-2 The HCl Fountain

The complete dissociation of HCl into H^+ and Cl^- makes HCl(g) extremely soluble in water.

$$HCl(g) \rightleftharpoons HCl(aq) \quad \textbf{(A)}$$

$$HCl(aq) \rightleftharpoons H^+(aq) + Cl^-(aq) \quad \textbf{(B)}$$

Net reaction: $$HCl(g) \rightleftharpoons H^+(aq) + Cl^-(aq) \quad \textbf{(C)}$$

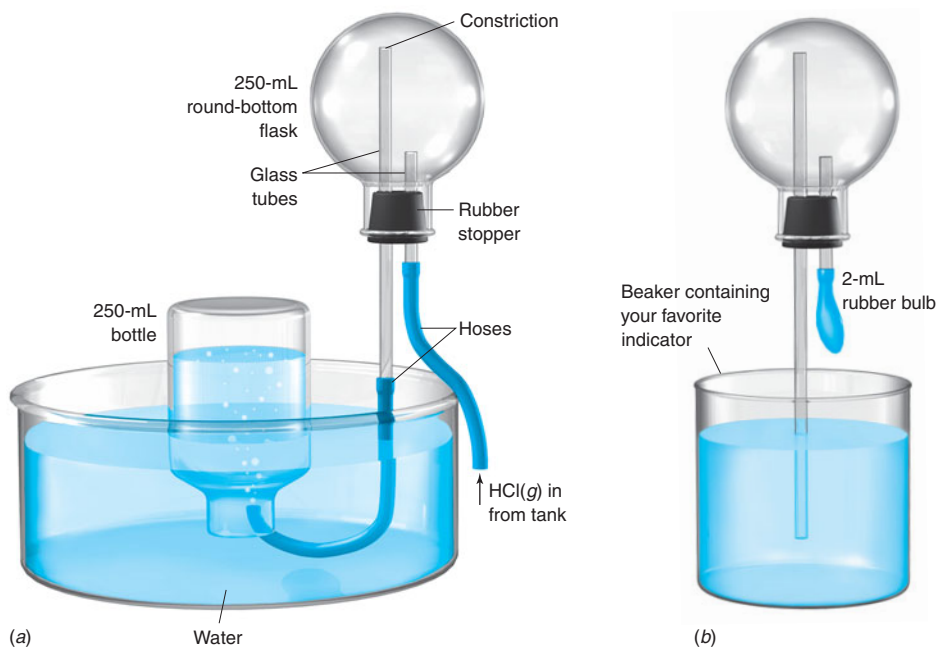
Because the equilibrium of Reaction B lies far to the right, it pulls Reaction A to the right as well.

Challenge The standard free energy change ($\Delta G°$) for Reaction C is -36.0 kJ/mol. Show that the equilibrium constant is 2.0×10^6.

The extreme solubility of HCl(g) in water is the basis for the HCl fountain,[23] assembled as shown below. In Figure *a*, an inverted 250-mL round-bottom flask containing air is set up with its inlet tube leading to a source of HCl(g) and its outlet tube directed into an inverted bottle of water. As HCl is admitted to the flask, air is displaced. When the bottle is filled with air, the flask is filled mostly with HCl(g).

The hoses are disconnected and replaced with a beaker of indicator and a rubber bulb (Figure *b*). For an indicator, we use slightly alkaline, commercial methyl purple solution, which is green above pH 5.4 and purple below pH 4.8. When ~1 mL of water is squirted from the rubber bulb into the flask, a vacuum is created and indicator solution is drawn up into the flask, making a fascinating fountain (Color Plate 1).

Question Why is a vacuum created when water is squirted into the flask, and why does the indicator change color when it enters the flask?



Even though the hydrogen halides HCl, HBr, and HI are strong acids, HF is *not* a strong acid, as explained in Box 6-3. For most purposes, the hydroxides of the alkaline earth metals (Mg^{2+}, Ca^{2+}, Sr^{2+}, and Ba^{2+}) can be considered to be strong bases, although they are far less soluble than alkali metal hydroxides and have some tendency to form MOH^+ complexes (Table 6-3). The strongest known base is the gas-phase molecule LiO^-.[25]

TABLE 6-3 Equilibria of alkaline earth metal hydroxides

$$M(OH)_2(s) \rightleftharpoons M^{2+} + 2OH^-$$
$$K_{sp} = [M^{2+}][OH^-]^2$$
$$M^{2+} + OH^- \rightleftharpoons MOH^+$$
$$K_1 = [MOH^+]/[M^{2+}][OH^-]$$

Metal	log K_{sp}	log K_1
Mg^{2+}	-11.15	2.58
Ca^{2+}	-5.19	1.30
Sr^{2+}	—	0.82
Ba^{2+}	—	0.64

NOTE: 25°C and ionic strength = 0.

Weak Acids and Bases

All weak acids, denoted HA, react with water by donating a proton to H_2O:

Dissociation of weak acid: $$HA + H_2O \overset{K_a}{\rightleftharpoons} H_3O^+ + A^- \quad \textbf{(6-23)}$$

which means exactly the same as

Dissociation of weak acid: $$HA \overset{K_a}{\rightleftharpoons} H^+ + A^- \qquad K_a = \frac{[H^+][A^-]}{[HA]} \quad \textbf{(6-24)}$$

Acid dissociation constant: $K_a = \dfrac{[H^+][A^-]}{[HA]}$.

The equilibrium constant is called K_a, the **acid dissociation constant.** By definition, a weak acid is one that is only partially dissociated in water, so K_a is "small."

BOX 6-3 The Strange Behavior of Hydrofluoric Acid[14]

The hydrogen halides HCl, HBr, and HI are all strong acids, which means that the reactions

$$HX(aq) + H_2O \rightarrow H_3O^+ + X^-$$

(X = Cl, Br, I) all go to completion. Why, then, does HF behave as a weak acid?

The answer is odd. First, HF does completely give up its proton to H_2O:

$$HF(aq) \rightarrow \underset{\text{Hydronium ion}}{H_3O^+} + \underset{\text{Fluoride ion}}{F^-}$$

But fluoride forms the strongest hydrogen bond of any ion. The hydronium ion remains tightly associated with F^- through a hydrogen bond. We call such an association an **ion pair.**

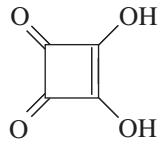
$$H_3O^+ + F^- \rightleftharpoons \underset{\text{An ion pair}}{F^- \cdots H_3O^+}$$

Ion pairs are common in aqueous solutions of any ion with a charge greater than 1. Ion pairs are the rule in nonaqueous solvents, which cannot promote ion dissociation as well as water.

Thus, HF does not behave as a strong acid because F^- and H_3O^+ remain associated with each other. Dissolving one mole of the strong acid HCl in water creates one mole of free H_3O^+. Dissolving one mole of the "weak" acid HF in water creates little free H_3O^+.

HF is not unique in its propensity to form ion pairs. Many moderately strong acids, such as those below, are thought to exist predominantly as ion pairs in aqueous solution ($HA + H_2O \rightleftharpoons A^- \cdots H_3O^+$).[24]

CF_3CO_2H
Trifluoroacetic acid
$K_a = 0.31$



Squaric acid
$K_a = 0.29$

Weak bases, B, react with water by abstracting a proton from H_2O:

Base hydrolysis constant: $K_b = \dfrac{[BH^+][OH^-]}{[B]}$

Hydrolysis refers to any reaction with water.

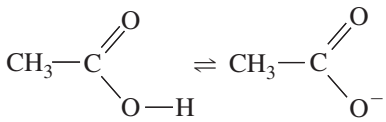
Base hydrolysis:

$$B + H_2O \xrightleftharpoons{K_b} BH^+ + OH^- \qquad K_b = \frac{[BH^+][OH^-]}{B} \tag{6-25}$$

The equilibrium constant K_b is the **base hydrolysis constant,** which is "small" for a weak base.

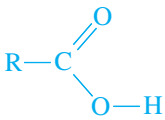
Common Classes of Weak Acids and Bases

Acetic acid is a typical weak acid.

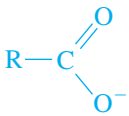


Acetic acid (HA) ⇌ Acetate (A^-) + H^+ $\qquad K_a = 1.75 \times 10^{-5}$ **(6-26)**

Acetic acid is a representative carboxylic acid, which has the general formula RCO_2H, where R is an organic substituent. *Most* **carboxylic acids** *are weak acids, and most* **carboxylate anions** *are weak bases.*



A carboxylic acid (weak acid, HA)

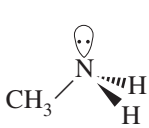


A carboxylate anion (weak base, A^-)

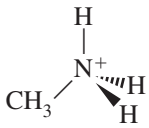
Methylamine is a typical weak base.

Carboxylic acids (RCO_2H) and ammonium ions (R_3NH^+) are weak acids.

Carboxylate anions (RCO_2^-) and amines (R_3N) are weak bases.



Methylamine B + H_2O ⇌



Methylammonium ion BH^+ + OH^- $\qquad K_b = 4.47 \times 10^{-4}$ **(6-27)**

Amines are nitrogen-containing compounds:

$R\ddot{N}H_2$	a primary amine	RNH_3^+	ammonium ions
$R_2\ddot{N}H$	a secondary amine	$R_2NH_2^+$	
$R_3\ddot{N}$	a tertiary amine	R_3NH^+	

Li^+ 13.64	Be													
Na^+ 13.9	Mg^{2+} 11.4											Al^{3+} 5.00		
K	Ca^{2+} 12.70	Sc^{3+} 4.3	Ti^{3+} 1.3	VO^{2+} 5.7	Cr^{2+} 5.5[a] Cr^{3+} 3.66	Mn^{2+} 10.6	Fe^{2+} 9.4 Fe^{3+} 2.19	Co^{2+} 9.7 Co^{3+} 0.5[b]	Ni^{2+} 9.9	Cu^{2+} 7.5	Zn^{2+} 9.0	Ga^{3+} 2.6	Ge	
Rb	Sr 13.18	Y^{3+} 7.7	Zr^{4+} –0.3	Nb	Mo	Tc	Ru	Rh^{3+} 3.33[c]	Pd^{2+} 1.0	Ag^+ 12.0	Cd^{2+} 10.1	In^{3+} 3.9	Sn^{2+} 3.4	Sb
Cs	Ba^{2+} 13.36	La^{3+} 8.5	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg_2^{2+} 5.3[d] Hg^{2+} 3.40	Tl^+ 13.21	Pb^{2+} 7.6	Bi^{3+} 1.1

Ce^{3+} 9.1[b]	Pr^{3+} 9.4[b]	Nd^{3+} 8.7[b]	Pm	Sm^{3+} 8.6[b]	Eu^{3+} 8.6[d]	Gd^{3+} 9.1[b]	Tb^{3+} 8.4[d]	Dy^{3+} 8.4[d]	Ho^{3+} 8.3	Er^{3+} 9.1[b]	Tm^{3+} 8.2[d]	Yb^{3+} 8.4[b]	Lu^{3+} 8.2[d]

Stronger acid

Ionic strength = 0 unless noted by superscript
a. Ionic strength = 1 M *b.* Ionic strength = 3 M *c.* Ionic strength = 2.5 M *d.* Ionic strength = 0.5 M

FIGURE 6-8 Acid dissociation constants (–log K_a) for aqueous metal ions: $M^{n+} + H_2O \overset{K_a}{\rightleftharpoons} MOH^{(n-1)+} + H^+$. For example, for Li^+, $K_a = 10^{-13.64}$. In Chapter 8, we will learn that the numbers in this table are called pK_a. Darkest shades are strongest acids. [Data from R. M. Smith, A. E. Martell, and R. J. Motekaitis, *NIST Critical Stability Constants of Metal Complexes Database 46* (Gaithersburg, MD: National Institute of Standards and Technology, 2001).]

Amines *are weak bases, and* **ammonium ions** *are weak acids.* The "parent" of all amines is ammonia, NH_3. When a base such as methylamine reacts with water, the product is the conjugate acid. That is, methylammonium ion produced in Reaction 6-27 is a weak acid:

$$\underset{BH^+}{CH_3\overset{+}{N}H_3} \overset{K_a}{\rightleftharpoons} \underset{B}{CH_3\ddot{N}H_2} + H^+ \qquad K_a = 2.26 \times 10^{-11} \qquad \textbf{(6-28)}$$

The methylammonium ion is the conjugate acid of methylamine.

You should learn to recognize whether a compound is acidic or basic. The salt methylammonium chloride, for example, dissociates in aqueous solution to give methylammonium cation and chloride:

$$\underset{\text{Methylammonium chloride}}{CH_3\overset{+}{N}H_3Cl^-(s)} \rightarrow \underset{\text{Methylammonium ion}}{CH_3\overset{+}{N}H_3(aq)} + Cl^-(aq) \qquad \textbf{(6-29)}$$

Methylammonium ion, being the conjugate acid of methylamine, is a weak acid (Reaction 6-28). Chloride is the conjugate base of HCl, a strong acid. In other words, Cl^- *has virtually no tendency to associate with* H^+, or else HCl would not be a strong acid. Methylammonium chloride is acidic because methylammonium ion is an acid and Cl^- is not a base.

Metal cations, M^{n+} act as weak acids by *acid hydrolysis* to form $M(OH)^{(n-1)+}$.[26] Figure 6-8 shows acid dissociation constants for the reaction

$$M^{n+} + H_2O \overset{K_a}{\rightleftharpoons} MOH^{(n-1)+} + H^+$$

Monovalent metal ions are very weak acids (Na^+, $K_a = 10^{-13.9}$). Divalent ions tend to be stronger (Fe^{2+}, $K_a = 10^{-9.4}$) and trivalent ions are stronger yet (Fe^{3+}, $K_a = 10^{-2.19}$).

Although we will usually write a **base** as **B** and an **acid** as **HA**, it is important to realize that **BH^+** is also an **acid** and **A^-** is also a **base**.

Methylammonium chloride is a weak acid because

1. It dissociates into $CH_3NH_3^+$ and Cl^-.

2. $CH_3NH_3^+$ is a weak acid, being conjugate to CH_3NH_2, a weak base.

3. Cl^- has no basic properties. It is conjugate to HCl, a strong acid. That is, HCl dissociates completely.

Challenge Phenol (C_6H_5OH) is a weak acid. Explain why a solution of the ionic compound potassium phenolate ($C_6H_5O^-K^+$) is basic.

Aqueous metal ions are associated with (*hydrated* by) several H_2O molecules, so a more accurate way to write the acid dissociation reaction is

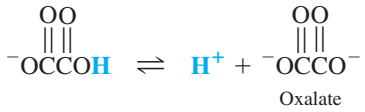
$$M(H_2O)_x^{n+} \rightleftharpoons M(H_2O)_{x-1}(OH)^{(n-1)} + H^+$$

Polyprotic Acids and Bases

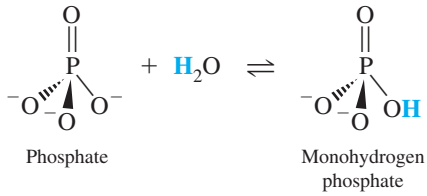
Polyprotic acids and bases are compounds that can donate or accept more than one proton. For example, oxalic acid is diprotic and phosphate is tribasic:

$$\underset{\text{Oxalic acid}}{HO\overset{O}{\overset{\|}{C}}\overset{O}{\overset{\|}{C}}OH} \rightleftharpoons H^+ + \underset{\text{Monohydrogen oxalate}}{{}^-O\overset{O}{\overset{\|}{C}}\overset{O}{\overset{\|}{C}}OH} \qquad K_{a1} = 5.37 \times 10^{-2} \qquad \textbf{(6-30)}$$

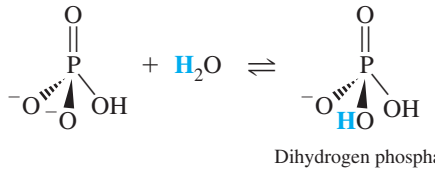
Notation for acid and base equilibrium constants: K_{a1} refers to the acidic species with the most protons and K_{b1} refers to the basic species with the least protons. The subscript "a" in acid dissociation constants will usually be omitted.



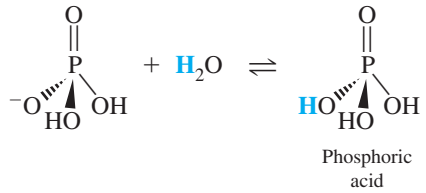
$K_{a2} = 5.42 \times 10^{-5}$ **(6-31)**



$K_{b1} = 2.3 \times 10^{-2}$ **(6-32)**



$K_{b2} = 1.60 \times 10^{-7}$ **(6-33)**



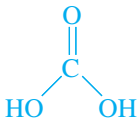
$K_{b3} = 1.42 \times 10^{-12}$ **(6-34)**

Standard notation for successive acid dissociation constants of a polyprotic acid is K_1, K_2, K_3, and so on, with the subscript "a" usually omitted. We retain or omit the subscript as dictated by clarity. For successive base hydrolysis constants, we retain the subscript "b." The preceding examples illustrate that K_{a1} (or K_1) *refers to the acidic species with the most protons, and* K_{b1} *refers to the basic species with the least number of protons*. Carbonic acid, a very important diprotic carboxylic acid derived from CO_2, is described in Box 6-4.

BOX 6-4 Carbonic Acid[27]

Carbonic acid is formed by the reaction of carbon dioxide with water:

$$CO_2(g) \rightleftharpoons CO_2(aq) \qquad K = \frac{[CO_2(aq)]}{P_{CO_2}} = 0.034\,4$$

$CO_2(aq) + H_2O \rightleftharpoons$  Carbonic acid

$$K = \frac{[H_2CO_3]}{[CO_2(aq)]} \approx 0.002$$

$$H_2CO_3 \rightleftharpoons \underset{\text{Bicarbonate}}{HCO_3^-} + H^+ \qquad K_{a1} = 4.46 \times 10^{-7}$$

$$HCO_3^- \rightleftharpoons \underset{\text{Carbonate}}{CO_3^{2-}} + H^+ \qquad K_{a2} = 4.69 \times 10^{-11}$$

Its behavior as a diprotic acid appears anomalous at first, because the value of K_{a1} is about 10^2 to 10^4 times smaller than K_a for other carboxylic acids.

CH_3CO_2H Acetic acid $K_a = 1.75 \times 10^{-5}$	HCO_2H Formic acid $K_a = 1.80 \times 10^{-4}$
$N{\equiv}CCH_2CO_2H$ Cyanoacetic acid $K_a = 3.37 \times 10^{-3}$	$HOCH_2CO_2H$ Glycolic acid $K_a = 1.48 \times 10^{-4}$

The reason for this anomaly is not that H_2CO_3 is unusual but, rather, that the value commonly given for K_{a1} applies to the equation

$$\underset{(= CO_2(aq) + H_2CO_3)}{\text{All dissolved } CO_2} \rightleftharpoons HCO_3^- + H^+$$

$$K_{a1} = \frac{[HCO_3^-][H^+]}{[CO_2(aq) + H_2CO_3]} = 4.46 \times 10^{-7}$$

Only about 0.2% of dissolved CO_2 is in the form H_2CO_3. When the true value of $[H_2CO_3]$ is used instead of the value $[H_2CO_3 + CO_2(aq)]$, the value of the equilibrium constant becomes

$$K_{a1} = \frac{[HCO_3^-][H^+]}{[H_2CO_3]} = 2 \times 10^{-4}$$

The hydration of CO_2 (reaction of CO_2 with H_2O) and dehydration of H_2CO_3 are slow reactions that can be demonstrated in a classroom.[27] Living cells utilize the enzyme *carbonic anhydrase* to speed the rate at which H_2CO_3 and CO_2 equilibrate in order to process this key metabolite. The enzyme provides an environment just right for the reaction of CO_2 with OH^-, lowering the *activation energy* (the energy barrier for the reaction) from 50 down to 26 kJ/mol and increasing the rate of reaction by more than a factor of 10^6.

Carbonic acid has limited stability in aqueous solution and is not well characterized. The dimer $(H_2CO_3)_2$ or oligomers $(H_2CO_3)_n$ appear to exist in the solid state.[28]

Relation Between K_a and K_b

A most important relation exists between K_a and K_b of a conjugate acid-base pair in aqueous solution. We can derive this result with the acid HA and its conjugate base A^-.

$$\cancel{HA} \rightleftharpoons H^+ + \cancel{A^-} \qquad K_a = \frac{[H^+][A^-]}{[HA]}$$

$$\cancel{A^-} + H_2O \rightleftharpoons \cancel{HA} + OH^- \qquad K_b = \frac{[HA][OH^-]}{[A^-]}$$

$$H_2O \rightleftharpoons H^+ + OH^- \qquad K_w = K_a \cdot K_b$$

$$= \frac{[H^+][\cancel{A^-}]}{[\cancel{HA}]} \cdot \frac{[\cancel{HA}][OH^-]}{[\cancel{A^-}]}$$

When the reactions are added, their equilibrium constants are multiplied to give

Relation between K_a and K_b for a conjugate pair:

$$K_a \cdot K_b = K_w \tag{6-35}$$

$K_a \cdot K_b = K_w$ for a conjugate acid-base pair in aqueous solution.

Equation 6-35 applies to any acid and its conjugate base in aqueous solution.

EXAMPLE Finding K_b for the Conjugate Base

K_a for acetic acid is 1.75×10^{-5} (Reaction 6-26). Find K_b for acetate ion.

Solution This one is trivial:†

$$K_b = \frac{K_w}{K_a} = \frac{1.0 \times 10^{-14}}{1.75 \times 10^{-5}} = 5.7 \times 10^{-10}$$

Test Yourself K_a for chloroacetic acid is 1.36×10^{-3}. Find K_b for chloroacetate ion. (***Answer:*** 7.4×10^{-12})

EXAMPLE Finding K_a for the Conjugate Acid

K_b for methylamine is 4.47×10^{-4} (Reaction 6-27). Find K_a for methylammonium ion.

Solution Once again,

$$K_a = \frac{K_w}{K_b} = 2.2 \times 10^{-11}$$

Test Yourself K_b for dimethylamine is 5.9×10^{-4}. Find K_a for dimethylammonium ion. (***Answer:*** 1.7×10^{-11})

For a diprotic acid, we can derive relationships between each of two acids and their conjugate bases:

$$\cancel{H_2A} \rightleftharpoons H^+ + \cancel{HA^-} \qquad K_{a1}$$
$$\cancel{HA^-} + H_2O \rightleftharpoons \cancel{H_2A} + OH^- \qquad K_{b2}$$
$$H_2O \rightleftharpoons H^+ + OH^- \qquad K_w$$

$$\cancel{HA^-} \rightleftharpoons H^+ + \cancel{A^{2-}} \qquad K_{a2}$$
$$\cancel{A^{2-}} + H_2O \rightleftharpoons \cancel{HA^-} + OH^- \qquad K_{b1}$$
$$H_2O \rightleftharpoons H^+ + OH^- \qquad K_w$$

The final results are

General relation between K_a and K_b:

$$K_{a1} \cdot K_{b2} = K_w \tag{6-36}$$

$$K_{a2} \cdot K_{b1} = K_w \tag{6-37}$$

† In this text, we use $K_w = 10^{-14.00} = 1.0 \times 10^{-14}$ at 25°C. The more accurate value from Table 6-1 is $K_w = 10^{-13.995}$. For acetic acid with $K_a = 10^{-4.756}$, the accurate value of K_b is $10^{-(13.995 - 4.756)} = 10^{-9.239} = 5.77 \times 10^{-10}$.

Challenge Derive the following results for a triprotic acid:

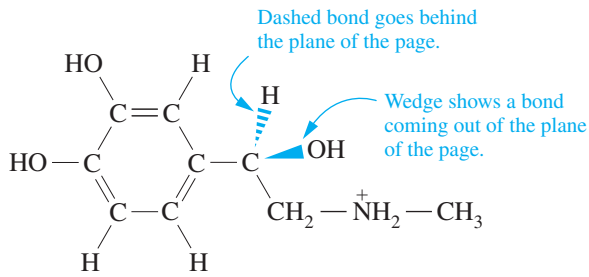
$$K_{a1} \cdot K_{b3} = K_w \tag{6-38}$$

$$K_{a2} \cdot K_{b2} = K_w \tag{6-39}$$

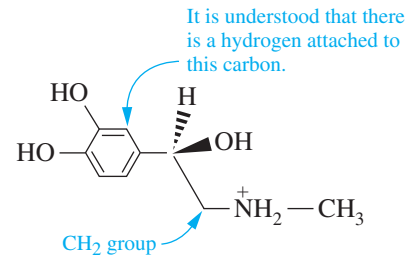
$$K_{a3} \cdot K_{b1} = K_w \tag{6-40}$$

Shorthand for Organic Structures

We are beginning to encounter organic (carbon-containing) compounds in this book. Chemists and biochemists use simple conventions for drawing molecules to avoid writing every atom. Each vertex of a structure is understood to be a carbon atom, unless otherwise labeled. In the shorthand, we usually omit bonds from carbon to hydrogen. Carbon forms four chemical bonds. If you see carbon forming fewer than four bonds, the remaining bonds are assumed to go to hydrogen atoms that are not written. Here is an example:

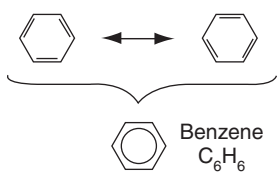


Epinephrine (also called adrenaline)



Shorthand drawing of epinephrine

Benzene, C_6H_6, has two equivalent resonance structures, so all C–C bonds are equivalent. We often draw benzene rings with a circle in place of three double bonds.



The shorthand shows that the carbon atom at the top right of the six-membered benzene ring forms three bonds to other carbon atoms (one single bond and one double bond), so there must be a hydrogen atom attached to this carbon atom. The carbon atom at the left side of the benzene ring forms three bonds to other carbon atoms and one bond to an oxygen atom. There is no hidden hydrogen atom attached to this carbon. In the CH_2 group adjacent to nitrogen, both hydrogen atoms are omitted in the shorthand structure.

Terms to Understand

acid
acid dissociation constant (K_a)
acidic solution
amine
ammonium ion
aprotic solvent
autoprotolysis
base
base hydrolysis constant (K_b)
basic solution
Brønsted-Lowry acid
Brønsted-Lowry base
carboxylate anion
carboxylic acid
common ion effect
complex ion
conjugate acid-base pair
coprecipitation
cumulative formation constant
disproportionation
endothermic
enthalpy change
entropy
equilibrium constant
exothermic
Gibbs free energy
hydronium ion
ion pair
Le Châtelier's principle
Lewis acid
Lewis base
ligand
neutralization
overall formation constant
pH
polyprotic acids
polyprotic bases
protic solvent
reaction quotient
salt
saturated solution
solubility product
standard state
stepwise formation constant

Summary

For the reaction $aA + bB \rightleftharpoons cC + dD$, the equilibrium constant is $K = [C]^c[D]^d/[A]^a[B]^b$. Solute concentrations should be expressed in moles per liter; gas concentrations should be in bars; and the concentrations of pure solids, liquids, and solvents are omitted. If the direction of a reaction is changed, $K' = 1/K$. If two reactions are added, $K_3 = K_1K_2$. The equilibrium constant can be calculated from the free-energy change for a chemical reaction: $K = e^{-\Delta G^\circ/RT}$. The equation $\Delta G = \Delta H - T\Delta S$ summarizes the observations that a reaction is favored if it liberates heat (exothermic, negative ΔH) or increases disorder (positive ΔS). Le Châtelier's principle predicts the effect on a chemical reaction when reactants or products are added or temperature is changed. The reaction quotient, Q, tells how a system must change to reach equilibrium.

The solubility product is the equilibrium constant for the dissolution of a solid salt into its constituent ions in aqueous solution. The common ion effect is the observation that, if one of the ions of that

salt is already present in the solution, the solubility of a salt is decreased. Sometimes, we can selectively precipitate one ion from a solution containing other ions by adding a suitable counterion. At high concentration of ligand, a precipitated metal ion may redissolve by forming soluble complex ions. In a metal-ion complex, the metal is a Lewis acid (electron pair acceptor) and the ligand is a Lewis base (electron pair donor).

Brønsted-Lowry acids are proton donors, and Brønsted-Lowry bases are proton acceptors. An acid increases the concentration of H_3O^+ in aqueous solution, and a base increases the concentration of OH^-. An acid-base pair related through the gain or loss of a single proton is described as conjugate. When a proton is transferred from one molecule to another molecule of a protic solvent, the reaction is called autoprotolysis.

The definition $pH = -\log[H^+]$ will be modified to include activity later. K_a is the equilibrium constant for the dissociation of an acid: $HA + H_2O \rightleftharpoons H_3O^+ + A^-$. The base hydrolysis constant for the reaction $B + H_2O \rightleftharpoons BH^+ + OH^-$ is K_b. When either K_a or K_b is large, the acid or base is said to be strong; otherwise, the acid or base is weak. Common strong acids and bases are listed in Table 6-2, which you should memorize. The most common weak acids are carboxylic acids (RCO_2H), and the most common weak bases are amines (R_3N:). Carboxylate anions (RCO_2^-) are weak bases, and ammonium ions (R_3NH^+) are weak acids. Metal cations are weak acids. For a conjugate acid-base pair in water, $K_a \cdot K_b = K_w$. For polyprotic acids, we denote successive acid dissociation constants as K_{a1}, K_{a2}, K_{a3}, $\cdots$, or just K_1, K_2, K_3, $\cdots$. For polybasic species, we denote successive hydrolysis constants K_{b1}, K_{b2}, K_{b3}, $\cdots$. For a diprotic system, the relations between successive acid and base equilibrium constants are $K_{a1} \cdot K_{b2} = K_w$ and $K_{a2} \cdot K_{b1} = K_w$. For a triprotic system, the relations are $K_{a1} \cdot K_{b3} = K_w$, $K_{a2} \cdot K_{b2} = K_w$, and $K_{a3} \cdot K_{b1} = K_w$.

In the chemists' shorthand for organic structures, each vertex is a carbon atom. If fewer than four bonds to that carbon are shown, it is understood that H atoms are attached to the carbon so that it makes four bonds.

Exercises

6-A. Consider the following equilibria in aqueous solution:

(1) $Ag^+ + Cl^- \rightleftharpoons AgCl(aq)$ $\quad K = 2.0 \times 10^3$

(2) $AgCl(aq) + Cl^- \rightleftharpoons AgCl_2^-$ $\quad K = 9.3 \times 10^1$

(3) $AgCl(s) \rightleftharpoons Ag^+ + Cl^-$ $\quad K = 1.8 \times 10^{-10}$

(a) Calculate the numerical value of the equilibrium constant for the reaction $AgCl(s) \rightleftharpoons AgCl(aq)$.

(b) Calculate the concentration of $AgCl(aq)$ in equilibrium with excess undissolved solid AgCl.

(c) Find the numerical value of K for the reaction $AgCl_2^- \rightleftharpoons AgCl(s) + Cl^-$.

6-B. Reaction 6-7 is allowed to come to equilibrium in a solution initially containing 0.010 0 M BrO_3^-, 0.010 0 M Cr^{3+}, and 1.00 M H^+. To find the concentrations at equilibrium, we can construct a table showing initial and final concentrations (see below). We use the stoichiometry coefficients of the reaction to say that if x mol of Br^- are created, then we must also make x mol of $Cr_2O_7^{2-}$ and $8x$ mol of H^+. To produce x mol of Br^-, we must have consumed x mol of BrO_3^- and $2x$ mol of Cr^{3+}.

(a) Write the equilibrium constant expression that you would use to solve for x to find the concentrations at equilibrium. Do not try to solve the equation.

(b) Because $K = 1 \times 10^{11}$, we suppose that the reaction will go nearly "to completion." That is, we expect both the concentration of Br^- and $Cr_2O_7^{2-}$ to be close to 0.005 00 M at equilibrium. (Why?) That is, $x \approx 0.005\,00$ M. With this value of x, $[H^+] = 1.00 + 8x = 1.04$ M and $[BrO_3^-] = 0.010\,0 - x = 0.005\,0$ M. However, we cannot say $[Cr^{3+}] = 0.010\,0 - 2x = 0$, because there must be some small concentration of Cr^{3+} at equilibrium. Write $[Cr^{3+}]$ for the concentration of Cr^{3+} and solve for $[Cr^{3+}]$. The *limiting reagent* in this example is Cr^{3+}. The reaction uses up Cr^{3+} before consuming BrO_3^-.

6-C. Find $[La^{3+}]$ in the solution when excess solid lanthanum iodate, $La(IO_3)_3$, is stirred with 0.050 M $LiIO_3$ until the system reaches equilibrium. Assume that IO_3^- from $La(IO_3)_3$ is negligible compared with IO_3^- from $LiIO_3$.

6-D. Which will be more soluble (moles of metal dissolved per liter of solution), $Ba(IO_3)_2$ ($K_{sp} = 1.5 \times 10^{-9}$) or $Ca(IO_3)_2$ ($K_{sp} = 7.1 \times 10^{-7}$)? Give an example of a chemical reaction that might occur that would reverse the predicted solubilities.

6-E. Fe(III) precipitates from acidic solution by addition of OH^- to form $Fe(OH)_3(s)$. At what concentration of OH^- will [Fe(III)] be reduced to 1.0×10^{-10} M? If Fe(II) is used instead, what concentration of OH^- will reduce [Fe(II)] to 1.0×10^{-10} M?

6-F. Is it possible to precipitate 99.0% of 0.010 M Ce^{3+} by adding oxalate ($C_2O_4^{2-}$) without precipitating 0.010 M Ca^{2+}?

CaC_2O_4 $\quad K_{sp} = 1.3 \times 10^{-8}$

$Ce_2(C_2O_4)_3$ $\quad K_{sp} = 5.9 \times 10^{-30}$

6-G. For a solution of Ni^{2+} and ethylenediamine, the following equilibrium constants apply at 20°C:

$$Ni^{2+} + \underset{\text{Ethylenediamine (abbreviated en)}}{H_2NCH_2CH_2NH_2} \rightleftharpoons Ni(en)^{2+} \qquad \log K_1 = 7.52$$

$$Ni(en)^{2+} + en \rightleftharpoons Ni(en)_2^{2+} \qquad \log K_2 = 6.32$$

$$Ni(en)_2^{2+} + en \rightleftharpoons Ni(en)_3^{2+} \qquad \log K_3 = 4.49$$

Calculate the concentration of free Ni^{2+} in a solution prepared by mixing 0.100 mol of en plus 1.00 mL of 0.010 0 M Ni^{2+} and diluting to 1.00 L with dilute base (which keeps all the en in its unprotonated form. Assume that nearly all nickel is in the form $Ni(en)_3^{2+}$, so $[Ni(en)_3^{2+}] = 1.00 \times 10^{-5}$ M. Calculate the concentrations of $Ni(en)^{2+}$ and $Ni(en)_2^{2+}$ to verify that they are negligible in comparison with $Ni(en)_3^{2+}$.

	BrO_3^-	+ $2Cr^{3+}$	+ $4H_2O$	$\rightleftharpoons$ Br^-	+ $Cr_2O_7^{2-}$	+ $8H^+$
Initial concentration	0.010 0	0.010 0				1.00
Final concentration	$0.010\,0 - x$	$0.010\,0 - 2x$		x	x	$1.00 + 8x$

6-H. If each compound is dissolved in water, will the solution be acidic, basic, or neutral?

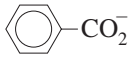
(a) Na^+Br^-

(b) $Na^+CH_3CO_2^-$

(c) $NH_4^+Cl^-$

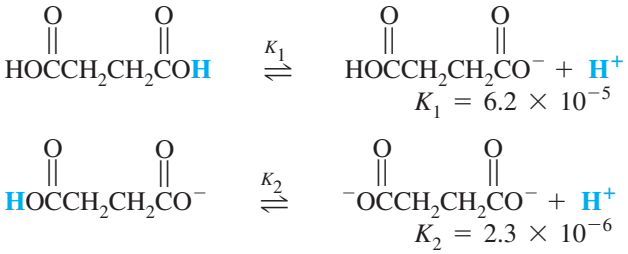
(d) K_3PO_4

(e) $(CH_3)_4N^+Cl^-$

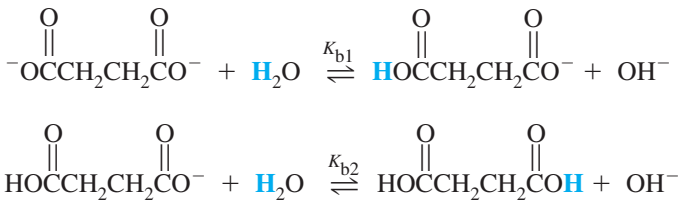
(f) $(CH_3)_4N^+$  $-CO_2^-$

(g) $Fe(NO_3)_3$

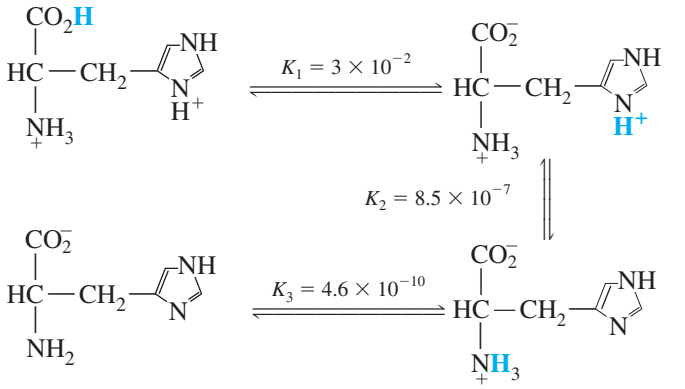
6-I. Succinic acid dissociates in two steps:



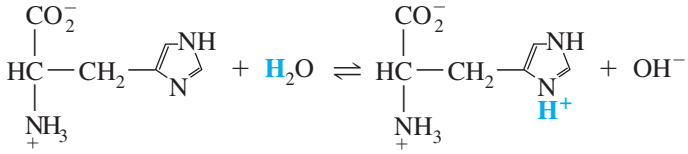
Calculate K_{b1} and K_{b2} for the following reactions:



6-J. Histidine is a triprotic amino acid:



What is the value of the equilibrium constant for the reaction



6-K. (a) From K_w in Table 6-1, calculate the pH of pure water at 0°, 20°, and 40°C.

(b) For the reaction $D_2O \rightleftharpoons D^+ + OD^-$, $K = [D^+][OD^-] = 1.35 \times 10^{-15}$ at 25°C. In this equation, D stands for deuterium, which is the isotope ^2H. What is the pD ($= -\log[D^+]$) for neutral D_2O?

Problems

Equilibrium and Thermodynamics

6-1. To evaluate the equilibrium constant in Equation 6-2, we must express concentrations of solutes in mol/L, gases in bars, and omit solids, liquids, and solvents. Explain why.

6-2. Why do we say that the equilibrium constant for the reaction $H_2O \rightleftharpoons H^+ + OH^-$ (or any other reaction) is dimensionless?

6-3. Explain the statement that predictions about the direction of a reaction based on Gibbs free energy or Le Châtelier's principle are *thermodynamic*, not *kinetic*.

6-4. Write the expression for the equilibrium constant for each of the following reactions. Write the pressure of a gaseous molecule, X, as P_X.

(a) $3Ag^+(aq) + PO_4^{3-}(aq) \rightleftharpoons Ag_3PO_4(s)$

(b) $C_6H_6(l) + \frac{15}{2}O_2(g) \rightleftharpoons 3H_2O(l) + 6CO_2(g)$

6-5. For the reaction $2A(g) + B(aq) + 3C(l) \rightleftharpoons D(s) + 3E(g)$, the concentrations at equilibrium are found to be

A: 2.8×10^3 Pa C: 12.8 M E: 3.6×10^4 Torr

B: 1.2×10^{-2} M D: 16.5 M

Find the numerical value of the equilibrium constant that would appear in a conventional table of equilibrium constants.

6-6. From the equations

$$HOCl \rightleftharpoons H^+ + OCl^- \qquad K = 3.0 \times 10^{-8}$$

$$HOCl + OBr^- \rightleftharpoons HOBr + OCl^- \qquad K = 15$$

find the value of K for the reaction $HOBr \rightleftharpoons H^+ + OBr^-$.

6-7. (a) A favorable entropy change occurs when ΔS is positive. Does the order of the system increase or decrease when ΔS is positive?

(b) A favorable enthalpy change occurs when ΔH is negative. Does the system absorb heat or give off heat when ΔH is negative?

(c) Write the relation between ΔG, ΔH, and ΔS. Use the results of parts **(a)** and **(b)** to state whether ΔG must be positive or negative for a spontaneous change.

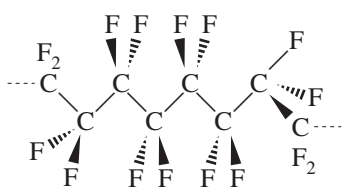
6-8. For the reaction $HCO_3^- \rightleftharpoons H^+ + CO_3^{2-}$, $\Delta G° = +59.0$ kJ/mol at 298.15 K. Find the value of K for the reaction.

6-9. The formation of tetrafluoroethylene from its elements is highly exothermic:

$$\underset{\text{Fluorine}}{2F_2(g)} + \underset{\text{Graphite}}{2C(s)} \rightleftharpoons \underset{\text{Tetrafluoroethylene}}{F_2C{=}CF_2(g)}$$

(a) If a mixture of F_2, graphite, and C_2F_4 is at equilibrium in a closed container, will the reaction go to the right or to the left if F_2 is added?

(b) Rare bacteria from the planet Teflon eat C_2F_4 and make Teflon for their cell walls. Will the reaction go to the right or to the left if these bacteria are added?



Teflon

(c) Will the reaction go right or left if solid graphite is added? (Neglect any effect of increased pressure due to the decreased volume in the vessel when solid is added.)

(d) Will the reaction go right or left if the container is crushed to one-eighth of its original volume?

(e) Does the equilibrium constant become larger or smaller if the container is heated?

6-10. $BaCl_2 \cdot H_2O(s)$ loses water when it is heated in an oven:

$$BaCl_2 \cdot H_2O(s) \rightleftharpoons BaCl_2(s) + H_2O(g)$$
$$\Delta H^\circ = 63.11 \text{ kJ/mol at } 25^\circ\text{C}$$
$$\Delta S^\circ = +148 \text{ J/(K} \cdot \text{mol) at } 25^\circ\text{C}$$

(a) Write the equilibrium constant for this reaction. Calculate the vapor pressure of gaseous H_2O (P_{H_2O}) above $BaCl_2 \cdot H_2O$ at 298 K.

(b) If ΔH° and ΔS° are not temperature dependent (a poor assumption), estimate the temperature at which P_{H_2O} above $BaCl_2 \cdot H_2O(s)$ will be 1 bar.

6-11. The equilibrium constant for the reaction of $NH_3(aq) + H_2O \rightleftharpoons NH_4^+ + OH^-$ is $K_b = 1.479 \times 10^{-5}$ at 5°C and 1.570×10^{-5} at 10°C.

(a) Assuming ΔH° and ΔS° are constant in the interval 5°–10°C (probably a good assumption for small ΔT), use Equation 6-8 to find ΔH° for the reaction in this temperature range.

(b) Describe how Equation 6-8 could be used to make a linear graph to determine ΔH°, if ΔH° and ΔS° were constant over some temperature range.

6-12. For $H_2(g) + Br_2(g) \rightleftharpoons 2HBr(g)$, $K = 7.2 \times 10^{-4}$ at 1 362 K and ΔH° is positive. A vessel is charged with 48.0 Pa HBr, 1 370 Pa H_2, and 3 310 Pa Br_2 at 1 362 K.

(a) Will the reaction proceed to the left or the right to reach equilibrium?

(b) Calculate the pressure (in pascals) of each species in the vessel at equilibrium.

(c) If the mixture at equilibrium is compressed to half of its original volume, will the reaction proceed to the left or the right to reestablish equilibrium?

(d) If the mixture at equilibrium is heated from 1 362 to 1 407 K, will HBr be formed or consumed in order to reestablish equilibrium?

6-13. *Henry's law* states that the concentration of a gas dissolved in a liquid is proportional to the pressure of the gas. This law is a consequence of the equilibrium

$$X(g) \overset{K_h}{\rightleftharpoons} X(aq) \qquad K_h = \frac{[X]}{P_X}$$

where K_h is called the Henry's law constant. (The same law applies to other solvents, but the value of K_h is different for each solvent.) For the gasoline additive MTBE, $K_h = 1.71$ M/bar. Suppose we have a closed container with aqueous solution and air in equilibrium. If the concentration of MTBE in the water is 1.00×10^2 ppm (= 100 μg MTBE/g solution ≈ 100 μg/mL), what is the pressure of MTBE in the air?

$CH_3—O—C(CH_3)_3$ Methyl-*t*-butylether (MTBE, FM 88.15)

Solubility Product

6-14. Find the concentration of Cu^+ in equilibrium with $CuBr(s)$ and 0.10 M Br^-.

6-15. What concentration of $Fe(CN)_6^{4-}$ (ferrocyanide) is in equilibrium with 1.0 μM Ag^+ and $Ag_4Fe(CN)_6(s)$. Express your answer with a prefix from Table 1-3.

6-16. Find $[Cu^{2+}]$ in a solution saturated with $Cu_4(OH)_6(SO_4)$ if $[OH^-]$ is *fixed* at 1.0×10^{-6} M. Note that $Cu_4(OH)_6(SO_4)$ gives 1 mol of SO_4^{2-} for 4 mol of Cu^{2+}.

$$Cu_4(OH)_6(SO_4)(s) \rightleftharpoons 4Cu^{2+} + 6OH^- + SO_4^{2-}$$
$$K_{sp} = 2.3 \times 10^{-69}$$

6-17. (a) From the solubility product of zinc ferrocyanide, $Zn_2Fe(CN)_6$, calculate the concentration of $Fe(CN)_6^{4-}$ in 0.10 mM $ZnSO_4$ saturated with $Zn_2Fe(CN)_6$. Assume that $Zn_2Fe(CN)_6$ is a negligible source of Zn^{2+}.

(b) What concentration of $K_4Fe(CN)_6$ should be in a suspension of solid $Zn_2Fe(CN)_6$ in water to give $[Zn^{2+}] = 5.0 \times 10^{-7}$ M?

6-18. Solubility products predict that cation A^{3+} can be 99.999% separated from cation B^{2+} by precipitation with anion X^-. When the separation is tried, we find 0.2% contamination of $AX_3(s)$ with B^{2+}. Explain what might be happening.

6-19. A solution contains 0.050 0 M Ca^{2+} and 0.030 0 M Ag^+. Can 99% of Ca^{2+} be precipitated by sulfate without precipitating Ag^+? What will be the concentration of Ca^{2+} when Ag_2SO_4 begins to precipitate?

6-20. A solution contains 0.010 M Ba^{2+} and 0.010 M Ag^+. Can 99.90% of either ion be precipitated by chromate (CrO_4^{2-}) without precipitating the other metal ion?

6-21. If a solution containing 0.10 M Cl^-, Br^-, I^-, and CrO_4^{2-} is treated with Ag^+, in what order will the anions precipitate?

Complex Formation

6-22. Explain why the total solubility of lead in Figure 6-3 first decreases and then increases as $[I^-]$ increases. Give an example of the chemistry in each of the two domains.

6-23. Identify the Lewis acids in the following reactions:

(a) $BF_3 + NH_3 \rightleftharpoons F_3\bar{B}—\overset{+}{N}H_3$

(b) $F^- + AsF_5 \rightleftharpoons AsF_6^-$

6-24. The cumulative formation constant for $SnCl_2(aq)$ in 1.0 M $NaNO_3$ is $\beta_2 = 12$. Find the concentration of $SnCl_2(aq)$ for a solution in which the concentrations of Sn^{2+} and Cl^- are both somehow fixed at 0.20 M.

6-25. Given the following equilibria, calculate the concentration of each zinc species in a solution saturated with $Zn(OH)_2(s)$ and containing $[OH^-]$ at a fixed concentration of 3.2×10^{-7} M.

$Zn(OH)_2(s)$	$K_{sp} = 3 \times 10^{-16}$
$Zn(OH)^+$	$\beta_1 = 1 \times 10^4$
$Zn(OH)_2(aq)$	$\beta_2 = 2 \times 10^{10}$
$Zn(OH)_3^-$	$\beta_3 = 8 \times 10^{13}$
$Zn(OH)_4^{2-}$	$\beta_4 = 3 \times 10^{15}$

6-26. Although KOH, RbOH, and CsOH have little association between metal and hydroxide in aqueous solution, Li^+ and Na^+ do form complexes with OH^-:

$$Li^+ + OH^- \rightleftharpoons LiOH(aq) \qquad K_1 = \frac{[LiOH(aq)]}{[Li^+][OH^-]} = 0.83$$

$$Na^+ + OH^- \rightleftharpoons NaOH(aq) \qquad K_1 = 0.20$$

Prepare a table like the one in Exercise 6-B showing initial and final concentrations of Na^+, OH^-, and $NaOH(aq)$ in 1 F NaOH

solution. Calculate the fraction of sodium in the form NaOH(*aq*) at equilibrium.

6-27. In Figure 6-3, the concentration of $PbI_2(aq)$ is independent of $[I^-]$. Use any of the equilibrium constants for Reactions 6-11 through 6-15 to find the equilibrium constant for the reaction $PbI_2(s) \rightleftharpoons PbI_2(aq)$, which is equal to the concentration of $PbI_2(aq)$.

Acids and Bases

6-28. Distinguish Lewis acids and bases from Brønsted-Lowry acids and bases. Give an example of each.

6-29. Fill in the blanks:

(a) The product of a reaction between a Lewis acid and a Lewis base is called _____.

(b) The bond between a Lewis acid and a Lewis base is called _____ or _____.

(c) Brønsted-Lowry acids and bases related by gain or loss of one proton are said to be _____.

(d) A solution is *acidic* if _____. A solution is *basic* if _____.

6-30. Why is the pH of distilled water usually <7? How can you prevent this from happening?

6-31. Gaseous SO_2 is created by combustion of sulfur-containing fuels, especially coal. Explain how SO_2 in the atmosphere makes acidic rain.

6-32. Use electron dot structures to show why tetramethylammonium hydroxide, $(CH_3)_4N^+OH^-$, is an ionic compound. That is, show why hydroxide is not covalently bound to the rest of the molecule.

6-33. Identify the Brønsted-Lowry acids among the reactants in the following reactions:

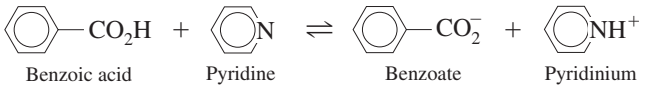
(a) $KCN + HI \rightleftharpoons HCN + KI$

(b) $PO_4^{3-} + H_2O \rightleftharpoons HPO_4^{2-} + OH^-$

6-34. Write the autoprotolysis reaction of H_2SO_4.

6-35. Identify the conjugate acid-base pairs in the following reactions:

(a) $H_3\overset{+}{N}CH_2CH_2\overset{+}{N}H_3 + H_2O \rightleftharpoons H_3\overset{+}{N}CH_2CH_2NH_2 + H_3O^+$

(b) 

pH

6-36. Calculate $[H^+]$ and pH for the following solutions:

(a) 0.010 M HNO_3

(b) 0.035 M KOH

(c) 0.030 M HCl

(d) 3.0 M HCl

(e) 0.010 M $[(CH_3)_4N^+]OH^-$
Tetramethylammonium hydroxide

6-37. Use Table 6-1 to calculate the pH of pure water at **(a)** 25°C and **(b)** 100°C.

6-38. The equilibrium constant for the reaction $H_2O \rightleftharpoons H^+ + OH^-$ is 1.0×10^{-14} at 25°C. What is the value of K for the reaction $4H_2O \rightleftharpoons 4H^+ + 4OH^-$?

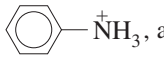
6-39. An acidic solution containing 0.010 M La^{3+} is treated with NaOH until $La(OH)_3$ precipitates. At what pH does this occur?

6-40. Use Le Châtelier's principle and K_w in Table 6-1 to decide whether the autoprotolysis of water is endothermic or exothermic at **(a)** 25°C; **(b)** 100°C; **(c)** 300°C.

Strengths of Acids and Bases

6-41. Make a list of the common strong acids and strong bases. Memorize this list.

6-42. Write the formulas and names for three classes of weak acids and two classes of weak bases.

6-43. Write the K_a reaction for trichloroacetic acid, Cl_3CCO_2H, for anilinium ion,  , and for lanthanum ion, La^{3+}.

6-44. Write the K_b reactions for pyridine and for sodium 2-mercaptoethanol.

Pyridine

$HOCH_2CH_2\ddot{S}:^-Na^+$
Sodium 2-mercaptoethanol

6-45. Write the K_a and K_b reactions of $NaHCO_3$.

6-46. Write the stepwise acid-base reactions for the following ions in water. Write the correct symbol (for example, K_{b1}) for the equilibrium constant for each reaction.

(a) $H_3\overset{+}{N}CH_2CH_2\overset{+}{N}H_3$
Ethylenediammonium ion

(b) $^-OC(=O)CH_2C(=O)O^-$
Malonate ion

6-47. Which is a stronger acid, **(a)** or **(b)**?

(a) $Cl_2HCC(=O)OH$
Dichloroacetic acid
$K_a = 8 \times 10^{-2}$

(b) $ClH_2CC(=O)OH$
Chloroacetic acid
$K_a = 1.36 \times 10^{-3}$

Which is a stronger base, **(c)** or **(d)**?

(c) H_2NNH_2
Hydrazine
$K_b = 1.1 \times 10^{-6}$

(d) $H_2NC(=O)NH_2$
Urea
$K_b = 1.5 \times 10^{-14}$

6-48. Write the K_b reaction of CN^-. Given that the K_a value for HCN is 6.2×10^{-10}, calculate K_b for CN^-.

6-49. Write the K_{a2} reaction of phosphoric acid (H_3PO_4) and the K_{b2} reaction of disodium oxalate ($Na_2C_2O_4$).

6-50. From the K_b values for phosphate in Equations 6-32 through 6-34, calculate the three K_a values of phosphoric acid.

6-51. From the following equilibrium constants, calculate the equilibrium constant for the reaction $HO_2CCO_2H \rightleftharpoons 2H^+ + C_2O_4^{2-}$.

$$\underset{\text{Oxalic acid}}{HOC(=O)C(=O)OH} \rightleftharpoons H^+ + HOC(=O)C(=O)O^- \qquad K_1 = 5.4 \times 10^{-2}$$

$$HOC(=O)C(=O)O^- \rightleftharpoons H^+ + \underset{\text{Oxalate}}{^-OC(=O)C(=O)O^-} \qquad K_2 = 5.4 \times 10^{-5}$$

6-52. **(a)** Using only K_{sp} from Table 6-3, calculate how many moles of $Ca(OH)_2$ will dissolve in 1.00 L of water.

(b) How will the solubility calculated in part **(a)** be affected by the K_1 reaction in Table 6-3?

6-53. The planet Aragonose (which is made mostly of the mineral aragonite, whose composition is $CaCO_3$) has an atmosphere containing methane and carbon dioxide, each at a pressure of 0.10 bar. The oceans are saturated with aragonite and have a concentration of H^+ equal to 1.8×10^{-7} M. Given the following equilibria, calculate how many grams of calcium are contained in 2.00 L of Aragonose seawater.

$$CaCO_3\,(s, \text{aragonite}) \rightleftharpoons Ca^{2+}(aq) + CO_3^{2-}(aq) \qquad K_{sp} = 6.0 \times 10^{-9}$$

$$CO_2(g) \rightleftharpoons CO_2(aq) \qquad K_{CO_2} = 3.4 \times 10^{-2}$$

$$CO_2(aq) + H_2O(l) \rightleftharpoons HCO_3^-(aq) + H^+(aq) \qquad K_1 = 4.5 \times 10^{-7}$$

$$HCO_3^-(aq) \rightleftharpoons H^+(aq) + CO_3^{2-}(aq) \qquad K_2 = 4.7 \times 10^{-11}$$

Don't panic! Reverse the first reaction, add all the reactions together, and see what cancels.

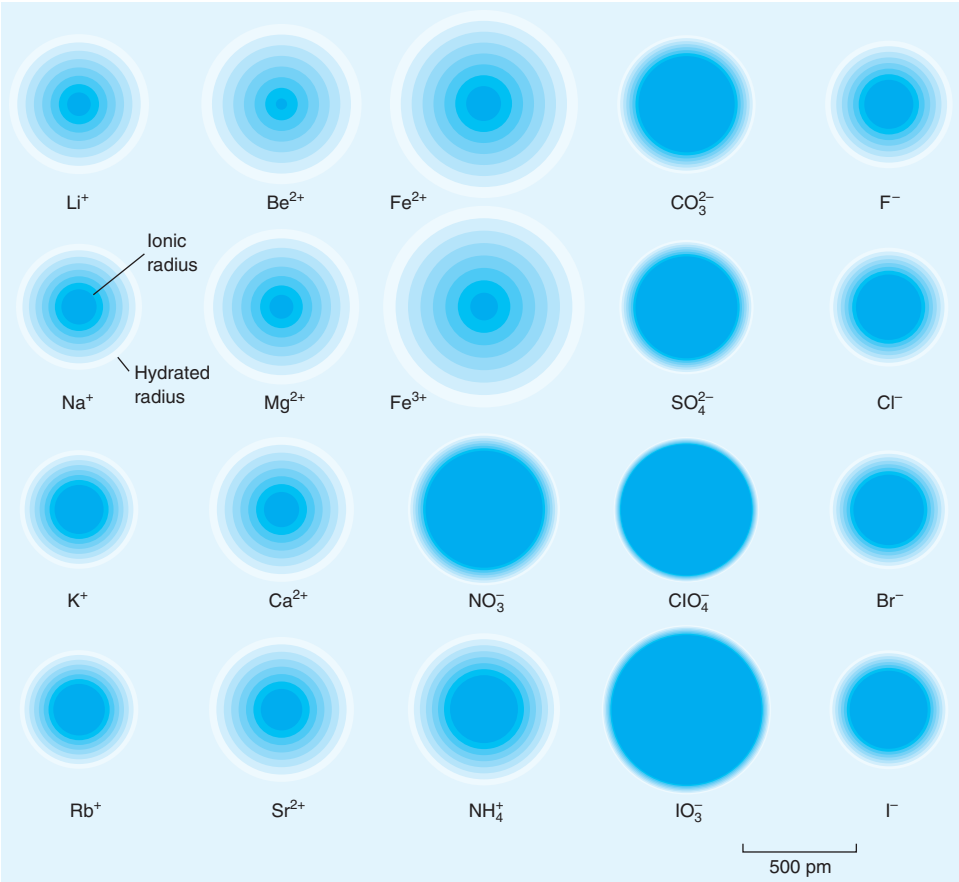
7 Activity and the Systematic Treatment of Equilibrium

HYDRATED IONS

Estimated number of waters of hydration

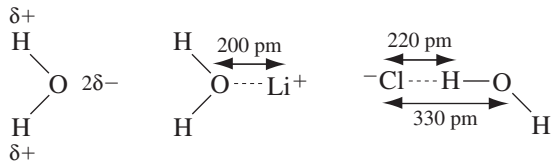
Molecule	Tightly bound H_2O
$CH_3CH_2CH_3$	0
C_6H_6	0
CH_3CH_2Cl	0
CH_3CH_2SH	0
$CH_3{-}O{-}CH_3$	1
CH_3CH_2OH	1
$(CH_3)_2C{=}O$	1.5
$CH_3CH{=}O$	1.5
CH_3CO_2H	2
$CH_3C{\equiv}N$	3
$CH_3C(=O)NHCH_3$	4
CH_3NO_2	5
$CH_3CO_2^-$	5
CH_3NH_2	6
CH_3SO_3H	7
NH_3	9
$CH_3SO_3^-$	10
NH_4^+	12

From S. Fu and C. A. Lucy, "Prediction of Electrophoretic Mobilities," Anal. Chem. ***1998,*** *70, 173.*



Ionic and hydrated radii of several ions. Smaller, more highly charged ions bind water molecules more tightly and behave as larger hydrated species.[3]

Ions and molecules in solution are surrounded by an organized sheath of solvent molecules. The oxygen atom of H_2O has a partial negative charge, and each hydrogen atom has half as much positive charge.



Water binds to cations through the oxygen atom. The first coordination sphere of Li^+, for example, is composed of ~4 H_2O molecules.[1] Cl^- binds ~6 H_2O molecules through hydrogen atoms.[1,2] H_2O exchanges rapidly between bulk solvent and ion-coordination sites.

Ionic radii in the figure are measured by X-ray diffraction of ions in crystals. Hydrated radii are estimated from diffusion coefficients of ions in solution and from the mobilities of aqueous ions in an electric field.[3,4] Smaller, more highly charged ions bind more water molecules and behave as larger species in solution. The *activity* of aqueous ions, which we study in this chapter, is related to the size of the hydrated species.

In Chapter 6, we wrote the equilibrium constant for a reaction in the form

$$\underset{\text{Pale yellow}}{Fe^{3+}} + \underset{\text{Colorless}}{SCN^-} \rightleftharpoons \underset{\text{Red}}{Fe(SCN)^{2+}} \qquad K = \frac{[Fe(SCN)^{2+}]}{[Fe^{3+}][SCN^-]} \tag{7-1}$$

Figure 7-1, Demonstration 7-1, and Color Plate 2 show that the concentration quotient in Equation 7-1 decreases if you add the "inert" salt KNO_3 to the solution. That is, the equilibrium "constant" is not really constant. This chapter explains why concentrations are replaced by *activities* in the equilibrium constant and how activities are used.

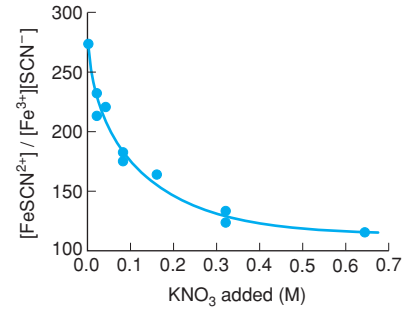


FIGURE 7-1 Student data showing that the equilibrium quotient of concentrations for the reaction $Fe^{3+} + SCN^- \rightleftharpoons Fe(SCN)^{2+}$ decreases as potassium nitrate is added to the solution. Color Plate 2 shows the fading of the red color of $Fe(SCN)^{2+}$ after KNO_3 has been added. Problem 12-11 gives more information on this chemical system. [From R. J. Stolzberg, "Discovering a Change in Equilibrium Constant with Change in Ionic Strength," *J. Chem. Ed.* **1999**, *76*, 640.]

7-1 The Effect of Ionic Strength on Solubility of Salts

Consider a saturated solution of $CaSO_4$ in distilled water.

$$CaSO_4(s) \rightleftharpoons Ca^{2+} + SO_4^{2-} \qquad K_{sp} = 2.4 \times 10^{-5} \tag{7-2}$$

Figure 6-1 showed that the solubility is 0.015 M. The dissolved species are mainly 0.010 M Ca^{2+}, 0.010 M SO_4^{2-}, and 0.005 M $CaSO_4(aq)$ (an ion pair).

Now an interesting effect is observed when a salt such as KNO_3 is added to the solution. Neither K^+ nor NO_3^- reacts with either Ca^{2+} or SO_4^{2-}. Yet, when 0.050 M KNO_3 is added to the saturated solution of $CaSO_4$, more solid dissolves until the concentrations of Ca^{2+} and SO_4^{2-} have each increased by about 30%.

In general, adding an "inert" salt (KNO_3) to a sparingly soluble salt ($CaSO_4$) increases the solubility of the sparingly soluble salt. "Inert" means that KNO_3 has no chemical reaction with $CaSO_4$. When we add salt to a solution, we say that the *ionic strength* of the solution increases. The definition of ionic strength will be given shortly.

Addition of an "inert" salt increases the solubility of an ionic compound.

The Explanation

Why does the solubility increase when salts are added to the solution? Consider one particular Ca^{2+} ion and one particular SO_4^{2-} ion in solution. The SO_4^{2-} ion is surrounded by cations (K^+, Ca^{2+}) and anions (NO_3^-, SO_4^{2-}) in solution. However, for the average anion, there will be more cations than anions nearby because cations are attracted to the anion, but anions are repelled. These interactions create a region of net positive charge around any particular anion. We call this region the **ionic atmosphere** (Figure 7-2). Ions continually diffuse into and out of the ionic atmosphere. The net charge in the atmosphere, averaged over time, is less than the charge of the anion at the center. Similarly, an atmosphere of negative charge surrounds any cation in solution.

The ionic atmosphere attenuates (decreases) the attraction between ions. The cation plus its negative atmosphere has less positive charge than the cation alone. The anion plus its ionic atmosphere has less negative charge than the anion alone. The net attraction between the cation with its ionic atmosphere and the anion with its ionic atmosphere is smaller than it would be between pure cation and anion in the absence of ionic atmospheres. *The greater the ionic strength of a solution, the higher the charge in the ionic atmosphere. Each ion-plus-atmosphere contains less net charge and there is less attraction between any particular cation and anion.*

An anion is surrounded by excess cations. A cation is surrounded by excess anions.

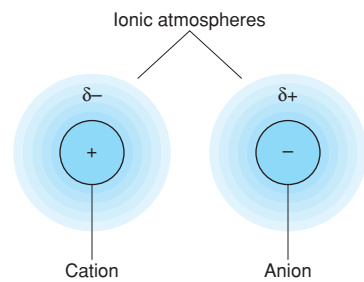


FIGURE 7-2 An ionic atmosphere, shown as a spherical cloud of charge δ+ or δ−, surrounds ions in solution. The charge of the atmosphere is less than the charge of the central ion. The greater the ionic strength of the solution, the greater the charge in each ionic atmosphere.

DEMONSTRATION 7-1 Effect of Ionic Strength on Ion Dissociation[5]

This experiment demonstrates the effect of ionic strength on the dissociation of the red iron(III) thiocyanate complex:

$$\underset{\text{Red}}{Fe(SCN)^{2+}} \rightleftharpoons \underset{\text{Pale yellow}}{Fe^{3+}} + \underset{\text{Colorless}}{SCN^-}$$

Prepare a solution of 1 mM $FeCl_3$ by dissolving 0.27 g of $FeCl_3 \cdot 6H_2O$ in 1 L of water containing 3 drops of 15 M (concentrated) HNO_3. The acid slows the precipitation of $Fe(OH)_3$, which occurs within a few days and necessitates the preparation of fresh solution for this demonstration.

To demonstrate the effect of ionic strength on the dissociation reaction, mix 300 mL of 1 mM $FeCl_3$ with 300 mL of 1.5 mM NH_4SCN or KSCN. Divide the pale red solution into two equal portions and add 12 g of KNO_3 to one of them to increase the ionic strength to 0.4 M. As KNO_3 dissolves, the red $Fe(SCN)^{2+}$ complex dissociates and the color fades (Color Plate 2).

Add a few crystals of NH_4SCN or KSCN to either solution to drive the reaction toward formation of $Fe(SCN)^{2+}$, thereby intensifying the red color. This reaction demonstrates Le Châtelier's principle—adding a product creates more reactant.

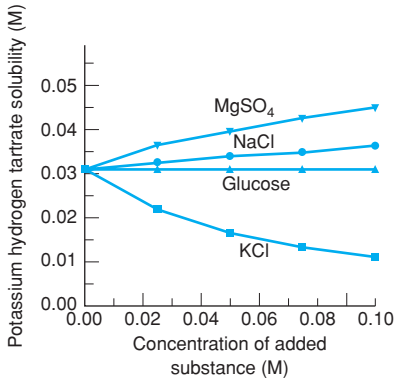
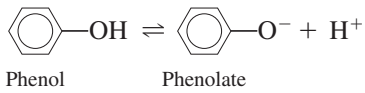


FIGURE 7-3 Solubility of potassium hydrogen tartrate increases when the salts $MgSO_4$ or NaCl are added. There is no effect when the neutral compound glucose is added. Addition of KCl decreases the solubility. (*Why?*) [From C. J. Marzzacco, "Effect of Salts and Nonelectrolytes on the Solubility of Potassium Bitartrate," *J. Chem. Ed.* **1998**, *75*, 1628.]

Increasing ionic strength therefore reduces the attraction between any particular Ca^{2+} ion and any SO_4^{2-} ion, relative to their attraction for each other in distilled water. The effect is to reduce their tendency to come together, thereby *increasing* the solubility of $CaSO_4$.

Increasing ionic strength promotes dissociation into ions. Thus, each of the following reactions is driven to the right if the ionic strength is raised from, say, 0.01 to 0.1 M:

$$Fe(SCN)^{2+} \rightleftharpoons Fe^{3+} + \underset{\text{Thiocyanate}}{SCN^-}$$



$$\underset{\text{Potassium hydrogen tartrate}}{HO_2CC(OH)H(OH)CHCO_2K(s)} \rightleftharpoons HO_2CC(OH)H(OH)CHCO_2^- + K^+$$

Figure 7-3 shows the effect of added salt on the solubility of potassium hydrogen tartrate.

What Do We Mean by "Ionic Strength"?

Ionic strength, μ, is a measure of the total concentration of ions in solution. The more highly charged an ion, the more it is counted.

Ionic strength:

$$\mu = \frac{1}{2}(c_1z_1^2 + c_2z_2^2 + \cdots) = \frac{1}{2}\sum_i c_iz_i^2 \qquad \textbf{(7-3)}$$

where c_i is the concentration of the ith species and z_i is its charge. The sum extends over *all* ions in solution.

EXAMPLE Calculation of Ionic Strength

Find the ionic strength of **(a)** 0.10 M $NaNO_3$; **(b)** 0.010 M Na_2SO_4; and **(c)** 0.020 M KBr plus 0.010 M Na_2SO_4.

Solution

(a) $\mu = \frac{1}{2}\{[Na^+]\cdot(+1)^2 + [NO_3^-]\cdot(-1)^2\}$

$= \frac{1}{2}\{0.10\cdot 1 + 0.10\cdot 1\} = 0.10\text{ M}$

(b) $\mu = \frac{1}{2}\{[Na^+]\cdot(+1)^2 + [SO_4^{2-}]\cdot(-2)^2\}$

$= \frac{1}{2}\{(0.020\cdot 1) + (0.010\cdot 4)\} = 0.030\text{ M}$

Note that $[Na^+] = 0.020$ M because there are two moles of Na^+ per mole of Na_2SO_4.

(c) $\mu = \frac{1}{2}\{[K^+]\cdot(+1)^2 + [Br^-]\cdot(-1)^2 + [Na^+]\cdot(+1)^2 + [SO_4^{2-}]\cdot(-2)^2\}$

$= \frac{1}{2}\{(0.020\cdot 1) + (0.020\cdot 1) + (0.020\cdot 1) + (0.010\cdot 4)\} = 0.050\text{ M}$

Test Yourself What is the ionic strength of 1 mM $CaCl_2$? (***Answer:*** 3 mM)

Electrolyte	Molarity	Ionic strength
1:1	M	M
2:1	M	3M
3:1	M	6M
2:2	M	4M

$NaNO_3$ is called a 1:1 electrolyte because the cation and the anion both have a charge of 1. For 1:1 electrolytes, ionic strength equals molarity. For other stoichiometries (such as the 2:1 electrolyte Na_2SO_4), ionic strength is greater than molarity.

Computing the ionic strength of any but the most dilute solutions is complicated because salts with ions of charge ≥ 2 are not fully dissociated. In Box 7-1, we find that, at a formal concentration of 0.025 M $MgSO_4$, 35% of Mg^{2+} is bound in the ion pair, $MgSO_4(aq)$. The higher the concentration and the higher the ionic charge, the more the ion pairing. There is no simple way to find the ionic strength of 0.025 M $MgSO_4$.

BOX 7-1 Salts with Ions of Charge ≥|2| Do Not Fully Dissociate[6]

Salts composed of cations and anions with charges of ±1 dissociate almost completely at concentrations <0.1 M in water. Salts containing ions with a charge ≥2 are less dissociated, even in dilute solution. Appendix J gives formation constants for *ion pairing*:

Ion-pair formation constant:

$$M^{n+}(aq) + L^{m-}(aq) \rightleftharpoons \underset{\text{Ion pair}}{M^{n+}L^{m-}(aq)}$$

$$K = \frac{[ML]\gamma_{ML}}{[M]\gamma_M[L]\gamma_L}$$

where the γ_i are activity coefficients. With constants from Appendix J, activity coefficients from Equation 7-6, craft, and persistence, you might calculate the following percentages of ion pairing in 0.025 F solutions:

Percentage of metal ion bound as ion pair in 0.025 F M_xL_y solution[a]

M \ L	Cl^-	SO_4^{2-}
Na^+	0.6%	4%
Mg^{2+}	8%	35%

a. The size of ML was taken as 500 pm to compute its activity coefficient.

The table tells us that 0.025 F NaCl is only 0.6% associated as $Na^+Cl^-(aq)$ and Na_2SO_4 is 4% associated as $NaSO_4^-(aq)$. For $MgSO_4$, 35% is ion paired. A solution of 0.025 F $MgSO_4$ contains 0.016 M Mg^{2+}, 0.016 M SO_4^{2-}, and 0.009 M $MgSO_4(aq)$. The ionic strength of 0.025 F $MgSO_4$ is not 0.10 M, but just 0.065 M. Problem 7-28 provides an example of the type of calculation in this box.

7-2 Activity Coefficients

Equation 7-1 does not predict any effect of ionic strength on a chemical reaction. To account for the effect of ionic strength, concentrations are replaced by **activities**:

Activity of C:

$$\mathcal{A}_C = [C]\gamma_C \qquad (7\text{-}4)$$

↑ Activity of C; ↑ Concentration of C; ↖ Activity coefficient of C

The activity of species C is its concentration multiplied by its **activity coefficient**. The activity coefficient measures the deviation of behavior from ideality. If the activity coefficient were 1, then the behavior would be ideal and the form of the equilibrium constant in Equation 7-1 would be correct.

Do not confuse the terms *activity* and *activity coefficient*.

The correct form of the equilibrium constant is

General form of equilibrium constant:

$$K = \frac{\mathcal{A}_C^c\,\mathcal{A}_D^d}{\mathcal{A}_A^a\,\mathcal{A}_B^b} = \frac{[C]^c\gamma_C^c[D]^d\gamma_D^d}{[A]^a\gamma_A^a\,[B]^b\gamma_B^b} \qquad (7\text{-}5)$$

Equation 7-5 is the "real" equilibrium constant. Equation 6-2, the concentration quotient, K_c, did not include activity coefficients:

$$K_c = \frac{[C]^c[D]^d}{[A]^a[B]^b} \qquad (6\text{-}2)$$

Equation 7-5 allows for the effect of ionic strength on a chemical equilibrium because the activity coefficients depend on ionic strength.

For Reaction 7-2, the equilibrium constant is

$$K_{sp} = \mathcal{A}_{Ca^{2+}}\mathcal{A}_{SO_4^{2-}} = [Ca^{2+}]\gamma_{Ca^{2+}}[SO_4^{2-}]\gamma_{SO_4^{2-}}$$

If the concentrations of Ca^{2+} and SO_4^{2-} are to *increase* when a second salt is added to increase ionic strength, the activity coefficients must *decrease* with increasing ionic strength.

At low ionic strength, activity coefficients approach unity, and the thermodynamic equilibrium constant (7-5) approaches the "concentration" equilibrium constant (6-2). One way to measure a thermodynamic equilibrium constant is to measure the concentration ratio (6-2) at successively lower ionic strengths and extrapolate to zero ionic strength. Commonly, tabulated equilibrium constants are not thermodynamic constants but just the concentration ratio (6-2) measured under a particular set of conditions.

EXAMPLE Exponents of Activity Coefficients

Write the solubility product expression for $La_2(SO_4)_3$ with activity coefficients.

Solution Exponents of activity coefficients are the same as exponents of concentrations:

$$K_{sp} = \mathcal{A}_{La^{3+}}^2\mathcal{A}_{SO_4^{2-}}^3 = [La^{3+}]^2\gamma_{La^{3+}}^2[SO_4^{2-}]^3\gamma_{SO_4^{2-}}^3$$

Test Yourself Write the equilibrium expression for $Ca^{2+} + 2Cl^- \rightleftharpoons CaCl_2(aq)$ with activity coefficients. $\left(\textit{Answer: } K = \dfrac{\mathcal{A}_{CaCl_2}}{\mathcal{A}_{Ca^{2+}}\mathcal{A}^2_{Cl^-}} = \dfrac{[CaCl_2]\gamma_{CaCl_2}}{[Ca^{2+}]\gamma_{Ca^{2+}}[Cl^-]^2\gamma^2_{Cl^-}}\right)$

Activity Coefficients of Ions

The ionic atmosphere model leads to the **extended Debye-Hückel equation,** relating activity coefficients to ionic strength:

Extended Debye-Hückel equation:

$$\log \gamma = \frac{-0.51z^2\sqrt{\mu}}{1 + (\alpha\sqrt{\mu}/305)} \quad \text{(at 25°C)} \qquad \textbf{(7-6)}$$

1 pm (picometer) = 10^{-12} m

In Equation 7-6, γ is the activity coefficient of an ion of charge $\pm z$ and size α (picometers, pm) in an aqueous solution of ionic strength μ. The equation works fairly well for $\mu \leq 0.1$ M. To find activity coefficients for ionic strengths above 0.1 M (up to molalities of 2–6 mol/kg for many salts), more complicated *Pitzer equations* are usually used.[7]

Table 7-1 lists sizes (α) and activity coefficients of many ions. All ions of the same size and charge appear in the same group and have the same activity coefficients. For example, Ba^{2+} and succinate ion [$^-O_2CCH_2CH_2CO_2^-$, listed as $(CH_2CO_2^-)_2$], each have a size of 500 pm and are listed among the charge ± 2 ions. At an ionic strength of 0.001 M, both of these ions have an activity coefficient of 0.868.

The ion size α in Equation 7-6 is an empirical parameter that provides agreement between measured activity coefficients and ionic strength up to $\mu \approx 0.1$ M. In theory, α is the diameter of the hydrated ion.[8] However, sizes in Table 7-1 cannot be taken literally. For example, the diameter of Cs^+ ion in crystals is 340 pm. The hydrated Cs^+ ion must be larger than the ion in the crystal, but the size of Cs^+ in Table 7-1 is only 250 pm.

Ionic and hydrated ion sizes are shown at the opening of this chapter.

Even though ion sizes in Table 7-1 are empirical parameters, trends among sizes are sensible. Small, highly charged ions bind solvent more tightly and have larger effective sizes than do larger or less highly charged ions. For example, the order of sizes in Table 7-1 is $Li^+ > Na^+ > K^+ > Rb^+$, even though crystallographic radii are $Li^+ < Na^+ < K^+ < Rb^+$.

Effect of Ionic Strength, Ion Charge, and Ion Size on the Activity Coefficient

Over the range of ionic strengths from 0 to 0.1 M, the effect of each variable on activity coefficients is as follows:

1. As ionic strength increases, the activity coefficient decreases (Figure 7-4). The activity coefficient (γ) approaches unity as the ionic strength (μ) approaches 0.
2. As the magnitude of the charge of the ion increases, the departure of its activity coefficient from unity increases. Activity corrections are more important for ions with a charge of ± 3 than for ions with a charge of ± 1 (Figure 7-4).
3. The smaller the ion size (α), the more important activity effects become.

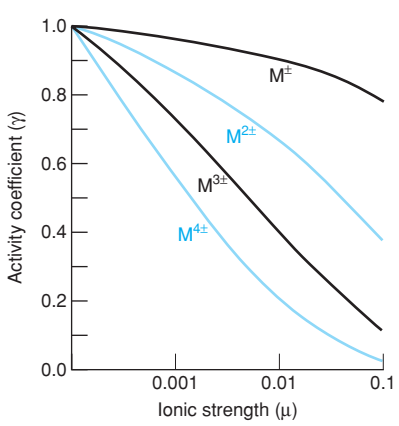


FIGURE 7-4 Activity coefficients for differently charged ions with a constant ionic size (α) of 500 pm. At zero ionic strength, $\gamma = 1$. The greater the charge of the ion, the more rapidly γ decreases as ionic strength increases. Note that the abscissa is logarithmic.

EXAMPLE **Using Table 7-1**

Find the activity coefficient of Ca^{2+} in a solution of 3.3 mM $CaCl_2$.

Solution The ionic strength is

$$\mu = \frac{1}{2}\{[Ca^{2+}] \cdot 2^2 + [Cl^-] \cdot (-1)^2\}$$

$$= \frac{1}{2}\{(0.003\,3) \cdot 4 + (0.006\,6) \cdot 1\} = 0.010 \text{ M}$$

In Table 7-1, Ca^{2+} is listed under the charge ± 2 and has a size of 600 pm. Thus $\gamma = 0.675$ when $\mu = 0.010$ M.

Test Yourself Find γ for Cl^- in 0.33 mM $CaCl_2$. (*Answer:* 0.964)

TABLE 7-1 Activity coefficients for aqueous solutions at 25°C

Ion	Ion size (α, pm)	Ionic strength (μ, M) 0.001	0.005	0.01	0.05	0.1
Charge = ±1		*Activity coefficient (γ)*				
H^+	900	0.967	0.933	0.914	0.86	0.83
$(C_6H_5)_2CHCO_2^-$, $(C_3H_7)_4N^+$	800	0.966	0.931	0.912	0.85	0.82
$(O_2N)_3C_6H_2O^-$, $(C_3H_7)_3NH^+$, $CH_3OC_6H_4CO_2^-$	700	0.965	0.930	0.909	0.845	0.81
Li^+, $C_6H_5CO_2^-$, $HOC_6H_4CO_2^-$, $ClC_6H_4CO_2^-$, $C_6H_5CH_2CO_2^-$, $CH_2{=}CHCH_2CO_2^-$, $(CH_3)_2CHCH_2CO_2^-$, $(CH_3CH_2)_4N^+$, $(C_3H_7)_2NH_2^+$	600	0.965	0.929	0.907	0.835	0.80
$Cl_2CHCO_2^-$, $Cl_3CCO_2^-$, $(CH_3CH_2)_3NH^+$, $(C_3H_7)NH_3^+$	500	0.964	0.928	0.904	0.83	0.79
Na^+, $CdCl^+$, ClO_2^-, IO_3^-, HCO_3^-, $H_2PO_4^-$, HSO_3^-, $H_2AsO_4^-$, $Co(NH_3)_4(NO_2)_2^+$, $CH_3CO_2^-$, $ClCH_2CO_2^-$, $(CH_3)_4N^+$, $(CH_3CH_2)_2NH_2^+$, $H_2NCH_2CO_2^-$	450	0.964	0.928	0.902	0.82	0.775
$^+H_3NCH_2CO_2H$, $(CH_3)_3NH^+$, $CH_3CH_2NH_3^+$	400	0.964	0.927	0.901	0.815	0.77
OH^-, F^-, SCN^-, OCN^-, HS^-, ClO_3^-, ClO_4^-, BrO_3^-, IO_4^-, MnO_4^-, HCO_2^-, $H_2citrate^-$, $CH_3NH_3^+$, $(CH_3)_2NH_2^+$	350	0.964	0.926	0.900	0.81	0.76
K^+, Cl^-, Br^-, I^-, CN^-, NO_2^-, NO_3^-	300	0.964	0.925	0.899	0.805	0.755
Rb^+, Cs^+, NH_4^+, Tl^+, Ag^+	250	0.964	0.924	0.898	0.80	0.75
Charge = ±2		*Activity coefficient (γ)*				
Mg^{2+}, Be^{2+}	800	0.872	0.755	0.69	0.52	0.45
$CH_2(CH_2CH_2CO_2^-)_2$, $(CH_2CH_2CH_2CO_2^-)_2$	700	0.872	0.755	0.685	0.50	0.425
Ca^{2+}, Cu^{2+}, Zn^{2+}, Sn^{2+}, Mn^{2+}, Fe^{2+}, Ni^{2+}, Co^{2+}, $C_6H_4(CO_2^-)_2$, $H_2C(CH_2CO_2^-)_2$, $(CH_2CH_2CO_2^-)_2$	600	0.870	0.749	0.675	0.485	0.405
Sr^{2+}, Ba^{2+}, Cd^{2+}, Hg^{2+}, S^{2-}, $S_2O_4^{2-}$, WO_4^{2-}, $H_2C(CO_2^-)_2$, $(CH_2CO_2^-)_2$, $(CHOHCO_2^-)_2$	500	0.868	0.744	0.67	0.465	0.38
Pb^{2+}, CO_3^{2-}, SO_3^{2-}, MoO_4^{2-}, $Co(NH_3)_5Cl^{2+}$, $Fe(CN)_5NO^{2-}$, $C_2O_4^{2-}$, $Hcitrate^{2-}$	450	0.867	0.742	0.665	0.455	0.37
Hg_2^{2+}, SO_4^{2-}, $S_2O_3^{2-}$, $S_2O_6^{2-}$, $S_2O_8^{2-}$, SeO_4^{2-}, CrO_4^{2-}, HPO_4^{2-}	400	0.867	0.740	0.660	0.445	0.355
Charge = ±3		*Activity coefficient (γ)*				
Al^{3+}, Fe^{3+}, Cr^{3+}, Sc^{3+}, Y^{3+}, In^{3+}, lanthanides[a]	900	0.738	0.54	0.445	0.245	0.18
$citrate^{3-}$	500	0.728	0.51	0.405	0.18	0.115
PO_4^{3-}, $Fe(CN)_6^{3-}$, $Cr(NH_3)_6^{3+}$, $Co(NH_3)_6^{3+}$, $Co(NH_3)_5H_2O^{3+}$	400	0.725	0.505	0.395	0.16	0.095
Charge = ±4		*Activity coefficient (γ)*				
Th^{4+}, Zr^{4+}, Ce^{4+}, Sn^{4+}	1 100	0.588	0.35	0.255	0.10	0.065
$Fe(CN)_6^{4-}$	500	0.57	0.31	0.20	0.048	0.021

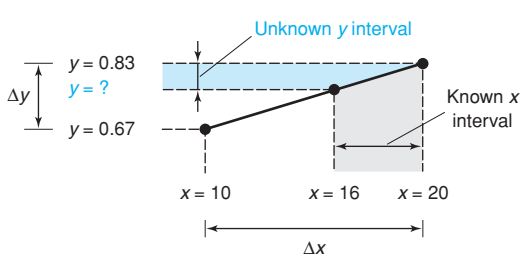
a. Lanthanides are elements 57–71 in the periodic table.
SOURCE: *J. Kielland, J. Am. Chem. Soc.* ***1937****, 59, 1675.*

How to Interpolate

If you need to find an activity coefficient for an ionic strength that is between values in Table 7-1, you can use Equation 7-6. Alternatively, in the absence of a spreadsheet, it not hard to interpolate in Table 7-1. In *linear interpolation*, we assume that values between two entries of a table lie on a straight line. For example, consider a table in which $y = 0.67$ when $x = 10$ and $y = 0.83$ when $x = 20$. What is the value of y when $x = 16$?

Interpolation is the estimation of a number that lies *between* two values in a table. Estimating a number that lies *beyond* values in a table is called *extrapolation*.

x value	y value
10	0.67
16	?
20	0.83



To interpolate a value of y, we can set up a proportion:

This calculation is equivalent to saying:

"16 is 60% of the way from 10 to 20. Therefore the y value will be 60% of the way from 0.67 to 0.83."

Interpolation:

$$\frac{\text{Unknown } y \text{ interval}}{\Delta y} = \frac{\text{known } x \text{ interval}}{\Delta x} \tag{7-7}$$

$$\frac{0.83 - y}{0.83 - 0.67} = \frac{20 - 16}{20 - 10} \Rightarrow y = 0.76_6$$

For $x = 16$, our estimate of y is 0.76_6.

EXAMPLE **Interpolating Activity Coefficients**

Calculate the activity coefficient of H^+ when $\mu = 0.025$ M.

Solution H^+ is the first entry in Table 7-1.

μ	γ for H^+
0.01	0.914
0.025	?
0.05	0.86

The linear interpolation is set up as follows:

$$\frac{\text{Unknown } \gamma \text{ interval}}{\Delta\gamma} = \frac{\text{known } \mu \text{ interval}}{\Delta\mu}$$

$$\frac{0.86 - \gamma}{0.86 - 0.914} = \frac{0.05 - 0.025}{0.05 - 0.01}$$

$$\gamma = 0.89_4$$

Another Solution A better and slightly more tedious calculation uses Equation 7-6, with the ion size $\alpha = 900$ pm listed for H^+ in Table 7-1:

$$\log \gamma_{H^+} = \frac{(-0.51)(1^2)\sqrt{0.025}}{1 + (900\sqrt{0.025}/305)} = -0.054_{98}$$

$$\gamma_{H^+} = 10^{-0.054_{98}} = 0.88_1$$

Test Yourself By interpolation, find γ for H^+ when $\mu = 0.06$ M. (***Answer:*** 0.85_4)

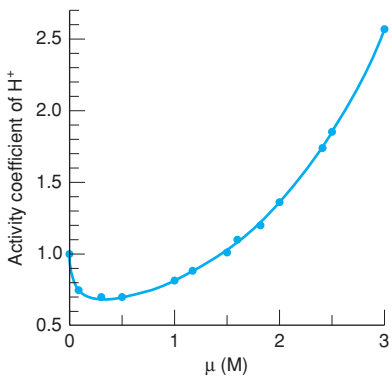


FIGURE 7-5 Activity coefficient of H^+ in solutions containing 0.010 0 M $HClO_4$ and varying amounts of $NaClO_4$. [Derived from L. Pezza, M. Molina, M. de Moraes, C. B. Melios, and J. O. Tognolli, *Talanta* 1996, *43*, 1689.] The authoritative source on electrolyte solutions is H. S. Harned and B. B. Owen, *The Physical Chemistry of Electrolyte Solutions* (New York: Reinhold, 1958 ed.).

Activity Coefficients of Nonionic Compounds

For neutral species, $\mathcal{A}_C \approx [C]$. A more accurate relation is $\log \gamma = k\mu$, where $k \approx 0$ for ion pairs, $k \approx 0.11$ for NH_3 and CO_2, and $k \approx 0.2$ for organic molecules. For an ionic strength of $\mu = 0.1$ M, $\gamma \approx 1.00$ for ion pairs, $\gamma \approx 1.03$ for NH_3, and $\gamma \approx 1.05$ for organic molecules.

Neutral molecules, such as benzene and acetic acid, have no ionic atmosphere because they have no charge. To a good approximation, their activity coefficients are unity when the ionic strength is less than 0.1 M. In this book, we set $\gamma = 1$ for neutral molecules. That is, *the activity of a neutral molecule will be assumed to be equal to its concentration*.

For gases such as H_2, the activity is written

$$\mathcal{A}_{H_2} = P_{H_2}\gamma_{H_2}$$

where P_{H_2} is pressure in bars. The activity of a gas is called its *fugacity*, and the activity coefficient is called the *fugacity coefficient*. Deviation of gas behavior from the ideal gas law results in deviation of the fugacity coefficient from unity. For gases at or below 1 bar, $\gamma \approx 1$. Therefore, for gases, *we will set* $\mathcal{A} = P$ (*bar*).

For gases, $\mathcal{A} \approx P$ (bar).

High Ionic Strengths

At high ionic strength, γ increases with increasing μ.

Above an ionic strength of ~1 M, activity coefficients of most ions increase, as shown for H^+ in $NaClO_4$ solutions in Figure 7-5. We should not be too surprised that activity coefficients in concentrated salt solutions are not the same as those in dilute aqueous solution. The "solvent" is no longer H_2O but, rather, a mixture of H_2O and $NaClO_4$. Hereafter, we limit our attention to dilute aqueous solutions.

EXAMPLE **Using Activity Coefficients**

Find the concentration of Ca^{2+} in equilibrium with 0.050 M NaF saturated with CaF_2. The solubility of CaF_2 is small, so the concentration of F^- is 0.050 M from NaF.

Solution We find $[Ca^{2+}]$ from the solubility product expression, including activity coefficients. The ionic strength of 0.050 M NaF is 0.050 M. At $\mu = 0.050\,0$ M in Table 7-1, we find $\gamma_{Ca^{2+}} = 0.485$ and $\gamma_{F^-} = 0.81$.

$$K_{sp} = [Ca^{2+}]\gamma_{Ca^{2+}}[F^-]^2\gamma_{F^-}^2$$
$$3.2 \times 10^{-11} = [Ca^{2+}](0.485)(0.050)^2(0.81)^2$$
$$[Ca^{2+}] = 4.0 \times 10^{-8}\ \text{M}$$

K_{sp} comes from Appendix F. Note that γ_{F^-} is squared.

Test Yourself Find $[Hg_2^{2+}]$ in equilibrium with 0.010 M KCl saturated with Hg_2Cl_2. (***Answer:*** 2.2×10^{-14} M)

7-3 pH Revisited

The definition pH $\approx -\log[H^+]$ in Chapter 6 is not exact. A better definition is

$$\mathbf{pH} = -\log \mathcal{A}_{H^+} = -\log[H^+]\gamma_{H^+} \qquad (7\text{-}8)$$

When we measure pH with a pH meter, we are measuring the negative logarithm of the hydrogen ion *activity*, not its concentration.

For a discussion of what pH really means and how the pH of primary standard solutions is measured, see B. Lunelli and F. Scagnolari, "pH Basics," *J. Chem. Ed.* **2009**, *86*, 246.

EXAMPLE **pH of Pure Water at 25°C**

Let's calculate the pH of pure water by using activity coefficients.

Solution The relevant equilibrium is

$$H_2O \underset{}{\overset{K_w}{\rightleftharpoons}} H^+ + OH^- \qquad (7\text{-}9)$$
$$K_w = \mathcal{A}_{H^+}\mathcal{A}_{OH^-} = [H^+]\gamma_{H^+}[OH^-]\gamma_{OH^-} \qquad (7\text{-}10)$$

H^+ and OH^- are produced in a 1:1 mole ratio, so their concentrations must be equal. Calling each concentration x, we write

$$K_w = 1.0 \times 10^{-14} = (x)\gamma_{H^+}(x)\gamma_{OH^-}$$

But the ionic strength of pure water is so small that it is reasonable to guess that $\gamma_{H^+} = \gamma_{OH^-} = 1$. Using these values in the preceding equation gives

$$1.0 \times 10^{-14} = (x)(1)(x)\,(1) = x^2 \Rightarrow x = 1.0 \times 10^{-7}\ \text{M}$$

The concentrations of H^+ and OH^- are both 1.0×10^{-7} M. The ionic strength is 1.0×10^{-7} M, so each activity coefficient is very close to 1.00. The pH is

$$\text{pH} = -\log[H^+]\gamma_{H^+} = -\log(1.0 \times 10^{-7})(1.00) = 7.00$$

EXAMPLE **pH of Water Containing a Salt**

Now let's calculate the pH of water containing 0.10 M KCl at 25°C.

Solution Reaction 7-9 tells us that $[H^+] = [OH^-]$. However, the ionic strength of 0.10 M KCl is 0.10 M. The activity coefficients of H^+ and OH^- in Table 7-1 are 0.83 and 0.76, respectively, when $\mu = 0.10$ M. Putting these values into Equation 7-10 gives

$$K_w = [H^+]\gamma_{H^+}[OH^-]\gamma_{OH^-}$$
$$1.0 \times 10^{-14} = (x)(0.83)(x)(0.76)$$
$$x = 1.26 \times 10^{-7}\ \text{M}$$

The concentrations of H^+ and OH^- are equal and are both greater than 1.0×10^{-7} M. The activities of H^+ and OH^- are not equal in this solution:

$$\mathcal{A}_{H^+} = [H^+]\gamma_{H^+} = (1.26 \times 10^{-7})(0.83) = 1.05 \times 10^{-7}$$
$$\mathcal{A}_{OH^-} = [OH^-]\gamma_{OH^-} = (1.26 \times 10^{-7})(0.76) = 0.96 \times 10^{-7}$$

Finally, we calculate $pH = -\log \mathcal{A}_{H^+} = -\log(1.05 \times 10^{-7}) = 6.98$.

Test Yourself Find $[H^+]$ and the pH of 0.05 M $LiNO_3$. (***Answer:*** $1.2_0 \times 10^{-7}$ M, 6.99)

The pH of water changes from 7.00 to 6.98 when we add 0.10 M KCl. KCl is not an acid or a base. The pH changes because KCl affects the activities of H^+ and OH^-. The pH change of 0.02 units lies at the limit of accuracy of pH measurements and is hardly important. However, the *concentration* of H^+ in 0.10 M KCl (1.26×10^{-7} M) is 26% greater than the concentration of H^+ in pure water (1.00×10^{-7} M).

7-4 Systematic Treatment of Equilibrium

The *systematic treatment of equilibrium* is a way to deal with all types of chemical equilibria, regardless of their complexity. After setting up general equations, we often introduce specific conditions or judicious approximations that allow simplification. Even simplified calculations are usually very tedious, so we make liberal use of spreadsheets for numerical solutions. When you have mastered the systematic treatment of equilibrium, you should be able to explore the behavior of complex systems.

The systematic procedure is to write as many independent algebraic equations as there are unknowns (species) in the problem. The equations are generated by writing all the chemical equilibrium conditions plus two more: the balances of charge and of mass. There is only one charge balance in a given system, but there could be several mass balances.

Charge Balance

Solutions must have zero total charge.

The **charge balance** is an algebraic statement of electroneutrality: *The sum of the positive charges in solution equals the sum of the negative charges in solution.*

Suppose that a solution contains the following ionic species: H^+, OH^-, K^+, $H_2PO_4^-$, HPO_4^{2-}, and PO_4^{3-}. The charge balance is

$$[H^+] + [K^+] = [OH^-] + [H_2PO_4^-] + 2[HPO_4^{2-}] + 3[PO_4^{3-}] \qquad \textbf{(7-11)}$$

The coefficient of each term in the charge balance equals the magnitude of the charge on each ion.

This statement says that the total charge contributed by H^+ and K^+ equals the magnitude of the charge contributed by all of the anions on the right side of the equation. *The coefficient in front of each species always equals the magnitude of the charge on the ion*. This statement is true because a mole of, say, PO_4^{3-} contributes three moles of negative charge. If $[PO_4^{3-}] = 0.01$ M, the negative charge is $3[PO_4^{3-}] = 3(0.01) = 0.03$ M.

Equation 7-11 appears unbalanced to many people. "The right side of the equation has much more charge than the left side!" you might think. But you would be wrong.

For example, consider a solution prepared by weighing out 0.025 0 mol of KH_2PO_4 plus 0.030 0 mol of KOH and diluting to 1.00 L. The concentrations of the species at equilibrium are calculated to be

$$[H^+] = 5.1 \times 10^{-12}\ \text{M} \qquad [H_2PO_4^-] = 1.3 \times 10^{-6}\ \text{M}$$
$$[K^+] = 0.055\,0\ \text{M} \qquad [HPO_4^{2-}] = 0.022\,0\ \text{M}$$
$$[OH^-] = 0.002\,0\ \text{M} \qquad [PO_4^{3-}] = 0.003\,0\ \text{M}$$

This calculation, which you should be able to do when you have finished studying acids and bases, takes into account the reaction of OH^- with $H_2PO_4^-$ to produce HPO_4^{2-} and PO_4^{3-}.

Are the charges balanced? Yes, indeed. Plugging into Equation 7-11, we find

$$[H^+] + [K^+] = [OH^-] + [H_2PO_4^-] + 2[HPO_4^{2-}] + 3[PO_4^{3-}]$$
$$5.1 \times 10^{-12} + 0.055\,0 = 0.002\,0 + 1.3 \times 10^{-6} + 2(0.022\,0) + 3(0.003\,0)$$
$$0.055\,0\ \text{M} = 0.055\,0\ \text{M}$$

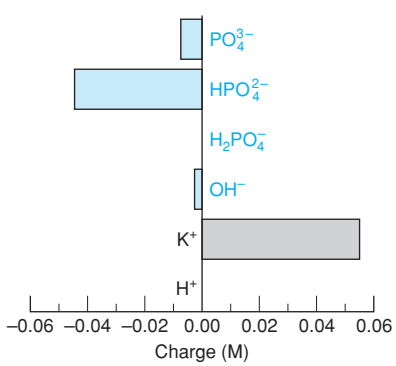


FIGURE 7-6 Charge contributed by each ion in 1.00 L of solution containing 0.025 0 mol KH_2PO_4 plus 0.030 0 mol KOH. The total positive charge equals the total negative charge.

The total positive charge is 0.055 0 M, and the total negative charge also is 0.055 0 M (Figure 7-6). Charges must balance in every solution. Otherwise, a beaker with excess positive charge would glide across the lab bench and smash into a beaker with excess negative charge.

The general form of the charge balance for any solution is

$$\textit{Charge balance:} \quad n_1[C_1] + n_2[C_2] + \cdots = m_1[A_1] + m_2[A_2] + \cdots \qquad (7\text{-}12)$$

where [C] is the concentration of a cation, n is the charge of the cation, [A] is the concentration of an anion, and m is the magnitude of the charge of the anion.

Σ[positive charges] = Σ[negative charges]

Activity coefficients do not appear in the charge balance. The charge contributed by 0.1 M H^+ is *exactly* 0.1 M. Think about this.

EXAMPLE **Writing a Charge Balance**

Write the charge balance for a solution containing H_2O, H^+, OH^-, ClO_4^-, $Fe(CN)_6^{3-}$, CN^-, Fe^{3+}, Mg^{2+}, CH_3OH, HCN, NH_3, and NH_4^+.

Solution Neutral species (H_2O, CH_3OH, HCN, and NH_3) contribute no charge, so the charge balance is

$$[H^+] + 3[Fe^{3+}] + 2[Mg^{2+}] + [NH_4^+] = [OH^-] + [ClO_4^-] + 3[Fe(CN)_6^{3-}] + [CN^-]$$

Test Yourself What would be the charge balance if you add $MgCl_2$ to the solution and it dissociates into $Mg^{2+} + 2Cl^-$? (***Answer:*** $[H^+] + 3[Fe^{3+}] + 2[Mg^{2+}] + [NH_4^+] = [OH^-] + [ClO_4^-] + 3[Fe(CN)_6^{3-}] + [CN^-] + [Cl^-]$)

Mass Balance

The **mass balance**, also called the *material balance*, is a statement of the conservation of matter. The mass balance states that *the quantity of all species in a solution containing a particular atom (or group of atoms) must equal the amount of that atom (or group) delivered to the solution*. It is easier to see this relation through examples than by a general statement.

The mass balance is a statement of the conservation of matter. It really refers to conservation of atoms, not to mass.

Suppose that a solution is prepared by dissolving 0.050 mol of acetic acid in water to give a total volume of 1.00 L. Acetic acid partially dissociates into acetate:

$$\underset{\text{Acetic acid}}{CH_3CO_2H} \rightleftharpoons \underset{\text{Acetate}}{CH_3CO_2^-} + H^+$$

The mass balance states that the quantity of dissociated and undissociated acetic acid in the solution must equal the amount of acetic acid put into the solution.

$$\textit{Mass balance for acetic acid in water:} \quad \underset{\text{What we put into the solution}}{0.050\ M} = \underset{\text{Undissociated product}}{[CH_3CO_2H]} + \underset{\text{Dissociated product}}{[CH_3CO_2^-]}$$

When a compound dissociates in several ways, the mass balance must include all the products. Phosphoric acid (H_3PO_4), for example, dissociates to $H_2PO_4^-$, HPO_4^{2-}, and PO_4^{3-}. The mass balance for a solution prepared by dissolving 0.025 0 mol of H_3PO_4 in 1.00 L is

Activity coefficients do not appear in the mass balance. The concentration of each species counts exactly the number of atoms of that species.

$$0.025\ 0\ M = [H_3PO_4] + [H_2PO_4^-] + [HPO_4^{2-}] + [PO_4^{3-}]$$

EXAMPLE **Mass Balance When the Total Concentration Is Known**

Write the mass balances for K^+ and for phosphate in a solution prepared by mixing 0.025 0 mol KH_2PO_4 plus 0.030 0 mol KOH and diluting to 1.00 L.

Solution The total K^+ is 0.025 0 M + 0.030 0 M, so one mass balance is

$$[K^+] = 0.055\ 0\ M$$

The total of *all forms* of phosphate is 0.025 0 M, so the mass balance for phosphate is

$$[H_3PO_4] + [H_2PO_4^-] + [HPO_4^{2-}] + [PO_4^{3-}] = 0.025\ 0\ M$$

Test Yourself Write two mass balances for a 1.00-L solution containing 0.100 mol of sodium acetate. (***Answer:*** $[Na^+] = 0.100$ M; $[CH_3CO_2H] + [CH_3CO_2^-] = 0.100$ M)

Now consider a solution prepared by dissolving $La(IO_3)_3$ in water.

$$La(IO_3)_3(s) \overset{K_{sp}}{\rightleftharpoons} La^{3+} + 3\underset{\text{Iodate}}{IO_3^-}$$

We do not know how much La^{3+} or IO_3^- is dissolved, but we do know that there must be three iodate ions for each lanthanum ion dissolved. That is, the iodate concentration must be three times the lanthanum concentration. If La^{3+} and IO_3^- are the only species derived from $La(IO_3)_3$, then the mass balance is

$$[IO_3^-] = 3[La^{3+}]$$

If the solution also contains the ion pair $LaIO_3^{2+}$ and the hydrolysis product $LaOH^{2+}$, the mass balance would be

$$[\text{Total iodate}] = 3[\text{total lanthanum}]$$
$$[IO_3^-] + [LaIO_3^{2+}] = 3\{[La^{3+}] + [LaIO_3^{2+}] + [LaOH^{2+}]\}$$

EXAMPLE **Mass Balance When the Total Concentration Is Unknown**

Write the mass balance for a saturated solution of the slightly soluble salt Ag_3PO_4, which produces PO_4^{3-} and $3Ag^+$ when it dissolves.

Solution If the phosphate in solution remained as PO_4^{3-}, we could write

$$[Ag^+] = 3[PO_4^{3-}]$$

because three silver ions are produced for each phosphate ion. However, phosphate reacts with water to give HPO_4^{2-}, $H_2PO_4^-$, and H_3PO_4, so the mass balance is

Atoms of Ag = 3(atoms of P)

$$[Ag^+] = 3\{[PO_4^{3-}] + [HPO_4^{2-}] + [H_2PO_4^-] + [H_3PO_4]\}$$

Box 7-2 illustrates the operation of a mass balance in natural waters.

That is, the number of atoms of Ag^+ must equal three times the total number of atoms of phosphorus, regardless of how many species contain phosphorus.

Test Yourself Write the mass balance for a saturated solution of $Ba(HSO_4)_2$ if the species in solution are Ba^{2+}, $BaSO_4(aq)$, HSO_4^-, SO_4^{2-}, and $BaOH^+$. (***Answer:*** $2 \times$ total barium = total sulfate, or $2\{[Ba^{2+}] + [BaSO_4(aq)] + [BaOH^+]\} = [SO_4^{2-}] + [HSO_4^-] + [BaSO_4(aq)]$)

Systematic Treatment of Equilibrium

Now that we have considered the charge and mass balances, we are ready for the systematic treatment of equilibrium.[11] Here is the general prescription:

Step 1 Write the *pertinent reactions*.
Step 2 Write the *charge balance* equation.
Step 3 Write *mass balance* equations. There may be more than one.
Step 4 Write the *equilibrium constant expression* for each chemical reaction. This step is the only one in which activity coefficients appear.
Step 5 *Count the equations and unknowns*. There should be as many equations as unknowns (chemical species). If not, you must either find more equilibria or fix some concentrations at known values.
Step 6 *Solve* for all unknowns.

Steps 1 and 6 are the heart of the problem. Guessing what chemical equilibria exist in a given solution requires a fair degree of chemical intuition. In this book, you will usually be given help with step 1. Unless we know all the relevant equilibria, it is not possible to calculate the composition of a solution correctly. Because we do not know all the chemical reactions, we undoubtedly oversimplify many equilibrium problems. Step 6—solving the equations—is likely to be your biggest challenge. With n equations and n unknowns, the problem can be solved, at least in principle. In the simplest cases, you can do this by hand, but, for most problems, approximations are made or a spreadsheet is employed.

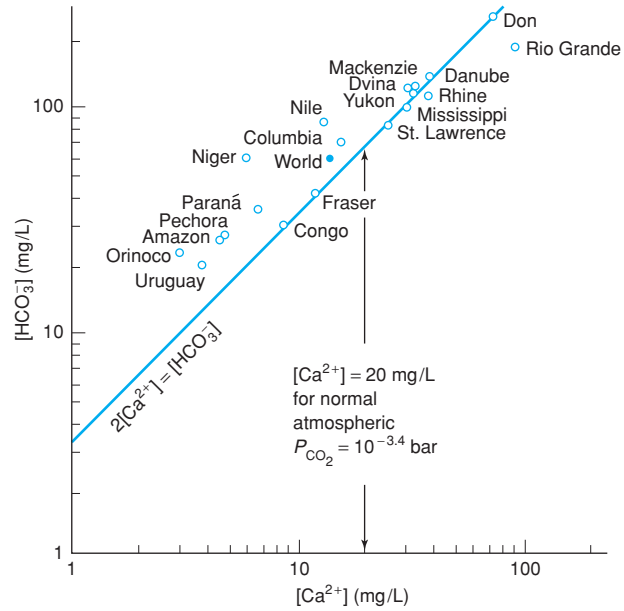
BOX 7-2 Calcium Carbonate Mass Balance in Rivers

Ca^{2+} is the most common cation in rivers and lakes. It comes from dissolution of the mineral calcite by the action of CO_2 to produce 2 moles of HCO_3^- for each mole of Ca^{2+}:

$$\underset{\text{Calcite}}{CaCO_3(s)} + CO_2(aq) + H_2O \rightleftharpoons Ca^{2+} + \underset{\text{Bicarbonate}}{2HCO_3^-} \qquad \textbf{(A)}$$

Near neutral pH, most of the product is bicarbonate, not CO_3^{2-} or H_2CO_3. The mass balance for the dissolution of calcite is therefore $[HCO_3^-] \approx 2[Ca^{2+}]$. Indeed, measurements of Ca^{2+} and HCO_3^- in many rivers conform to this mass balance, shown by the straight line on the graph. Rivers such as the Danube, the Mississippi, and the Congo, which lie on the line $[HCO_3^-] = 2[Ca^{2+}]$, appear to be saturated with calcium carbonate. If the river water were in equilibrium with atmospheric CO_2 ($P_{CO_2} = 10^{-3.4}$ bar), the concentration of Ca^{2+} would be 20 mg/L (see Problem 7-30). Rivers with more than 20 mg of Ca^{2+} per liter have a higher concentration of dissolved CO_2 produced by respiration or from inflow of groundwaters with a high CO_2 content. Rivers such as the Nile, the Niger, and the Amazon, for which $2[Ca^{2+}] < [HCO_3^-]$, are not saturated with $CaCO_3$.

Between 1960 and 2008, atmospheric CO_2 increased by 20% (Figure 0-4, page 4)—mostly from our burning of fossil fuel. This increase drives Reaction A to the right and threatens the existence of coral reefs,[9] which are living structures consisting largely of $CaCO_3$. Coral reefs are a unique habitat for many aquatic species. Continued buildup of atmospheric CO_2 threatens certain plankton with $CaCO_3$ shells,[10] a loss that, in turn, threatens higher members of the food chain.



Concentrations of bicarbonate and calcium in many rivers conform to the mass balance $[HCO_3^-] \approx 2[Ca^{2+}]$. [Data from W. Stumm and J. J. Morgan, *Aquatic Chemistry*, 3rd ed. (New York: Wiley-Interscience, 1996), p. 189; and H. D. Holland, *The Chemistry of the Atmosphere and Oceans* (New York: Wiley-Interscience, 1978).]

7-5 Applying the Systematic Treatment of Equilibrium

Now we examine some problems to learn to apply the systematic treatment of equilibrium and to illustrate what can be done by hand and when a spreadsheet is really helpful.

A Solution of Ammonia

Let's find the concentrations of species in an aqueous solution containing 0.010 0 mol NH_3 in 1.000 L. The primary equilibrium is

$$NH_3 + H_2O \overset{K_b}{\rightleftharpoons} NH_4^+ + OH^- \qquad K_b = 1.76 \times 10^{-5} \text{ at } 25°C \qquad \textbf{(7-13)}$$

A second equilibrium in every aqueous solution is

$$H_2O \overset{K_w}{\rightleftharpoons} H^+ + OH^- \qquad K_w = 1.0 \times 10^{-14} \text{ at } 25°C \qquad \textbf{(7-14)}$$

Our goal is to find $[NH_3]$, $[NH_4^+]$, $[H^+]$, and $[OH^-]$.

Step 1 Pertinent reactions. They are 7-13 and 7-14.

Step 2 Charge balance. The sum of positive charge equals the sum of negative charge:

$$[NH_4^+] + [H^+] = [OH^-] \qquad \textbf{(7-15)}$$

Step 3 Mass balance. All of the ammonia delivered to the solution is either in the form NH_3 or NH_4^+. These two must add up to 0.010 0 M.

$$[NH_3] + [NH_4^+] = 0.010\,0 \text{ M} \equiv F \qquad \textbf{(7-16)}$$

The symbol ≡ means "is defined as."

where F stands for formal concentration.

Step 4 Equilibrium expressions.

$$K_b = \frac{[NH_4^+]\gamma_{NH_4^+}[OH^-]\gamma_{OH^-}}{[NH_3]\gamma_{NH_3}} = 1.76 \times 10^{-5} \qquad \textbf{(7-17)}$$

$$K_w = [H^+]\gamma_{H^+}[OH^-]\gamma_{OH^-} = 1.0 \times 10^{-14} \qquad \textbf{(7-18)}$$

This is the only step in which activity coefficients enter the problem.

We need n equations to solve for n unknowns.

Step 5 Count equations and unknowns. We have four equations, 7-15 to 7-18, and four unknowns ($[NH_3]$, $[NH_4^+]$, $[H^+]$, and $[OH^-]$). We have enough information to solve the problem.

Step 6 Solve.

This "simple" problem is complicated. Let's start by ignoring activity coefficients; we will return to them later. Our approach is to eliminate one variable at a time until only one unknown is left. For an acid-base problem, I choose to express each concentration in terms of $[H^+]$. A substitution we can always make is $[OH^-] = K_w/[H^+]$. Putting this expression for $[OH^-]$ into the charge balance 7-15 gives

$$[NH_4^+] + [H^+] = \frac{K_w}{[H^+]}$$

from which we can solve for $[NH_4^+]$:

$$[NH_4^+] = \frac{K_w}{[H^+]} - [H^+] \tag{7-19}$$

The mass balance tells us that $[NH_3] = F - [NH_4^+]$. We can substitute the expression for $[NH_4^+]$ from Equation 7-19 into the mass balance to express $[NH_3]$ in terms of $[H^+]$:

$$[NH_3] = F - [NH_4^+] = F - \left(\frac{K_w}{[H^+]} - [H^+]\right) \tag{7-20}$$

Equation 7-19 gives $[NH_4^+]$ in terms of $[H^+]$. Equation 7-20 gives $[NH_3]$ in terms of $[H^+]$.

We can generate an equation in which the only unknown is $[H^+]$ by substituting our expressions for $[NH_4^+]$, $[NH_3]$, and $[OH^-]$ into the K_b equilibrium (still ignoring activity coefficients):

$$K_b = \frac{[NH_4^+][OH^-]}{[NH_3]} = \frac{\left(\frac{K_w}{[H^+]} - [H^+]\right)\left(\frac{K_w}{[H^+]}\right)}{\left(F - \frac{K_w}{[H^+]} + [H^+]\right)} \tag{7-21}$$

Equation 7-21 is horrible, but $[H^+]$ is the only unknown. One way you could solve for $[H^+]$ is to *guess* a value of $[H^+]$, put it into the right side of the equation, and see if the right side is equal to K_b on the left side. Of course, your guess would not make the right side of the equation equal to K_b. So guess a little smaller value of $[H^+]$ and see if you come closer to K_b. If your second answer is better than the first one, continue guessing smaller values of $[H^+]$ until you have solved the equation. If your second answer was worse than the first one, guess larger values of $[H^+]$ until you have solved the equation.

Excel has a procedure called Goal Seek, which follows a systematic guessing process to find the answer. We will learn to use Goal Seek later in this chapter.

After solving for $[H^+]$, we could calculate $[OH^-] = K_w/[H^+]$. We could find $[NH_4^+]$ from Equation 7-19 and we could compute $[NH_3]$ from the K_b equilibrium expression. Then we would have all four concentrations.

What could we do about the activity coefficients? From $[NH_4^+]$, $[H^+]$, and $[OH^-]$, we could calculate the ionic strength and then find the activity coefficients with Table 7-1 or the extended Debye-Hückel equation. Then we could put these coefficients into Equations 7-17 and 7-18 and solve the problem all over again. The new concentrations would be different from what we found without activity coefficients. We could use the new concentrations to find a new ionic strength and new activity coefficients and another set of new concentrations. We could repeat this process until differences between successive answers become negligible (say, less than 1%). At that point, we have solved the problem.

You should now appreciate that applying the systematic treatment of equilibrium to even the simplest of problems is not simple. In most equilibrium problems, we will make simplifying approximations to reach a good answer with a reasonable effort. After solving a problem, we must always verify that our approximations are valid.

Here is an approximation to simplify the ammonia problem. Ammonia is a base, so we expect that $[OH^-] \gg [H^+]$. For example, suppose the pH comes out to 9. Then $[H^+] = 10^{-9}$ M and $[OH^-](= K_w/[H^+]) = 10^{-14}/10^{-9} = 10^{-5}$ M. That is, $[OH^-] \gg [H^+]$. In the first term of the numerator of Equation 7-21, we can neglect $[H^+]$ in comparison with $K_w/[H^+]$.

In the denominator, we can also neglect $[H^+]$ in comparison with $K_w/[H^+]$. With these approximations, Equation 7-21 becomes

$$K_b = \frac{\left(\frac{K_w}{[H^+]} - \cancel{[H^+]}\right)\left(\frac{K_w}{[H^+]}\right)}{\left(F - \frac{K_w}{[H^+]} + \cancel{[H^+]}\right)} = \frac{\left(\frac{K_w}{[H^+]}\right)\left(\frac{K_w}{[H^+]}\right)}{\left(F - \frac{K_w}{[H^+]}\right)} = \frac{[OH^-]^2}{F - [OH^-]} \tag{7-22}$$

Equation 7-22 is quadratic with one variable $[OH^-]$. We can solve for $[OH^-]$ by algebra. We will deal with equations of this type extensively in the next chapter on acids and bases.

Next, we take two examples all the way through to numerical answers.

Solubility of Calcium Sulfate

Let's find the concentrations of the major species in a saturated solution of $CaSO_4$.

Step 1 Pertinent reactions. Even in such a simple system, there are quite a few reactions:

$$CaSO_4(s) \overset{K_{sp}}{\rightleftharpoons} Ca^{2+} + SO_4^{2-} \qquad K_{sp} = 2.4 \times 10^{-5} \tag{7-23}$$

$$CaSO_4(s) \overset{K_{ion\ pair}}{\rightleftharpoons} CaSO_4(aq) \qquad K_{ion\ pair} = 5.0 \times 10^{-3} \tag{7-24}$$

$$Ca^{2+} + H_2O \overset{K_{acid}}{\rightleftharpoons} CaOH^+ + H^+ \qquad K_{acid} = 2.0 \times 10^{-13} \tag{7-25}$$

$$SO_4^{2-} + H_2O \overset{K_{base}}{\rightleftharpoons} HSO_4^- + OH^- \qquad K_{base} = 9.8 \times 10^{-13} \tag{7-26}$$

$$H_2O \overset{K_w}{\rightleftharpoons} H^+ + OH^- \qquad K_w = 1.0 \times 10^{-14} \tag{7-27}$$

Caveat Emptor! In all equilibrium problems, we are limited by how much of the system's chemistry is understood. Without all relevant equilibria, it is impossible to calculate the composition.

There is no way you can be expected to come up with all of these reactions, so you will be given help with this step.

Step 2 Charge balance. Equating positive and negative charges gives

$$2[Ca^{2+}] + [CaOH^+] + [H^+] = 2[SO_4^{2-}] + [HSO_4^-] + [OH^-] \tag{7-28}$$

Multiply $[Ca^{2+}]$ and $[SO_4^{2-}]$ by 2 because 1 mol of each ion has 2 mol of charge.

Step 3 Mass balance. Reaction 7-23 produces 1 mole of sulfate for each mole of calcium. No matter what happens to these ions, the total concentration of all species with sulfate must equal the total concentration of all species with calcium:

$$[\text{Total calcium}] = [\text{total sulfate}]$$

$$[Ca^{2+}] + [CaSO_4(aq)] + [CaOH^+] = [SO_4^{2-}] + [HSO_4^-] + [CaSO_4(aq)] \tag{7-29}$$

Step 4 Equilibrium constant expressions. There is one for each chemical reaction.

$$K_{sp} = [Ca^{2+}]\gamma_{Ca^{2+}}[SO_4^{2-}]\gamma_{SO_4^{2-}} = 2.4 \times 10^{-5} \tag{7-30}$$

$$K_{ion\ pair} = [CaSO_4(aq)] = 5.0 \times 10^{-3} \tag{7-31}$$

$$K_{acid} = \frac{[CaOH^+]\gamma_{CaOH^+}[H^+]\gamma_{H^+}}{[Ca^{2+}]\gamma_{Ca^{2+}}} = 2.0 \times 10^{-13} \tag{7-32}$$

$$K_{base} = \frac{[HSO_4^-]\gamma_{HSO_4^-}[OH^-]\gamma_{OH^-}}{[SO_4^{2-}]\gamma_{SO_4^{2-}}} = 9.8 \times 10^{-13} \tag{7-33}$$

$$K_w = [H^+]\gamma_{H^+}[OH^-]\gamma_{OH^-} = 1.0 \times 10^{-14} \tag{7-34}$$

Step 4 is the only one where activity coefficients come in.

Step 5 Count equations and unknowns. There are seven equations (7-28 through 7-34) and seven unknowns: $[Ca^{2+}]$, $[SO_4^{2-}]$, $[CaSO_4(aq)]$, $[CaOH^+]$, $[HSO_4^-]$, $[H^+]$, and $[OH^-]$.

Step 6 Solve. Well, this is not easy! We don't know the ionic strength, so we cannot evaluate activity coefficients. Also, where do we start when there are seven unknowns?

Just when the world looks grim, a Good Chemist comes galloping down the hill on her white stallion to rescue us with some hints. "First of all," she says, "Reactions 7-25 and 7-26 have small equilibrium constants, so they are not very important compared with Reactions 7-23 and 7-24. As for activity coefficients, you can begin by setting them all equal to 1 and solving for all concentrations. Then you can calculate the ionic strength and find values for the activity coefficients. With these coefficients, you can solve the

problem a second time and find a new set of concentrations. You can repeat this process a few times until you reach a constant answer."

On the advice of the Good Chemist, we neglect the acid-base reactions 7-25 and 7-26. The remaining reactions of calcium sulfate, 7-23 and 7-24, are not reactions with H_2O. Therefore, in our approximation, Reaction 7-27 is independent of the calcium sulfate chemistry. Reaction 7-27 produces $[H^+]$ and $[OH^-]$, which we know are 1×10^{-7} M. These concentrations of H^+ and OH^- are not exactly correct, because we have neglected Reactions 7-25 and 7-26, which do play a role in determining $[H^+]$ and $[OH^-]$.

These approximations leave just Reactions 7-23 and 7-24. In the charge balance 7-28, $CaOH^+$ and HSO_4^- are neglected. Also, $[H^+] = [OH^-]$, so they cancel. The charge balance becomes $2[Ca^{2+}] = 2[SO_4^{2-}]$. In the mass balance 7-29, we discard $CaOH^+$ and HSO_4^- because we neglect reactions 7-25 and 7-26. The term $[CaSO_4(aq)]$ cancels, leaving $[Ca^{2+}] = [SO_4^{2-}]$, which is the same as the charge balance. We have three unknowns ($[Ca^{2+}]$, $[SO_4^{2-}]$, $[CaSO_4(aq)]$) and three equations:

The activity coefficient of the neutral species $CaSO_4(aq)$ is 1.

$$K_{sp} = [Ca^{2+}]\gamma_{Ca^{2+}}[SO_4^{2-}]\gamma_{SO_4^{2-}} = 2.4 \times 10^{-5} \quad \textbf{(7-30)}$$

$$K_{\text{ion pair}} = [CaSO_4(aq)] = 5.0 \times 10^{-3} \quad \textbf{(7-31)}$$

$$[Ca^{2+}] = [SO_4^{2-}] \quad \textbf{(7-35)}$$

Equation 7-31 says $[CaSO_4(aq)] = 5.0 \times 10^{-3}$ M, so $[CaSO_4(aq)]$ is known.

The simplified problem is reduced to Equations 7-30 and 7-35. We find a first approximate solution by setting activity coefficients to 1:

$$[Ca^{2+}]_1\gamma_{Ca^{2+}}[SO_4^{2-}]_1\gamma_{SO_4^{2-}} = 2.4 \times 10^{-5} \quad \textbf{(7-36)}$$

$$[Ca^{2+}]_1(1)[SO_4^{2-}]_1(1) = 2.4 \times 10^{-5}$$

$$[Ca^{2+}]_1(1)[Ca^{2+}]_1(1) = 2.4 \times 10^{-5} \Rightarrow [Ca^{2+}]_1 = 4.9 \times 10^{-3}\ \text{M}$$

where the subscript 1 means it is our first approximation. If $[Ca^{2+}] = [SO_4^{2-}] = 4.9 \times 10^{-3}$ M, then the ionic strength is $\mu = 4(4.9 \times 10^{-3}\ \text{M}) = 0.020$ M. Interpolating in Table 7-1, we find the activity coefficients $\gamma_{Ca^{2+}} = 0.628$ and $\gamma_{SO_4^{2-}} = 0.606$. Putting these coefficients back into Equation 7-36 provides a second approximation:

We are carrying out a method of *successive approximations*. Each cycle is called an *iteration*.

$$[Ca^{2+}]_2(0.628)[Ca^{2+}]_2(0.606) = 2.4 \times 10^{-5} \Rightarrow [Ca^{2+}]_2 = 7.9 \times 10^{-3}\ \text{M}$$

$$\Rightarrow \mu = 0.032\ \text{M}$$

Repeating this process gives the following results:

Iteration	$\gamma_{Ca^{2+}}$	$\gamma_{SO_4^{2-}}$	$[Ca^{2+}]$ (M)	μ (M)
1	1	1	0.004 9	0.020
2	0.628	0.606	0.007 9	0.032
3	0.570	0.542	0.008 8	0.035
4	0.556	0.526	0.009 1	0.036
5	0.551	0.520	0.009 2	0.037
6	0.547	0.515	0.009 2	0.037

The sixth iteration gives the same concentration as the fifth, so we have reached a constant answer.

Total concentration of dissolved sulfate

$= [SO_4^{2-}] + [CaSO_4(aq)]$
$= 0.009\ 2 + 0.005\ 0 = 0.014\ 2$ M

which is near the measured value in Figure 6-1. With the extended Debye-Hückel equation, instead of interpolation, total dissolved sulfate = 0.014 7 M.

With the advice of the Good Chemist, we simplified the problem tremendously. Now we need to know if her advice was good. From $[Ca^{2+}] = [SO_4^{2-}] = 0.009\ 2$ M and $[H^+] = [OH^-] = 1.0 \times 10^{-7}$ M, we can estimate $[CaOH^+]$ and $[HSO_4^-]$ to see if they are negligible. We are just looking for orders of magnitude, so we ignore activity coefficients. From Equation 7-32, we have

$$\frac{[CaOH^+][H^+]}{[Ca^{2+}]} = 2.0 \times 10^{-13}$$

$$[CaOH^+] \approx \frac{(2.0 \times 10^{-13})[Ca^{2+}]}{[H^+]} = \frac{(2.0 \times 10^{-13})[0.009\ 2]}{[1.0 \times 10^{-7}]} = 2 \times 10^{-8}\ \text{M}$$

From Equation 7-33, we estimate

$$[HSO_4^-] \approx \frac{(9.8 \times 10^{-13})[SO_4^{2-}]}{[OH^-]} = \frac{(9.8 \times 10^{-13})[0.009\ 2]}{[1.0 \times 10^{-7}]} = 9 \times 10^{-8}\ \text{M}$$

Both $[CaOH^+]$ and $[HSO_4^-]$ are $\sim 10^5$ times less than $[Ca^{2+}]$ and $[SO_4^{2-}]$, so it was reasonable to neglect $[CaOH^+]$ and $[HSO_4^-]$ in the charge and mass balances.

We simplified the problem to the point where we could assume that the pH is close to 7.00. If you need a better answer, Section 12-3 provides a method to find the pH using all five chemical reactions 7-23 through 7-27. The result in Problem 12-13 is pH = 7.06.

We Will Usually Omit Activity Coefficients

Although it is proper to write equilibrium constants in terms of activities, the complexity of manipulating activity coefficients is a nuisance. Most of the time, we will omit activity coefficients unless there is a particular point to be made. Occasional problems will remind you how to use activities.

Solubility of Magnesium Hydroxide

Let's find the concentrations of species in a saturated solution of $Mg(OH)_2$, given the following chemistry. For simplicity, we ignore activity coefficients.

$$Mg(OH)_2(s) \overset{K_{sp}}{\rightleftharpoons} Mg^{2+} + 2OH^- \qquad K_{sp} = [Mg^{2+}][OH^-]^2 = 7.1 \times 10^{-12} \quad \textbf{(7-37)}$$

$$Mg^{2+} + OH^- \overset{K_1}{\rightleftharpoons} MgOH^+ \qquad K_1 = \frac{[MgOH^+]}{[Mg^{2+}][OH^-]} = 3.8 \times 10^2 \quad \textbf{(7-38)}$$

$$H_2O \overset{K_w}{\rightleftharpoons} H^+ + OH^- \qquad K_w = [H^+][OH^-] = 1.0 \times 10^{-14} \quad \textbf{(7-39)}$$

Step 1 Pertinent reactions are listed above.

Step 2 Charge balance:

$$2[Mg^{2+}] + [MgOH^+] + [H^+] = [OH^-] \quad \textbf{(7-40)}$$

Step 3 Mass balance. This is a little tricky. From Reaction 7-37, we could say that the concentrations of all species containing OH^- equal two times the concentrations of all magnesium species. However, Reaction 7-39 also creates 1 OH^- for each H^+. The mass balance accounts for both sources of OH^-:

$$\underbrace{[OH^-] + [MgOH^+]}_{\text{Species containing } OH^-} = 2\underbrace{\{[Mg^{2+}] + [MgOH^+]\}}_{\text{Species containing } Mg^{2+}} + [H^+] \quad \textbf{(7-41)}$$

After all this work, Equation 7-41 is equivalent to Equation 7-40.

Step 4 Equilibrium constant expressions are in Equations 7-37 through 7-39.

Step 5 Count equations and unknowns. We have four equations (7-37 to 7-40) and four unknowns: $[Mg^{2+}]$, $[MgOH^+]$, $[H^+]$, and $[OH^-]$.

Step 6 Solve.

Before hitting the algebra, we can make one simplification. The solution must be basic because we made it from $Mg(OH)_2$. In basic solution, $[OH^-] \gg [H^+]$, so we can neglect $[H^+]$ on the left side of Equation 7-40 in comparison with $[OH^-]$ on the right side. The charge balance simplifies to

$$2[Mg^{2+}] + [MgOH^+] = [OH^-] \quad \textbf{(7-42)}$$

From the K_1 expression 7-38, we write $[MgOH^+] = K_1[Mg^{2+}][OH^-]$. Substituting this expression for $[MgOH^+]$ into Equation 7-42 gives

$$2[Mg^{2+}] + K_1[Mg^{2+}][OH^-] = [OH^-]$$

which we solve for $[Mg^{2+}]$:

$$[Mg^{2+}] = \frac{[OH^-]}{2 + K_1[OH^-]}$$

Substituting this expression for $[Mg^{2+}]$ into the solubility product reduces the equation to a single variable:

$$K_{sp} = [Mg^{2+}][OH^-]^2 = \left(\frac{[OH^-]}{2 + K_1[OH^-]}\right)[OH^-]^2 = \frac{[OH^-]^3}{2 + K_1[OH^-]} \quad \textbf{(7-43)}$$

	A	B	C	D
1	$Mg(OH)_2$ Solubility			
2				
3	K_{sp} =		$[OH^-]_{guess}$ =	$[OH^-]^3/(2 + K_1[OH^-])$ =
4	7.1E-12		0.0002459	7.1000E-12
5	K_1 =			
6	3.8E+02		$[Mg^{2+}]$ =	$[MgOH^+]$ =
7			0.0001174	0.0000110
8				
9	D4 = C4^3/(2+A6*C4)			
10	C7 = A4/C4^2			
11	D8 = A6*C7*C4			

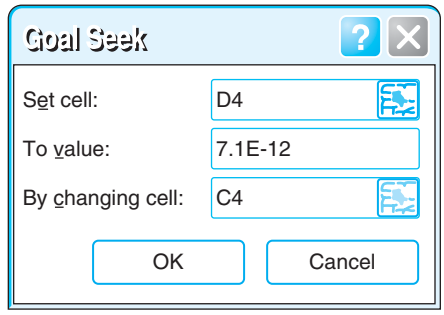


FIGURE 7-7 Spreadsheet for solving Equation 7-43.

We are down to solving the ugly Equation 7-43 for $[OH^-]$. Just when the world looks grim again, the Good Chemist says, "Use a spreadsheet to vary $[OH^-]$ until Equation 7-43 is satisfied." We do this in Figure 7-7, where we *guess* a value of $[OH^-]$ in cell C4 and evaluate the right side of Equation 7-43 in cell D4. When we have guessed the correct value of $[OH^-]$, cell D4 is equal to K_{sp}. Guessing is done by systematically changing $[OH^-]$ in cell C4 until cell D4 has the desired value of 7.1×10^{-12}.

Solving Equations with Excel Goal Seek®

Excel Goal Seek

A better procedure to solve Equation 7-43 is to use Excel Goal Seek to vary cell C4 until cell D4 is equal to K_{sp}. Put any guess for $[OH^-]$, such as 0.01, into cell C4 in Figure 7-7. Before using Goal Seek in Excel 2007, click the Microsoft Office button at the upper left of the spreadsheet. At the bottom of the Office window, click Excel Options. At the left side of the next window, select Formulas. In Calculation Options, set Maximum Change to 1e-24, which enables Excel to look for differences smaller than the target value of 7.1×10^{-12}. Click OK. Return to the spreadsheet and select the Data ribbon. In Data Tools, click What-If Analysis and select Goal Seek. When the window at the right of Figure 7-7 appears, fill in the underlined values: Set cell D4 To value 7.1e-12 by changing cell C4. Click OK and Excel varies cell C4 until cell D4 is equal to 7.1E-12. We find $[OH^-] = 2.459 \times 10^{-4}$ M. Figure 7-7 also computes $[Mg^{2+}]$ and $[MgOH^+]$ from Equations 7-37 and 7-38. The results confirm the approximation we made at the outset: $[H^+] = K_w/[OH^-] = 4.1 \times 10^{-11}$ M $\ll [OH^-]$.

In earlier versions of Excel, before using Goal Seek, go to the Tools menu and select Options. Select the Calculations tab and set Maximum change to 1e-24. Go back to Tools, select Goal Seek, and proceed as described above.

Terms to Understand

activity
activity coefficient
charge balance
extended Debye-Hückel equation
ionic atmosphere
ionic strength
mass balance
pH

Summary

The thermodynamic equilibrium constant for the reaction $aA + bB \rightleftharpoons cC + dD$ is $K = \mathcal{A}_C^c \mathcal{A}_D^d/(\mathcal{A}_A^a \mathcal{A}_B^b)$, where $\mathcal{A}_i$ is the activity of the ith species. The activity is the product of the concentration (c) and the activity coefficient (γ): $\mathcal{A}_i = c_i\gamma_i$. For nonionic compounds and gases, $\gamma_i \approx 1$. For ionic species, the activity coefficient depends on the ionic strength, defined as $\mu = \frac{1}{2}\Sigma c_i z_i^2$, where z_i is the charge of an ion. The activity coefficient decreases as ionic strength increases, at least for low ionic strengths (≤ 0.1 M). Dissociation of ionic compounds increases with ionic strength because the ionic atmosphere of each ion diminishes the attraction of ions for one another. You should be able to estimate activity coefficients by interpolation in Table 7-1. pH is defined in terms of the activity of H^+: $pH = -\log \mathcal{A}_{H^+} = -\log[H^+]\gamma_{H^+}$.

In the systematic treatment of equilibrium, we write pertinent equilibrium expressions, as well as the charge and mass balances. The charge balance states that the sum of all positive charges in solution equals the sum of all negative charges. The mass balance states that the moles of all forms of an element in solution must equal the moles of that element delivered to the solution. We make certain that we have as many equations as unknowns and then solve for the concentrations by using algebra, approximations, spreadsheets, magic, or anything else.

Exercises

7-A. Assuming complete dissociation of the salts, calculate the ionic strength of **(a)** 0.2 mM KNO_3; **(b)** 0.2 mM Cs_2CrO_4; **(c)** 0.2 mM $MgCl_2$ plus 0.3 mM $AlCl_3$.

7-B. Find the activity (not the activity coefficient) of the $(C_3H_7)_4N^+$ (tetrapropylammonium) ion in a solution containing 0.005 0 M $(C_3H_7)_4N^+Br^-$ plus 0.005 0 M $(CH_3)_4N^+Cl^-$.

7-C. Using activities, find $[Ag^+]$ in 0.060 M KSCN saturated with AgSCN(s).

7-D. Using activities, calculate the pH and concentration of H^+ in 0.050 M LiBr at 25°C.

7-E. A 40.0-mL solution of 0.040 0 M $Hg_2(NO_3)_2$ was titrated with 60.0 mL of 0.100 M KI to precipitate Hg_2I_2 ($K_{sp} = 4.6 \times 10^{-29}$).

(a) Show that 32.0 mL of KI are needed to reach the equivalence point.

(b) When 60.0 mL of KI have been added, virtually all Hg_2^{2+} has precipitated, along with 3.20 mmol of I^-. Considering all ions remaining in the solution, calculate the ionic strength when 60.0 mL of KI have been added.

(c) Using activities, calculate $pHg_2^{2+} (= -\log \mathcal{A}_{Hg_2^{2+}})$ for part **(b)**.

7-F. (a) Write the mass balance for $CaCl_2$ in water if the species are Ca^{2+} and Cl^-.

(b) Write the mass balance if the species are Ca^{2+}, Cl^-, $CaCl^+$, and $CaOH^+$.

(c) Write the charge balance for part **(b)**.

7-G. Write the charge and mass balances for dissolving CaF_2 in water if the reactions are

$$CaF_2(s) \rightleftharpoons Ca^{2+} + 2F^-$$
$$Ca^{2+} + H_2O \rightleftharpoons CaOH^+ + H^+$$
$$Ca^{2+} + F^- \rightleftharpoons CaF^+$$
$$CaF_2(s) \rightleftharpoons CaF_2(aq)$$
$$F^- + H^+ \rightleftharpoons HF(aq)$$
$$HF(aq) + F^- \rightleftharpoons HF_2^-$$

7-H. Write charge and mass balances for aqueous $Ca_3(PO_4)_2$ if the species are Ca^{2+}, $CaOH^+$, $CaPO_4^-$, PO_4^{3-}, HPO_4^{2-}, $H_2PO_4^-$, and H_3PO_4.

7-I. (*Warning: long problem!*) *Using activities*, find the concentrations of the major species in 0.10 M $NaClO_4$ saturated with $Mn(OH)_2$. Take the ionic strength to be 0.10 M and suppose that the ion size of $MnOH^+$ is the same as Mn^{2+}. Consider just the following chemistry:

$$Mn(OH)_2(s) \xrightleftharpoons{K_{sp}} Mn^{2+} + 2OH^- \qquad K_{sp} = 1.6 \times 10^{-13}$$
$$Mn^{2+} + OH^- \xrightleftharpoons{K_1} MnOH^+ \qquad K_1 = 2.5 \times 10^3$$
$$H_2O \xrightleftharpoons{K_w} H^+ + OH^- \qquad K_w = 1.0 \times 10^{-14}$$

Problems

Activity Coefficients

7-1. Explain why the solubility of an ionic compound increases as the ionic strength of the solution increases (at least up to ~0.5 M).

7-2. Which statements are true? In the ionic strength range 0–0.1 M, activity coefficients decrease with **(a)** increasing ionic strength; **(b)** increasing ionic charge; **(c)** decreasing hydrated radius.

7-3. Calculate the ionic strength of **(a)** 0.008 7 M KOH and **(b)** 0.000 2 M $La(IO_3)_3$ (assuming complete dissociation at this low concentration and no hydrolysis reaction to make $LaOH^{2+}$).

7-4. Find the activity coefficient of each ion at the indicated ionic strength:

(a) SO_4^{2-} ($\mu = 0.01$ M)
(b) Sc^{3+} ($\mu = 0.005$ M)
(c) Eu^{3+} ($\mu = 0.1$ M)
(d) $(CH_3CH_2)_3NH^+$ ($\mu = 0.05$ M)

7-5. Interpolate in Table 7-1 to find the activity coefficient of H^+ when $\mu = 0.030$ M.

7-6. Calculate the activity coefficient of Zn^{2+} when $\mu = 0.083$ M by using **(a)** Equation 7-6; **(b)** linear interpolation in Table 7-1.

7-7. Calculate the activity coefficient of Al^{3+} when $\mu = 0.083$ M by linear interpolation in Table 7-1.

7-8. The equilibrium constant for dissolution in water of a nonionic compound, such as diethyl ether ($CH_3CH_2OCH_2CH_3$), can be written

$$\text{ether}(l) \rightleftharpoons \text{ether}(aq) \qquad K = [\text{ether}(aq)]\gamma_{\text{ether}}$$

At low ionic strength, $\gamma \approx 1$ for neutral compounds. At high ionic strength, most neutral molecules can be *salted out* of aqueous solution. That is, when a high concentration (typically >1 M) of a salt such as NaCl is added to an aqueous solution, neutral molecules usually become *less* soluble. Does the activity coefficient, γ_{ether}, increase or decrease at high ionic strength?

7-9. Including activity coefficients, find $[Hg_2^{2+}]$ in saturated Hg_2Br_2 in 0.001 00 M KBr.

7-10. Including activity coefficients, find the concentration of Ba^{2+} in a 0.100 M $(CH_3)_4NIO_3$ solution saturated with $Ba(IO_3)_2$.

7-11. Find the activity coefficient of H^+ in a solution containing 0.010 M HCl plus 0.040 M $KClO_4$. What is the pH of the solution?

7-12. Using activities, calculate the pH of a solution containing 0.010 M NaOH plus 0.012 0 M $LiNO_3$. What would be the pH if you neglected activities?

7-13. The temperature-dependent form of the extended Debye-Hückel equation 7-6 is

$$\log \gamma = \frac{(-1.825 \times 10^6)(\varepsilon T)^{-3/2} z^2 \sqrt{\mu}}{1 + \alpha\sqrt{\mu}/(2.00\sqrt{\varepsilon T})}$$

where ε is the (dimensionless) dielectric constant† of water, T is temperature (K), z is the charge of the ion, μ is ionic strength (mol/L), and α is the ion size parameter (pm). The dependence of ε on temperature is

$$\varepsilon = 79.755e^{(-4.6\times10^{-3})(T-293.15)}$$

Calculate the activity coefficient of SO_4^{2-} at 50.00°C when μ = 0.100 M. Compare your value with the one in Table 7-1.

7-14. *Extended Debye-Hückel equation.* Use Equation 7-6 to calculate the activity coefficient (γ) as a function of ionic strength (μ) for μ = 0.000 1, 0.000 3, 0.001, 0.003, 0.01, 0.03, and 0.1 M.

(a) For an ionic charge of ±1 and a size α = 400 pm, make a table of γ (= 10^(log γ)) for each value of μ.

(b) Do the same for ionic charges of ±2, ±3, and ±4.

(c) Plot γ versus log μ to obtain a graph similar to Figure 7-4.

7-15. *Activity coefficient of a neutral molecule.* We use the approximation that the activity coefficient (γ) of neutral molecules is 1.00. A more accurate relation is $\log \gamma = k\mu$, where μ is ionic strength and $k \approx 0.11$ for NH_3 and CO_2 and $k \approx 0.2$ for organic molecules. With activity coefficients for HA, A^-, and H^+, predict the value of the quotient below for benzoic acid (HA ≡ $C_6H_5CO_2H$). The observed quotient is 0.63 ± 0.03.[12]

$$\text{Concentration quotient} = \frac{\dfrac{[H^+][A^-]}{[HA]}(\text{at } \mu = 0)}{\dfrac{[H^+][A^-]}{[HA]}(\text{at } \mu = 0.1\text{ M})}$$

Systematic Treatment of Equilibrium

7-16. State the meaning of the charge and mass balance equations.

7-17. Why do activity coefficients not appear in the charge and mass balance equations?

7-18. Write the charge balance for a solution containing H^+, OH^-, Ca^{2+}, HCO_3^-, CO_3^{2-}, $Ca(HCO_3)^+$, $Ca(OH)^+$, K^+, and ClO_4^-.

7-19. Write the charge balance for a solution of H_2SO_4 in water if H_2SO_4 ionizes to HSO_4^- and SO_4^{2-}.

7-20. Write the charge balance for an aqueous solution of arsenic acid, H_3AsO_4, in which the acid can dissociate to $H_2AsO_4^-$, $HAsO_4^{2-}$, and AsO_4^{3-}. Look up the structure of arsenic acid in Appendix G and write the structure of $HAsO_4^{2-}$.

7-21. (a) Write the charge and mass balances for a solution made by dissolving $MgBr_2$ to give Mg^{2+}, Br^-, $MgBr^+$, and $MgOH^+$.

(b) Modify the mass balance if the solution was made by dissolving 0.2 mol $MgBr_2$ in 1 L.

†The dimensionless *dielectric constant*, ε, measures how well a solvent can separate oppositely charged ions. The force of attraction (newtons) between ions of charge q_1 and q_2 (coulombs) separated by distance r (meters) is

$$\text{Force} = -(8.988\times10^9)\frac{q_1q_2}{\varepsilon r^2}$$

The larger the value of ε, the smaller the attraction between ions. Water, with $\varepsilon \approx 80$, separates ions very well. Here are some values of ε: methanol, 33; ethanol, 24; benzene, 2; vacuum and air, 1. Ionic compounds dissolved in solvents less polar than water may exist predominantly as ion pairs, not separate ions.

7-22. What would happen if charge balance did not exist in a solution? The force between two charges is given in the footnote on this page. Find the force between two beakers separated by 1.5 m of air if one contains 250 mL with 1.0×10^{-6} M excess negative charge and the other has 250 mL with 1.0×10^{-6} M excess positive charge. There are 9.648×10^4 coulombs per mole of charge. Convert force from N into pounds (0.224 8 pounds/N). Could two elephants hold the beakers apart?

7-23. For a 0.1 M aqueous solution of sodium acetate, $Na^+CH_3CO_2^-$, one mass balance is simply $[Na^+]$ = 0.1 M. Write a mass balance involving acetate.

7-24. Consider the dissolution of the compound X_2Y_3, which gives $X_2Y_2^{2+}$, X_2Y^{4+}, $X_2Y_3(aq)$, and Y^{2-}. Use the mass balance to find an expression for $[Y^{2-}]$ in terms of the other concentrations. Simplify your answer as much as possible.

7-25. Write a mass balance for a solution of $Fe_2(SO_4)_3$ if the species are Fe^{3+}, $Fe(OH)^{2+}$, $Fe(OH)_2^+$, $Fe_2(OH)_2^{4+}$, $FeSO_4^+$, SO_4^{2-}, and HSO_4^-.

7-26. (a) Following the example of ammonia in Section 7-5, write the equilibria and charge and mass balances needed to find the composition of 0.01 M sodium acetate, which you should abbreviate as Na^+A^-. *Include activity coefficients* where appropriate.

(b) Neglect activity coefficients for this part and call the formal concentration F. Following the example of ammonia, reduce the equations to a single equation with $[H^+]$ as the sole unknown. Do not try to simplify the equation.

(c) Use Excel Goal Seek to solve for $[H^+]$. Use the value $K_b = 5.7\times10^{-10}$. Before using Goal Seek in Excel 2007, click the Microsoft Office button, then Excel Options, and select Formulas. In Calculation Options, set Maximum Change to 1e-14. In earlier versions of Excel, go to Tools and Options. Select the Calculations tab and set Maximum change to 1e-14. From $[H^+]$, find $[OH^-]$, $[A^-]$, and [HA].

7-27. (a) Following the example of $Mg(OH)_2$ in Section 7-5, write the equations needed to find the solubility of $Ca(OH)_2$. *Include activity coefficients* where appropriate. Equilibrium constants are in Appendixes F and I.

(b) Neglecting activity coefficients, compute the concentrations of all species and compute the solubility of $Ca(OH)_2$ in g/L.

7-28. Look up the equilibrium constant for the *ion-pairing* reaction $Zn^{2+} + SO_4^{2-} \rightleftharpoons ZnSO_4(aq)$ in Appendix J.

(a) Use the systematic treatment of equilibrium to find $[Zn^{2+}]$ in 0.010 F $ZnSO_4$. Neglect activity coefficients and any other reactions.

(b) Use the answer from part **(a)** to compute the ionic strength and activity coefficients of Zn^{2+} and SO_4^{2-}. Then repeat the calculation using activity coefficients. Repeat the procedure two more times to find a good estimate of $[Zn^{2+}]$. What percentage is ion paired? What is the ionic strength of the solution?

(c) Two possibly important reactions that we did not consider are acid hydrolysis of Zn^{2+} and base hydrolysis of SO_4^{2-}. Write these two reactions and find their equilibrium constants in Appendixes I and G.

7-29. *Finding solubility by iteration.* Use the systematic treatment of equilibrium to find the concentrations of the major species in a saturated aqueous solution of LiF. Consider these reactions:

$$LiF(s) \rightleftharpoons Li^+ + F^- \qquad K_{sp} = [Li^+]\gamma_{Li^+}[F^-]\gamma_{F^-} = 0.001\,7$$

$$LiF(s) \rightleftharpoons LiF(aq) \qquad K_{\text{ion pair}} = LiF(aq)\gamma_{LiF(aq)} = 0.002\,9$$

(a) Initially, set the ionic strength to 0 and solve for all concentrations. Then compute the ionic strength and activity coefficients and find new concentrations. Use several iterations to home in on the correct solution.

(b) In the systematic treatment, you will find that the calculation simplifies to $[Li^+] = [F^-] = \sqrt{K_{sp}/(\gamma_{Li^+}\gamma_{F^-})}$. Set up the following spreadsheet, in which ionic strength in cell B4 is initially given the value 0. Activity coefficients in cells B6 and B8 are from the extended Debye-Hückel equation. Cell B10 computes $[Li^+] = [F^-] = \sqrt{K_{sp}/(\gamma_{Li^+}\gamma_{F^-})}$. With 0 in cell B4, your spreadsheet should compute 1 in cells B6 and B8 and $[Li^+] = [F^-] =$ 0.041 23 M in cell B10.

	A	B	C
1	Spreadsheet for iterative LiF solubility computation		
2			
3	Size (pm) of Li^+ =	Ionic strength =	
4	600	0.00000	
5	Size (pm) of F^- =	Activity coeff Li^+ =	
6	350	1	
7	K_{sp} =	Activity coeff F^- =	
8	0.0017	1	
9		$[Li^+] = [F^-]$ =	
10		0.04123	
11			
12	B6 = 10^((−0.51)*SQRT(B4)/(1+A4*SQRT(B4)/305))		
13	B8 = 10^((−0.51)*SQRT(B4)/(1+A6*SQRT(B4)/305))		
14	B10 = SQRT(A8/(B6*B8))		

Because the ionic strength of a 1:1 electrolyte is equal to the concentration, copy the value 0.041 23 from cell B10 into cell B4. (To transfer a numerical value, rather than a formula, copy cell B10 and then highlight cell B4. In Excel 2007, go to the Home ribbon, select Paste, and then click on Paste Values. The numerical value from B10 will be pasted into B4. In earlier versions of Excel, go to the Edit menu, select Paste Special, and then choose Value.) This procedure gives new activity coefficients in cells B6 and B8 and a new concentration in cell B10. Copy the new concentration from cell B10 into cell B4 and repeat this procedure several times until you have a constant answer.

(c) *Using circular references in Excel*. Take your spreadsheet and enter 0 in cell B4. The value 0.041 23 is computed in cell B10. Ideally, you would like to write "=B10" in cell B4 so that the value from B10 would be copied to B4. Excel gives a "circular reference" error message because cell B10 depends on B4 and cell B4 depends on B10. To get around this problem, in Excel 2007, click the Microsoft Office button at the upper left of the spreadsheet. Click on Excel Options at the bottom of the window. Select Formulas. In Calculation Options, check Enable iterative calculation and set Maximum Change to 0.000 01. Click OK and Excel merrily iterates between cells B10 and B4 until the two values agree within 0.000 01. In earlier versions of Excel, go to the Tools menu and choose Options. Select Calculation and choose Iteration. Set Maximum change to 0.000 01.

7-30. *Heterogeneous equilibria and calcite solubility*. If river water in Box 7-2 is saturated with calcite ($CaCO_3$), $[Ca^{2+}]$ is governed by the following equilibria:

$$CaCO_3(s) \rightleftharpoons Ca^{2+} + CO_3^{2-} \qquad K_{sp} = 4.5 \times 10^{-9}$$
$$CO_2(g) \rightleftharpoons CO_2(aq) \qquad K_{CO_2} = 0.032$$
$$CO_2(aq) + H_2O \rightleftharpoons HCO_3^- + H^+ \qquad K_1 = 4.46 \times 10^{-7}$$
$$HCO_3^- \rightleftharpoons CO_3^{2-} + H^+ \qquad K_2 = 4.69 \times 10^{-11}$$

(a) From these reactions, find the equilibrium constant for the reaction

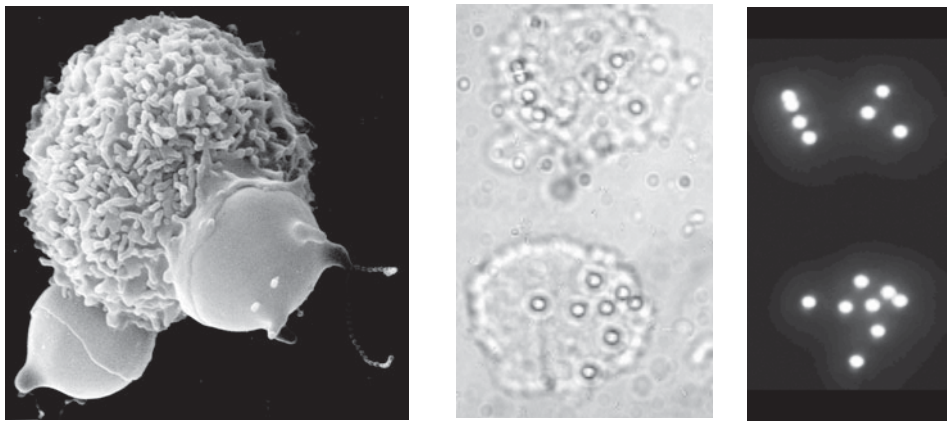
$$CaCO_3(s) + CO_2(aq) + H_2O \rightleftharpoons Ca^{2+} + 2HCO_3^- \qquad K = ? \quad \textbf{(A)}$$

(b) The mass balance for Reaction A is $[HCO_3^-] = 2[Ca^{2+}]$. Find $[Ca^{2+}]$ (in mol/L and in mg/L) in equilibrium with atmospheric CO_2 if $P_{CO_2} = 3.8 \times 10^{-4}$ bar. Locate this point on the line in Box 7-2.

(c) The concentration of Ca^{2+} in the Don River is 80 mg/L. What effective P_{CO_2} is in equilibrium with this much Ca^{2+}? How can the river have this much CO_2?

8 Monoprotic Acid-Base Equilibria

MEASURING pH INSIDE CELLULAR COMPARTMENTS



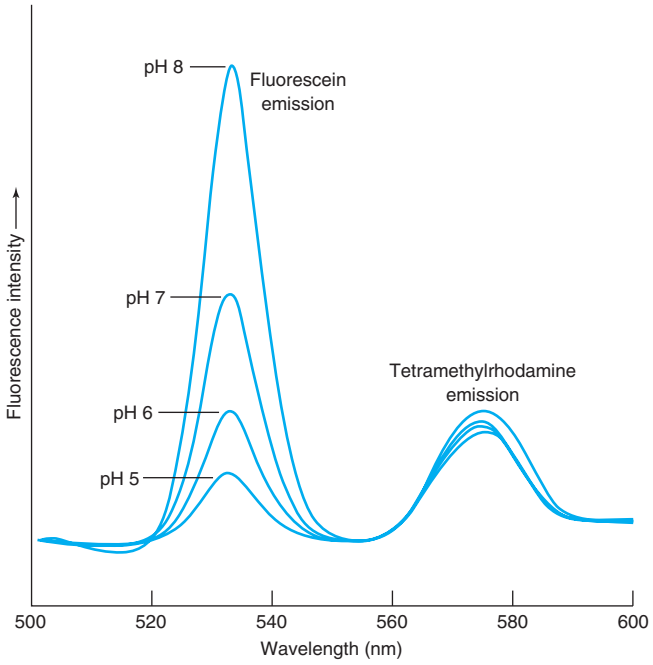
(*a*) (*b*) (*c*)

(*a*) Mouse macrophage engulfs two foreign red blood cells as phagocytosis begins. [From J. P. Revel in B. Alberts, D. Bray, J. Lewis, M. Raff, K. Roberts, and J. D. Watson, *Molecular Biology of the Cell*, 2nd ed. (New York: Garland Publishing, 1989.]
(*b*) Macrophages with ingested 1.6-μm-diameter fluorescent beads.
(*c*) Fluorescence image of panel *b*. [From K. P. McNamara, T. Nguyen, G. Dumitrascu, J. Ji, N. Rosenzweig, and Z. Rosenzweig, "Synthesis, Characterization, and Application of Fluorescence Sensing Lipobeads for Intracellular pH Measurements," *Anal. Chem.* **2001,** *73*, 3240.]

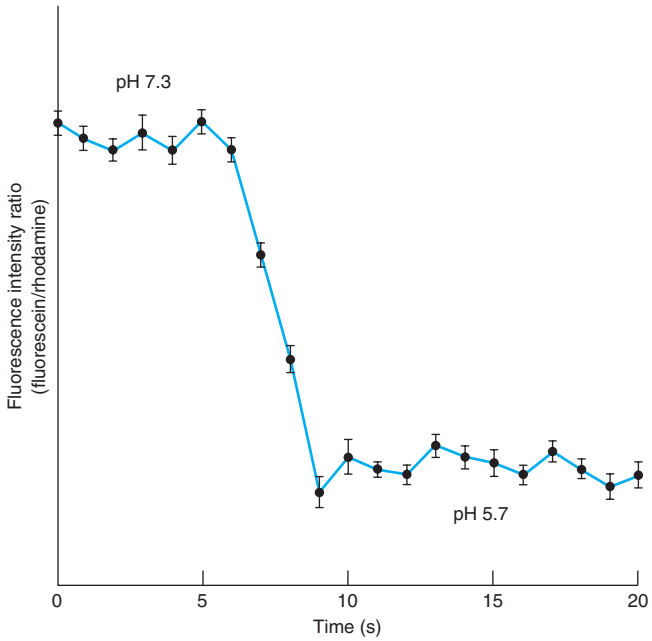
Macrophages are white blood cells that fight infection by ingesting and dissolving foreign cells—a process called *phagocytosis*. The compartment containing the ingested foreign cell merges with compartments called *lysosomes*, which contain digestive enzymes that are most active in acid. Low enzyme activity above pH 7 protects the cell from enzymes that leak into the cell.

One way to measure pH inside the compartment containing the ingested particle and digestive enzymes is to present macrophages with polystyrene beads coated with a lipid membrane to which fluorescent (light-emitting) dyes are covalently bound. Panel *d* shows that fluorescence intensity from the dye fluorescein depends on pH, but fluorescence from tetramethylrhodamine does not. The ratio of emission from the dyes is a measure of pH. Panel *e* shows the fluorescence intensity ratio changing in 3 s as the bead is ingested and the pH around the bead drops from 7.3 to 5.7 to allow digestion to commence.

(*d*) Fluorescence spectra of lipobeads in solutions at pH 5–8. (*e*) pH change during phagocytosis of a single bead by a macrophage. [From McNamara et al., ibid.]



(*d*)



(*e*)

Acids and bases are essential to virtually every application of chemistry and for the intelligent use of analytical procedures such as chromatography and electrophoresis. It would be difficult to have a meaningful discussion of, say, protein purification or the weathering of rocks without understanding acids and bases. This chapter covers acid-base equilibria and buffers. Chapter 9 treats polyprotic systems involving two or more acidic protons. Nearly every biological macromolecule is polyprotic. Chapter 10 describes acid-base titrations. Now is the time to review fundamentals of acids and bases in Sections 6-5 through 6-7.

8-1 Strong Acids and Bases

What could be easier than calculating the pH of 0.10 M HBr? HBr is a **strong acid,** so the reaction

$$HBr + H_2O \rightarrow H_3O^+ + Br^-$$

goes to completion, and the concentration of H_3O^+ is 0.10 M. It will be our custom to write H^+ instead of H_3O^+, and we can say

$$pH = -\log[H^+] = -\log(0.10) = 1.00$$

Table 6-2 gave a list of strong acids and bases that you must memorize.

Equilibrium constants for the reaction[1]

$HX(aq) + H_2O \rightleftharpoons H_3O^+ + X^-$

HCl	$K_a = 10^{3.9}$
HBr	$K_a = 10^{5.8}$
HI	$K_a = 10^{10.4}$
HNO_3	$K_a = 10^{1.4}$

HNO_3 is discussed in Box 8-1.

EXAMPLE Activity Coefficient in a Strong-Acid Calculation

Calculate the pH of 0.10 M HBr, using activity coefficients.

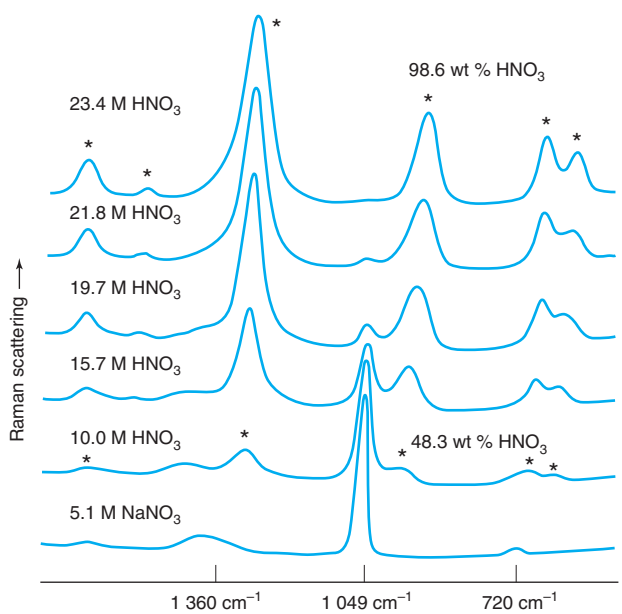
Solution The ionic strength of 0.10 M HBr is $\mu = 0.10$ M, at which the activity coefficient of H^+ is 0.83 (Table 7-1). Remember that pH is $-\log \mathcal{A}_{H^+}$, not $-\log[H^+]$:

$$pH = -\log[H^+]\gamma_{H^+} = -\log(0.10)(0.83) = 1.08$$

Test Yourself Calculate the pH of 0.010 M HBr in 0.090 M KBr. (***Answer:*** 2.08)

BOX 8-1 Concentrated HNO_3 Is Only Slightly Dissociated[2]

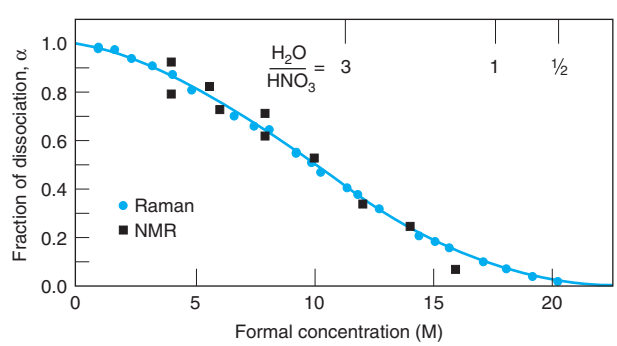
Strong acids in dilute solution are essentially completely dissociated. As concentration increases, the degree of dissociation decreases. The figure shows a *Raman spectrum* of solutions of nitric acid of increasing concentration. The spectrum measures scattering of light whose energy corresponds to vibrational energies of molecules. The sharp signal at 1 049 cm^{-1} in the spectrum of 5.1 M $NaNO_3$ is characteristic of free NO_3^- anion.



Raman spectrum of aqueous HNO_3 at 25°C. Signals at 1 360, 1 049, and 720 cm^{-1} arise from NO_3^- anion. Signals denoted by asterisks are from undissociated HNO_3. The wavenumber unit, cm^{-1}, is 1/wavelength.

A 10.0 M HNO_3 solution has a strong NO_3^- signal at 1 049 cm^{-1} from dissociated acid. Bands denoted by asterisks arise from *undissociated* HNO_3. As concentration increases, the 1 049 cm^{-1} signal disappears and signals attributed to undissociated HNO_3 increase. The graph shows the fraction of dissociation deduced from spectroscopic measurements. It is instructive to realize that, in 20 M HNO_3, there are fewer H_2O molecules than there are molecules of HNO_3. Dissociation decreases because there is not enough solvent to stabilize the free ions.

Theoretical studies indicate that dilute HNO_3 at a water-air *interface* is also a weak acid because there are not enough H_2O molecules to solvate the free ions.[3] This finding has implications for atmospheric chemistry at the surface of microscopic droplets in clouds.



Temperature (°C)	Acid dissociation constant (K_a)
0	46.8
25	26.8
50	14.9

Now that we have reminded you of activity coefficients, you can breathe a sigh of relief because we will neglect activity coefficients unless there is a specific point to be made.

How do we calculate the pH of 0.10 M KOH? KOH is a **strong base** (completely dissociated), so $[OH^-] = 0.10$ M. Using $K_w = [H^+][OH^-]$, we write

From $[OH^-]$, you can always find $[H^+]$:

$$[H^+] = \frac{K_w}{[OH^-]}$$

$$[H^+] = \frac{K_w}{[OH^-]} = \frac{1.0 \times 10^{-14}}{0.10} = 1.0 \times 10^{-13}\ \text{M}$$

$$\text{pH} = -\log[H^+] = 13.00$$

Finding the pH of other concentrations of KOH is pretty trivial:

$[OH^-]$ (M)	$[H^+]$ (M)	pH
$10^{-3.00}$	$10^{-11.00}$	11.00
$10^{-4.00}$	$10^{-10.00}$	10.00
$10^{-5.00}$	$10^{-9.00}$	9.00

A generally useful relation is

The temperature dependence of K_w was given in Table 6-1.

Relation between pH and pOH:

$$\text{pH} + \text{pOH} = -\log K_w = 14.00 \text{ at } 25°\text{C} \qquad \textbf{(8-1)}$$

The Dilemma

Well, life seems simple enough so far. Now we ask, "What is the pH of 1.0×10^{-8} M KOH?" Applying our usual reasoning, we calculate

Adding base to water cannot *lower* the pH. (Lower pH is more *acidic*.) There must be something wrong.

$$[H^+] = K_w/(1.0 \times 10^{-8}) = 1.0 \times 10^{-6}\ \text{M} \Rightarrow \text{pH} = 6.00$$

How can the base KOH produce an acidic solution (pH < 7)? It's impossible.

The Cure

Clearly, there is something wrong with our calculation. In particular, we have not considered the contribution of OH^- from the ionization of water. In pure water, $[OH^-] = 1.0 \times 10^{-7}$ M, which is greater than the amount of KOH added to the solution. To handle this problem, we resort to the systematic treatment of equilibrium.

Step 1 *Pertinent reactions*. The only one is $H_2O \overset{K_w}{\rightleftharpoons} H^+ + OH^-$

Step 2 *Charge balance*. The species in solution are K^+, OH^-, and H^+. So,

$$[K^+] + [H^+] = [OH^-] \qquad \textbf{(8-2)}$$

Step 3 *Mass balance*. All K^+ comes from the KOH, so $[K^+] = 1.0 \times 10^{-8}$ M

Step 4 *Equilibrium constant*. $K_w = [H^+][OH^-] = 1.0 \times 10^{-14}$

Step 5 *Count*. There are three equations and three unknowns ($[H^+]$, $[OH^-]$, $[K^+]$), so we have enough information to solve the problem.

If we had been using activities, step 4 is the only point at which activity coefficients would have entered.

Step 6 *Solve*. We seek the pH, so let's set $[H^+] = x$. Writing $[K^+] = 1.0 \times 10^{-8}$ M in Equation 8-2, we get

$$[OH^-] = [K^+] + [H^+] = 1.0 \times 10^{-8} + x$$

Putting $[OH^-] = 1.0 \times 10^{-8} + x$ into the K_w equilibrium enables us to solve the problem:

$$[H^+][OH^-] = K_w$$

$$(x)(1.0 \times 10^{-8} + x) = 1.0 \times 10^{-14}$$

$$x^2 + (1.0 \times 10^{-8})x - (1.0 \times 10^{-14}) = 0$$

Solution of a quadratic equation:

$$ax^2 + bx + c = 0$$

$$x = \frac{-b \pm \sqrt{b^2 - 4ac}}{2a}$$

Retain all digits in your calculator because b^2 is sometimes nearly equal to $4ac$. If you round off before computing $b^2 - 4ac$, your answer may be garbage.

$$x = \frac{-1.0 \times 10^{-8} \pm \sqrt{(1.0 \times 10^{-8})^2 - 4(1)(-1.0 \times 10^{-14})}}{2(1)}$$

$$= 9.6 \times 10^{-8}\ \text{M} \qquad \text{or} \qquad -1.1 \times 10^{-7}\ \text{M}$$

Rejecting the negative concentration, we conclude that

$$[H^+] = 9.6 \times 10^{-8}\ \text{M} \Rightarrow \text{pH} = -\log[H^+] = 7.02$$

This pH is eminently reasonable, because 10^{-8} M KOH should be very slightly basic.

Figure 8-1 shows the pH calculated for different concentrations of strong base or strong acid in water. There are three regions:

1. When the concentration is "high" ($\geq 10^{-6}$ M), pH is calculated by just considering the added H^+ or OH^-. That is, the pH of $10^{-5.00}$ M KOH *is* 9.00.
2. When the concentration is "low" ($\leq 10^{-8}$ M), the pH is 7.00. We have not added enough acid or base to change the pH of the water itself.
3. At intermediate concentrations of 10^{-6} to 10^{-8} M, the effects of water ionization and the added acid or base are comparable. Only in this region is a systematic equilibrium calculation necessary.

Region 1 is the only practical case. Unless you were to protect 10^{-7} M KOH from the air, the pH would be governed by dissolved CO_2, not KOH.

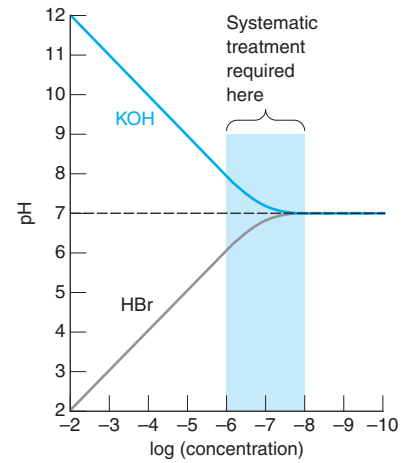


FIGURE 8-1 Calculated pH as a function of concentration of strong acid or strong base in water.

Water Almost Never Produces 10^{-7} M H^+ and 10^{-7} M OH^-

The misconception that dissociation of water always produces 10^{-7} M H^+ and 10^{-7} M OH^- is true *only* in pure water with no added acid or base. In 10^{-4} M HBr, for example, the pH is 4. The concentration of OH^- is $[OH^-] = K_w/[H^+] = 10^{-10}$ M. But the only source of $[OH^-]$ is dissociation of water. If water produces 10^{-10} M OH^-, it must also produce 10^{-10} M H^+ because it makes one H^+ for every OH^-. In 10^{-4} M HBr solution, water dissociation produces only 10^{-10} M OH^- and 10^{-10} M H^+.

Any acid or base suppresses water ionization, as predicted by Le Châtelier's principle.

Question What concentrations of H^+ and OH^- are produced by H_2O dissociation in 0.01 M NaOH?

8-2 Weak Acids and Bases

Let's review the meaning of the **acid dissociation constant,** K_a, for the acid HA:

Weak-acid equilibrium:

$$HA \overset{K_a}{\rightleftharpoons} H^+ + A^- \qquad K_a = \frac{[H^+][A^-]}{[HA]} \tag{8-3}$$

Of course, you know that K_a should really be expressed in terms of activities, not concentrations:

$$K_a = \mathcal{A}_{H^+}\mathcal{A}_{A^-}/\mathcal{A}_{HA}$$

A **weak acid** is one that is not completely dissociated. That is, Reaction 8-3 does not go to completion. For a base, B, the **base hydrolysis constant,** K_b, is defined by the reaction

Weak-base equilibrium:

$$B + H_2O \overset{K_b}{\rightleftharpoons} BH^+ + OH^- \qquad K_b = \frac{[BH^+][OH^-]}{[B]} \tag{8-4}$$

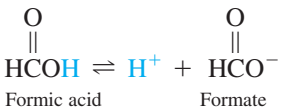
Hydrolysis is reaction with water.

A **weak base** is one for which Reaction 8-4 does not go to completion.

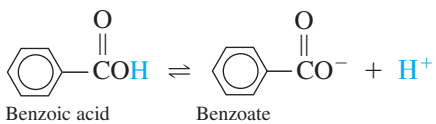
p*K* is the negative logarithm of an equilibrium constant:

$$pK_w = -\log K_w$$
$$pK_a = -\log K_a$$
$$pK_b = -\log K_b$$

As K increases, pK decreases, and vice versa. Comparing formic and benzoic acids, we see that formic acid is stronger, with a larger K_a and smaller pK_a, than benzoic acid.



$K_a = 1.80 \times 10^{-4}$
$\mathbf{pK_a} = 3.744$



$K_a = 6.28 \times 10^{-5}$
$\mathbf{pK_a} = 4.202$

As K_a increases, pK_a decreases. Smaller pK_a means stronger acid.

The acid HA and its corresponding base, A^-, are said to be a **conjugate acid-base pair,** because they are related by the gain or loss of a proton. Similarly, B and BH^+ are a conjugate pair. The important relation between K_a and K_b for a conjugate acid-base pair is

HA and A^- are a *conjugate acid-base pair*. B and BH^+ also are conjugate.

Relation between K_a and K_b for conjugate pair:

$$K_a \cdot K_b = K_w \tag{8-5}$$

Weak Is Conjugate to Weak

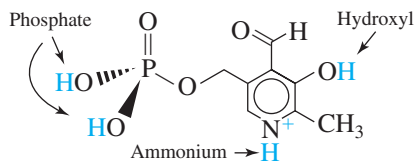
The conjugate base of a weak acid is a weak base. The conjugate acid of a weak base is a weak acid. *Weak is conjugate to weak.*

The conjugate base of a weak acid is a weak base. The conjugate acid of a weak base is a weak acid. Consider a weak acid, HA, with $K_a = 10^{-4}$. The conjugate base, A^-, has $K_b = K_w/K_a = 10^{-10}$. That is, if HA is a weak acid, A^- is a weak base. If K_a were 10^{-5}, then K_b would be 10^{-9}. As HA becomes a weaker acid, A^- becomes a stronger base (but never a strong base). Conversely, the greater the acid strength of HA, the less the base strength of A^-. However, if either A^- or HA is weak, so is its conjugate. If HA is strong (such as HCl), its conjugate base (Cl^-) is *so* weak that it is not a base at all in water.

Using Appendix G

Appendix G lists acid dissociation constants. Each compound is shown in its *fully protonated form*. Diethylamine, for example, is shown as $(CH_3CH_2)_2NH_2^+$, which is really the diethylammonium ion. The value of K_a (1.0×10^{-11}) given for diethylamine is actually K_a for the diethylammonium ion. To find K_b for diethylamine, we write $K_b = K_w/K_a = 1.0 \times 10^{-14}/1.0 \times 10^{-11} = 1.0 \times 10^{-3}$.

For polyprotic acids and bases, several K_a values are given. Pyridoxal phosphate is given in its fully protonated form as follows:[4]

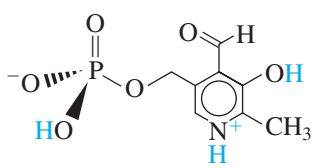


Pyridoxal phosphate
(a derivative of vitamin B_6)

pK_a	K_a
1.4 (POH)	0.04
3.51 (OH)	3.1×10^{-4}
6.04 (POH)	9.1×10^{-7}
8.25 (NH)	5.6×10^{-9}

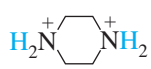
pK_1 (1.4) is for dissociation of one of the phosphate protons, and pK_2 (3.51) is for the hydroxyl proton. The third most acidic proton is the other phosphate proton, for which $pK_3 = 6.04$, and the NH^+ group is the least acidic ($pK_4 = 8.25$).

Species drawn in Appendix G are fully protonated. If a structure in Appendix G has a charge other than 0, it is not the structure that belongs with the name in the appendix. *Names refer to neutral molecules*. The neutral molecule pyridoxal phosphate is not the species drawn above, which has a +1 charge. The neutral molecule pyridoxal phosphate is

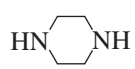


We took away a POH proton, not the NH^+ proton, because POH is the most acidic group in the molecule ($pK_a = 1.4$).

As another example, consider the molecule piperazine:



Structure shown for piperazine in Appendix G



Actual structure of piperazine, which *must be neutral*

K_a at $\mu = 0$ is the *thermodynamic acid dissociation constant* that applies at any ionic strength when activity coefficients are used for that ionic strength:

$$K_a = \frac{\mathcal{A}_{H^+}\mathcal{A}_{A^-}}{\mathcal{A}_{HA}} = \frac{[H^+]\gamma_{H^+}[A^-]\gamma_{A^-}}{[HA]\gamma_{HA}}$$

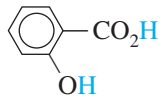
K_a at $\mu = 0.1$ M is the quotient of concentrations when the ionic strength is 0.1 M:

$$K_a\ (\mu = 0.1\ \text{M}) = \frac{[H^+][A^-]}{[HA]}$$

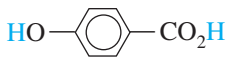
Appendix G gives pK_a for ionic strengths of 0 and 0.1 M, when available. We will use pK_a for $\mu = 0$ unless there is no value listed or we need $\mu = 0.1$ M for a specific purpose. For pyridoxal phosphate, we used values for $\mu = 0.1$ M because none are listed for $\mu = 0$.

8-3 Weak-Acid Equilibria

Let's compare the ionization of *ortho*- and *para*-hydroxybenzoic acids:



o-Hydroxybenzoic acid
(salicylic acid)
$pK_a = 2.97$

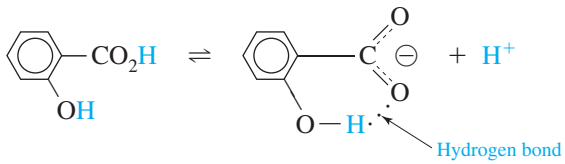


p-Hydroxybenzoic acid

$pK_a = 4.54$

Why is the *ortho* isomer 30 times more acidic than the *para* isomer? Any effect that increases the stability of the product of a reaction drives the reaction forward. In the *ortho*

isomer, the product of the acid dissociation reaction can form a strong, internal hydrogen bond.



The *para* isomer cannot form such a bond because the —OH and $—CO_2^-$ groups are too far apart. By stabilizing the product, the internal hydrogen bond is thought to make *o*-hydroxybenzoic acid more acidic than *p*-hydroxybenzoic acid.

A Typical Weak-Acid Problem

The problem is to find the pH of a solution of the weak acid HA, given the formal concentration of HA and the value of K_a.[5] Let's call the formal concentration F and use the systematic treatment of equilibrium:

Formal concentration is the total number of moles of a compound dissolved in a liter. The formal concentration of a weak acid is the total amount of HA placed in the solution, regardless of the fact that some has changed into A^-.

Reactions: $HA \overset{K_a}{\rightleftharpoons} H^+ + A^-$ $\quad H_2O \overset{K_w}{\rightleftharpoons} H^+ + OH^-$

Charge balance: $$[H^+] = [A^-] + [OH^-] \tag{8-6}$$

Mass balance: $$F = [A^-] + [HA] \tag{8-7}$$

Equilibrium expressions: $$K_a = \frac{[H^+][A^-]}{[HA]} \tag{8-8}$$

$$K_w = [H^+][OH^-]$$

There are four equations and four unknowns ($[A^-]$, $[HA]$, $[H^+]$, $[OH^-]$), so the problem is solved if we can just do the algebra.

But it's not so easy to solve these simultaneous equations. If you combine them, you will discover that a cubic equation results. At this point, the Good Chemist rides down again from the mountain on her white stallion to rescue us and cries, "Wait! There is no reason to solve a cubic equation. We can make an excellent, simplifying approximation. (Besides, I have trouble solving cubic equations.)"

For any respectable weak acid, $[H^+]$ from HA will be much greater than $[H^+]$ from H_2O. When HA dissociates, it produces A^-. When H_2O dissociates, it produces OH^-. If dissociation of HA is much greater than dissociation of H_2O, then $[A^-] \gg [OH^-]$, and Equation 8-6 reduces to

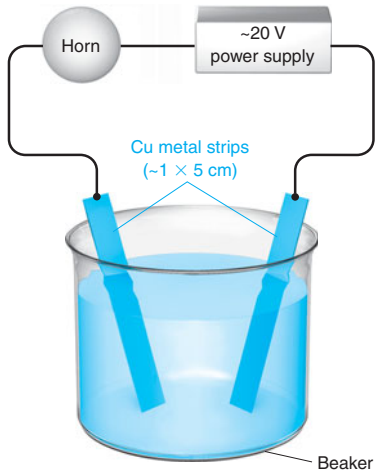
$$[H^+] \approx [A^-] \tag{8-9}$$

DEMONSTRATION 8-1 Conductivity of Weak Electrolytes[6]

The relative conductivity of strong and weak acids is related to their different degrees of dissociation in aqueous solution. To demonstrate conductivity, we use a Radio Shack piezo alerting buzzer, but any kind of buzzer or light bulb could easily be substituted. The voltage required will depend on the buzzer or light chosen.

When a conducting solution is placed in the beaker, the horn sounds. First show that distilled water and sucrose solution are nonconductive. Solutions of the strong electrolytes NaCl or HCl are conductive. Compare strong and weak electrolytes by demonstrating that 1 mM HCl gives a loud sound, whereas 1 mM acetic acid gives little or no sound. With 10 mM acetic acid, the strength of the sound varies noticeably as the electrodes are moved away from each other in the beaker.

When CO_2 is absorbed by pure water, the conductivity increases from dissociation of the H_2CO_3 (carbonic acid) formed. Atmospheric CO_2 can be measured by conductivity.[7]



To solve the problem, first set $[H^+] = x$. Equation 8-9 says that $[A^-]$ also is equal to x. Equation 8-7 says that $[HA] = F - [A^-] = F - x$. Putting these expressions into Equation 8-8 gives

$x = [H^+]$ in weak-acid problems.

$$K_a = \frac{[H^+][A^-]}{[HA]} = \frac{(x)(x)}{F - x}$$

Setting $F = 0.050\,0$ M and $K_a = 1.0_7 \times 10^{-3}$ for *o*-hydroxybenzoic acid, we can solve the equation, because it is just a quadratic equation.

$$\frac{x^2}{0.050\,0 - x} = 1.0_7 \times 10^{-3}$$

$$x^2 = (1.0_7 \times 10^{-3})(0.050\,0 - x)$$

$$x^2 + (1.07 \times 10^{-3})x - 5.35 \times 10^{-5} = 0$$

$$x = 6.8_0 \times 10^{-3}\ \text{M (negative root rejected)}$$

$$[H^+] = [A^-] = x = 6.8_0 \times 10^{-3}\ \text{M}$$

$$[HA] = F - x = 0.043_2\ \text{M}$$

$$pH = -\log x = 2.17$$

For uniformity, we express pH to the 0.01 decimal place, regardless of the number of places justified by significant figures. Ordinary pH measurements are not more accurate than ±0.02 pH units.

Was the approximation $[H^+] \approx [A^-]$ justified? The calculated pH is 2.17, which means that $[OH^-] = K_w/[H^+] = 1.5 \times 10^{-12}$ M.

$$[A^-]\text{(from HA dissociation)} = 6.8 \times 10^{-3}\ \text{M}$$

$$\Rightarrow [H^+]\ \text{from HA dissociation} = 6.8 \times 10^{-3}\ \text{M}$$

$$[OH^-]\text{(from } H_2O \text{ dissociation)} = 1.5 \times 10^{-12}\ \text{M}$$

$$\Rightarrow [H^+]\ \text{from } H_2O \text{ dissociation} = 1.5 \times 10^{-12}\ \text{M}$$

In a solution of a weak acid, H^+ is derived almost entirely from HA, not from H_2O.

The assumption that H^+ is derived mainly from HA is excellent.

Fraction of Dissociation

The **fraction of dissociation, α,** is defined as the fraction of the acid in the form A^-:

α is the fraction of HA that has dissociated:

$$\alpha = \frac{[A^-]}{[A^-] + [HA]}$$

Fractions of dissociation of an acid:

$$\alpha = \frac{[A^-]}{[A^-] + [HA]} = \frac{x}{x + (F - x)} = \frac{x}{F} \qquad \textbf{(8-10)}$$

For 0.050 0 M *o*-hydroxybenzoic acid, we find

$$\alpha = \frac{6.8 \times 10^{-3}\ \text{M}}{0.050\,0\ \text{M}} = 0.14$$

That is, the acid is 14% dissociated at a formal concentration of 0.050 0 M.

The variation of α with formal concentration is shown in Figure 8-2. **Weak electrolytes** (compounds that are only partially dissociated) dissociate more as they are diluted. *o*-Hydroxybenzoic acid is more dissociated than *p*-hydroxybenzoic acid at the same formal concentration because the *ortho* isomer is a stronger acid. Demonstration 8-1 and Box 8-2 illustrate weak-acid properties.

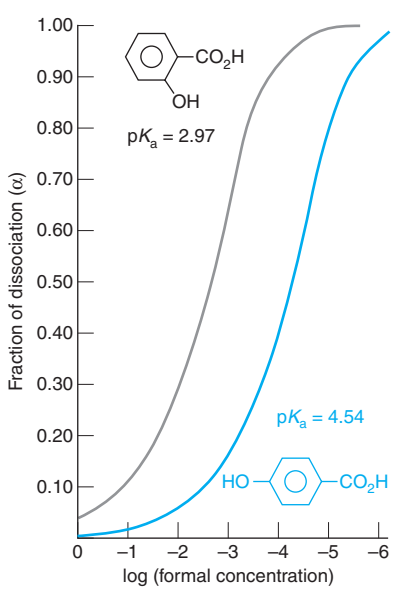


FIGURE 8-2 Fraction of dissociation of a weak electrolyte increases as electrolyte is diluted. The stronger acid is more dissociated than the weaker acid at all concentrations.

The Essence of a Weak-Acid Problem

When faced with finding the pH of a weak acid, you should immediately realize that $[H^+] = [A^-] = x$ and proceed to set up and solve the equation

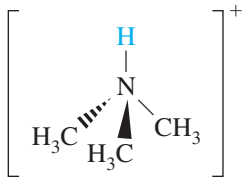
Equation for weak acids:

$$\frac{[H^+][A^-]}{[HA]} = \frac{x^2}{F - x} = K_a \qquad \textbf{(8-11)}$$

where F is the formal concentration of HA. The approximation $[H^+] = [A^-]$ would be poor only if the acid were too dilute or too weak, neither of which constitutes a practical problem.

EXAMPLE A Weak-Acid Problem

Find the pH of 0.050 M trimethylammonium chloride.



Trimethylammonium chloride

Solution We assume that ammonium halide salts are completely dissociated to give $(CH_3)_3NH^+$ and Cl^-.† We then recognize that trimethylammonium ion is a weak acid, being the conjugate acid of trimethylamine, $(CH_3)_3N$, a weak base. Cl^- has no basic or acidic properties and should be ignored. In Appendix G, we find trimethylammonium ion listed as trimethylamine but drawn as trimethylammonium ion, with $pK_a = 9.799$, at an ionic strength of $\mu = 0$. So,

Cl^- has no acidic or basic properties because it is the conjugate base of the strong acid, HCl. If Cl^- had appreciable basicity, HCl would not be completely dissociated.

$$K_a = 10^{-pK_a} = 10^{-9.799} = 1.59 \times 10^{-10}$$

From here, everything is downhill.

$$\underset{F - x}{(CH_3)_3NH^+} \overset{K_a}{\rightleftharpoons} \underset{x}{(CH_3)_3N} + \underset{x}{H^+}$$

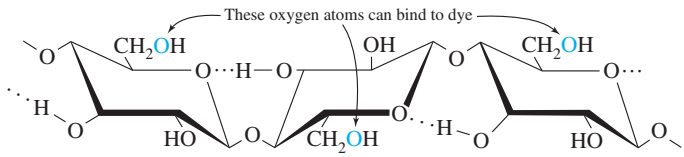
$$\frac{x^2}{0.050 - x} = 1.59 \times 10^{-10} \qquad \textbf{(8-12)}$$

$$x = 2.8 \times 10^{-6}\,M \Rightarrow pH = 5.55$$

Test Yourself Find the pH of 0.050 M triethylammonium bromide. (***Answer:*** 6.01)

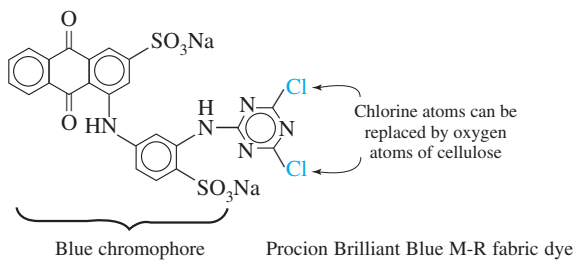
BOX 8-2 Dyeing Fabrics and the Fraction of Dissociation[8]

Cotton fabrics are largely cellulose, a polymer with repeating units of the sugar glucose:

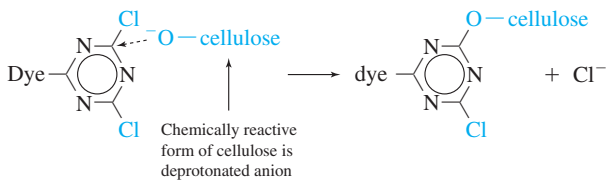


Structure of cellulose. Hydrogen bonding between glucose units helps make the structure rigid.

Dyes are colored molecules that can form covalent bonds to fabric. For example, Procion Brilliant Blue M-R is a dye with a blue *chromophore* (the colored part) attached to a reactive dichlorotriazine ring:



Oxygen atoms of the —CH_2OH groups on cellulose can replace Cl atoms of the dye to form covalent bonds that fix the dye permanently to the fabric:



After the fabric has been dyed in cold water, excess dye is removed with a hot wash. During the hot wash, the second Cl group of the dye is replaced by a second cellulose or by water (giving dye—OH).

The chemically reactive form of cellulose is the conjugate base:

$$\underset{ROH}{\text{Cellulose—}CH_2OH} \overset{K_a \approx 10^{-15}}{\rightleftharpoons} \underset{\substack{RO^- \\ \text{(conjugate base)}}}{\text{cellulose—}CH_2O^-} + H^+$$

To promote dissociation of the cellulose—CH_2OH proton, dyeing is carried out in sodium carbonate solution with a pH around 10.6. The fraction of reactive cellulose is given by the fraction of dissociation of the weak acid at pH 10.6:

$$\text{Fraction of dissociation} = \frac{[RO^-]}{[ROH] + [RO^-]} \approx \frac{[RO^-]}{[ROH]}$$

Because the fraction of dissociation of the very weak acid is so small, $[ROH] >> [RO^-]$ in the denominator, which is therefore approximately just [ROH]. The quotient $[RO^-]/[ROH]$ can be calculated from K_a and the pH:

$$K_a = \frac{[RO^-][H^+]}{[ROH]} \Rightarrow \frac{[RO^-]}{[ROH]} = \frac{K_a}{[H^+]} \approx \frac{10^{-15}}{10^{-10.6}}$$

$$= 10^{-4.4} \approx \text{fraction of dissociation}$$

Only about one cellulose—CH_2OH group in 10^4 is in the reactive form at pH 10.6.

†$R_4N^+X^-$ salts are not completely dissociated, because there are some *ion pairs*, $R_4N^+X^-(aq)$ (Box 7-1). Equilibrium constants for $R_4N^+ + X^- \rightleftharpoons R_4N^+X^-(aq)$ are given below. For 0.050 F solutions, the fraction of ion pairing, calculated with activity coefficients, is 4% in $(CH_3)_4N^+Br^-$, 7% in $(CH_3CH_2)_4N^+Br^-$, and 9% in $(CH_3CH_2CH_2)_4N^+Br^-$.

R_4N^+	X^-	$K_{ion\ pair}$ ($\mu = 0$)	R_4N^+	X^-	$K_{ion\ pair}$ ($\mu = 0$)
Me_4N^+	Cl^-	1.1	Me_4N^+	I^-	2.0
Bu_4N^+	Cl^-	2.5	Et_4N^+	I^-	2.9
Me_4N^+	Br^-	1.4	Pr_4N^+	I^-	4.6
Et_4N^+	Br^-	2.4	Bu_4N^+	I^-	6.0
Pr_4N^+	Br^-	3.1			

Me = CH_3—, Et = CH_3CH_2—, Pr = $CH_3CH_2CH_2$—, Bu = $CH_3CH_2CH_2CH_2$—

A handy tip: Equation 8-11 can always be solved with the quadratic formula. However, an easier method worth trying first is to neglect x in the denominator. If x comes out much smaller than F, then your approximation was good and you need not use the quadratic formula. For Equation 8-12, the approximation works like this:

Approximation Neglect x in denominator. If x comes out to be less than 1% of F, accept the approximation.

$$\frac{x^2}{0.050 - x} \approx \frac{x^2}{0.050} = 1.59 \times 10^{-10} \Rightarrow x = \sqrt{(0.050)(1.59 \times 10^{-10})} = 2.8 \times 10^{-6}\ \text{M}$$

The approximate solution ($x \approx 2.8 \times 10^{-6}$) is much smaller than the term 0.050 in the denominator of Equation 8-12. Therefore, the approximate solution is fine. A reasonable rule of thumb is to accept the approximation if x comes out to be less than 1% of F.

8-4 Weak-Base Equilibria

The treatment of weak bases is almost the same as that of weak acids.

As K_b increases, pK_b decreases and the base becomes stronger.

$$B + H_2O \overset{K_b}{\rightleftharpoons} BH^+ + OH^- \qquad K_b = \frac{[BH^+][OH^-]}{[B]}$$

We suppose that nearly all OH^- comes from the reaction of $B + H_2O$, and little comes from dissociation of H_2O. Setting $[OH^-] = x$, we must also set $[BH^+] = x$, because one BH^+ is produced for each OH^-. Calling the formal concentration of base F ($= [B] + [BH^+]$), we write

$$[B] = F - [BH^+] = F - x$$

Plugging these values into the K_b equilibrium expression, we get

A weak-base problem has the same algebra as a weak-acid problem, except $K = K_b$ and $x = [OH^-]$.

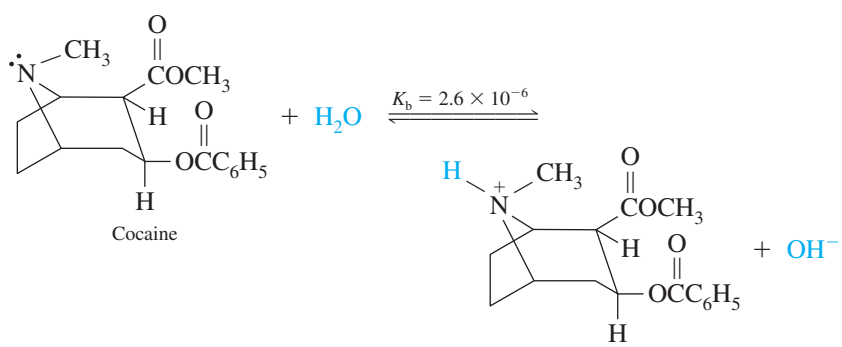
Equation for weak base:

$$\frac{[BH^+][OH^-]}{[B]} = \frac{x^2}{F - x} = K_b \qquad \textbf{(8-13)}$$

which looks a lot like a weak-acid problem, except that now $x = [OH^-]$.

A Typical Weak-Base Problem

Consider the commonly occurring weak base, cocaine.



If the formal concentration is 0.037 2 M, the problem is formulated as follows:

$$\underset{0.037\,2 - x}{B} + H_2O \rightleftharpoons \underset{x}{BH^+} + \underset{x}{OH^-}$$

$$\frac{x^2}{0.037\,2 - x} = 2.6 \times 10^{-6} \Rightarrow x = 3.1 \times 10^{-4}\ \text{M}$$

Because $x = [OH^-]$, we can write

Question What concentration of OH^- is produced by H_2O dissociation in this solution? Was it justified to neglect water dissociation as a source of OH^-?

$$[H^+] = K_w/[OH^-] = 1.0 \times 10^{-14}/3.1 \times 10^{-4} = 3.2 \times 10^{-11}\ \text{M}$$

$$pH = -\log[H^+] = 10.49$$

This is a reasonable pH for a weak base.

What fraction of cocaine has reacted with water? We can formulate α for a base, called the **fraction of association:**

For a base, α is the fraction that has reacted with water.

Fraction of association of a base:

$$\alpha = \frac{[BH^+]}{[BH^+] + [B]} = \frac{x}{F} = 0.008\,3 \qquad \textbf{(8-14)}$$

Only 0.83% of the base has reacted.

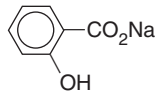
Conjugate Acids and Bases—Revisited

Earlier, we noted that **the conjugate base of a weak acid is a weak base,** and **the conjugate acid of a weak base is a weak acid.** We also derived an exceedingly important relation between the equilibrium constants for a conjugate acid-base pair: $K_a \cdot K_b = K_w$.

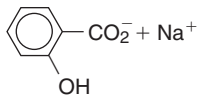
HA and A^- are a conjugate acid-base pair. So are BH^+ and B.

In Section 8-3, we considered *o*- and *p*-hydroxybenzoic acids, designated HA. Now consider their conjugate bases. For example, the salt sodium *o*-hydroxybenzoate dissolves to give Na^+ (which has no acid-base chemistry) and *o*-hydroxybenzoate, which is a weak base.

In aqueous solution,

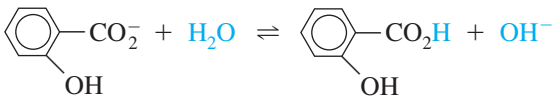


gives



o-Hydroxybenzoate

The acid-base chemistry is the reaction of *o*-hydroxybenzoate with water:



(8-15)

A^-(*o*-hydroxybenzoate)	HA	
$F - x$	x	x

$$\frac{x^2}{F - x} = K_b$$

From K_a for each isomer, we calculate K_b for the conjugate base.

Isomer of hydroxybenzoic acid	K_a	$K_b = K_w/K_a$
ortho	$1.0_7 \times 10^{-3}$	9.3×10^{-12}
para	2.9×10^{-5}	3.5×10^{-10}

Using each value of K_b and letting F = 0.050 0 M, we find

$$\text{pH of 0.050 0 M } o\text{-hydroxybenzoate} = 7.83$$
$$\text{pH of 0.050 0 M } p\text{-hydroxybenzoate} = 8.62$$

These are reasonable pH values for solutions of weak bases. Furthermore, as expected, the conjugate base of the stronger acid is the weaker base.

EXAMPLE A Weak-Base Problem

Find the pH of 0.10 M ammonia.

Solution When ammonia is dissolved in water, its reaction is

$$\underset{\substack{\text{Ammonia}\\ F - x}}{NH_3} + H_2O \overset{K_b}{\rightleftharpoons} \underset{\substack{\text{Ammonium ion}\\ x}}{NH_4^+} + \underset{x}{OH^-}$$

In Appendix G, we find ammonium ion, NH_4^+, listed next to ammonia. pK_a for ammonium ion is 9.245. Therefore, K_b for NH_3 is

$$K_b = \frac{K_w}{K_a} = \frac{10^{-14.00}}{10^{-9.245}} = 1.76 \times 10^{-5}$$

To find the pH of 0.10 M NH_3, we set up and solve the equation

$$\frac{[NH_4^+][OH^-]}{[NH_3]} = \frac{x^2}{0.10 - x} = K_b = 1.76 \times 10^{-5}$$

$$x = [OH^-] = 1.3_2 \times 10^{-3}\,\text{M}$$

$$[H^+] = \frac{K_w}{[OH^-]} = 7.6 \times 10^{-12}\,\text{M} \Rightarrow \text{pH} = -\log[H^+] = 11.12$$

Test Yourself Find the pH of 0.10 M methylamine. (***Answer:*** 11.80)

8-5 Buffers

A buffered solution resists changes in pH when acids or bases are added or when dilution occurs. The **buffer** is a mixture of an acid and its conjugate base. There must be comparable amounts of the conjugate acid and base (within a factor of ~10) to exert significant buffering.

The importance of buffers in all areas of science is immense. At the outset of this chapter, we saw that digestive enzymes in lysosomes operate best in acid, a constraint that allows a cell

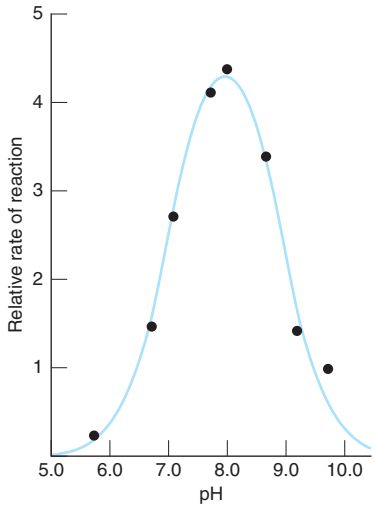
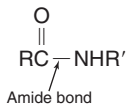


FIGURE 8-3 pH dependence of the rate of cleavage of an amide bond by the enzyme chymotrypsin, which helps digest proteins in your intestine. [M. L. Bender, G. E. Clement, F. J. Kézdy, and H. A. Heck, "The Correlation of the pH (pD) Dependence and the Stepwise Mechanism of α-Chymotrypsin-Catalyzed Reactions," *J. Am. Chem. Soc.* **1964**, *86*, 3680.]



to protect itself from its own enzymes. If enzymes leak into the buffered, neutral cytoplasm, they have low reactivity and do less damage to the cell than they would at their optimum pH. Figure 8-3 shows the pH dependence of an enzyme-catalyzed reaction that is fastest near pH 8.0. For an organism to survive, it must control the pH of each subcellular compartment so that each reaction proceeds at the proper rate.

Mixing a Weak Acid and Its Conjugate Base

If you mix A moles of a weak acid with B moles of its conjugate base, the moles of acid remain close to A and the moles of base remain close to B. Little reaction occurs to change either concentration.

To understand why this should be so, look at the K_a and K_b reactions in terms of Le Châtelier's principle. Consider an acid with $pK_a = 4.00$ and its conjugate base with $pK_b = 10.00$. Let's calculate the fraction of acid that dissociates in a 0.10 M solution of HA.

$$\underset{0.10-x}{HA} \rightleftharpoons \underset{x}{H^+} + \underset{x}{A^-} \qquad pK_a = 4.00$$

$$\frac{x^2}{F - x} = K_a \Rightarrow x = 3.1 \times 10^{-3}\ M$$

$$\text{Fraction of dissociation} = \alpha = \frac{x}{F} = 0.031$$

The acid is only 3.1% dissociated under these conditions.

In a solution containing 0.10 mol of A^- dissolved in 1.00 L, the extent of reaction of A^- with water is even smaller.

$$\underset{0.10-x}{A^-} + H_2O \rightleftharpoons \underset{x}{HA} + \underset{x}{OH^-} \qquad pK_b = 10.00$$

$$\frac{x^2}{F - x} = K_b \Rightarrow x = 3.2 \times 10^{-6}$$

$$\text{Fraction of association} = \alpha = \frac{x}{F} = 3.2 \times 10^{-5}$$

When you mix a weak acid with its conjugate base, you get what you mix!

HA dissociates very little, and adding extra A^- to the solution makes HA dissociate even less. Similarly, A^- does not react much with water, and adding extra HA makes A^- react even less. If 0.050 mol of A^- plus 0.036 mol of HA are added to water, there will be close to 0.050 mol of A^- and close to 0.036 mol of HA in the solution at equilibrium.

The approximation that the concentrations of HA and A^- remain unchanged breaks down for dilute solutions or at extremes of pH. We test the validity of the approximation on page 180.

Henderson-Hasselbalch Equation

The central equation for buffers is the **Henderson-Hasselbalch equation,** which is merely a rearranged form of the K_a equilibrium expression.

$$K_a = \frac{[H^+][A^-]}{[HA]}$$

$$\log K_a = \log \frac{[H^+][A^-]}{[HA]} = \log[H^+] + \log \frac{[A^-]}{[HA]}$$

$$\underbrace{-\log[H^+]}_{pH} = \underbrace{-\log K_a}_{pK_a} + \log \frac{[A^-]}{[HA]}$$

$\log xy = \log x + \log y$

Henderson-Hasselbalch equation for an acid:

$HA \overset{K_a}{\rightleftharpoons} H^+ + A^-$

$$pH = pK_a + \log \frac{[A^-]}{[HA]} \qquad \textbf{(8-16)}$$

L. J. Henderson was a physician who wrote $[H^+] = K_a[\text{acid}]/[\text{salt}]$ in a physiology article in 1908, a year before the word "buffer" and the concept of pH were invented by the biochemist S. P. L. Sørensen. Henderson's contribution was the approximation of setting [acid] equal to the concentration of HA placed in solution and [salt] equal to the concentration of A^- placed in solution. In 1916, K. A. Hasselbalch wrote what we call the Henderson-Hasselbalch equation in a biochemical journal.[9]

The Henderson-Hasselbalch equation tells us the pH of a solution, provided we know the ratio of the concentrations of conjugate acid and base, as well as pK_a for the acid. If a solution is prepared from the weak base B and its conjugate acid, the analogous equation is

Henderson-Hasselbalch equation for a base:

$BH^+ \overset{K_a = K_w/K_b}{\rightleftharpoons} B + H^+$

$$pH = pK_a + \log \frac{[B]}{[BH^+]} \qquad \textbf{(8-17)}$$

pK_a applies to *this* acid

where pK_a is the acid dissociation constant of the weak acid BH^+. The important features of Equations 8-16 and 8-17 are that the base (A^- or B) appears in the numerator of both equations, and the equilibrium constant is K_a of the acid in the denominator.

Equations 8-16 and 8-17 are only sensible when the base (A^- or B) is in the *numerator*. When the concentration of base increases, the log term increases and the pH increases.

Challenge Show that, when activities are included, the Henderson-Hasselbalch equation is

$$pH = pK_a + \log \frac{[A^-]\gamma_{A^-}}{[HA]\gamma_{HA}} \tag{8-18}$$

The Henderson-Hasselbalch equation is not an approximation. It is just a rearranged form of the equilibrium expression. The approximations we make are the values of $[A^-]$ and [HA]. In most cases, it is valid to assume that what we mix is what we get in solution. At the end of this chapter, we treat the case in which what we mix is not what we get because the solution is too dilute or the acid is too strong.

Properties of the Henderson-Hasselbalch Equation

In Equation 8-16, we see that, if $[A^-] = [HA]$, then $pH = pK_a$.

$$pH = pK_a + \log \frac{[A^-]}{[HA]} = pK_a + \log 1 = pK_a$$

When $[A^-] = [HA]$, $pH = pK_a$.

Regardless of how complex a solution may be, whenever $pH = pK_a$, for a particular acid, $[A^-]$ must equal [HA] for that acid.

All equilibria must be satisfied simultaneously in any solution at equilibrium. If there are 10 different acids and bases in the solution, the 10 forms of Equation 8-16 will have 10 different quotients $[A^-]/[HA]$, but all 10 equations must give the same pH, because **there can be only one concentration of H^+ in a solution**.

Another feature of the Henderson-Hasselbalch equation is that, for every power-of-10 change in the ratio $[A^-]/[HA]$, the pH changes by one unit (Table 8-1). As the base (A^-) increases, the pH goes up. As the acid (HA) increases, the pH goes down. For any conjugate acid-base pair, you can say, for example, that if $pH = pK_a - 1$, there must be 10 times as much HA as A^-. Ten-elevenths is in the form HA and one-eleventh is in the form A^-.

TABLE 8-1 Effect of $[A^-]/[HA]$ on pH

$[A^-]/[HA]$	pH
100:1	$pK_a + 2$
10:1	$pK_a + 1$
1:1	pK_a
1:10	$pK_a - 1$
1:100	$pK_a - 2$

EXAMPLE Using the Henderson-Hasselbalch Equation

Sodium hypochlorite (NaOCl, the active ingredient of almost all bleaches) was dissolved in a solution buffered to pH 6.20. Find the ratio $[OCl^-]/[HOCl]$ in this solution.

Solution In Appendix G, we find that $pK_a = 7.53$ for hypochlorous acid, HOCl. The pH is known, so the ratio $[OCl^-]/[HOCl]$ can be calculated from the Henderson-Hasselbalch equation.

$$HOCl \rightleftharpoons H^+ + OCl^-$$

$$pH = pK_a + \log \frac{[OCl^-]}{[HOCl]}$$

$$6.20 = 7.53 + \log \frac{[OCl^-]}{[HOCl]}$$

$$-1.33 = \log \frac{[OCl^-]}{[HOCl]}$$

$$10^{-1.33} = 10^{\log([OCl^-]/[HOCl])} = \frac{[OCl^-]}{[HOCl]}$$

$10^{\log z} = z$

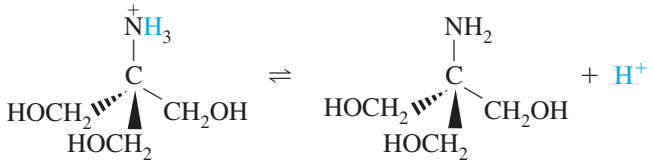
$$0.047 = \frac{[OCl^-]}{[HOCl]}$$

The ratio $[OCl^-]/[HOCl]$ is set by pH and pK_a. We do not need to know how much NaOCl was added, or the volume.

Test Yourself Find $[OCl^-]/[HOCl]$ if pH is raised by one unit to 7.20. (***Answer:*** 0.47)

A Buffer in Action

For illustration, we choose a widely used buffer called "tris," which is short for tris(hydroxymethyl)aminomethane.



BH^+ — $pK_a = 8.072$ | B — This form is "tris"

In Appendix G, we find $pK_a = 8.072$ for the conjugate acid of tris. An example of a salt containing the BH^+ cation is tris hydrochloride, which is BH^+Cl^-. When BH^+Cl^- is dissolved in water, it dissociates to BH^+ and Cl^-.

EXAMPLE A Buffer Solution

Find the pH of a 1.00-L aqueous solution prepared with 12.43 g of tris (FM 121.135) plus 4.67 g of tris hydrochloride (FM 157.596).

Solution The concentrations of B and BH^+ added to the solution are

$$[B] = \frac{12.43\ \text{g/L}}{121.135\ \text{g/mol}} = 0.102\,6\ \text{M} \qquad [BH^+] = \frac{4.67\ \text{g/L}}{157.596\ \text{g/mol}} = 0.029\,6\ \text{M}$$

Assuming that what we mixed stays in the same form, we plug these concentrations into the Henderson-Hasselbalch equation to find the pH:

$$\text{pH} = pK_a + \log\frac{[B]}{[BH^+]} = 8.072 + \log\frac{0.102\,6}{0.029\,6} = 8.61$$

Test Yourself Find the pH if we add another 1.00 g of tris hydrochloride. (***Answer:*** 8.53)

The pH of a buffer is nearly independent of volume.

Notice that *the volume of solution is irrelevant*, because volume cancels in the numerator and denominator of the log term:

$$\text{pH} = pK_a + \log\frac{\text{moles of B}/\cancel{\text{L of solution}}}{\text{moles of BH}^+/\cancel{\text{L of solution}}}$$

$$= pK_a + \log\frac{\text{moles of B}}{\text{moles of BH}^+}$$

BOX 8-3 Strong Plus Weak Reacts Completely

Strong acid reacts with a weak base essentially "completely" because the equilibrium constant is large.

$$\underset{\text{Weak base}}{B} + \underset{\text{Strong acid}}{H^+} \rightleftharpoons BH^+ \qquad K = \frac{1}{K_a\,(\text{for } BH^+)}$$

If B is tris(hydroxymethyl)aminomethane, the equilibrium constant for reaction with HCl is

$$K = \frac{1}{K_a} = \frac{1}{10^{-8.072}} = 1.2 \times 10^8$$

Strong base reacts "completely" with a weak acid because the equilibrium constant is, again, very large.

$$\underset{\text{Strong base}}{OH^-} + \underset{\text{Weak acid}}{HA} \rightleftharpoons A^- + H_2O \qquad K = \frac{1}{K_b\,(\text{for } A^-)}$$

If HA is acetic acid, then the equilibrium constant for reaction with NaOH is

$$K = \frac{1}{K_b} = \frac{K_a\,(\text{for HA})}{K_w} = 1.7 \times 10^9$$

The reaction of a strong acid with a strong base is even more complete than a strong plus weak reaction:

$$\underset{\text{Strong acid}}{H^+} + \underset{\text{Strong base}}{OH^-} \rightleftharpoons H_2O \qquad K = \frac{1}{K_w} = 10^{14}$$

If you mix a strong acid, a strong base, a weak acid, and a weak base, the strong acid and strong base will neutralize each other until one is used up. The remaining strong acid or strong base will then react with the weak base or weak acid.

EXAMPLE Effect of Adding Acid to a Buffer

If we add 12.0 mL of 1.00 M HCl to the solution in the previous example, what will be the new pH?

Solution The key is to realize that, *when a strong acid is added to a weak base, they react completely to give* BH^+ (Box 8-3). We are adding 12.0 mL of 1.00 M HCl, which contains (0.012 0 L)(1.00 mol/L) = 0.012 0 mol of H^+. This much H^+ consumes 0.012 0 mol of B to create 0.012 0 mol of BH^+:

	B (Tris)	+	H^+ (From HCl)	→	BH^+
Initial moles	0.102 6		0.012 0		0.029 6
Final moles	0.090 6		—		0.041 6
	(0.102 6 − 0.012 0)				(0.029 6 + 0.012 0)

Information in the table allows us to calculate the pH:

$$pH = pK_a + \log \frac{\text{moles of B}}{\text{moles of } BH^+}$$

$$= 8.072 + \log \frac{0.090\,6}{0.041\,6} = 8.41$$

The volume of the solution is irrelevant.

Question Does the pH change in the right direction when HCl is added?

Test Yourself Find the pH if only 6.0 instead of 12.0 mL HCl were added. (***Answer:*** 8.51)

A buffer resists changes in pH . . .

We see that *the pH of a buffer does not change very much when a limited amount of strong acid or base is added*. Addition of 12.0 mL of 1.00 M HCl changed the pH from 8.61 to 8.41. Addition of 12.0 mL of 1.00 M HCl to 1.00 L of unbuffered solution would have lowered the pH to 1.93.

. . . because the buffer consumes the added acid or base.

But *why* does a buffer resist changes in pH? It does so because the strong acid or base is consumed by B or BH^+. If you add HCl to tris, B is converted into BH^+. If you add NaOH, BH^+ is converted into B. As long as you don't use up B or BH^+ by adding too much HCl or NaOH, the log term of the Henderson-Hasselbalch equation does not change much and pH does not change much. Demonstration 8-2 illustrates what happens when buffer does get used up. The buffer has its maximum capacity to resist changes of pH when pH = pK_a. We return to this point later.

EXAMPLE Calculating How to Prepare a Buffer Solution

How many milliliters of 0.500 M NaOH should be added to 10.0 g of tris hydrochloride to give a pH of 7.60 in a final volume of 250 mL?

Solution The moles of tris hydrochloride are (10.0 g)/(157.596 g/mol) = 0.063 5 mol. We can make a table to help solve the problem:

Reaction with OH^-:	BH^+	+	OH^-	→	B
Initial moles	0.063 5		x		—
Final moles	0.063 5 − x		—		x

The Henderson-Hasselbalch equation allows us to find x, because we know pH and pK_a.

$$pH = pK_a + \log \frac{\text{mol B}}{\text{mol } BH^+}$$

$$7.60 = 8.072 + \log \frac{x}{0.063\,5 - x}$$

$$-0.472 = \log \frac{x}{0.063\,5 - x}$$

$$10^{-0.472} = \frac{x}{0.063\,5 - x} \Rightarrow x = 0.016\,0 \text{ mol}$$

This many moles of NaOH is contained in

$$\frac{0.016\,0 \text{ mol}}{0.500 \text{ mol/L}} = 0.032\,0 \text{ L} = 32.0 \text{ mL}$$

Test Yourself How many mL of 0.500 M NaOH should be added to 10.0 g of tris hydrochloride to give a pH of 7.40 in a final volume of 500 mL? (***Answer*:** 22.3 mL)

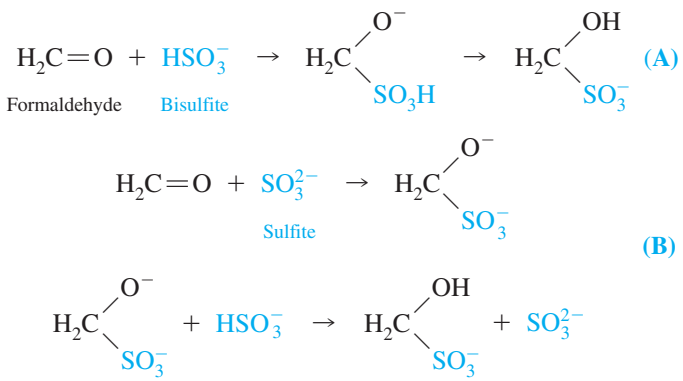
DEMONSTRATION 8-2 How Buffers Work

A buffer resists changes in pH because added acid or base is consumed by buffer. As buffer is used up, it becomes less resistant to changes in pH.

In this demonstration,[10] a mixture containing approximately a 10:1 mole ratio of HSO_3^-:SO_3^{2-} is prepared. Because pK_a for HSO_3^- is 7.2, the pH should be approximately

$$\text{pH} = \text{p}K_a + \log \frac{[SO_3^{2-}]}{[HSO_3^-]} = 7.2 + \log \frac{1}{10} = 6.2$$

When formaldehyde is added, the net reaction is the consumption of HSO_3^-, but not of SO_3^{2-}:



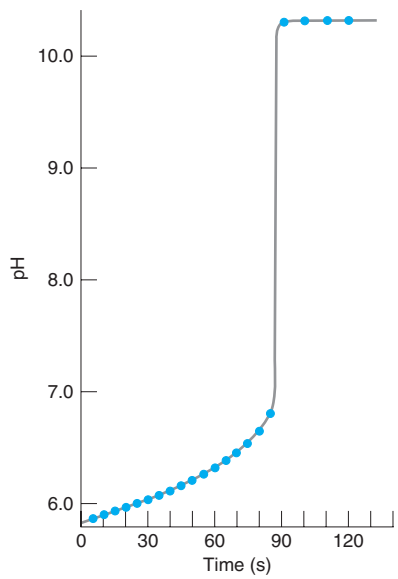
(In sequence A, bisulfite is consumed directly. In sequence B, the net reaction is destruction of HSO_3^-, with no change in the SO_3^{2-} concentration.)

We can prepare a table showing how the pH should change as the HSO_3^- reacts.

Percentage of reaction completed	$[SO_3^{2-}]$: $[HSO_3^-]$	Calculated pH
0	1 : 10	6.2
90	1 : 1	7.2
99	1 : 0.1	8.2
99.9	1 : 0.01	9.2
99.99	1 : 0.001	10.2

Through 90% completion, the pH should rise by just 1 unit. In the next 9% of the reaction, the pH will rise by another unit. At the end of the reaction, the change in pH is very abrupt.

In the formaldehyde *clock reaction*,[11] formaldehyde is added to a solution containing HSO_3^-, SO_3^{2-}, and phenolphthalein indicator. Phenolphthalein is colorless below pH 8 and red above this pH. The solution remains colorless for more than a minute. Suddenly pH shoots up and the liquid turns pink. Monitoring pH with a glass electrode gave the results in the graph.



Graph of pH versus time in the formaldehyde clock reaction.

Procedure: Solutions must be fresh. Prepare a solution of formaldehyde by diluting 9 mL of 37 wt% formaldehyde to 100 mL. Dissolve 1.4 g of $Na_2S_2O_5$ (sodium metabisulfite)[12] and 0.18 g of Na_2SO_3 in 400 mL of water, and add ~1 mL of phenolphthalein solution (Table 10-3). Add 23 mL of formaldehyde solution to the well-stirred solution to initiate the reaction. Reaction time can be adjusted by changing temperature, concentrations, or volume.

A less toxic variant of this demonstration uses glyoxal ($HC(=O)—CH(=O)$) in place of formaldehyde.[13] A day before the demonstration, dilute 2.9 g 40 wt% glyoxal (20.0 mmol) to 25 mL. Dissolve 0.90 g $Na_2S_2O_5$ (4.7 mmol), 0.15 g Na_2SO_3 (1.2 mmol), and 0.18 g $Na_2EDTA{\cdot}2H_2O$ (0.48 mmol, to protect sulfite from metal-catalyzed air oxidation) in 50 mL. A mole of $Na_2S_2O_5$ makes 2 moles of HSO_3^- by reaction with H_2O. For the demonstration, add 0.5 mL phenol red indicator (Table 10-3) to 400 mL H_2O plus 5.0 mL sulfite solution. Add 2.5 mL glyoxal solution to the well-stirred sulfite solution to start the clock reaction.

Preparing a Buffer in Real Life!

If you really wanted to prepare a tris buffer of pH 7.60, you would *not* do it by calculating what to mix. Suppose that you wish to prepare 1.00 L of buffer containing 0.100 M tris at a pH of 7.60. You have available solid tris hydrochloride and approximately 1 M NaOH. Here's how I would do it:

1. Weigh out 0.100 mol of tris hydrochloride and dissolve it in a beaker containing about 800 mL of water.
2. Place a calibrated pH electrode in the solution and monitor the pH.
3. Add NaOH solution until the pH is exactly 7.60.
4. Transfer the solution to a volumetric flask and wash the beaker a few times. Add the washings to the volumetric flask.
5. Dilute to the mark and mix.

You do not simply add the calculated quantity of NaOH because it would not give exactly the desired pH. The reason for using 800 mL of water in the first step is so that the volume will be reasonably close to the final volume during pH adjustment. Otherwise, the pH will change slightly when the sample is diluted to its final volume and the ionic strength changes.

Reasons why a calculation could be wrong:

1. Activity coefficients were not considered.

2. The temperature might not be 25°C, for which pK_a is listed.

3. The approximations [HA] = F_{HA} and [A^-] = F_{A^-} could be in error.

4. pK_a listed for tris in your favorite table is probably not exactly what you would measure.

5. Other ions besides the acid and base species affect pH by ion-pairing reactions with acid and base species.

Buffer Capacity[14]

Buffer capacity, β, is a measure of how well a solution resists changes in pH when strong acid or base is added. Buffer capacity is defined as

Buffer capacity:

$$\beta = \frac{dC_b}{d\text{pH}} = -\frac{dC_a}{d\text{pH}} \tag{8-19}$$

where C_a and C_b are the number of moles of strong acid and strong base per liter needed to produce a unit change in pH. The greater the buffer capacity, the more resistant the solution is to pH change.

Figure 8-4a shows C_b versus pH for a solution containing 0.100 F HA with pK_a = 5.00. The ordinate (C_b) is the formal concentration of strong base needed to be mixed with 0.100 F HA to give the indicated pH. For example, a solution containing 0.050 F OH^- plus 0.100 F HA would have a pH of 5.00 (neglecting activities).

Figure 8-4b, which is the derivative of the upper curve, shows buffer capacity for the same system. Buffer capacity reaches a maximum when pH = pK_a. That is, *a buffer is most effective in resisting changes in pH when pH = pK_a* (that is, when [HA] = [A^-]).

In choosing a buffer, *seek one whose pK_a is as close as possible to the desired pH. The useful pH range of a buffer is usually considered to be pK_a ± 1 pH unit.* Outside this range, there is not enough of either the weak acid or the weak base to react with added base or acid. Buffer capacity can be increased by increasing the concentration of the buffer.

Choose a buffer whose pK_a is close to the desired pH.

Buffer capacity in Figure 8-4b continues upward at high pH (and at low pH, which is not shown) simply because there is a high concentration of OH^- at high pH (or H^+ at low pH). Addition of a small amount of acid or base to a large amount of OH^- (or H^+) will not have a large effect on pH. A solution of high pH is buffered by the H_2O/OH^- conjugate acid-conjugate base pair. A solution of low pH is buffered by the H_3O^+/H_2O conjugate acid-conjugate base pair.

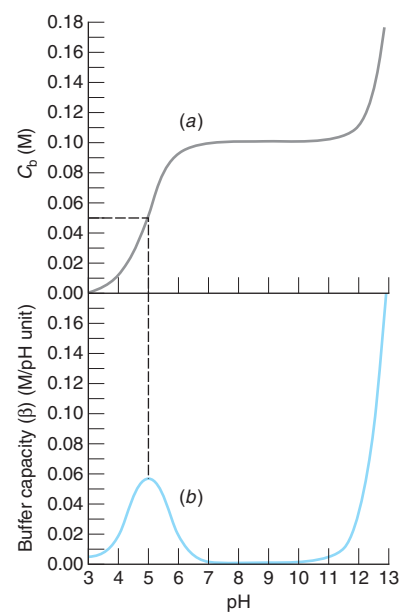


FIGURE 8-4 (*a*) C_b versus pH for a solution containing 0.100 F HA with pK_a = 5.00. (*b*) Buffer capacity versus pH for the same system reaches a maximum when pH = pK_a. The lower curve is the derivative of the upper curve.

Buffer pH Depends on Ionic Strength and Temperature

The correct Henderson-Hasselbalch equation, 8-18, includes activity coefficients. The most important reason why the calculated pH of a buffer is not equal to the observed pH is because the ionic strength is not 0, so activity coefficients are not 1. Table 8-2 lists pK_a values for common buffers that are widely used in biochemistry. Values are listed for ionic strengths of 0 and 0.1 M. If a buffer solution has an ionic strength closer to 0.1 M than to 0, it is sensible to use pK_a for μ = 0.1 to obtain a more realistic calculation of pH.

If we mix 0.200 mol boric acid with 0.100 mol NaOH in 1.00 L, we generate a 1:1 mixture of boric acid and its conjugate base with an ionic strength of 0.10 M:

$$\underset{\text{Boric acid (HA)}}{B(OH)_3} + OH^- \rightarrow \underset{\text{Borate } (A^-)}{(HO)_2BO^-} + H_2O$$

For boric acid in Table 8-2 we find pK_a = 9.24 at μ = 0 and pK_a = 8.98 at μ = 0.1 M. We predict that the pH of a 1:1 mixture of boric acid and borate will have pH near pK_a = 9.24 at low ionic strength and near 8.98 at μ = 0.1 M. As another example of ionic strength effects,

TABLE 8-2 Structures and pK_a values for common buffers[a,b,c,d]

Name	Structure	pK_a[e] $\mu = 0$	pK_a[e] $\mu = 0.1$ M	Formula mass	$\Delta(pK_a)/\Delta T$ (K^{-1})
N-2-Acetamidoiminodiacetic acid (ADA)	$H_2N\overset{O}{\overset{\|\|}{C}}CH_2\overset{+}{N}H(CH_2CO_2H)_2$	— (CO_2H)	1.59	190.15	—
N-Tris(hydroxymethyl)methylglycine (TRICINE)	$(HOCH_2)_3C\overset{+}{N}H_2CH_2CO_2H$	2.02 (CO_2H)	—	179.17	−0.003
Phosphoric acid	H_3PO_4	2.15 (pK_1)	1.92	98.00	0.005
N,N-Bis(2-hydroxyethyl)glycine (BICINE)	$(HOCH_2CH_2)_2\overset{+}{N}HCH_2CO_2H$	2.23 (CO_2H)	—	163.17	—
ADA	(see above)	2.48 (CO_2H)	2.31	190.15	—
Piperazine-*N,N′*-bis(2-ethanesulfonic acid) (PIPES)	$^-O_3SCH_2CH_2\overset{+}{N}H\ H\overset{+}{N}CH_2CH_2SO_3^-$	— (pK_1)	2.67	302.37	—
Citric acid	$HO_2CCH_2C(OH)(CO_2H)CH_2CO_2H$	3.13 (pK_1)	2.90	192.12	−0.002
Glycylglycine	$H_3\overset{+}{N}CH_2\overset{O}{\overset{\|\|}{C}}NHCH_2CO_2H$	3.14 (CO_2H)	3.11	132.12	0.000
Piperazine-*N,N′*-bis(3-propanesulfonic acid) (PIPPS)	$^-O_3S(CH_2)_3\overset{+}{N}H\ H\overset{+}{N}(CH_2)_3SO_3^-$	— (pK_1)	3.79	330.42	—
Piperazine-*N,N′*-bis(4-butanesulfonic acid) (PIPBS)	$^-O_3S(CH_2)_4\overset{+}{N}H\ H\overset{+}{N}(CH_2)_4SO_3^-$	— (pK_1)	4.29	358.47	—
N,N′-Diethylpiperazine dihydrochloride (DEPP-2HCl)	$CH_3CH_2\overset{+}{N}H\ H\overset{+}{N}CH_2CH_3\cdot 2Cl^-$	— (pK_1)	4.48	215.16	—
Citric acid	(see above)	4.76 (pK_2)	4.35	192.12	−0.001
Acetic acid	CH_3CO_2H	4.76	4.62	60.05	0.000
N,N′-Diethylethylenediamine-*N,N′*-bis(3-propanesulfonic acid) (DESPEN)	$^-O_3S(CH_2)_3\overset{+}{N}(CH_3CH_2)H\overset{+}{N}(CH_2CH_3)(CH_2)_3SO_3^-$	— (pK_1)	5.62	360.49	—
2-(*N*-Morpholino)ethanesulfonic acid (MES)	$O(CH_2)_4\overset{+}{N}HCH_2CH_2SO_3^-$	6.27	6.06	195.24	−0.009
Citric acid	(see above)	6.40 (pK_3)	5.70	192.12	0.002
N,N,N′,N′-Tetraethylethylenediamine dihydrochloride (TEEN·2HC1)	$Et_2\overset{+}{N}HCH_2CH_2H\overset{+}{N}Et_2\cdot 2Cl^-$	— (pK_1)	6.58	245.23	—
1,3-Bis[tris(hydroxymethyl)methylamino] propane hydrochloride (BIS-TRIS propane-2HCl)	$(HOCH_2)_3C\overset{+}{N}H_2(CH_2)_3\overset{+}{N}H_2(CH_2OH)_3C\cdot 2Cl^-$	6.65 (pK_1)	—	355.26	—
ADA	(see above)	6.84 (NH)	6.67	190.15	−0.007

a. The protonated form of each molecule is shown. Acidic hydrogen atoms are shown in ***bold*** *type. pK_a is for 25°C.*

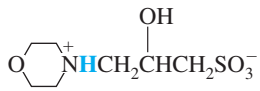
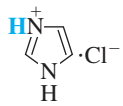
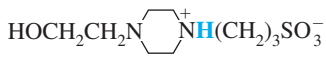
b. Many buffers in this table are widely used in biomedical research because of their weak metal binding and physiologic inertness (C. L. Bering, J. Chem. Ed. ***1987,*** *64, 803). In one study, where MES and MOPS had no discernible affinity for Cu^{2+}, a minor impurity in HEPES and HEPPS had a strong affinity for Cu^{2+} and MOPSO bound Cu^{2+} stoichiometrically (H. E. Marsh, Y.-P. Chin, L. Sigg, R. Hari, and H. Xu, Anal. Chem.* ***2003,*** *75, 671). ADA, BICINE, ACES, and TES have some metal-binding ability (R. Nakon and C. R. Krishnamoorthy, Science* ***1983,*** *221, 749). Lutidine buffers for the pH range 3 to 8 with limited metal-binding power have been described by U. Bips, H. Elias, M. Hauröder, G. Kleinhans, S. Pfeifer, and K. J. Wannowius, Inorg. Chem.* ***1983,*** *22, 3862.*

c. Some data from R. N. Goldberg, N. Kishore, and R. M. Lennen, J. Phys. Chem. Ref. Data ***2002,*** *31, 231. This paper gives the temperature dependence of pK_a.*

d. Temperature and ionic strength dependence of pK_a for buffers: HEPES—D. Feng, W. F. Koch, and Y. C. Wu, Anal. Chem. ***1989,*** *61, 1400; MOPSO—Y. C. Wu, P. A. Berezansky, D. Feng, and W. F. Koch, Anal. Chem.* ***1993,*** *65, 1084; ACES and CHES—R. N. Roy, J. Bice, J. Greer, J. A. Carlsten, J. Smithson, W. S. Good, C. P. Moore, L. N. Roy, and K. M. Kuhler, J. Chem. Eng. Data* ***1997,*** *42, 41; TEMN, TEEN, DEPP, DESPEN, PIPES, PIPPS, PIPBS, MES, MOPS, and MOBS—A. Kandegedara and D. B. Rorabacher, Anal. Chem.* ***1999,*** *71, 3140. This last set of buffers was specifically developed for low metal-binding ability (Q. Yu, A. Kandegedara, Y. Xu, and D. B. Rorabacher, Anal. Biochem.* ***1997,*** *253, 50).*

e. See marginal note on page 166 for the distinction between pK_a at $\mu = 0$ and at $\mu = 0.1$ M.

TABLE 8-2 (continued) **Structures and pK_a values for common buffers**[a,b,c,d]

Name	Structure	pK_a $\mu = 0$	pK_a $\mu = 0.1$ M	Formula mass	$\Delta(pK_a)/\Delta T$ (K^{-1})
N-2-Acetamido-2-aminoethane-sulfonic acid (ACES)	$H_2NC(=O)CH_2\overset{+}{N}H_2CH_2CH_2SO_3^-$	6.85	6.75	182.20	−0.018
3-(*N*-Morpholino)-2-hydroxy-propanesulfonic acid (MOPSO)		6.90	—	225.26	−0.015
Imidazole hydrochloride		6.99	7.00	104.54	−0.022
PIPES	(see above)	7.14 (pK_2)	6.93	302.37	−0.007
3-(*N*-Morpholino)propanesulfonic acid (MOPS)		7.18	7.08	209.26	−0.012
Phosphoric acid	H_3PO_4	7.20 (pK_2)	6.71	98.00	−0.002
4-(*N*-Morpholino)butanesulfonic acid (MOBS)		—	7.48	223.29	—
N-Tris(hydroxymethyl)methyl-2-aminoethanesulfonic acid (TES)	$(HOCH_2)_3C\overset{+}{N}H_2CH_2CH_2SO_3^-$	7.55	7.60	229.25	−0.019
N-2-Hydroxyethylpiperazine-*N*′-2-ethanesulfonic acid (HEPES)		7.56	7.49	238.30	−0.012
PIPPS	(see above)	— (pK_2)	7.97	330.42	—
N-2-Hydroxyethylpiperazine-*N*′-3-propanesulfonic acid (HEPPS)		7.96	7.87	252.33	−0.013
Glycine amide hydrochloride	$H_3\overset{+}{N}CH_2C(=O)NH_2 \cdot Cl^-$	—	8.04	110.54	—
Tris(hydroxymethyl)aminomethane hydrochloride (TRIS·HCl)	$(HOCH_2)_3C\overset{+}{N}H_3 \cdot Cl^-$	8.07	8.10	157.60	−0.028
TRICINE	(see above)	8.14 (NH)	—	179.17	−0.018
Glycylglycine	(see above)	8.26 (NH)	8.09	132.12	−0.026
BICINE	(see above)	8.33 (NH)	8.22	163.17	−0.015
PIPBS	(see above)	— (pK_2)	8.55	358.47	—
DEPP·2HCl	(see above)	— (pK_2)	8.58	207.10	—
DESPEN	(see above)	— (pK_2)	9.06	360.49	—
BIS-TRIS propane·2HCl	(see above)	9.10 (pK_2)	—	355.26	—
Ammonia	NH_4^+	9.24	—	17.03	−0.031
Boric acid	$B(OH)_3$	9.24 (pK_1)	8.98	61.83	−0.008
Cyclohexylaminoethanesulfonic acid (CHES)		9.39	—	207.29	−0.023
TEEN·2HCl	(see above)	— (pK_2)	9.88	245.23	—
3-(Cyclohexylamino)propanesulfonic acid (CAPS)		10.50	10.39	221.32	−0.028
N,N,N′,N′–Tetraethylmethylene-diamine·2HCl (TEMN·2HC1)	$Et_2\overset{+}{N}HCH_2H\overset{+}{N}Et_2 \cdot 2Cl^-$	— (pK_2)	11.01	231.21	—
Phosphoric acid	H_3PO_4	12.35 (pK_3)	11.52	98.00	−0.009
Boric acid	$B(OH)_3$	12.74 (pK_2)	—	61.83	—

Changing ionic strength changes pH.

when a 0.5 M stock solution of phosphate buffer at pH 6.6 is diluted to 0.05 M, the pH rises to 6.9—a rather significant effect.

For almost all problems in this book we use pK_a for $\mu = 0$. As a practical matter, when there is no value of pK_a listed for $\mu = 0$, use pK_a for $\mu = 0.1$ M.

Changing temperature changes pH.

Buffer pK_a depends on temperature, as indicated in the last column of Table 8-2. Tris has an exceptionally large dependence, -0.028 pK_a units per degree, near room temperature. A solution of tris with pH 8.07 at 25°C will have pH ≈ 8.7 at 4°C and pH ≈ 7.7 at 37°C.

When What You Mix Is Not What You Get

What you mix is not what you get in dilute solutions or at extremes of pH.

In dilute solution or at extremes of pH, the concentrations of HA and A^- are not equal to their formal concentrations. Suppose we mix F_{HA} moles of HA and F_{A^-} moles of the salt Na^+A^-. The mass and charge balances are

Mass balance: $$F_{HA} + F_{A^-} = [HA] + [A^-]$$

Charge balance: $$[Na^+] + [H^+] = [OH^-] + [A^-]$$

The substitution $[Na^+] = F_{A^-}$ and a little algebra leads to the equations

$$[HA] = F_{HA} - [H^+] + [OH^-] \tag{8-20}$$

$$[A^-] = F_{A^-} + [H^+] - [OH^-] \tag{8-21}$$

So far we have assumed that $[HA] \approx F_{HA}$ and $[A^-] \approx F_{A^-}$, and we used these values in the Henderson-Hasselbalch equation. A more rigorous procedure is to use Equations 8-20 and 8-21. If F_{HA} or F_{A^-} is small, or if $[H^+]$ or $[OH^-]$ is large, then the approximations $[HA] \approx F_{HA}$ and $[A^-] \approx F_{A^-}$ are not good. In acidic solutions, $[H^+] >> [OH^-]$, so $[OH^-]$ can be ignored in Equations 8-20 and 8-21. In basic solutions, $[H^+]$ can be neglected.

EXAMPLE A Dilute Buffer Prepared from a Moderately Strong Acid

What will be the pH if 0.010 0 mol of HA (with $pK_a = 2.00$) and 0.010 0 mol of A^- are dissolved in water to make 1.00 L of solution?

Solution The solution is acidic ($pH \approx pK_a = 2.00$), so we neglect $[OH^-]$ in Equations 8-20 and 8-21. Setting $[H^+] = x$ in Equations 8-20 and 8-21, we use the K_a equation to find $[H^+]$:

$$\underset{0.010\,0 - x}{HA} \rightleftharpoons \underset{x}{H^+} + \underset{0.010\,0 + x}{A^-}$$

$$K_a = \frac{[H^+][A^-]}{[HA]} = \frac{(x)(0.010\,0 + x)}{(0.010\,0 - x)} = 10^{-2.00} \tag{8-22}$$

$$\Rightarrow x = 0.004\,14 \text{ M} \quad \Rightarrow \quad pH = -\log[H^+] = 2.38$$

The pH is 2.38 instead of 2.00. [HA] and $[A^-]$ are not what we mixed:

HA in this solution is more than 40% dissociated. The acid is too strong for the approximation $[HA] \approx F_{HA}$.

$$[HA] = F_{HA} - [H^+] = 0.005\,86 \text{ M}$$

$$[A^-] = F_{A^-} + [H^+] = 0.014\,1 \text{ M}$$

In this example, HA is too strong and the concentrations are too low for HA and A^- to be equal to their formal concentrations.

Test Yourself Find pH if $pK_a = 3.00$ instead of 2.00. Does the answer make sense? (***Answer:*** 3.07)

The Henderson-Hasselbalch equation (with activity coefficients) is *always* true, because it is just a rearrangement of the K_a equilibrium expression. Approximations that are not always true are the statements $[HA] \approx F_{HA}$ and $[A^-] \approx F_{A^-}$.

In summary, a buffer consists of a mixture of a weak acid and its conjugate base. The buffer is most useful when $pH \approx pK_a$. Over a reasonable range of concentration, the pH of a buffer is nearly independent of concentration. A buffer resists changes in pH because it reacts with added acids or bases. If too much acid or base is added, the buffer will be consumed and will no longer resist changes in pH.

EXAMPLE **Excel's Goal Seek Tool and Naming of Cells**

We saw at the end of Chapter 7 that Goal Seek solves numerical equations. In setting up Equation 8-22, we made the (superb) approximation $[H^+] >> [OH^-]$ and neglected $[OH^-]$. With Goal Seek, it is easy to use Equations 8-20 and 8-21 without approximations:

$$K_a = \frac{[H^+][A^-]}{[HA]} = \frac{[H^+](F_{A^-} + [H^+] - [OH^-])}{F_{HA} - [H^+] + [OH^-]} \quad \textbf{(8-23)}$$

The spreadsheet illustrates Goal Seek and the naming of cells to make formulas more meaningful. In column A, enter labels for K_a, K_w, F_{HA}, F_A (= F_{A^-}), H (= $[H^+]$), and OH (= $[OH^-]$). Write numerical values for K_a, K_w, F_{HA}, and F_{A^-} in B1:B4. In cell B5, enter a *guess* for $[H^+]$.

	A	B	C	D	E
1	Ka =	0.01		Reaction quotient	
2	Kw =	1.00E-1.4		for Ka =	
3	FHA =	0.01		[H+][A–]/[HA] =	
4	FA =	0.01		0.001222222	
5	H =	1.000E-03	<–Vary H with Goal Seek until D4 = Ka		
6	OH = Kw/H =	1E-11		D4 = H*(FA + H – OH)/(FHA – H + OH)	
7	pH = –log(H) =	3.00			

Now we want to name cells B1 through B6. In Excel 2007, select cell B1, go to the Formula ribbon, and click on Define Name. The dialog box will ask if you want to use the name "Ka" that appears in cell A1. If you like this name, click OK. Now when you select cell B1, the name box at the upper left of the spreadsheet displays Ka instead of B1. In earlier versions of Excel, select cell B1, go to the Insert menu, select Name and then Define. By this procedure, name the other cells in column B "Kw", "FHA", "FA", "H", and "OH". Now when you write a formula referring to cell B2, you can write Kw instead of B2. Kw is an *absolute reference* to cell $B$2.

In cell B6 enter the formula "=Kw/H" and Excel returns the value 1E-11 for $[OH^-]$. The beauty of naming cells is that "=Kw/H" is easier to understand than "=$B$2/$B$5". In cell B7, enter the formula "= −log(H)" for the pH.

In cell D4, write "=H*(FA+H-OH)/(FHA-H+OH)", which is the quotient in Equation 8-23. Excel returns the value 0.001 222 based on the guess $[H^+] = 0.001$ in cell B5.

Now use Goal Seek to vary $[H^+]$ in cell B5 until the reaction quotient in cell D4 equals 0.01, which is the value of K_a. Before using Goal Seek in Excel 2007, click the Microsoft Office button at the top left of the spreadsheet, click on Excel Options and then on Formulas. Set Maximum Change to a small number such as 1e-20 to find an answer with high precision. To execute Goal Seek, go to the Data ribbon, click on What-If Analysis and then on Goal Seek. In the dialog box, Set cell D4 To value 0.01 By changing cell B5. Click OK and Excel varies cell B5 until the value $[H^+] = 4.142 \times 10^{-3}$ gives a reaction quotient of 0.01 in cell D4. Different guesses for H might give negative solutions or might not reach a solution. Only one positive value of H satisfies Equation 8-23. For earlier versions of Excel, in the Tools menu, select Options and go to Calculation. Set Maximum Change to 1e-20. In the Tools menu, select Goal Seek and proceed as described above.

Test Yourself Find H if $K_a = 0.001$. (***Answer:*** $H = 8.44 \times 10^{-4}$, pH = 3.07)

Terms to Understand

acid dissociation constant, K_a
base hydrolysis constant, K_b
buffer
buffer capacity
conjugate acid-base pair
fraction of association, α (of a base)
fraction of dissociation, α (of an acid)
Henderson-Hasselbalch equation
p*K*
strong acid
strong base
weak acid
weak base
weak electrolyte

Summary

Strong acids or bases. For practical concentrations ($\gtrsim 10^{-6}$ M), pH or pOH is obtained directly from the formal concentration of acid or base. When the concentration is near 10^{-7} M, we use the systematic treatment of equilibrium to calculate pH. At still lower concentrations, the pH is 7.00, set by autoprotolysis of the solvent.

Weak acids. For the reaction $HA \rightleftharpoons H^+ + A^-$, we set up and solve the equation $K_a = x^2/(F - x)$, where $[H^+] = [A^-] = x$, and $[HA] = F - x$. The fraction of dissociation is given by $\alpha = [A^-]/([HA] + [A^-]) = x/F$. The term pK_a is defined as $pK_a = -\log K_a$.

Weak bases. For the reaction $B + H_2O \rightleftharpoons BH^+ + OH^-$, we set up and solve the equation $K_b = x^2/(F - x)$, where $[OH^-] = [BH^+] = x$, and $[B] = F - x$. The conjugate acid of a weak base is a weak acid, and the conjugate base of a weak acid is a weak base. For a conjugate acid-base pair, $K_a \cdot K_b = K_w$.

Buffers. A buffer is a mixture of a weak acid and its conjugate base. It resists changes in pH because it reacts with added acid or base. The pH is given by the Henderson-Hasselbalch equation:

$$pH = pK_a + \log \frac{[A^-]}{[HA]}$$

where pK_a applies to the species in the denominator. The concentrations of HA and A^- are essentially unchanged from those used to prepare the solution. The pH of a buffer is nearly independent of dilution, but buffer capacity increases as the concentration of buffer increases. The maximum buffer capacity is at $pH = pK_a$, and the useful range is $pH = pK_a \pm 1$.

The conjugate base of a weak acid is a weak base. The weaker the acid, the stronger the base. However, if one member of a conjugate pair is weak, so is its conjugate. The relation between K_a for an acid and K_b for its conjugate base in aqueous solution is $K_a \cdot K_b = K_w$. When a strong acid (or base) is added to a weak base (or acid), they react nearly completely.

Exercises

8-A. Using activity coefficients correctly, find the pH of 1.0×10^{-2} M NaOH.

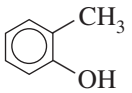
8-B. (Without activities), calculate the pH of

(a) 1.0×10^{-8} M HBr

(b) 1.0×10^{-8} M H_2SO_4 (H_2SO_4 dissociates completely to $2H^+$ plus SO_4^{2-} at this low concentration.)

8-C. What is the pH of a solution prepared by dissolving 1.23 g of 2-nitrophenol (FM 139.11) in 0.250 L?

8-D. The pH of 0.010 M *o*-cresol is 6.16. Find pK_a for this weak acid.



o-Cresol

8-E. Calculate the limiting value of the fraction of dissociation (α) of a weak acid ($pK_a = 5.00$) as the concentration of HA approaches 0. Repeat the same calculation for $pK_a = 9.00$.

8-F. Find the pH of 0.050 M sodium butanoate (the sodium salt of butanoic acid, also called butyric acid).

8-G. The pH of 0.10 M ethylamine is 11.82.

(a) Without referring to Appendix G, find K_b for ethylamine.

(b) Using results from part **(a)**, calculate the pH of 0.10 M ethylammonium chloride.

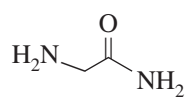
8-H. Which of the following bases would be most suitable for preparing a buffer of pH 9.00? (i) NH_3 (ammonia, $K_b = 1.76 \times 10^{-5}$); (ii) $C_6H_5NH_2$ (aniline, $K_b = 3.99 \times 10^{-10}$); (iii) H_2NNH_2 (hydrazine, $K_b = 1.05 \times 10^{-6}$); (iv) C_5H_5N (pyridine, $K_b = 1.58 \times 10^{-9}$)

8-I. A solution contains 63 different conjugate acid-base pairs. Among them is acrylic acid and acrylate ion, with the equilibrium ratio [acrylate]/[acrylic acid] = 0.75. What is the pH of the solution?

$H_2C{=}CHCO_2H$ $\quad pK_a = 4.25$

Acrylic acid

8-J. (a) Find the pH of a solution prepared by dissolving 1.00 g of glycine amide hydrochloride (Table 8-2) plus 1.00 g of glycine amide in 0.100 L.



Glycine amide
$C_2H_6N_2O$
FM 74.08

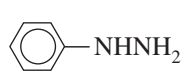
(b) How many grams of glycine amide should be added to 1.00 g of glycine amide hydrochloride to give 100 mL of solution with pH 8.00?

(c) What would be the pH if the solution in part **(a)** were mixed with 5.00 mL of 0.100 M HCl?

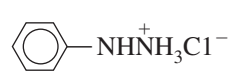
(d) What would be the pH if the solution in part **(c)** were mixed with 10.00 mL of 0.100 M NaOH?

(e) What would be the pH if the solution in part **(a)** were mixed with 90.46 mL of 0.100 M NaOH? (This is exactly the quantity of NaOH required to neutralize the glycine amide hydrochloride.)

8-K. A solution with an ionic strength of 0.10 M containing 0.010 0 M phenylhydrazine has a pH of 8.13. Using activity coefficients correctly, find pK_a for the phenylhydrazinium ion found in phenylhydrazine hydrochloride. Assume that $\gamma_{BH^+} = 0.80$.



Phenylhydrazine
B



Phenylhydrazine hydrochloride
BH^+Cl^-

8-L. Use the Goal Seek spreadsheet at the end of the chapter to find the pH of 1.00 L of solution containing 0.030 mol HA ($pK_a = 2.50$) and 0.015 mol NaA. What would the pH be with the approximations $[HA] = 0.030$ and $[A^-] = 0.015$?

Problems

Strong Acids and Bases

8-1. Why doesn't water dissociate to produce 10^{-7} M H^+ and 10^{-7} M OH^- when some HBr is added?

8-2. Calculate the pH of **(a)** 1.0×10^{-3} M HBr; **(b)** 1.0×10^{-2} M KOH.

8-3. Calculate the pH of 5.0×10^{-8} M $HClO_4$. What fraction of the total H^+ in this solution is derived from dissociation of water?

8-4. (a) The measured pH of 0.100 M HCl at 25°C is 1.092. From this information, calculate the activity coefficient of H^+ and compare your answer with that in Table 7-1.

(b) The measured pH of 0.010 0 M HCl + 0.090 0 M KCl at 25°C is 2.102. From this information, calculate the activity coefficient of H^+ in this solution.

(c) The ionic strengths of the solutions in parts (**a**) and (**b**) are the same. What can you conclude about the dependence of activity coefficients on the particular ions in a solution?

Weak-Acid Equilibria

8-5. Write the chemical reaction whose equilibrium constant is

(a) K_a for benzoic acid, $C_6H_5CO_2H$

(b) K_b for benzoate ion, $C_6H_5CO_2^-$

(c) K_b for aniline, $C_6H_5NH_2$

(d) K_a for anilinium ion, $C_6H_5NH_3^+$

8-6. Find the pH and fraction of dissociation (α) of a 0.100 M solution of the weak acid HA with $K_a = 1.00 \times 10^{-5}$.

8-7. $BH^+ClO_4^-$ is a salt formed from the base B ($K_b = 1.00 \times 10^{-4}$) and perchloric acid. It dissociates into BH^+, a weak acid, and ClO_4^-, which is neither an acid nor a base. Find the pH of 0.100 M $BH^+ClO_4^-$.

8-8. Find the pH and concentrations of $(CH_3)_3N$ and $(CH_3)_3NH^+$ in a 0.060 M solution of trimethylammonium chloride.

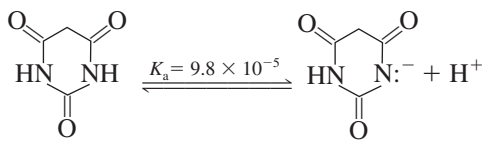
8-9. Use the reaction quotient, Q, to explain why the fraction of dissociation of weak acid, HA, increases when the solution is diluted by a factor of 2.

8-10. *When is a weak acid weak and when is a weak acid strong?* Show that the weak acid HA will be 92% dissociated when dissolved in water if the formal concentration is one-tenth of K_a ($F = K_a/10$). Show that the fraction of dissociation is 27% when $F = 10K_a$. At what formal concentration will the acid be 99% dissociated? Compare your answer with the left-hand curve in Figure 8-2.

8-11. A 0.045 0 M solution of benzoic acid has a pH of 2.78. Calculate pK_a for this acid.

8-12. A 0.045 0 M solution of HA is 0.60% dissociated. Calculate pK_a for this acid.

8-13. Barbituric acid dissociates as follows:



Barbituric acid HA — A^-

(a) Calculate the pH and fraction of dissociation of $10^{-2.00}$ M barbituric acid.

(b) Calculate the pH and fraction of dissociation of $10^{-10.00}$ M barbituric acid.

8-14. Using activity coefficients, find the pH and fraction of dissociation of 50.0 mM hydroxybenzene (phenol) in 0.050 M LiBr. Take the size of $C_6H_5O^-$ to be 600 pm.

8-15. Cr^{3+} is acidic by virtue of the hydrolysis reaction

$$Cr^{3+} + H_2O \overset{K_{a1}}{\rightleftharpoons} Cr(OH)^{2+} + H^+$$

[Further reactions produce $Cr(OH)_2^+$, $Cr(OH)_3$, and $Cr(OH)_4^-$.] Find the value of K_{a1} in Figure 6-8. Considering only the K_{a1} reaction, find the pH of 0.010 M $Cr(ClO_4)_3$. What fraction of chromium is in the form $Cr(OH)^{2+}$?

8-16. From the dissociation constant of HNO_3 at 25°C in Box 8-1, find the percent dissociated in 0.100 M HNO_3 and in 1.00 M HNO_3.

8-17. *Excel Goal Seek*. Solve the equation $x^2/(F - x) = K$ by using Goal Seek. Guess a value of x in cell A4 and evaluate $x^2/(F - x)$ in cell B4. Use Goal Seek to vary the value of x until $x^2/(F - x)$ is equal to K. Use your spreadsheet to check your answer to Problem 8-6.

	A	B
1	Using Excel Goal Seek	
2		
3	x =	x^2/(F-x) =
4	0.01	1.1111E-03
5	F =	
6	0.1	

Weak-Base Equilibria

8-18. Covalent compounds generally have higher vapor pressure than ionic compounds. The "fishy" smell of fish arises from amines in the fish. Explain why squeezing lemon (which is acidic) onto fish reduces the fishy smell (and taste).

8-19. Find the pH and fraction of association (α) of a 0.100 M solution of the weak base B with $K_b = 1.00 \times 10^{-5}$.

8-20. Find the pH and concentrations of $(CH_3)_3N$ and $(CH_3)_3NH^+$ in a 0.060 M solution of trimethylamine.

8-21. Find the pH of 0.050 M NaCN.

8-22. Calculate the fraction of association (α) for 1.00×10^{-1}, 1.00×10^{-2}, and 1.00×10^{-12} M sodium acetate. Does α increase or decrease with dilution?

8-23. A 0.10 M solution of a base has pH = 9.28. Find K_b.

8-24. A 0.10 M solution of a base is 2.0% hydrolyzed ($\alpha = 0.020$). Find K_b.

8-25. Show that the limiting fraction of association of a base in water, as the concentration of base approaches 0, is $\alpha = 10^7 K_b / (1 + 10^7 K_b)$. Find the limiting value of α for $K_b = 10^{-4}$ and for $K_b = 10^{-10}$.

Buffers

8-26. Describe how to prepare 100 mL of 0.200 M acetate buffer, pH 5.00, starting with pure liquid acetic acid and solutions containing ~3 M HCl and ~3 M NaOH.

8-27. Why is the pH of a buffer nearly independent of concentration?

8-28. Why does buffer capacity increase as the concentration of buffer increases?

8-29. Why does buffer capacity increase as a solution becomes very acidic (pH ≈ 1) or very basic (pH ≈ 13)?

8-30. Why does the buffer capacity reach a maximum when $pH = pK_a$?

8-31. Explain the following statement: The Henderson-Hasselbalch equation (with activity coefficients) is *always* true; what may not be correct are the values of $[A^-]$ and [HA] that we choose to use in the equation.

8-32. Which of the following acids would be most suitable for preparing a buffer of pH 3.10? (i) hydrogen peroxide; (ii) propanoic acid; (iii) cyanoacetic acid; (iv) 4-aminobenzenesulfonic acid.

8-33. A buffer was prepared by dissolving 0.100 mol of the weak acid HA ($K_a = 1.00 \times 10^{-5}$) plus 0.050 mol of its conjugate base Na^+A^- in 1.00 L. Find the pH.

8-34. Write the Henderson-Hasselbalch equation for a solution of formic acid. Calculate the quotient $[HCO_2^-]/[HCO_2H]$ at **(a)** pH 3.000; **(b)** pH 3.744; **(c)** pH 4.000.

8-35. Calculate the quotient $[HCO_2^-]/[HCO_2H]$ at pH 3.744 if the ionic strength is 0.1 M by using the effective equilibrium constant listed for $\mu = 0.1$ in Appendix G.

8-36. Given that pK_b for nitrite ion (NO_2^-) is 10.85, find the quotient $[HNO_2]/[NO_2^-]$ in a solution of sodium nitrite at **(a)** pH 2.00; **(b)** pH 10.00.

8-37. (a) Would you need NaOH or HCl to bring the pH of 0.050 0 M HEPES (Table 8-2) to 7.45?

(b) Describe how to prepare 0.250 L of 0.050 0 M HEPES, pH 7.45.

8-38. How many milliliters of 0.246 M HNO_3 should be added to 213 mL of 0.006 66 M 2,2′-bipyridine to give a pH of 4.19?

8-39. (a) Write the chemical reactions whose equilibrium constants are K_b and K_a for imidazole and imidazole hydrochloride, respectively.

(b) Calculate the pH of a solution prepared by mixing 1.00 g of imidazole with 1.00 g of imidazole hydrochloride and diluting to 100.0 mL.

(c) Calculate the pH of the solution if 2.30 mL of 1.07 M $HClO_4$ are added.

(d) How many milliliters of 1.07 M $HClO_4$ should be added to 1.00 g of imidazole to give a pH of 6.993?

8-40. Calculate the pH of a solution prepared by mixing 0.080 0 mol of chloroacetic acid plus 0.040 0 mol of sodium chloroacetate in 1.00 L of water.

(a) First do the calculation by assuming that the concentrations of HA and A^- equal their formal concentrations.

(b) Then do the calculation, using the real values of [HA] and $[A^-]$ in the solution.

(c) Using first your head, and then the Henderson-Hasselbalch equation, find the pH of a solution prepared by dissolving all the following compounds in one beaker containing a total volume of 1.00 L: 0.180 mol $ClCH_2CO_2H$, 0.020 mol $ClCH_2CO_2Na$, 0.080 mol HNO_3, and 0.080 mol $Ca(OH)_2$. Assume that $Ca(OH)_2$ dissociates completely.

8-41. Calculate how many milliliters of 0.626 M KOH should be added to 5.00 g of MOBS (Table 8-2) to give a pH of 7.40.

8-42. (a) Use Equations 8-20 and 8-21 to find the pH and concentrations of HA and A^- in a solution prepared by mixing 0.002 00 mol of acetic acid plus 0.004 00 mol of sodium acetate in 1.00 L of water.

(b) After working part **(a)** by hand, use Excel Goal Seek to find the same answers.

8-43. (a) Calculate the pH of a solution prepared by mixing 0.010 0 mol of the base B ($K_b = 10^{-2.00}$) with 0.020 0 mol of BH^+Br^- and diluting to 1.00 L. First calculate the pH by assuming [B] = 0.010 0 and $[BH^+]$ = 0.020 0 M. Compare this answer with the pH calculated without making such an assumption.

(b) After working part **(a)** by hand, use Excel Goal Seek to find the same answers.

8-44. *Effect of ionic strength on* pK_a. K_a for the $H_2PO_4^-/HPO_4^{2-}$ buffer is

$$K_a = \frac{[HPO_4^{2-}][H^+]\gamma_{HPO_4^{2-}}\gamma_{H^+}}{[H_2PO_4^-]\gamma_{H_2PO_4^-}} = 10^{-7.20}$$

If you mix a 1:1 mole ratio of $H_2PO_4^-$ and HPO_4^{2-} at 0 ionic strength, the pH is 7.20. Using activity coefficients from Table 7-1, calculate the pH of a 1:1 mixture of $H_2PO_4^-$ and HPO_4^{2-} at an ionic strength of 0.10. Remember that $pH = -\log \mathcal{A}_{H^+} = -\log[H^+]\gamma_{H^+}$.

8-45. *Systematic treatment of equilibrium.* The acidity of Al^{3+} is determined by the following reactions. Write the equations needed to find the pH of $Al(ClO_4)_3$ at a formal concentration F.

$$Al^{3+} + H_2O \overset{\beta_1}{\rightleftharpoons} AlOH^{2+} + H^+$$

$$Al^{3+} + 2H_2O \overset{\beta_2}{\rightleftharpoons} Al(OH)_2^+ + 2H^+$$

$$2Al^{3+} + 2H_2O \overset{K_{22}}{\rightleftharpoons} Al_2(OH)_2^{4+} + 2H^+$$

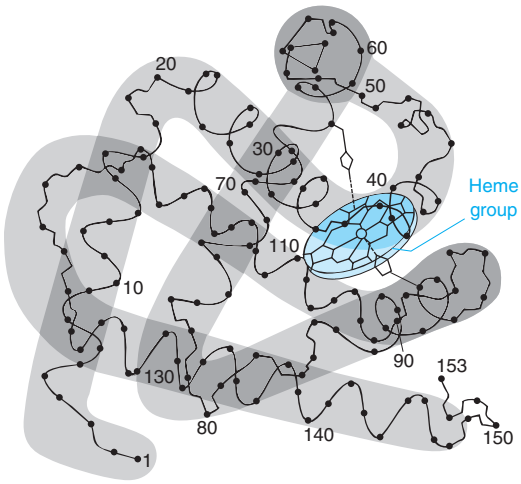
$$Al^{3+} + 3H_2O \overset{\beta_3}{\rightleftharpoons} Al(OH)_3(aq) + 3H^+$$

$$Al^{3+} + 4H_2O \overset{\beta_4}{\rightleftharpoons} Al(OH)_4^- + 4H^+$$

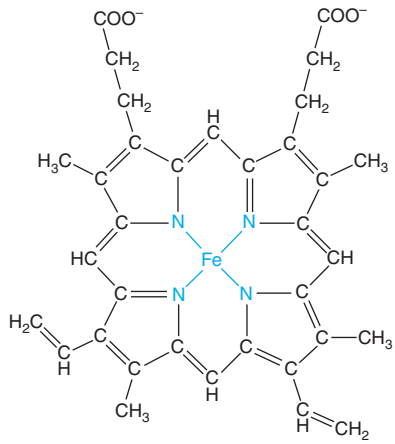
$$3Al^{3+} + 4H_2O \overset{K_{43}}{\rightleftharpoons} Al_3(OH)_4^{5+} + 4H^+$$

9 Polyprotic Acid-Base Equilibria

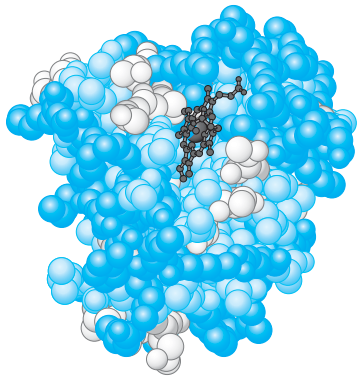
PROTEINS ARE POLYPROTIC ACIDS AND BASES



(*a*) Myoglobin backbone



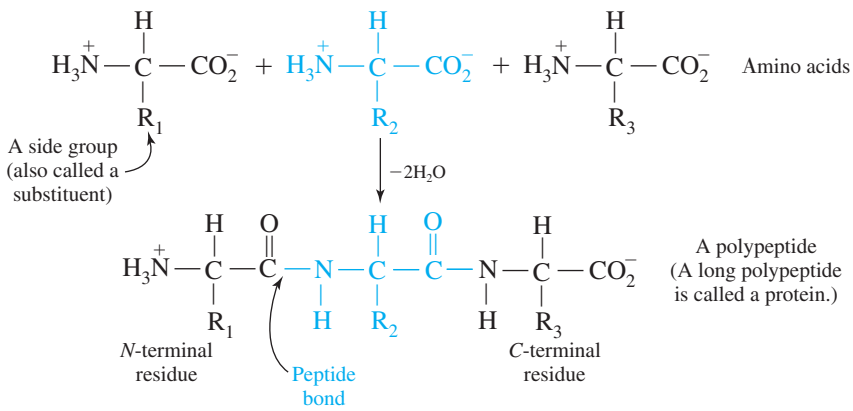
(*b*) Heme structure



(*c*) Space-filling model of myoglobin

(*a*) Amino acid backbone of the protein myoglobin, which stores oxygen in muscle tissue. Substituents (R groups from Table 9-1) are omitted for clarity. The flat *heme* group at the right side of the protein contains an iron atom that can bind O_2, CO, and other small molecules. [From M. F. Perutz, "The Hemoglobin Molecule." Copyright © 1964 by Scientific American, Inc.] (*b*) Structure of heme. (*c*) Space-filling model of myoglobin, with charged acidic and basic amino acids in dark color and *hydrophobic* (nonpolar, water-repelling) amino acids in light color. White amino acids are *hydrophilic* (polar, water-loving), but not charged. The surface of this water-soluble protein is dominated by charged and hydrophilic groups. [From J. M. Berg, J. L. Tymoczko, and L. Stryer, *Biochemistry*, 5th ed. (New York: Freeman, 2002).]

Proteins perform biological functions such as structural support, catalysis of chemical reactions, immune response to foreign substances, transport of molecules across membranes, and control of genetic expression. The three-dimensional structure and function of a protein is determined by the sequence of *amino acids* from which the protein is made. The diagram below shows how amino acids are connected to make a *polypeptide*. Of the 20 common amino acids, three have basic substituents and four have acidic substituents. Myoglobin, shown above, folds into several helical (spiral) regions that control access of oxygen and other small molecules to the heme group, whose function is to store O_2 in muscle cells. Of the 153 amino acids in sperm-whale myoglobin, 35 have basic side groups and 23 are acidic.

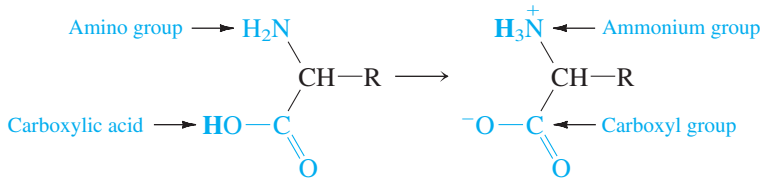


Polyprotic acids and bases are those that can donate or accept more than one proton. After we have studied **diprotic** systems (with two acidic or basic sites), the extension to three or more acidic sites is straightforward. Then we step back and take a qualitative look at the big picture and think about which species are dominant at any given pH.

9-1 Diprotic Acids and Bases

Amino acids from which proteins are built have an acidic carboxylic acid group, a basic amino group, and a variable substituent designated R. The carboxyl group is a stronger acid than the ammonium group, so the nonionized form rearranges spontaneously to the **zwitterion,** which has both positive and negative sites:

A *zwitterion* is a molecule with both positive and negative charges.



Zwitterion

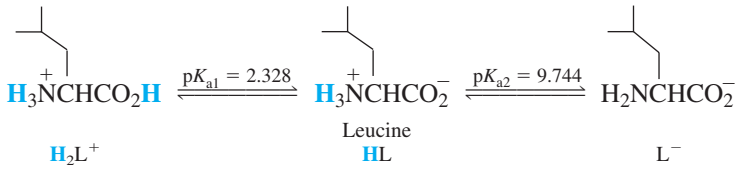
pK_a values of amino acids in living cells are somewhat different from those in Table 9-1 because physiologic temperature is not 25°C and the ionic strength is not 0.

At low pH, both the ammonium group and the carboxyl group are protonated. At high pH, neither is protonated. Acid dissociation constants of amino acids are listed in Table 9-1, where each compound is drawn in its fully protonated form.

Zwitterions are stabilized in solution by interactions of $—NH_3^+$ and $—CO_2^-$ with water. The zwitterion is also the stable form of the amino acid in the solid state, where hydrogen bonding from $—NH_3^+$ to $—CO_2^-$ of neighboring molecules occurs. In the gas phase, there are no neighbors to stabilize the charges, so the nonionized structure in Figure 9-1, with intramolecular hydrogen bonding from $—NH_2$ to a carboxyl oxygen, predominates.

Our discussion will focus on the amino acid leucine, designated HL.

The substituent R in leucine is an isobutyl group: $(CH_3)_2CHCH_2—$



The equilibrium constants refer to the following reactions:

We customarily omit the subscript "a" in K_{a1} and K_{a2}. We will always write the subscript "b" in K_{b1} and K_{b2}.

Diprotic acid:

$$H_2L^+ \rightleftharpoons HL + H^+ \qquad K_{a1} \equiv K_1 \qquad (9\text{-}1)$$

$$HL \rightleftharpoons L^- + H^+ \qquad K_{a2} \equiv K_2 \qquad (9\text{-}2)$$

Diprotic base:

$$L^- + H_2O \rightleftharpoons HL + OH^- \qquad K_{b1} \qquad (9\text{-}3)$$

$$HL + H_2O \rightleftharpoons H_2L^+ + OH^- \qquad K_{b2} \qquad (9\text{-}4)$$

Recall that the relations between the acid and base equilibrium constants are

Relations between K_a and K_b:

$$K_{a1} \cdot K_{b2} = K_w \qquad (9\text{-}5)$$

$$K_{a2} \cdot K_{b1} = K_w \qquad (9\text{-}6)$$

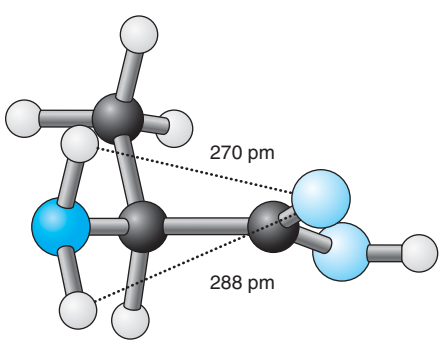


FIGURE 9-1 Gas-phase structure of alanine, determined by microwave spectroscopy. [From S. Blanco, A. Lesarri, J. C. López, and J. L. Alonso, "The Gas-Phase Structure of Alanine," *J. Am. Chem. Soc.* **2004**, *126*, 11675.]

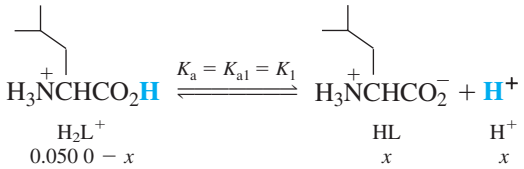
We now set out to calculate the pH and composition of individual solutions of 0.050 0 M H_2L^+, 0.050 0 M HL, and 0.050 0 M L^-. Our methods are general. They do not depend on the charge type of the acids and bases. That is, *we would use the same procedure to find the pH of the diprotic* H_2A, where A is anything, or H_2L^+, where HL is leucine.

The Acidic Form, H_2L^+

Leucine hydrochloride contains the protonated species, H_2L^+, which can dissociate twice (Reactions 9-1 and 9-2). Because $K_1 = 4.70 \times 10^{-3}$, H_2L^+ is a weak acid. HL is an even weaker acid, because $K_2 = 1.80 \times 10^{-10}$. It appears that the H_2L^+ will dissociate only partly, and the resulting HL will hardly dissociate at all. For this reason, we make the (superb) approximation that a solution of H_2L^+ behaves as a monoprotic acid, with $K_a = K_1$.

With this approximation, finding the pH of 0.050 0 M H_2L^+ is easy.

H_2L^+ can be treated as monoprotic, with $K_a = K_{a1}$.



$$K_a = K_1 = 4.70 \times 10^{-3}$$

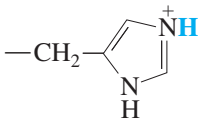
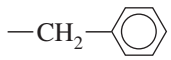
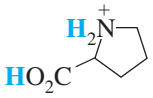
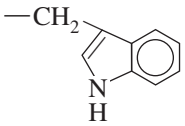
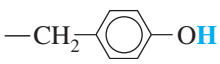
$$\frac{x^2}{F - x} = K_a \Rightarrow x = 1.32 \times 10^{-2}\ M$$ Solve for x with the quadratic equation.

$$[HL] = x = 1.32 \times 10^{-2}\ M$$

$$[H^+] = x = 1.32 \times 10^{-2}\ M \Rightarrow pH = 1.88$$

$$[H_2L^+] = F - x = 3.68 \times 10^{-2}\ M$$

TABLE 9-1 Acid dissociation constants of amino acids

Amino acid[a]	Substituent[a]	Carboxylic acid[b] pK_a	Ammonium[b] pK_a	Substituent[b] pK_a	Formula mass
Alanine (A)	$—CH_3$	2.344	9.868		89.09
Arginine (R)	$—CH_2CH_2CH_2NHC(=NH_2^+)NH_2$	1.823	8.991	(12.1[c])	174.20
Asparagine (N)	$—CH_2C(=O)NH_2$	2.16[c]	8.73[c]		132.12
Aspartic acid (D)	$—CH_2CO_2H$	1.990	10.002	3.900	133.10
Cysteine (C)	$—CH_2SH$	(1.7)	10.74	8.36	121.16
Glutamic acid (E)	$—CH_2CH_2CO_2H$	2.16	9.96	4.30	147.13
Glutamine (Q)	$—CH_2CH_2C(=O)NH_2$	2.19[c]	9.00[c]		146.15
Glycine (G)	$—H$	2.350	9.778		75.07
Histidine (H)		(1.6)	9.28	5.97	155.16
Isoleucine (I)	$—CH(CH_3)(CH_2CH_3)$	2.318	9.758		131.17
Leucine (L)	$—CH_2CH(CH_3)_2$	2.328	9.744		131.17
Lysine (K)	$—CH_2CH_2CH_2CH_2NH_3^+$	(1.77)	9.07	10.82	146.19
Methionine (M)	$—CH_2CH_2SCH_3$	2.18[c]	9.08[c]		149.21
Phenylalanine (F)		2.20	9.31		165.19
Proline (P)	 Structure of entire amino acid	1.952	10.640		115.13
Serine (S)	$—CH_2OH$	2.187	9.209		105.09
Threonine (T)	$—CH(CH_3)(OH)$	2.088	9.100		119.12
Tryptophan (W)		2.37[c]	9.33[c]		204.23
Tyrosine (Y)		2.41[c]	8.67[c]	11.01[c]	181.19
Valine (V)	$—CH(CH_3)_2$	2.286	9.719		117.15

*a. The acidic protons are shown in **bold** type. Each amino acid is written in its fully protonated form. Standard abbreviations are shown in parentheses.*
b. pK_a values refer to 25°C and zero ionic strength unless marked by c. Values considered to be uncertain are enclosed in parentheses. Appendix G gives pK_a for $\mu = 0.1$ M.
c. For these entries, the ionic strength is 0.1 M, and the constant refers to a product of concentrations instead of activities.

SOURCE: *A. E. Martell and R. J. Motekaitis, NIST Database 46 (Gaithersburg, MD: National Institute of Standards and Technology, 2001).*

What is the concentration of L^- in the solution? We have already assumed that it is very small, but it cannot be 0. We can calculate $[L^-]$ from the K_2 equation, with the concentrations of HL and H^+ that we just computed.

$$K_2 = \frac{[H^+][L^-]}{[HL]} \Rightarrow [L^-] = \frac{K_2[HL]}{[H^+]} \tag{9-7}$$

$$[L^-] = \frac{(1.80 \times 10^{-10})(1.32 \times 10^{-2})}{(1.32 \times 10^{-2})} = 1.80 \times 10^{-10}\ \text{M}\ (= K_2)$$

The approximation $[H^+] \approx [HL]$ reduces Equation 9-7 to $[L^-] = K_2$.

Our approximation is confirmed by this last result. The concentration of L^- is about eight orders of magnitude smaller than that of HL. The dissociation of HL is indeed negligible relative to the dissociation of H_2L^+. For most diprotic acids, K_1 is sufficiently larger than K_2 for this approximation to be valid. Even if K_2 were just 10 times less than K_1, $[H^+]$ calculated by ignoring the second ionization would be in error by only 4%. The error in pH would be only 0.01 pH unit. In summary, *a solution of a diprotic acid behaves like a solution of a monoprotic acid, with* $K_a = K_1$.

Dissolved carbon dioxide is one of the most important diprotic acids in Earth's ecosystem. Box 9-1 describes imminent danger to the entire ocean food chain as a result of increasing atmospheric CO_2 dissolving in the oceans. Reaction A in Box 9-1 lowers the concentration of CO_3^{2-} in the oceans. As a result, $CaCO_3$ shells and skeletons of creatures at the bottom of the food chain will dissolve by Reaction B. This effect is far more certain than the effects of atmospheric CO_2 on Earth's climate.

The Basic Form, L^-

The species L^-, found in a salt such as sodium leucinate, can be prepared by treating leucine (HL) with an equimolar quantity of NaOH. Dissolving sodium leucinate in water gives a solution of L^-, the fully basic species. K_b values for this dibasic anion are

$$L^- + H_2O \rightleftharpoons HL + OH^- \qquad K_{b1} = K_w/K_{a2} = 5.55 \times 10^{-5}$$

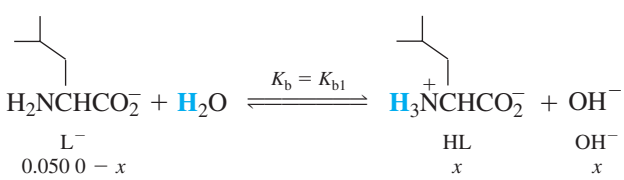
$$HL + H_2O \rightleftharpoons H_2L^+ + OH^- \qquad K_{b2} = K_w/K_{a1} = 2.13 \times 10^{-12}$$

Hydrolysis is the reaction of anything with water. Specifically, the reaction $L^- + H_2O \rightleftharpoons HL + OH^-$ is called hydrolysis.

K_{b1} tells us that L^- will not *hydrolyze* (react with water) very much to give HL. Furthermore, K_{b2} tells us that the resulting HL is such a weak base that hardly any further reaction to make H_2L^+ will occur.

We therefore treat L^- as a monobasic species, with $K_b = K_{b1}$. The results of this (fantastic) approximation are outlined as follows:

L^- can be treated as monobasic, with $K_b = K_{b1}$.



$$K_b = K_{b1} = \frac{K_w}{K_{a2}} = 5.55 \times 10^{-5}$$

$$\frac{x^2}{F - x} = 5.55 \times 10^{-5} \Rightarrow x = 1.64 \times 10^{-3}\ \text{M}$$

$$[HL] = x = 1.64 \times 10^{-3}\ \text{M}$$

$$[H^+] = K_w/[OH^-] = K_w/x = 6.11 \times 10^{-12}\ \text{M} \Rightarrow \text{pH} = 11.21$$

$$[L^-] = F - x = 4.84 \times 10^{-2}\ \text{M}$$

The concentration of H_2L^+ can be found from the K_{b2} (or K_{a1}) equilibrium.

$$K_{b2} = \frac{[H_2L^+][OH^-]}{[HL]} = \frac{[H_2L^+]x}{x} = [H_2L^+]$$

We find that $[H_2L^+] = K_{b2} = 2.13 \times 10^{-12}$ M, and the approximation that $[H_2L^+]$ is insignificant relative to [HL] is well justified. In summary, if there is any reasonable separation between K_{a1} and K_{a2} (and, therefore, between K_{b1} and K_{b2}), *the fully basic form of a diprotic acid can be treated as monobasic, with* $K_b = K_{b1}$.

BOX 9-1 Carbon Dioxide in the Air and Ocean

The graph on the opening page of Chapter 0 shows that atmospheric CO_2 has oscillated between about 180 and 280 ppm by volume (μL/L) for 800 000 years. Burning of fossil fuel and destruction of Earth's forests since 1800 caused an exponential increase in CO_2 that threatens to alter Earth's climate in your lifetime.

Increasing atmospheric CO_2 increases the concentration of CO_2 dissolved in the ocean, which consumes carbonate and lowers the pH:[1]

$$CO_2(aq) + H_2O + \underset{\text{Carbonate}}{CO_3^{2-}} \rightleftharpoons \underset{\text{Bicarbonate}}{2HCO_3^-} \qquad \textbf{(A)}$$

The pH of the ocean has already decreased from its preindustrial value of 8.16 to 8.04 today.[2] Without changes in our activities, the pH could be 7.7 by 2100.

Low carbonate concentration promotes dissolution of solid calcium carbonate:

$$\underset{\text{Calcium carbonate}}{CaCO_3(s)} \rightleftharpoons Ca^{2+} + CO_3^{2-} \qquad \textbf{(B)}$$

Le Châtelier's principle tells us that decreasing $[CO_3^{2-}]$ draws the reaction to the right

If $[CO_3^{2-}]$ in the ocean decreases enough, organisms such as plankton and coral with $CaCO_3$ shells or skeletons will not survive.[3] Calcium carbonate has two crystalline forms called calcite and aragonite. Aragonite is more soluble than calcite. Aquatic organisms have either calcite or aragonite in their shells and skeletons.

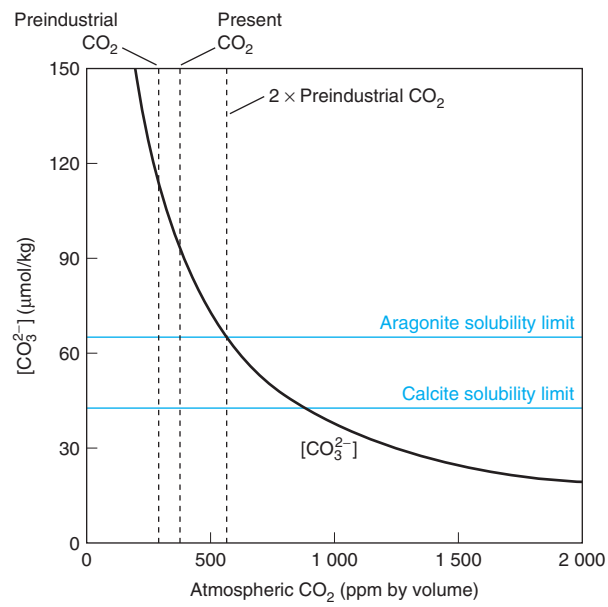
Pteropods are a type of zooplankton also known as winged snails. When pteropods collected from the subarctic Pacific Ocean are kept in water that is less than saturated with aragonite, their shells begin to dissolve within 48 h. Animals such as the pteropod lie at the base of the food chain. Their destruction would reverberate throughout the entire ocean.

Today, ocean surface waters contain more than enough CO_3^{2-} to sustain aragonite and calcite. As atmospheric CO_2 inexorably increases during the twenty-first century, ocean surface waters will become undersaturated with respect to aragonite—killing off organisms that depend on this mineral for their structure. Polar regions will suffer this fate first because CO_2 is more soluble in cold water than in warm water and K_{a1} and K_{a2} at low temperature favor HCO_3^- and $CO_2(aq)$ relative to CO_3^{2-} (Problem 9-12).

Panel *b* shows the predicted concentration of CO_3^{2-} in polar ocean surface water as a function of atmospheric CO_2. The upper horizontal line is the concentration of CO_3^{2-} below which aragonite dissolves. Atmospheric CO_2 is presently near 400 ppm and $[CO_3^{2-}]$ is near 100 μmol/kg of seawater—more than enough to precipitate aragonite or calcite. When atmospheric CO_2 reaches 600 ppm near the middle of the present century, $[CO_3^{2-}]$ will decrease to 60 μmol/kg and creatures with aragonite structures will begin to disappear from polar waters. At still higher atmospheric CO_2 concentration, extinctions will move to lower latitudes and will overtake organisms with calcite structures as well as aragonite structures. *How long will we put CO_2 into the atmosphere to see if these predictions are borne out?*

(*a*)

Pteropods. The shell of a live pteropod begins to dissolve after 48 h in water that is undersaturated with aragonite. [David Wrobel/Visuals Unlimited.]



(*b*)

Calculated $[CO_3^{2-}]$ in polar ocean surface waters as a function of atmospheric CO_2. When $[CO_3^{2-}]$ drops below the upper horizontal line, argonite dissolves. [Adapted from J. C. Orr et al., *Nature* 2005, *437*, 681.[4]] Reference 1 gives equations that allow you to calculate the curve in this figure.

Nature counteracts some changes to mitigate their effects. For example, phytoplankton called coccolithophores are marine organisms with a $CaCO_3$ skeleton several micrometers in diameter. These organisms produce about one-third of all $CaCO_3$ in the ocean. In the past 220 years, as atmospheric CO_2 increased, the average mass of the coccolithophore species *Emiliania huxleyi* has increased by 40%, thereby removing some CO_2 from the ocean.[5] Coccolithophores can mitigate CO_2 increases up to a point. It is not likely that any *calcifying* ($CaCO_3$-producing) marine organism can survive if CO_2 increases to the level where $CaCO_3$ is no longer thermodynamically stable.

A tougher problem.

The Intermediate Form, HL

A solution prepared from leucine, HL, is more complicated than one prepared from either H_2L^+ or L^-, because HL is both an acid and a base.

HL is both an acid and a base.

$$HL \rightleftharpoons H^+ + L^- \qquad K_a = K_{a2} = 1.80 \times 10^{-10} \tag{9-8}$$

$$HL + H_2O \rightleftharpoons H_2L^+ + OH^- \qquad K_b = K_{b2} = 2.13 \times 10^{-12} \tag{9-9}$$

A molecule that can both donate and accept a proton is said to be **amphiprotic.** The acid dissociation reaction (9-8) has a larger equilibrium constant than the base hydrolysis reaction (9-9), so we expect that a solution of leucine will be acidic.

However, we cannot simply ignore Reaction 9-9, even if K_a and K_b differ by several orders of magnitude. Both reactions proceed to nearly equal extent, because H^+ produced in Reaction 9-8 reacts with OH^- from Reaction 9-9, thereby driving Reaction 9-9 to the right.

To treat this case, we resort to the systematic treatment of equilibrium. The procedure is applied to leucine, whose intermediate form (HL) has no net charge. However, the results apply to the intermediate form of *any* diprotic acid, regardless of its charge.

Problem 9-10 leads you through the same derivation for the intermediate form Na^+HA^-.

For Reactions 9-8 and 9-9, the charge balance is

$$[H^+] + [H_2L^+] = [L^-] + [OH^-] \quad \text{or} \quad [H_2L^+] - [L^-] + [H^+] - [OH^-] = 0$$

From the acid dissociation equilibria, we replace $[H_2L^+]$ with $[HL][H^+]/K_1$, and $[L^-]$ with $[HL]K_2/[H^+]$. Also, we can always write $[OH^-] = K_w/[H^+]$. Putting these expressions into the charge balance gives

$$\frac{[HL][H^+]}{K_1} - \frac{[HL]K_2}{[H^+]} + [H^+] - \frac{K_w}{[H^+]} = 0$$

which can be solved for $[H^+]$. First, multiply all terms by $[H^+]$:

$$\frac{[HL][H^+]^2}{K_1} - [HL]K_2 + [H^+]^2 - K_w = 0$$

Then rearrange and factor out $[H^+]^2$:

$$[H^+]^2\left(\frac{[HL]}{K_1} + 1\right) = K_2[HL] + K_w$$

$$[H^+]^2 = \frac{K_2[HL] + K_w}{\dfrac{[HL]}{K_1} + 1}$$

Now multiply the numerator and denominator by K_1 and take the square root:

$$[H^+] = \sqrt{\frac{K_1K_2[HL] + K_1K_w}{K_1 + [HL]}} \tag{9-10}$$

Up to this point, we have made no approximations, except to neglect activity coefficients. We solved for $[H^+]$ in terms of known constants plus the single unknown, [HL]. Where do we proceed from here?

The missing insight!

Just as we are feeling desperate, the Good Chemist again gallops down from the mountains to provide the missing insight: "The major species is HL, because it is both a weak acid and a weak base. Neither Reaction 9-8 nor Reaction 9-9 goes very far. For [HL] in Equation 9-10, you can simply substitute the formal concentration, 0.050 0 M."

Taking the Good Chemist's advice, we write Equation 9-10 in its most useful form.

K_1 and K_2 in this equation are both *acid* dissociation constants (K_{a1} and K_{a2}).

Intermediate form of diprotic acid:

$$[H^+] \approx \sqrt{\frac{K_1K_2F + K_1K_w}{K_1 + F}} \tag{9-11}$$

where F is the formal concentration of HL (= 0.050 0 M in the present case).

At long last, we can calculate the pH of 0.050 0 M leucine:

$$[H^+] = \sqrt{\frac{(4.70 \times 10^{-3})(1.80 \times 10^{-10})(0.050\,0) + (4.70 \times 10^{-3})(1.0 \times 10^{-14})}{4.70 \times 10^{-3} + 0.050\,0}}$$

$$= 8.80 \times 10^{-7}\ \text{M} \Rightarrow \text{pH} = 6.06$$

The concentrations of H_2L^+ and L^- can be found from the K_1 and K_2 equilibria, using $[H^+] = 8.80 \times 10^{-7}$ M and [HL] = 0.050 0 M.

$$[H_2L^+] = \frac{[H^+][HL]}{K_1} = \frac{(8.80 \times 10^{-7})(0.050\,0)}{4.70 \times 10^{-3}} = 9.36 \times 10^{-6}\ \text{M}$$

$$[L^-] = \frac{K_2[HL]}{[H^+]} = \frac{(1.80 \times 10^{-10})(0.050\,0)}{8.80 \times 10^{-7}} = 1.02 \times 10^{-5}\ \text{M}$$

Was the approximation [HL] ≈ 0.050 0 M a good one? It certainly was, because $[H_2L^+]$ (= 9.36×10^{-6} M) and $[L^-]$ (= 1.02×10^{-5} M) are small in comparison with [HL] (≈ 0.050 0 M). Nearly all the leucine remained in the form HL. Note also that $[H_2L^+]$ is nearly equal to $[L^-]$. This result confirms that Reactions 9-8 and 9-9 proceed equally, even though K_a is 84 times bigger than K_b for leucine.

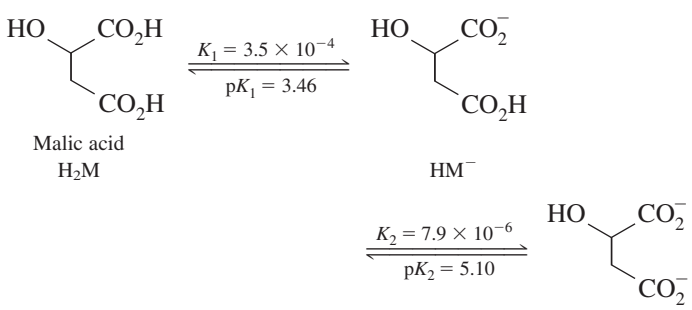
If $[H_2L^+] + [L^-]$ is not much less than [HL] and if you wish to refine your values of $[H_2L^+]$ and $[L^-]$, try the method in Box 9-2.

A summary of results for leucine is given here. Notice the relative concentrations of H_2L^+, HL, and L^- in each solution and notice the pH of each solution.

Solution	pH	$[H^+]$ (M)	$[H_2L^+]$ (M)	[HL] (M)	$[L^-]$ (M)
0.050 0 M H_2A	1.88	1.32×10^{-2}	3.68×10^{-2}	1.32×10^{-2}	1.80×10^{-10}
0.050 0 M HA^-	6.06	8.80×10^{-7}	9.36×10^{-6}	5.00×10^{-2}	1.02×10^{-5}
0.050 0 M HA^{2-}	11.21	6.11×10^{-12}	2.13×10^{-12}	1.64×10^{-3}	4.84×10^{-2}

BOX 9-2 Successive Approximations

The method of *successive approximations* is a good way to deal with difficult equations that do not have simple solutions. For example, Equation 9-11 is not a good approximation when the concentration of the intermediate species of a diprotic acid is not close to F, the formal concentration. This situation arises when K_1 and K_2 are nearly equal and F is small. Consider a solution of 1.00×10^{-3} M HM^-, the intermediate form of malic acid.



For a first approximation, assume that $[HM^-] \approx 1.00 \times 10^{-3}$ M. Plugging this value into Equation 9-10, we calculate first approximations for $[H^+]$, $[H_2M]$, and $[M^{2-}]$.

$$[H^+]_1 = \sqrt{\frac{K_1K_2(0.001\,00) + K_1K_w}{K_1 + (0.001\,00)}} = 4.53 \times 10^{-5}\ \text{M}$$

$$\Rightarrow [H_2M]_1 = \frac{[H^+][HM^-]}{K_1} = \frac{(4.53 \times 10^{-5})(1.00 \times 10^{-3})}{3.5 \times 10^{-4}} = 1.29 \times 10^{-4}\ \text{M}$$

$$[M^{2-}]_1 = \frac{K_2[HM^-]}{[H^+]} = \frac{(7.9 \times 10^{-6})(1.00 \times 10^{-3})}{4.53 \times 10^{-5}} = 1.75 \times 10^{-4}\ \text{M}$$

Clearly, $[H_2M]$ and $[M^{2-}]$ are not negligible relative to F = 1.00×10^{-3} M, so we need to revise our estimate of $[HM^-]$. The mass balance gives us a second approximation:

$$[HM^-]_2 = F - [H_2M]_1 - [M^{2-}]_1 = 0.001\,00 - 0.000\,129 - 0.000\,175 = 0.000\,696\ \text{M}$$

Inserting $[HM^-]_2 = 0.000\,696$ into Equation 9-10 gives

$$[H^+]_2 = \sqrt{\frac{K_1K_2(0.000\,696) + K_1K_w}{K_1 + (0.000\,696)}} = 4.29 \times 10^{-5}\ \text{M}$$

$$\Rightarrow [H_2M]_2 = 8.53 \times 10^{-5}\ \text{M}$$

$$[M^{2-}]_2 = 1.28 \times 10^{-4}\ \text{M}$$

$[H_2M]_2$ and $[M^{2-}]_2$ can be used to calculate a third approximation for $[HM^-]$:

$$[HM^-]_3 = F - [H_2M]_2 - [M^{2-}]_2 = 0.000\,786\ \text{M}$$

Plugging $[HM^-]_3$ into Equation 9-10 gives

$$[H^+]_3 = 4.37 \times 10^{-5}\ \text{M}$$

and the procedure can be repeated to get

$$[H^+]_4 = 4.35 \times 10^{-5}\ \text{M}$$

We are homing in on an estimate of $[H^+]$ in which the precision is already less than 1%. The fourth approximation gives pH = 4.36, compared with pH = 4.34 from the first approximation and pH = 4.28 from the formula pH ≈ $\frac{1}{2}(pK_1 + pK_2)$. Considering the uncertainty in pH measurements, all this calculation was hardly worth the effort. However, the concentration $[HM^-]_5$ is 0.000 768 M, which is 23% less than the original estimate of 0.001 00 M. Successive approximations can be carried out by hand, but the process is more easily and reliably performed with a spreadsheet.

Simplified Calculation for the Intermediate Form

Usually Equation 9-11 is a fair-to-excellent approximation. An even simpler form results from two conditions that usually exist. First, if $K_2F \gg K_w$, the second term in the numerator of Equation 9-11 can be dropped.

$$[H^+] \approx \sqrt{\frac{K_1K_2F + \cancel{K_1K_w}}{K_1 + F}}$$

Then, if $K_1 \ll F$, the first term in the denominator also can be neglected.

$$[H^+] \approx \sqrt{\frac{K_1K_2F}{\cancel{K_1} + F}}$$

Canceling F in the numerator and denominator gives

$$[H^+] \approx \sqrt{K_1K_2}$$

or

$$\log[H^+] \approx \frac{1}{2}(\log K_1 + \log K_2)$$

$$-\log[H^+] \approx -\frac{1}{2}(\log K_1 + \log K_2)$$

Recall that

$\log(x^{1/2}) = \frac{1}{2}\log x$

$\log(xy) = \log x + \log y$

$\log(x/y) = \log x - \log y$

The pH of the intermediate form of a diprotic acid is close to midway between the two pK_a values and is almost independent of concentration.

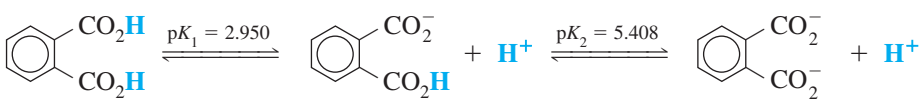
Intermediate form of diprotic acid:

$$pH \approx \frac{1}{2}(pK_1 + pK_2) \qquad \textbf{(9-12)}$$

Equation 9-12 is really good to keep in your head. It gives a pH of 6.04 for leucine, compared with pH = 6.06 from Equation 9-11. Equation 9-12 says that *the pH of the intermediate form of a diprotic acid is close to midway between pK_1 and pK_2, regardless of the formal concentration*.

EXAMPLE pH of the Intermediate Form of a Diprotic Acid

Potassium hydrogen phthalate, KHP, is a salt of the intermediate form of phthalic acid. Calculate the pH of 0.10 M and 0.010 M KHP.



Phthalic acid H_2P — Monohydrogen phthalate HP^- — Phthalate P^{2-}

(Potassium hydrogen phthalate = K^+HP^-)

Solution With Equation 9-12, the pH of potassium hydrogen phthalate is estimated as $\frac{1}{2}(pK_1 + pK_2) = 4.18$, regardless of concentration. With Equation 9-11, we calculate pH = 4.18 for 0.10 M K^+HP^- and pH = 4.20 for 0.010 M K^+HP^-.

Test Yourself Find the pH of 0.002 M K^+HP^- with Equation 9-11. (***Answer:*** 4.28)

Advice When faced with the intermediate form of a diprotic acid, use Equation 9-11 to calculate pH. The answer should be close to $\frac{1}{2}(pK_1 + pK_2)$.

Summary of Diprotic Acid Calculations

Here is how we calculate the pH and composition of solutions prepared from different forms of a diprotic acid (H_2A, HA^-, or A^{2-}).

Solution of H_2A

1. Treat H_2A as a monoprotic acid with $K_a = K_1$ to find $[H^+]$, $[HA^-]$, and $[H_2A]$.

$$\underset{F-x}{H_2A} \overset{K_1}{\rightleftharpoons} \underset{x}{H^+} + \underset{x}{HA^-} \qquad \frac{x^2}{F-x} = K_1$$

2. Use the K_2 equilibrium to solve for $[A^{2-}]$.

$$[A^{2-}] = \frac{K_2\cancel{[HA^-]}}{\cancel{[H^+]}} = K_2$$

Solution of HA^-

1. Use the approximation $[HA^-] \approx F$ and find the pH with Equation 9-11.

$$[H^+] = \sqrt{\frac{K_1K_2F + K_1K_w}{K_1 + F}}$$

The pH should be close to $\frac{1}{2}(pK_1 + pK_2)$.

2. With $[H^+]$ from step 1 and $[HA^-] \approx F$, solve for $[H_2A]$ and $[A^{2-}]$, using the K_1 and K_2 equilibria.

$$[H_2A] = \frac{[HA^-][H^+]}{K_1} \qquad [A^{2-}] = \frac{K_2[HA^-]}{[H^+]}$$

Solution of A^{2-}

1. Treat A^{2-} as monobasic, with $K_b = K_{b1} = K_w/K_{a2}$ to find $[A^{2-}]$, $[HA^-]$, and $[H^+]$.

$$\underset{F-x}{A^{2-}} + H_2O \overset{K_{b1}}{\rightleftharpoons} \underset{x}{HA^-} + \underset{x}{OH^-} \qquad \frac{x^2}{F-x} = K_{b1} = \frac{K_w}{K_{a2}}$$

$$[H^+] = \frac{K_w}{[OH^-]} = \frac{K_w}{x}$$

2. Use the K_1 equilibrium to solve for $[H_2A]$.

$$[H_2A] = \frac{[HA^-][H^+]}{K_{a1}} = \frac{\cancel{[HA^-]}(K_w/\cancel{[OH^-]})}{K_{a1}} = K_{b2}$$

The calculations we have been doing are really important to understand and use. However, we should not get too cocky about our great powers, because there could be equilibria we have not considered. For example, Na^+ or K^+ in solutions of HA^- or A^{2-} form weak ion pairs that we have neglected:[6]

$K^+ + A^{2-} \rightleftharpoons \{K^+A^{2-}\}$

$K^+ + HA^- \rightleftharpoons \{K^+HA^-\}$

9-2 Diprotic Buffers

A buffer made from a diprotic (or polyprotic) acid is treated in the same way as a buffer made from a monoprotic acid. For the acid H_2A, we can write *two* Henderson-Hasselbalch equations, both of which are *always* true. If we happen to know $[H_2A]$ and $[HA^-]$, then we will use the pK_1 equation. If we know $[HA^-]$ and $[A^{2-}]$, we will use the pK_2 equation.

$$pH = pK_1 + \log\frac{[HA^-]}{[H_2A]} \qquad pH = pK_2 + \log\frac{[A^{2-}]}{[HA^-]}$$

All Henderson-Hasselbalch equations (with activity coefficients) are always true for a solution at equilibrium.

EXAMPLE A Diprotic Buffer System

Find the pH of a solution prepared by dissolving 1.00 g of potassium hydrogen phthalate and 1.20 g of disodium phthalate in 50.0 mL of water.

Solution Monohydrogen phthalate and phthalate were shown in the preceding example. The formula masses are $KHP = C_8H_5O_4K = 204.221$ and $Na_2P = C_8H_4O_4Na_2 = 210.094$. We know $[HP^-]$ and $[P^{2-}]$, so we use the pK_2 Henderson-Hasselbalch equation to find the pH:

$$pH = pK_2 + \log\frac{[P^{2-}]}{[HP^-]} = 5.408 + \log\frac{(1.20\text{ g})/(210.094\text{ g/mol})}{(1.00\text{ g})/(204.221\text{ g/mol})} = 5.47$$

K_2 is the acid dissociation constant of HP^-, which appears in the denominator of the log term. Notice that the volume of solution was not used to answer the question.

Test Yourself Find the pH with 1.50 g Na_2P instead of 1.20 g. (***Answer:*** 5.57)

EXAMPLE Preparing a Buffer in a Diprotic System

How many milliliters of 0.800 M KOH should be added to 3.38 g of oxalic acid to give a pH of 4.40 when diluted to 500 mL?

Oxalic acid (H_2Ox)
Formula mass = 90.035

$pK_1 = 1.250$
$pK_2 = 4.266$

Solution The desired pH is above pK_2. We know that a 1:1 mole ratio of HOx^- : Ox^{2-} would have pH = pK_2 = 4.266. If the pH is to be 4.40, there must be more Ox^{2-} than HOx^- present. We must add enough base to convert all of the H_2Ox into HOx^-, plus enough additional base to convert the right amount of HOx^- into Ox^{2-}.

$$H_2Ox + OH^- \rightarrow \underset{\substack{\uparrow \\ pH \approx \frac{1}{2}(pK_1 + pK_2) = 2.76}}{\mathbf{HOx^-}} + H_2O$$

$$\underset{\substack{\uparrow \\ \text{A 1:1 mixture would have} \\ pH = pK_2 = 4.266}}{\mathbf{HOx^-}} + OH^- \rightarrow \mathbf{Ox^{2-}} + H_2O$$

In 3.38 g of H_2Ox, there are $0.037\ 5_4$ mol. The volume of 0.800 M KOH needed to react with this much H_2Ox to make HOx^- is $(0.037\ 5_4 \text{ mol})/(0.800 \text{ M}) = 46.9_3$ mL.

To produce a pH of 4.40 requires more OH^-:

	HOx^-	+	OH^-	→	Ox^{2-}
Initial moles	$0.037\ 5_4$		x		—
Final moles	$0.037\ 5_4 - x$		—		x

$$pH = pK_2 + \log\frac{[Ox^{2-}]}{[HOx^-]}$$

$$4.40 = 4.266 + \log\frac{x}{0.037\ 5_4 - x} \Rightarrow x = 0.021\ 6_6 \text{ mol}$$

The volume of KOH needed to deliver $0.021\ 6_6$ mole is $(0.021\ 6_4 \text{ mol})/(0.800 \text{ M}) = 27.0_5$ mL. The total volume of KOH needed to bring the pH to 4.40 is $46.9_3 + 27.0_5 = 73.9_8$ mL.

Test Yourself What volume of KOH would bring the pH to 4.50? (***Answer:*** 76.5_6 mL)

9-3 Polyprotic Acids And Bases

The treatment of diprotic acids and bases can be extended to polyprotic systems. By way of review, let's write the pertinent equilibria for a triprotic system.

$$H_3A \rightleftharpoons H_2A^- + H^+ \qquad K_{a1} = K_1$$
$$H_2A^- \rightleftharpoons HA^{2-} + H^+ \qquad K_{a2} = K_2$$
$$HA^{2-} \rightleftharpoons A^{3-} + H^+ \qquad K_{a3} = K_3$$
$$A^{3-} + H_2O \rightleftharpoons HA^{2-} + OH^- \qquad K_{b1} = K_w/K_{a3}$$
$$HA^{2-} + H_2O \rightleftharpoons H_2A^- + OH^- \qquad K_{b2} = K_w/K_{a2}$$
$$H_2A^- + H_2O \rightleftharpoons H_3A + OH^- \qquad K_{b3} = K_w/K_{a1}$$

We deal with triprotic systems as follows:

1. H_3A is treated as a monoprotic weak acid, with $K_a = K_1$.
2. H_2A^- is treated as the intermediate form of a diprotic acid.

The K values in Equations 9-13 and 9-14 are K_a values for the triprotic acid.

$$[H^+] \approx \sqrt{\frac{K_1K_2F + K_1K_w}{K_1 + F}} \tag{9-13}$$

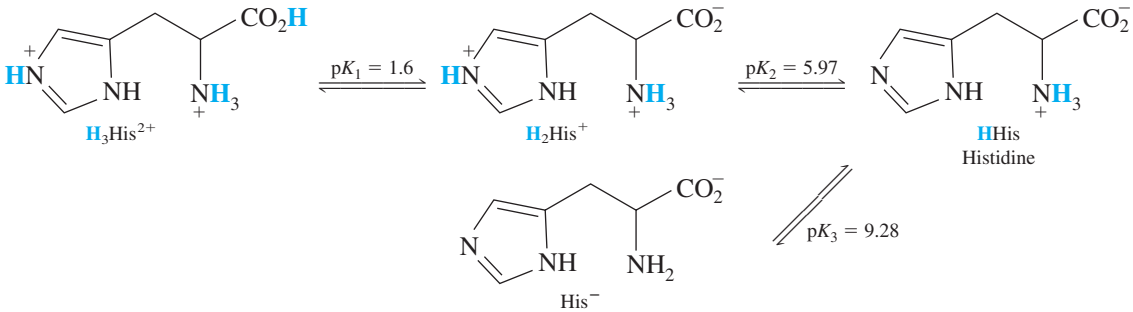
3. HA^{2-} is also treated as the intermediate form of a diprotic acid. However, HA^{2-} is "surrounded" by H_2A^- and A^{3-}, so the equilibrium constants to use are K_2 and K_3, instead of K_1 and K_2.

$$[H^+] \approx \sqrt{\frac{K_2K_3F + K_2K_w}{K_2 + F}} \tag{9-14}$$

4. A^{3-} is treated as monobasic, with $K_b = K_{b1} = K_w / K_{a3}$.

EXAMPLE A Triprotic System

Find the pH of 0.10 M H_3His^{2+}, 0.10 M H_2His^{+}, 0.10 M HHis, and 0.10 M His^{-}, where His stands for the amino acid histidine.



Solution *0.10 M H_3His^{2+}:* Treating H_3His^{2+} as a monoprotic acid, we write

$$\underset{F-x}{H_3His^{2+}} \rightleftharpoons \underset{x}{H_2His^{+}} + \underset{x}{H^{+}}$$

$$\frac{x^2}{F-x} = K_1 = 10^{-1.6} \Rightarrow x = 3._9 \times 10^{-2}\ M \Rightarrow pH = 1.41$$

0.10 M H_2His^{+}: Using Equation 9-13, we find

$$[H^+] = \sqrt{\frac{(10^{-1.6})(10^{-5.97})(0.10) + (10^{-1.6})(1.0 \times 10^{-14})}{10^{-1.6} + 0.10}}$$

$$= 1.4_7 \times 10^{-4}\ M \Rightarrow pH = 3.83$$

which is close to $\frac{1}{2}(pK_1 + pK_2) = 3.78$.

0.10 M HHis: Equation 9-14 gives

$$[H^+] = \sqrt{\frac{(10^{-5.97})(10^{-9.28})(0.10) + (10^{-5.97})(1.0 \times 10^{-14})}{10^{-5.97} + 0.10}}$$

$$= 2.3_7 \times 10^{-8}\ M \Rightarrow pH = 7.62$$

which is the same as $\frac{1}{2}(pK_2 + pK_3) = 7.62$.

0.10 M His^{-}: Treating His^{-} as monobasic, we can write

$$\underset{F-x}{His^{-}} + H_2O \rightleftharpoons \underset{x}{HHis} + \underset{x}{OH^{-}}$$

$$\frac{x^2}{F-x} = K_{b1} = \frac{K_w}{K_{a3}} = 1.9 \times 10^{-5} \Rightarrow x = 1.3_7 \times 10^{-3}\ M$$

$$pH = -\log\left(\frac{K_w}{x}\right) = 11.14$$

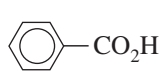
Test Yourself Compute the pH of 0.010 M HHis. (***Answer:*** 7.62)

We have reduced acid-base problems to just three types. When you encounter an acid or base, decide whether you are dealing with an *acidic*, *basic*, or *intermediate* form. Then do the appropriate arithmetic to answer the question at hand.

Three forms of acids and bases:
- acidic
- basic
- intermediate (amphiprotic)

9-4 Which Is the Principal Species?

We sometimes must identify which species of acid, base, or intermediate predominates under given conditions. For example, "What is the principal form of benzoic acid at pH 8?"



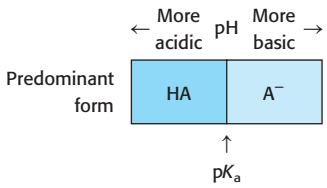
$pK_a = 4.20$

Benzoic acid

An example of when you need to know principal species is when you design a chromatographic or electrophoretic separation. You would use different strategies for separating cations, anions, and neutral compounds.

$$pH = pK_a + \log\frac{[A^-]}{[HA]}$$

pH	Major species
$< pK_a$	HA
$> pK_a$	A^-



pK_a for benzoic acid is 4.20. So, at pH 4.20, there is a 1:1 mixture of benzoic acid (HA) and benzoate ion (A^-). At pH = pK_a + 1 (= 5.20), the quotient $[A^-]/[HA]$ is 10:1. At pH = pK_a + 2 (= 6.20), the quotient $[A^-]/[HA]$ is 100:1. As pH increases, the quotient $[A^-]/[HA]$ increases still further.

For a monoprotic system, the basic species A^- is the predominant form when pH > pK_a. The acidic species, HA, is the predominant form when pH < pK_a. The predominant form of benzoic acid at pH 8 is the benzoate anion, $C_6H_5CO_2^-$.

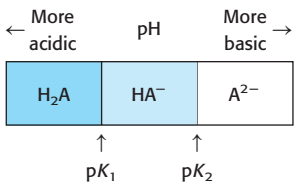
EXAMPLE Principal Species—Which One and How Much?

What is the predominant form of ammonia in a solution at pH 7.0? Approximately what fraction is in this form?

Solution In Appendix G, we find pK_a = 9.24 for the ammonium ion (NH_4^+, the conjugate acid of ammonia, NH_3). At pH = 9.24, $[NH_4^+] = [NH_3]$. Below pH 9.24, NH_4^+ will be the predominant form. Because pH = 7.0 is about 2 pH units below pK_a, the quotient $[NH_4^+]/[NH_3]$ will be about 100:1. More than 99% is in the form NH_4^+.

Test Yourself Approximately what fraction of ammonia is in the form NH_3 at pH 11? (***Answer:*** somewhat less than 99% because pH is almost 2 units above pK_a)

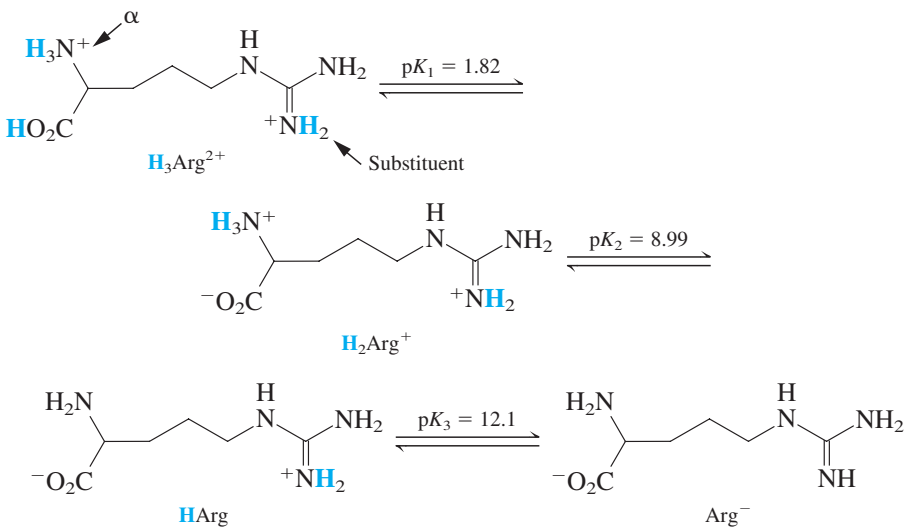
pH	Major species
$pH < pK_1$	H_2A
$pK_1 < pH < pK_2$	HA^-
$pH > pK_2$	A^{2-}



For polyprotic systems, our reasoning is similar, but there are several values of pK_a. Consider oxalic acid, H_2Ox, with pK_1 = 1.25 and pK_2 = 4.27. At pH = pK_1, $[H_2Ox] = [HOx^-]$. At pH = pK_2, $[HOx^-] = [Ox^{2-}]$. The chart in the margin shows the major species in each pH region.

EXAMPLE Principal Species in a Polyprotic System

The amino acid arginine has the following forms:



Appendix G tells us that the α-ammonium group (at the left) is more acidic than the substituent (at the right). What is the principal form of arginine at pH 10.0? Approximately what fraction is in this form? What is the second most abundant form at this pH?

Solution We know that at pH = pK_2 = 8.99, $[H_2Arg^+] = [HArg]$. At pH = pK_3 = 12.1, $[HArg] = [Arg^-]$. At pH = 10.0, the major species is HArg. Because pH 10.0 is about one pH unit higher than pK_2, we can say that $[HArg]/[H_2Arg^+] \approx 10:1$. About 90% of arginine is in the form HArg. The second most important species is H_2Arg^+, which makes up about 10% of the arginine.

Test Yourself What is the predominant form of arginine at pH 11? What is the second major species? (***Answer:*** HArg, Arg^-)

EXAMPLE **More on Polyprotic Systems**

In the pH range 1.82 to 8.99, H_2Arg^+ is the principal form of arginine. Which is the second most prominent species at pH 6.0? at pH 5.0?

Solution We know that the pH of the pure intermediate (amphiprotic) species, H_2Arg^+, is

$$\text{pH of } H_2Arg^+ \approx \frac{1}{2}(pK_1 + pK_2) = 5.40$$

Above pH 5.40 (and below pH = pK_2), HArg, the conjugate base of H_2Arg^+, will be the second most important species. Below pH 5.40 (and above pH = pK_1), H_3Arg^{2+} will be the second most important species.

Test Yourself At what pH does $[H_2Arg^+] = [Arg^-]$? (***Answer:*** 10.54)

Figure 9-2 summarizes how we think of a triprotic system. We determine the principal species by comparing the pH of the solution with the pK_a values.

Go back and read the Example, "Preparing a Buffer in a Diprotic System," on page 193. See if it makes more sense now.

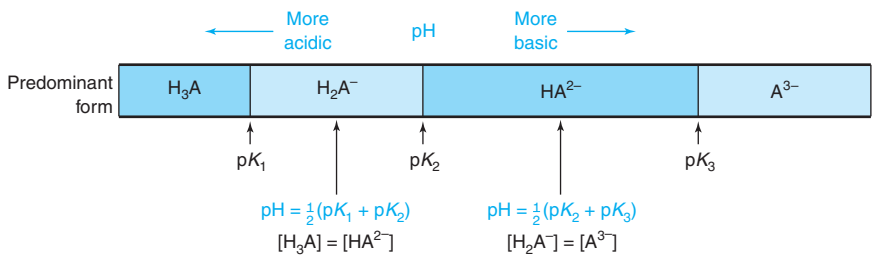


FIGURE 9-2 The predominant molecular form of a triprotic system (H_3A) in the various pH intervals.

Speciation describes the distribution of analyte among possible species. For an acid or base, speciation describes how much of each protonated form is present. When you ingest inorganic arsenic ($AsO(OH)_3$ and $As(OH)_3$) from drinking water, it is methylated to species such as $(CH_3)AsO(OH)_2$, $(CH_3)As(OH)_2$, $(CH_3)_2AsO(OH)$, $(CH_3)_2As(OH)$, $(CH_3)_3AsO$, and $(CH_3)_3As$. Speciation describes the forms and quantities that are present.

9-5 Fractional Composition Equations

We now derive equations that give the fraction of each species of acid or base at a given pH. These equations will be useful for acid-base and EDTA titrations, as well as for electrochemical equilibria. They are of key value in Chapter 12.

Monoprotic Systems

Our goal is to find an expression for the fraction of an acid in each form (HA and A^-) as a function of pH. We can do this by combining the equilibrium constant with the mass balance. Consider an acid with formal concentration F:

$$HA \overset{K_a}{\rightleftharpoons} H^+ + A^- \qquad K_a = \frac{[H^+][A^-]}{[HA]}$$

$$\text{Mass balance:} \quad F = [HA] + [A^-]$$

Rearranging the mass balance gives $[A^-] = F - [HA]$, which can be plugged into the K_a expression to give

$$K_a = \frac{[H^+](F - [HA])}{[HA]}$$

or, with a little algebra,

$$[HA] = \frac{[H^+]F}{[H^+] + K_a} \tag{9-15}$$

The *fraction* of molecules in the form HA is called $\boldsymbol{\alpha_{HA}}$.

$$\alpha_{HA} = \frac{[HA]}{[HA] + [A^-]} = \frac{[HA]}{F} \tag{9-16}$$

α_{HA} = fraction of species in the form HA
α_{A^-} = fraction of species in the form A^-

$$\alpha_{HA} + \alpha_{A^-} = 1$$

The fraction denoted here as α_{A^-} is the same thing we called the *fraction of dissociation* (α) previously.

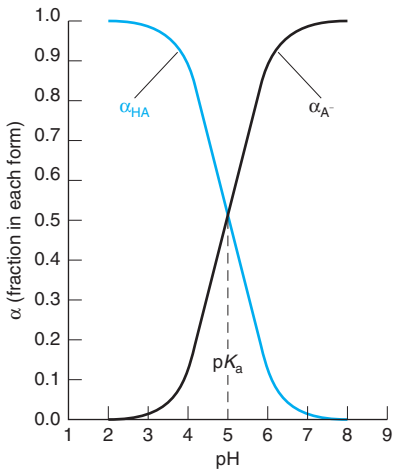


FIGURE 9-3 Fractional composition diagram of a monoprotic system with $pK_a = 5.00$. Below pH 5, HA is the dominant form, whereas, above pH 5, A^- dominates.

Dividing Equation 9-15 by F gives

$$\textit{Fraction in the form HA:} \qquad \alpha_{HA} = \frac{[HA]}{F} = \frac{[H^+]}{[H^+] + K_a} \tag{9-17}$$

In a similar manner, the fraction in the form A^-, designated $\boldsymbol{\alpha_{A^-}}$, can be obtained:

$$\textit{Fraction in the form } A^-\textit{:} \qquad \alpha_{A^-} = \frac{[A^-]}{F} = \frac{K_a}{[H^+] + K_a} \tag{9-18}$$

Figure 9-3 shows α_{HA} and α_{A^-} for a system with $pK_a = 5.00$. At low pH, almost all of the acid is in the form HA. At high pH, almost everything is in the form A^-.

Diprotic Systems

The derivation of fractional composition equations for a diprotic system follows the same pattern used for the monoprotic system.

$$H_2A \overset{K_1}{\rightleftharpoons} H^+ + HA^-$$

$$HA^- \overset{K_2}{\rightleftharpoons} H^+ + A^{2-}$$

$$K_1 = \frac{[H^+][HA^-]}{[H_2A]} \Rightarrow [HA^-] = \underbrace{[H_2A]\frac{K_1}{[H^+]}}$$

$$K_2 = \frac{[H^+][A^{2-}]}{[HA^-]} \Rightarrow [A^{2-}] = [HA^-]\frac{K_2}{[H^+]} = [H_2A]\frac{K_1K_2}{[H^+]^2}$$

Mass balance: $F = [H_2A] + [HA^-] + [A^{2-}]$

$$F = [H_2A] + \frac{K_1}{[H^+]}[H_2A] + \frac{K_1K_2}{[H^+]^2}[H_2A]$$

$$F = [H_2A]\left(1 + \frac{K_1}{[H^+]} + \frac{K_1K_2}{[H^+]^2}\right) = [H_2A]\frac{[H^+]^2 + [H^+]K_1 + K_1K_2}{[H^+]^2}$$

α_{H_2A} = fraction of species in the form H_2A
α_{HA^-} = fraction of species in the form HA^-
$\alpha_{A^{2-}}$ = fraction of species in the form A^{2-}

$$\alpha_{H_2A} + \alpha_{HA^-} + \alpha_{A^{2-}} = 1$$

For a diprotic system, we designate the fraction in the form H_2A as $\boldsymbol{\alpha_{H_2A}}$, the fraction in the form HA^- as $\boldsymbol{\alpha_{HA^-}}$, and the fraction in the form A^{2-} as $\boldsymbol{\alpha_{A^{2-}}}$. From the definition of α_{H_2A}, we can write

$$\textit{Fraction in the form } H_2A\textit{:} \quad \alpha_{H_2A} = \frac{[H_2A]}{F} = \frac{[H^+]^2}{[H^+]^2 + [H^+]K_1 + K_1K_2} \tag{9-19}$$

In a similar manner, we can derive the following equations:

$$\textit{Fraction in the form } HA^-\textit{:} \quad \alpha_{HA^-} = \frac{[HA^-]}{F} = \frac{K_1[H^+]}{[H^+]^2 + [H^+]K_1 + K_1K_2} \tag{9-20}$$

$$\textit{Fraction in the form } A^{2-}\textit{:} \quad \alpha_{A^{2-}} = \frac{[A^{2-}]}{F} = \frac{K_1K_2}{[H^+]^2 + [H^+]K_1 + K_1K_2} \tag{9-21}$$

The general form of α for the polyprotic acid H_nA is

$$\alpha_{H_nA} = \frac{[H^+]^n}{D}$$

$$\alpha_{H_{n-1}A} = \frac{K_1[H^+]^{n-1}}{D}$$

$$\alpha_{H_{n-j}A} = \frac{K_1K_2 \ldots K_j[H^+]^{n-j}}{D}$$

where $D = [H^+]^n + K_1[H^+]^{n-1} + K_1K_2[H^+]^{n-2} + \cdots + K_1K_2K_3 \cdots K_n$.

Figure 9-4 shows the fractions α_{H_2A}, α_{HA^-}, and $\alpha_{A^{2-}}$ for fumaric acid, whose two pK_a values are only 1.46 units apart. α_{HA^-} rises only to 0.73 because the two pK values are so close together. There are substantial quantities of H_2A and A^{2-} in the region $pK_1 < pH < pK_2$.

How to apply fractional composition equations to bases

Equations 9-19 through 9-21 apply equally well to B, BH^+, and BH_2^{2+} obtained from the base B. The fraction α_{H_2A} applies to the acidic form BH_2^{2+}. α_{HA^-} applies to BH^+, and $\alpha_{A^{2-}}$ applies to B. The constants K_1 and K_2 are the *acid* dissociation constants of BH_2^{2+} ($K_1 = K_w/K_{b2}$ and $K_2 = K_w/K_{b1}$).

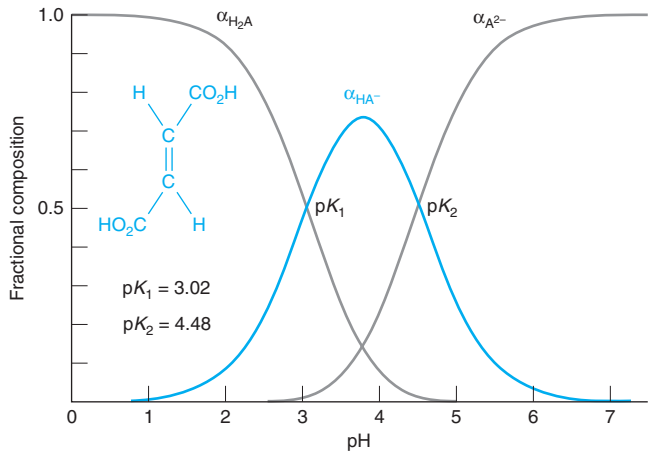


FIGURE 9-4 Fractional composition diagram for fumaric acid (*trans*-butenedioic acid). At low pH, H_2A is dominant. At intermediate pH, HA^- is dominant; and, at high pH, A^{2-} dominates. Because pK_1 and pK_2 are not separated very much, the fraction of HA^- never gets very close to unity.

9-6 Isoelectric and Isoionic pH

Biochemists speak of the isoelectric or isoionic pH of polyprotic molecules, such as proteins. These terms can be understood in terms of a diprotic system, such as the amino acid alanine.

$$\underset{\substack{\text{Alanine cation}\\ H_2A^+}}{H_3\overset{+}{N}CH(CH_3)CO_2H} \rightleftharpoons \underset{\substack{\text{Neutral zwitterion}\\ HA}}{H_3\overset{+}{N}CH(CH_3)CO_2^-} + H^+ \qquad pK_1 = 2.34$$

$$H_3\overset{+}{N}CH(CH_3)CO_2^- \rightleftharpoons \underset{\substack{\text{Alanine anion}\\ A^-}}{H_2NCH(CH_3)CO_2^-} + H^+ \qquad pK_2 = 9.87$$

The **isoionic point** (or isoionic pH) is the pH obtained when the pure, neutral polyprotic acid HA (the neutral zwitterion) is dissolved in water. The only ions are H_2A^+, A^-, H^+, and OH^-. Most alanine is in the form HA, and the concentrations of H_2A^+ and A^- are *not* equal to each other.

Isoionic pH is the pH of the pure, neutral, polyprotic acid.

The **isoelectric point** (or isoelectric pH) is the pH at which the *average* charge of the polyprotic acid is 0. Most of the molecules are in the uncharged form HA, and the concentrations of H_2A^+ and A^- *are* equal to each other. There is always some H_2A^+ and some A^- in equilibrium with HA.

Isoelectric pH is the pH at which average charge of the polyprotic acid is 0.

When alanine is dissolved in water, the pH of the solution, by definition, is the *isoionic* pH. Because alanine (HA) is the intermediate form of the diprotic acid, H_2A^+, $[H^+]$ is given by

Isoionic point:

$$[H^+] = \sqrt{\frac{K_1K_2F + K_1K_w}{K_1 + F}} \qquad \textbf{(9-22)}$$

Alanine is the intermediate form of a diprotic acid, so we use Equation 9-11 to find the pH.

where F is the formal concentration of alanine. For 0.10 M alanine, the isoionic pH is found from

$$[H^+] = \sqrt{\frac{K_1K_2(0.10) + K_1K_w}{K_1 + (0.10)}} = 7.7 \times 10^{-7}\ \text{M} \Rightarrow \text{pH} = 6.11$$

From $[H^+]$, K_1, and K_2, you could calculate $[H_2A^+] = 1.68 \times 10^{-5}$ M and $[A^-] = 1.76 \times 10^{-5}$ M for pure alanine in water (the *isoionic* solution). There is a slight excess of A^- because HA is a slightly stronger acid than it is a base. It dissociates to make A^- a little more than it reacts with water to make H_2A^+.

The *isoelectric* point is the pH at which $[H_2A^+] = [A^-]$, and, therefore, the average charge of alanine is 0. To go from the *isoionic* solution (pure HA in water) to the isoelectric solution, we could add just enough strong acid to decrease $[A^-]$ and increase $[H_2A^+]$ until they are equal. Adding acid necessarily lowers the pH. For alanine, the isoelectric pH must be lower than the isoionic pH.

We calculate the isoelectric pH by first writing expressions for $[H_2A^+]$ and $[A^-]$:

$$[H_2A^+] = \frac{[HA][H^+]}{K_1} \qquad [A^-] = \frac{K_2[HA]}{[H^+]}$$

Setting $[H_2A^+] = [A^-]$, we find

$$\frac{[HA][H^+]}{K_1} = \frac{K_2[HA]}{[H^+]} \Rightarrow [H^+] = \sqrt{K_1K_2}$$

which gives

The isoelectric point is midway between the two pK_a values "surrounding" the neutral, intermediate species.

Isoelectric point:

$$pH = \frac{1}{2}(pK_1 + pK_2) \quad \textbf{(9-23)}$$

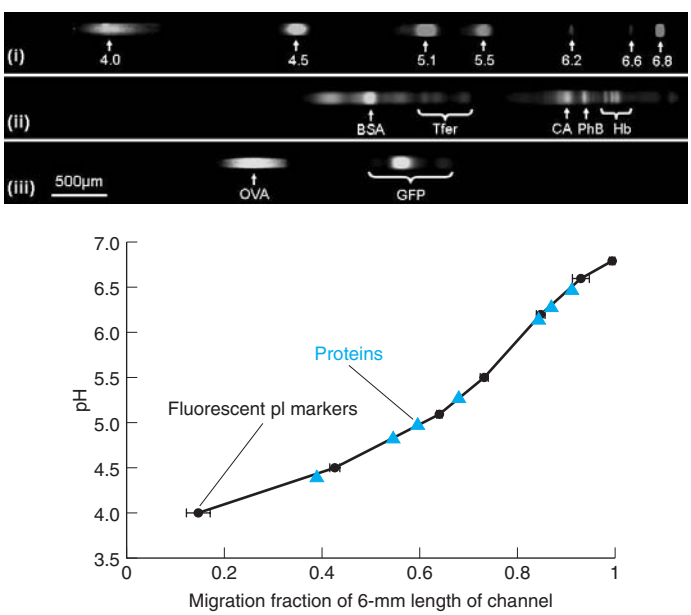
For a diprotic amino acid, the isoelectric pH is halfway between the two pK_a values. The isoelectric pH of alanine is $\frac{1}{2}(2.34 + 9.87) = 6.10$.

The isoelectric and isoionic points for a polyprotic acid are almost the same. At the isoelectric pH, the average charge of the molecule is 0; thus $[H_2A^+] = [A^-]$ and $pH = \frac{1}{2}(pK_1 + pK_2)$. At the isoionic point, the pH is given by Equation 9-22, and $[H_2A^+]$ is not exactly equal to $[A^-]$.

For a protein, the *isoionic* pH is the pH of a solution of pure protein with no other ions except H^+ and OH^-. Proteins are usually isolated in a charged form together with counterions such as Na^+, NH_4^+, or Cl^-. When the protein is subjected to intensive *dialysis* (Demonstration 26-1) against pure water, the pH in the protein compartment approaches the isoionic point if

BOX 9-3 Isoelectric Focusing

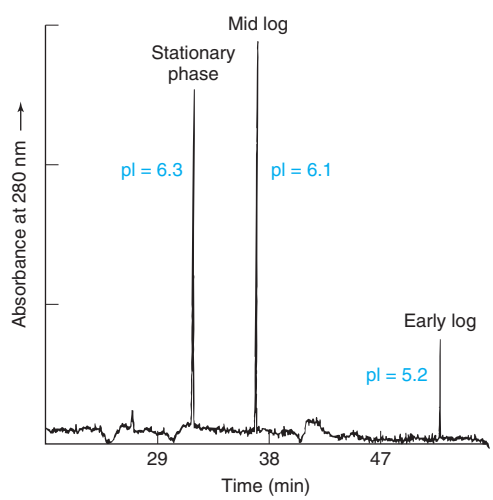
At its *isoelectric point*, the average charge of all forms of a protein is 0. It will therefore not migrate in an electric field at its isoelectric pH. This effect is the basis of a technique of protein separation called **isoelectric focusing.** A protein mixture is subjected to a strong electric field in a medium specifically designed to have a pH gradient. Positively charged molecules move toward the negative pole and negatively charged molecules move toward the positive pole. Each protein migrates until it reaches the point where the pH is the same as its isoelectric pH. At this point, the protein has no net charge and no longer moves. Each protein in the mixture is focused in one region at its isoelectric pH.



Lab-on-a-chip isoelectric focusing. (i) Fluorescent pI markers. (ii) and (iii) Separation of fluorescence-labeled proteins: (OVA) ovalbumin; (GFP) green fluorescent protein; (BSA) bovine serum albumin; (Tfer) transferrin; (CA) carbonic anhydrase; (PhB) phosphorylase B; and (Hb) hemoglobin. [G. J. Sommer, A. K. Singh, and A. V. Hatch, "On-Chip Isoelectric Focusing Using Photopolymerized Immobilized pH Gradients," *Anal. Chem.* **2008**, *80*, 3327.]

Isoelectric focusing in a 6-mm-long × 100 μm-wide × 25-μm-deep capillary etched into silica glass is shown at the left below. Panel (i) shows fluorescent markers with known isoelectric pH (called pI) run as standards. Panels (ii) and (iii) show separations of fluorescence-labeled proteins. Proteins migrate until they reach their isoelectric pH and then stop migrating. If a molecule diffuses out of its isoelectric region, it becomes charged and immediately migrates back to its isoelectric zone. The graph shows measured pH versus distance in the capillary. Separations or reactions conducted in capillaries in glass or polymer chips are examples of *lab-on-a-chip* operations (Section 25-8).

The figure at the lower right shows separation of whole yeast cells at three different stages of growth (called early log, mid log, and stationary phase) by isoelectric focusing in a silica capillary tube. Acid-base properties (and, therefore, pI) of cell surfaces change during growth of the colony.



Capillary isoelectric focusing of whole yeast cells taken from three growth stages. After cells have been focused at their isoelectric pH, the inlet end of the capillary was elevated and liquid drained out of the capillary past an ultraviolet detector, creating three peaks observed here. The abscissa is the time required for the bands to reach the detector. [From R. Shen, S. J. Berger, and R. D. Smith, "Capillary Isoelectric Focusing of Yeast Cells," *Anal. Chem.* **2000**, *72*, 4603.]

the counterions are free to pass through the semipermeable dialysis membrane that retains the protein. The *isoelectric* point is the pH at which the protein has no net charge. Box 9-3 tells how proteins can be separated on the basis of their different isoelectric points.

Related properties—of interest to geology, environmental science, and ceramics—are the surface acidity of a solid[7] and the pH of zero charge.[8] Mineral, clay, and even organic surfaces behave as acids and bases. The silica (SiO_2) surface of sand or glass can be simplistically thought of as a diprotic acid:

$$\equiv\text{Si—OH}_2^+ \overset{K_{a1}}{\rightleftharpoons} \equiv\text{Si—OH} + \text{H}^+ \qquad K_{a1} = \frac{\{\text{SiOH}\}[\text{H}^+]}{\{\text{SiOH}_2^+\}} \tag{9-24}$$

$$\equiv\text{Si—OH} \overset{K_{a2}}{\rightleftharpoons} \equiv\text{Si—O}^- + \text{H}^+ \qquad K_{a2} = \frac{\{\text{SiO}^-\}[\text{H}^+]}{\{\text{SiOH}\}} \tag{9-25}$$

The notation $\equiv$Si represents a surface silicon atom. Silanol groups ($\equiv$Si—OH) can donate or accept a proton to give the surface a negative or positive charge. In the equilibrium constants, the concentrations of the surface species $\{SiOH_2^+\}$, $\{SiOH\}$, and $\{SiO^-\}$ are measured in moles per gram of solid.

The *pH of zero charge* is the pH at which $\{SiOH_2^+\} = \{SiO^-\}$ and, therefore, the surface has no net charge. Like the isoelectric point of a diprotic acid, the pH of zero charge is $\frac{1}{2}(pK_{a1} + pK_{a2})$. *Colloidal particles* (those with diameters in the range 1–500 nm) tend to remain dispersed when they are charged, but they *flocculate* (come together and precipitate) near the pH of zero charge. In capillary electrophoresis (Chapter 25), the surface charge of the silica capillary governs the rate at which solvent moves through the capillary.

Terms to Understand

amino acid
amphiprotic
diprotic acids and bases
hydrolysis
isoelectric focusing
isoelectric point
isoionic point
polyprotic acids and bases
speciation
zwitterion

Summary

Diprotic acids and bases fall into three categories:

1. The fully acidic form, H_2A, behaves as a monoprotic acid, $H_2A \rightleftharpoons H^+ + HA^-$, for which we solve the equation $K_{a1} = x^2/(F - x)$, where $[H^+] = [HA^-] = x$, and $[H_2A] = F - x$. From $[HA^-]$ and $[H^+]$, $[A^{2-}]$ can be found from the K_{a2} equilibrium.
2. The fully basic form, A^{2-}, behaves as a base, $A^{2-} + H_2O \rightleftharpoons HA^- + OH^-$, for which we solve the equation $K_{b1} = x^2/(F - x)$, where $[OH^-] = [HA^-] = x$, and $[A^{2-}] = F - x$. From these concentrations, $[H_2A]$ can be found from the K_{a1} or K_{b2} equilibrium.
3. The intermediate (amphiprotic) form, HA^-, is both an acid and a base. Its pH is given by

$$[\text{H}^+] = \sqrt{\frac{K_1K_2\text{F} + K_1K_w}{K_1 + \text{F}}}$$

where K_1 and K_2 are acid dissociation constants for H_2A, and F is the formal concentration of the intermediate. In most cases, this equation reduces to the form $pH \approx \frac{1}{2}(pK_1 + pK_2)$, in which pH is independent of concentration.

In triprotic systems, there are two intermediate forms. The pH of each is found with an equation analogous to that for the intermediate form of a diprotic system. Triprotic systems also have one fully acidic and one fully basic form; these species can be treated as monoprotic for the purpose of calculating pH. For polyprotic buffers, we write the Henderson-Hasselbalch equation connecting the two principal species in the system. pK_a in this equation is the one that applies to the acid in the denominator of the log term.

The principal species of a monoprotic or polyprotic system is found by comparing the pH with the pK_a values. For $pH < pK_1$, the fully protonated species, H_nA, is the predominant form. For $pK_1 < pH < pK_2$, the form $H_{n-1}A^-$ is favored; and, at each successive pK value, the next deprotonated species becomes principal. Finally, at pH values higher than the highest pK, the fully basic form (A^{n-}) is dominant. The fractional composition of a solution is expressed by α, given in Equations 9-17 and 9-18 for a monoprotic system and Equations 9-19 through 9-21 for a diprotic system.

The isoelectric pH of a polyprotic compound is that pH at which the average charge of all species is 0. For a diprotic amino acid whose amphiprotic form is neutral, the isoelectric pH is given by $pH = \frac{1}{2}(pK_1 + pK_2)$. The isoionic pH of a polyprotic species is the pH that would exist in a solution containing only ions derived from the neutral polyprotic species and from H_2O. For a diprotic amino acid whose amphiprotic form is neutral, the isoionic pH is found from $[H^+] = \sqrt{(K_1K_2F + K_1K_w)/(K_1 + F)}$, where F is the formal concentration of the amino acid.

Exercises

9-A. Find the pH and the concentrations of H_2SO_3, HSO_3^-, and SO_3^{2-} in each solution: **(a)** 0.050 M H_2SO_3; **(b)** 0.050 M $NaHSO_3$; **(c)** 0.050 M Na_2SO_3.

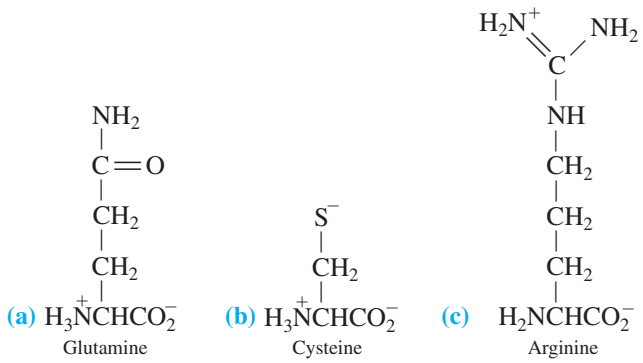
9-B. (a) How many grams of $NaHCO_3$ (FM 84.007) must be added to 4.00 g of K_2CO_3 (FM 138.206) to give a pH of 10.80 in 500 mL of water?

(b) What will be the pH if 100 mL of 0.100 M HCl are added to the solution in part **(a)**?

(c) How many milliliters of 0.320 M HNO_3 should be added to 4.00 g of K_2CO_3 to give a pH of 10.00 in 250 mL?

9-C. How many milliliters of 0.800 M KOH should be added to 5.02 g of 1,5-pentanedioic acid ($C_5H_8O_4$, FM 132.11) to give a pH of 4.40 when diluted to 250 mL?

9-D. Calculate the pH of a 0.010 M solution of each amino acid in the form drawn here.



9-E. (a) Draw the structure of the predominant form (principal species) of 1,3-dihydroxybenzene at pH 9.00 and at pH 11.00.

(b) What is the second most prominent species at each pH?

(c) Calculate the percentage in the major form at each pH.

9-F. Draw the structures of the predominant forms of glutamic acid and tyrosine at pH 9.0 and pH 10.0. What is the second most abundant species at each pH?

9-G. Calculate the isoionic pH of 0.010 M lysine.

9-H. Neutral lysine can be written HL. The other forms of lysine are H_3L^{2+}, H_2L^+, and L^-. The isoelectric point is the pH at which the *average* charge of lysine is 0. Therefore, at the isoelectric point, $2[H_3L^{2+}] + [H_2L^+] = [L^-]$. Use this condition to calculate the isoelectric pH of lysine.

Problems

Diprotic Acids and Bases

9-1. Consider HA^-, the intermediate form of a diprotic acid. K_a for this species is 10^{-4} and K_b is 10^{-8}. Nonetheless, the K_a and K_b reactions proceed to nearly the same extent when NaHA is dissolved in water. Explain.

9-2. Write the general structure of an amino acid. Why do some amino acids in Table 9-1 have two pK values and others three?

9-3. Write the chemical reactions whose equilibrium constants are K_{b1} and K_{b2} for the amino acid proline. Find the values of K_{b1} and K_{b2}.

9-4. Consider the diprotic acid H_2A with $K_1 = 1.00 \times 10^{-4}$ and $K_2 = 1.00 \times 10^{-8}$. Find the pH and concentrations of H_2A, HA^-, and A^{2-} in **(a)** 0.100 M H_2A; **(b)** 0.100 M NaHA; **(c)** 0.100 M Na_2A.

9-5. We will abbreviate malonic acid, $CH_2(CO_2H)_2$, as H_2M. Find the pH and concentrations of H_2M, HM^-, and M^{2-} in **(a)** 0.100 M H_2M; **(b)** 0.100 M NaHM; **(c)** 0.100 M Na_2M.

9-6. Calculate the pH of 0.300 M piperazine. Calculate the concentration of each form of piperazine in this solution.

9-7. Use the method of Box 9-2 to calculate the concentrations of H^+, H_2A, HA^-, and A^{2-} in 0.001 00 M monosodium oxalate, NaHA.

9-8. *Activity*. In this problem, we calculate the pH of the intermediate form of a diprotic acid, taking activities into account.

(a) Including activity coefficients, derive Equation 9-11 for potassium hydrogen phthalate (K^+HP^- in the example following Equation 9-12).

(b) Calculate the pH of 0.050 M KHP, using the results in part **(a)**. Assume that the sizes of both HP^- and P^{2-} are 600 pm.

9-9. *Intermediate form of diprotic acid.* Use the method in Box 9-2 to find the pH and concentration of HA^- in a 0.01 F solution of the amphiprotic salt Na^+HA^- derived from the diprotic acid H_2A with pK_1 = 4 and **(a)** pK_2 = 8 or **(b)** pK_2 = 5.

9-10. *Derivation of Equation 9-10 for pH of the intermediate form Na^+HA^-.* The derivation in the chapter was for HL, the intermediate form of H_2L^+. Write the mass and charge balances for Na^+HA^- at formal concentration F. Substitute $[H_2A] + [HA^-] + [A^{2-}]$ for $[Na^+]$ in the charge balance. After canceling like terms on both sides of the charge balance, express all concentrations in terms of $[HA^-]$ and $[H^+]$. Solve for $[H^+]$ and show that you end up with the same expression as Equation 9-10.

9-11. *Heterogeneous equilibrium.* CO_2 dissolves in water to give "carbonic acid" (which is mostly dissolved CO_2, as described in Box 6-4).

$$CO_2(g) \rightleftharpoons CO_2(aq) \qquad K = 10^{-1.5}$$

(The equilibrium constant is called the *Henry's law constant* for carbon dioxide, because Henry's law states that the solubility of a gas in a liquid is proportional to the pressure of the gas.) The acid dissociation constants listed for "carbonic acid" in Appendix G apply to $CO_2(aq)$. Given that P_{CO_2} in the atmosphere is $10^{-3.4}$ atm, find the pH of water in equilibrium with the atmosphere.

9-12. *Effect of temperature on carbonic acid acidity and the solubility of $CaCO_3$.*[9] Box 9-1 states that marine life with $CaCO_3$ shells and skeletons will be threatened with extinction in cold polar waters before that will happen in warm tropical waters. The following equilibrium constants apply to seawater at 0° and 30°C, when concentrations are measured in moles per kilogram of seawater and pressure is in bars:

$$CO_2(g) \rightleftharpoons CO_2(aq) \qquad \textbf{(A)}$$

$$K_H = \frac{[CO_2(aq)]}{P_{CO_2}} = 10^{-1.2073}\ \text{mol kg}^{-1}\ \text{bar}^{-1} \text{ at } 0°\text{C}$$

$$= 10^{-1.6048}\ \text{mol kg}^{-1}\ \text{bar}^{-1} \text{ at } 30°\text{C}$$

$$CO_2(aq) + H_2O \rightleftharpoons HCO_3^- + H^+ \quad \textbf{(B)}$$

$$K_{a1} = \frac{[HCO_3^-][H^+]}{[CO_2(aq)]} = 10^{-6.1004}\ \text{mol kg}^{-1} \text{ at } 0°C$$

$$= 10^{-5.8008}\ \text{mol kg}^{-1} \text{ at } 30°C$$

$$HCO_3^- \rightleftharpoons CO_3^{2-} + H^+ \quad \textbf{(C)}$$

$$K_{a2} = \frac{[CO_3^{2-}][H^+]}{[HCO_3^-]} = 10^{-9.3762}\ \text{mol kg}^{-1} \text{ at } 0°C$$

$$= 10^{-8.8324}\ \text{mol kg}^{-1} \text{ at } 30°C$$

$$CaCO_3(s, \textit{aragonite}) \rightleftharpoons Ca^{2+} + CO_3^{2-} \quad \textbf{(D)}$$

$$K_{sp}^{arg} = [Ca^{2+}][CO_3^{2-}] = 10^{-6.1113}\ \text{mol}^2\ \text{kg}^{-2} \text{ at } 0°C$$

$$= 10^{-6.1391}\ \text{mol}^2\ \text{kg}^{-2} \text{ at } 30°C$$

$$CaCO_3(s, \textit{calcite}) \rightleftharpoons Ca^{2+} + CO_3^{2-} \quad \textbf{(E)}$$

$$K_{sp}^{cal} = [Ca^{2+}][CO_3^{2-}] = 10^{-6.3652}\ \text{mol}^2\ \text{kg}^{-2} \text{ at } 0°C$$

$$= 10^{-6.3713}\ \text{mol}^2\ \text{kg}^{-2} \text{ at } 30°C$$

The first equilibrium constant is called K_H for Henry's law (Problem 9-11). Units are given to remind you what units you must use.

(a) Combine the expressions for K_H, K_{a1}, and K_{a2} to find an expression for $[CO_3^{2-}]$ in terms of P_{CO_2} and $[H^+]$.

(b) From the result of **(a)**, calculate $[CO_3^{2-}]$ (mol kg^{-1}) at P_{CO_2} = 800 μbar and pH = 7.8 at temperatures of 0° (polar ocean) and 30°C (tropical ocean). These are conditions that could be reached around the year 2100 if we continue to release CO_2 at the present rate.

(c) The concentration of Ca^{2+} in the ocean is 0.010 M. Predict whether aragonite and calcite will dissolve under the conditions in **(b)**.

Diprotic Buffers

9-13. How many grams of Na_2CO_3 (FM 105.99) should be mixed with 5.00 g of $NaHCO_3$ (FM 84.01) to produce 100 mL of buffer with pH 10.00?

9-14. How many milliliters of 0.202 M NaOH should be added to 25.0 mL of 0.023 3 M salicylic acid (2-hydroxybenzoic acid) to adjust the pH to 3.50?

9-15. Describe how you would prepare exactly 100 mL of 0.100 M picolinate buffer, pH 5.50. Possible starting materials are pure picolinic acid (pyridine-2-carboxylic acid, FM 123.11), 1.0 M HCl, and 1.0 M NaOH. Approximately how many milliliters of the HCl or NaOH will be required?

9-16. How many grams of Na_2SO_4 (FM 142.04) should be added to how many grams of sulfuric acid (FM 98.08) to give 1.00 L of buffer with pH 2.80 and a total sulfur (= SO_4^{2-} + HSO_4^- + H_2SO_4) concentration of 0.200 M?

Polyprotic Acids and Bases

9-17. Phosphate at 0.01 M is one of the main buffers in blood plasma, whose pH is 7.45. Would phosphate be as useful if the plasma pH were 8.5?

9-18. Starting with the fully protonated species, write the stepwise acid dissociation reactions of the amino acids glutamic acid and tyrosine. Be sure to remove the protons in the correct order. Which species are the neutral molecules that we call glutamic acid and tyrosine?

9-19. **(a)** Calculate the quotient $[H_3PO_4]/[H_2PO_4^-]$ in 0.050 0 M KH_2PO_4.

(b) Find the same quotient for 0.050 0 M K_2HPO_4.

9-20. **(a)** Which two of the following compounds would you mix to make a buffer of pH 7.45: H_3PO_4 (FM 98.00), NaH_2PO_4 (FM 119.98), Na_2HPO_4 (FM 141.96), and Na_3PO_4 (FM 163.94)?

(b) If you wanted to prepare 1.00 L of buffer with a total phosphate concentration of 0.050 0 M, how many grams of each of the two selected compounds would you mix together?

(c) If you did what you calculated in part **(b)**, you would not get a pH of exactly 7.45. Explain how you would really prepare this buffer in the lab.

9-21. Find the pH and the concentration of each species of lysine in a solution of 0.010 0 M lysine · HCl, lysine monohydrochloride.

9-22. How many milliliters of 1.00 M KOH should be added to 100 mL of solution containing 10.0 g of histidine hydrochloride (His · HCl, FM 191.62) to get a pH of 9.30?

9-23. **(a)** Using activity coefficients, calculate the pH of a solution containing a 2.00:1.00 mole ratio of HC^{2-}:C^{3-} (H_3C = citric acid). The ionic strength is 0.010 M.

(b) What will be the pH if the ionic strength is raised to 0.10 M and the mole ratio HC^{2-}:C^{3-} is kept constant?

Which Is the Principal Species?

9-24. The acid HA has pK_a = 7.00.

(a) Which is the principal species, HA or A^-, at pH 6.00?

(b) Which is the principal species at pH 8.00?

(c) What is the quotient $[A^-]/[HA]$ at pH 7.00? at pH 6.00?

9-25. The diprotic acid H_2A has pK_1 = 4.00 and pK_2 = 8.00.

(a) At what pH is $[H_2A] = [HA^-]$?

(b) At what pH is $[HA^-] = [A^{2-}]$?

(c) Which is the principal species at pH 2.00: H_2A, HA^-, or A^{2-}?

(d) Which is the principal species at pH 6.00?

(e) Which is the principal species at pH 10.00?

9-26. The base B has pK_b = 5.00.

(a) What is the value of pK_a for the acid BH^+?

(b) At what pH is $[BH^+] = [B]$?

(c) Which is the principal species at pH 7.00: B or BH^+?

(d) What is the quotient $[B]/[BH^+]$ at pH 12.00?

9-27. Draw the structure of the predominant form of pyridoxal-5-phosphate at pH 7.00.

Fractional Composition Equations

9-28. The acid HA has pK_a = 4.00. Use Equations 9-17 and 9-18 to find the fraction in the form HA and the fraction in the form A^- at pH = 5.00. Does your answer agree with what you expect for the quotient $[A^-]/[HA]$ at pH 5.00?

9-29. A dibasic compound, B, has pK_{b1} = 4.00 and pK_{b2} = 6.00. Find the fraction in the form BH_2^{2+} at pH 7.00, using Equation 9-19. Note that K_1 and K_2 in Equation 9-19 are acid dissociation constants for BH_2^{2+}($K_1 = K_w/K_{b2}$ and $K_2 = K_w/K_{b1}$).

9-30. What fraction of ethane-1,2-dithiol is in each form (H_2A, HA^-, A^{2-}) at pH 8.00? at pH 10.00?

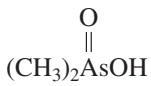
9-31. Calculate α_{H_2A}, α_{HA^-}, and $\alpha_{A^{2-}}$ for *cis*-butenedioic acid at pH 1.00, 1.92, 6.00, 6.27, and 10.00.

9-32. **(a)** Derive equations for α_{H_3A}, $\alpha_{H_2A^-}$, $\alpha_{HA^{2-}}$ and $\alpha_{A^{3-}}$ for a triprotic system.

(b) Calculate the values of these fractions for phosphoric acid at pH 7.00.

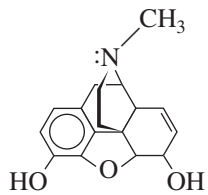
9-33. A solution containing acetic acid, oxalic acid, ammonia, and pyridine has a pH of 9.00. What fraction of ammonia is not protonated?

9-34. A solution was prepared from 10.0 mL of 0.100 M cacodylic acid and 10.0 mL of 0.080 0 M NaOH. To this mixture was added 1.00 mL of 1.27×10^{-6} M morphine. Calling morphine B, calculate the fraction of morphine present in the form BH^+.



Cacodylic acid

$K_a = 6.4 \times 10^{-7}$



Morphine

$K_b = 1.6 \times 10^{-6}$

9-35. *Fractional composition in a diprotic system.* Create a spreadsheet with Equations 9-19 through 9-21 to compute the three curves in Figure 9-4. Plot the three curves in a beautifully labeled figure.

9-36. *Fractional composition in a triprotic system.* For a triprotic system, the fractional composition equations are

$$\alpha_{H_3A} = \frac{[H^+]^3}{D} \qquad \alpha_{HA^{2-}} = \frac{K_1K_2[H^+]}{D}$$

$$\alpha_{H_2A^-} = \frac{K_1[H^+]^2}{D} \qquad \alpha_{A^{3-}} = \frac{K_1K_2K_3}{D}$$

where $D = [H^+]^3 + K_1[H^+]^2 + K_1K_2[H^+] + K_1K_2K_3$. Use these equations to create a fractional composition diagram analogous to Figure 9-4 for the amino acid tyrosine. What is the fraction of each species at pH 10.00?

9-37. *Fractional composition in a tetraprotic system.* Prepare a fractional composition diagram analogous to Figure 9-4 for the tetraprotic system derived from hydrolysis of Cr^{3+}:

$$Cr^{3+} + H_2O \rightleftharpoons Cr(OH)^{2+} + H^+ \qquad K_{a1} = 10^{-3.80}$$

$$Cr(OH)^{2+} + H_2O \rightleftharpoons Cr(OH)_2^+ + H^+ \qquad K_{a2} = 10^{-6.40}$$

$$Cr(OH)_2^+ + H_2O \rightleftharpoons Cr(OH)_3(aq) + H^+ \qquad K_{a3} = 10^{-6.40}$$

$$Cr(OH)_3(aq) + H_2O \rightleftharpoons Cr(OH)_4^- + H^+ \qquad K_{a4} = 10^{-11.40}$$

(Yes, the values of K_{a2} and K_{a3} are equal.)

(a) Use these equilibrium constants to prepare a fractional composition diagram for this tetraprotic system.

(b) You should do this part with your head and your calculator, not your spreadsheet. The solubility of $Cr(OH)_3$ is given by

$$Cr(OH)_3(s) \rightleftharpoons Cr(OH)_3(aq) \qquad K = 10^{-6.84}$$

What concentration of $Cr(OH)_3(aq)$ is in equilibrium with solid $Cr(OH)_3(s)$?

(c) What concentration of $Cr(OH)^{2+}$ is in equilibrium with $Cr(OH)_3(s)$ if the solution pH is adjusted to 4.00?

Isoelectric and Isoionic pH

9-38. What is the difference between the isoelectric pH and the isoionic pH of a protein with many different acidic and basic substituents?

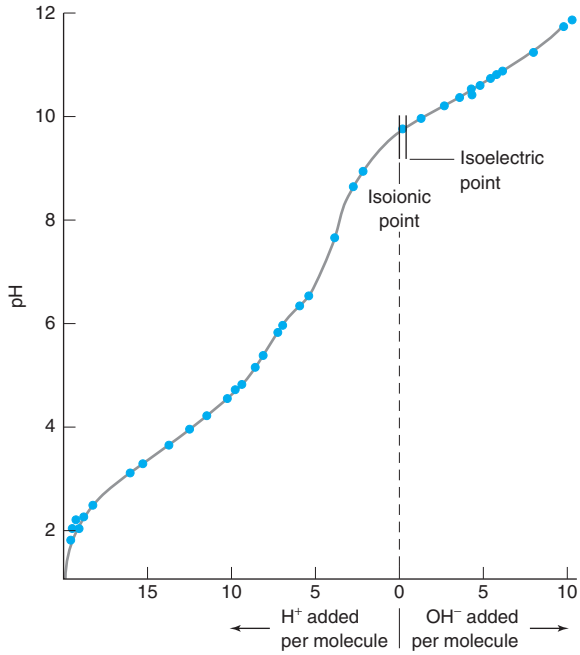
9-39. Explain what is wrong with the following statement: At its isoelectric point, the charge on all molecules of a particular protein is 0.

9-40. Calculate the isoelectric and isoionic pH of 0.010 M threonine.

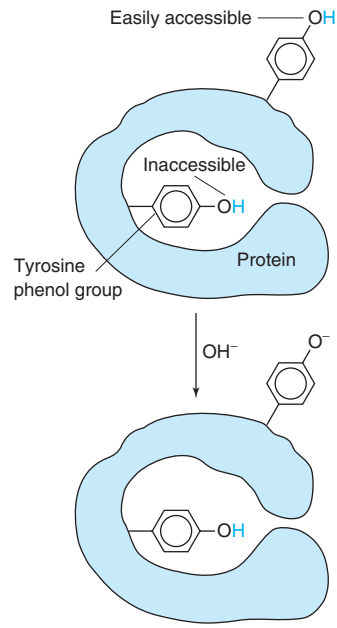
9-41. Explain how isoelectric focusing works.

10 Acid-Base Titrations

ACID-BASE TITRATION OF A PROTEIN



Acid-base titration of the enzyme ribonuclease. The isoionic point is the pH of the pure protein with no ions present except H^+ and OH^-. The isoelectric point is the pH at which the average charge on the protein is zero. [From C. T. Tanford and J. D. Hauenstein, "Hydrogen Ion Equilibria of Ribonuclease," *J. Am. Chem. Soc.* **1956**, *78*, 5287.]



If tyrosine is buried deep inside the protein, it is not readily accessible and a high concentration of OH^- is required to remove the proton from the phenol group.

Ribonuclease is an enzyme with 124 amino acids. Its function is to cleave ribonucleic acid (RNA) into small fragments. A solution containing pure protein, with no other ions present except H^+ and OH^- derived from the protein and water, is said to be *isoionic*. From the isoionic point near pH 9.6 in the graph, the protein can be titrated with acid or base. Of the 124 amino acids, 16 can be protonated by acid and 20 can lose protons to added base. From the shape of the titration curve, it is possible to deduce the approximate pK_a for each titratable group.[1,2] This information provides insight into the environment of that amino acid in the protein. In ribonuclease, three tyrosine residues have "normal" values of pK_a ($\approx$10) (Table 9-1) and three others have $pK_a > 12$. An interpretation is that three tyrosine groups are accessible to OH^-, and three are buried inside the protein where they cannot be easily titrated. The curve in the illustration is calculated from pK_a values for all titratable groups.

Theoretical titration curves for enzymes can be calculated from known crystal structures and first principles of electrostatics. Key amino acids at the active site where catalysis occurs have significantly perturbed pK_a values and unusual behavior in which they are partially protonated over a wide pH region.[3] In principle, such titration calculations can identify the active site of a protein whose structure is known, but whose function is not.

Lipophilicity is a measure of solubility in nonpolar solvents. It is determined from the equilibrium distribution of a drug between water and octanol.

$$\text{Drug}(aq) \rightleftharpoons \text{drug}(\textit{in octanol})$$

$$\text{Lipophilicity} = \log\left(\frac{[\text{drug}\ (\textit{in octanol})]}{[\text{drug}\ (aq)]}\right)$$

From an acid-base titration curve, we can deduce the quantities and pK_a values of acidic and basic substances in a mixture. In medicinal chemistry, the pK_a and *lipophilicity* of a candidate drug predict how easily it will cross cell membranes. From pK_a and pH, we can compute the charge of a polyprotic acid. Usually, the more highly charged a drug, the harder it is for that drug to cross a cell membrane. In this chapter, we learn to predict the shapes of titration curves and to find end points with electrodes and indicators.

10-1 Titration of Strong Base with Strong Acid

For each type of titration in this chapter, *our goal is to construct a graph showing how pH changes as titrant is added*. If you can do this, then you understand what is happening during the titration, and you will be able to interpret an experimental titration curve. pH is usually measured with a glass electrode whose operation is explained in Section 14-5.

First, write the reaction between *titrant* and *analyte*.

The first step in each case is to write the chemical reaction between titrant and analyte. Then use that reaction to calculate the composition and pH after each addition of titrant. As a simple example, let's focus on the titration of 50.00 mL of 0.020 00 M KOH with 0.100 0 M HBr. The chemical reaction between titrant and analyte is merely

The titration reaction.

$$H^+ + OH^- \rightarrow H_2O \qquad K = 1/K_w = 10^{14}$$

Because the equilibrium constant for this reaction is 10^{14}, it is fair to say that it "goes to completion." *Any amount of H^+ added will consume a stoichiometric amount of* OH^-.

It is useful to know the volume of HBr (V_e) needed to reach the equivalence point, which we find by equating moles of KOH being titrated to moles of added HBr:

$$\underbrace{(V_e\,(\cancel{L}))\left(0.100\,0\,\frac{\text{mol}}{\cancel{L}}\right)}_{\substack{\text{mol of HBr}\\ \text{at equivalence point}}} = \underbrace{(0.050\,00\,\cancel{L})\left(0.020\,00\,\frac{\text{mol}}{\cancel{L}}\right)}_{\substack{\text{mol of OH}^-\\ \text{being titrated}}} \Rightarrow V_e = 0.010\,00\ \text{L}$$

Instead of multiplying $\cancel{L} \times (\text{mol}/\cancel{L})$ to get mol, we frequently multiply mL × (mol/L), which is the same as $\cancel{\text{mL}} \times (\text{mmol}/\cancel{\text{mL}}) = \text{mmol}$:

$$\text{mL} \times \frac{\text{mol}}{\text{L}} = \cancel{\text{mL}} \times \frac{\text{mmol}}{\cancel{\text{mL}}} = \text{mmol}$$

$$\underbrace{(V_e\,(\text{mL}))(0.100\,0\ \text{M})}_{\substack{\text{mmol of HBr}\\ \text{at equivalence point}}} = \underbrace{(50.00\ \text{mL})(0.020\,00\ \text{M})}_{\substack{\text{mmol of OH}^-\\ \text{being titrated}}} \Rightarrow V_e = 10.00\ \text{mL}$$

When 10.00 mL of HBr have been added, the titration is complete. Prior to this point, there is excess, unreacted OH^- present. After V_e, there is excess H^+ in the solution.

In the titration of any strong base with any strong acid, there are three regions of the titration curve that require different kinds of calculations:

1. Before the equivalence point, the pH is determined by excess OH^- in the solution.
2. At the equivalence point, H^+ is just sufficient to react with all OH^- to make H_2O. The pH is determined by dissociation of water.
3. After the equivalence point, pH is determined by excess H^+ in the solution.

We will do one sample calculation for each region. Complete results are shown in Table 10-1 and Figure 10-1. As a reminder, the *equivalence point* occurs when added titrant is exactly enough for stoichiometric reaction with the analyte. The equivalence point is the ideal result we seek in a titration. What we actually measure is the *end point*, which is marked by a sudden physical change, such as indicator color or an electrode potential.

Region 1: Before the Equivalence Point

Before the equivalence point, there is excess OH^-.

We will do this calculation once by the method you would have learned in general chemistry, and then we will streamline the process. When 3.00 mL of HBr have been added, the total volume is 53.00 mL. HBr is consumed by NaOH, leaving excess NaOH. The moles of added HBr are (0.100 0 M)(0.003 00 L) = 0.300×10^{-3} mol HBr = 0.300 mmol HBr. The initial moles of NaOH were (0.020 00 M)(0.050 00 L) = 1.000×10^{-3} mol NaOH = 1.000 mmol NaOH. Unreacted OH^- is the difference 1.000 mmol − 0.300 mmol = 0.700 mmol. The concentration of unreacted OH^- is (0.700 mmol)/(53.00 mL) = 0.013 2 M. So, $[H^+] = K_w/[OH^-] = 7.57 \times 10^{-13}$ M and pH = $-\log[H^+]$ = 12.12.

In your sleep,

$$\frac{\text{mmol}}{\text{mL}} = \frac{\text{mol}}{\text{L}} = \text{M}$$

Now here is the streamlined calculation: When 3.00 mL of HBr have been added, the reaction is three-tenths complete because V_e = 10.00 mL. The fraction of OH^- left unreacted

TABLE 10-1 Calculation of the titration curve for 50.00 mL of 0.020 00 M KOH treated with 0.100 0 M HBr

	mL HBr added (V_a)	Concentration of unreacted OH^- (M)	Concentration of excess H^+ (M)	pH
Region 1 (excess OH^-)	0.00	0.020 0		12.30
	1.00	0.017 6		12.24
	2.00	0.015 4		12.18
	3.00	0.013 2		12.12
	4.00	0.011 1		12.04
	5.00	0.009 09		11.95
	6.00	0.007 14		11.85
	7.00	0.005 26		11.72
	8.00	0.003 45		11.53
	9.00	0.001 69		11.22
	9.50	0.000 840		10.92
	9.90	0.000 167		10.22
	9.99	0.000 016 6		9.22
Region 2	10.00	—	—	7.00
Region 3 (excess H^+)	10.01		0.000 016 7	4.78
	10.10		0.000 166	3.78
	10.50		0.000 826	3.08
	11.00		0.001 64	2.79
	12.00		0.003 23	2.49
	13.00		0.004 76	2.32
	14.00		0.006 25	2.20
	15.00		0.007 69	2.11
	16.00		0.009 09	2.04

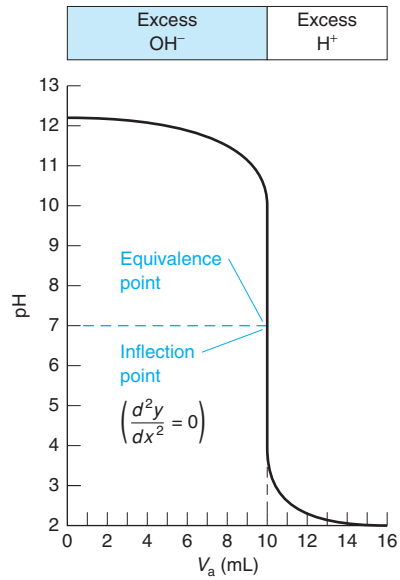


FIGURE 10-1 Calculated titration curve, showing how pH changes as 0.100 0 M HBr is added to 50.00 mL of 0.020 00 M KOH. The equivalence point is an inflection point at which the second derivative is zero.

is seven-tenths. The concentration of remaining OH^- is the product of the fraction remaining, the initial concentration, and a dilution factor:

$$[OH^-] = \underbrace{\left(\frac{10.00 - 3.00}{10.00}\right)}_{\text{Fraction of OH}^- \text{ remaining}} \underbrace{(0.020\,00\text{ M})}_{\text{Initial concentration of OH}^-} \underbrace{\left(\frac{50.00}{50.00 + 3.00}\right)}_{\text{Dilution factor}} = 0.013\,2\text{ M} \qquad \textbf{(10-1)}$$

Initial volume of OH^- (50.00); Total volume of solution (50.00 + 3.00)

$$[H^+] = \frac{K_w}{[OH^-]} = \frac{1.0 \times 10^{-14}}{0.013\,2} = 7.5_7 \times 10^{-13}\text{ M} \Rightarrow \text{pH} = 12.12$$

Equation 10-1 tells us that $[OH^-]$ is equal to a certain fraction of the initial concentration, with a correction for dilution. The dilution factor equals the initial volume of analyte divided by the total volume of solution.

In Table 10-1, the volume of acid added is designated V_a. pH is expressed to the 0.01 decimal place, regardless of what is justified by significant figures. We do this for the sake of consistency and also because 0.01 is near the limit of accuracy in pH measurements.

Challenge Using a setup similar to Equation 10-1, calculate $[OH^-]$ when 6.00 mL of HBr have been added. Check your pH against the value in Table 10-1.

Region 2: At the Equivalence Point

Region 2 is the equivalence point, where just enough H^+ has been added to consume OH^-. We could prepare the same solution by dissolving KBr in water. pH is determined by dissociation of water:

$$H_2O \rightleftharpoons \underset{x}{H^+} + \underset{x}{OH^-}$$

$$K_w = x^2 \Rightarrow x = 1.00 \times 10^{-7}\text{ M} \Rightarrow \text{pH} = 7.00$$

The pH at the equivalence point in the titration of any strong base (or acid) with strong acid (or base) will be 7.00 at 25°C.

At the equivalence point, pH = 7.00, but *only* in a strong-acid–strong-base reaction.

We will soon discover that *the pH is **not** 7.00 at the equivalence point in the titration of weak acids or bases*. The pH is 7.00 only if the titrant and analyte are both strong.

Region 3: After the Equivalence Point

Beyond the equivalence point, we are adding excess HBr to the solution. The concentration of excess H^+ at, say, 10.50 mL is given by

After the equivalence point, there is excess H^+.

$$[H^+] = \underbrace{(0.100\,0\text{ M})}_{\substack{\text{Initial}\\\text{concentration}\\\text{of } H^+}}\underbrace{\left(\frac{0.50}{50.00 + 10.50}\right)}_{\substack{\text{Dilution}\\\text{factor}}} = 8.26 \times 10^{-4}\text{ M}$$

Volume of excess H^+

Total volume of solution

$$\text{pH} = -\log[H^+] = 3.08$$

At $V_a = 10.50$ mL, there is an excess of just $V_a - V_e = 10.50 - 10.00 = 0.50$ mL of HBr. That is the reason why 0.50 appears in the dilution factor.

The Titration Curve

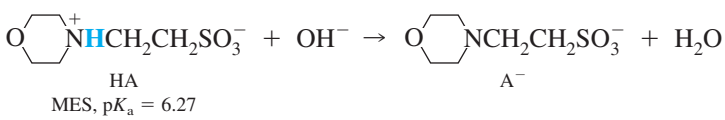
The titration curve in Figure 10-1 exhibits a rapid change in pH near the equivalence point. The equivalence point is where the slope ($d\text{pH}/dV_a$) is greatest (and the second derivative is 0, which makes it an *inflection point*). To repeat an important statement, the pH at the equivalence point is 7.00 *only* in a strong-acid–strong-base titration. If one or both of the reactants is weak, the equivalence point pH is *not* 7.00.

10-2 Titration of Weak Acid with Strong Base

The titration of a weak acid with a strong base allows us to put all our knowledge of acid-base chemistry to work. The example we examine is the titration of 50.00 mL of 0.020 00 M MES with 0.100 0 M NaOH. MES is an abbreviation for 2-(*N*-morpholino)ethanesulfonic acid, which is a weak acid with $pK_a = 6.27$.

The *titration reaction* is

Always start by writing the titration reaction.



(10-2)

Reaction 10-2 is the reverse of the K_b reaction for the base A^-. Therefore, the equilibrium constant for Reaction 10-2 is $K = 1/K_b = 1/(K_w/K_a \text{ (for HA)}) = 5.4 \times 10^7$. The equilibrium constant is so large that we can say that the reaction goes "to completion" after each addition of OH^-. As we saw in Box 8-3, *strong plus weak react completely*.

Strong + weak → complete reaction

Let's first calculate the volume of base, V_b, needed to reach the equivalence point:

$$\underbrace{(V_b\text{ (mL)})(0.100\,0\text{ M})}_{\text{mmol of base}} = \underbrace{(50.00\text{ mL})(0.020\,00\text{ M})}_{\text{mmol of HA}} \Rightarrow V_b = 10.00\text{ mL}$$

The titration calculations for this problem are of four types:

1. Before any base is added, the solution contains just HA in water. This is a weak acid whose pH is determined by the equilibrium

$$HA \overset{K_a}{\rightleftharpoons} H^+ + A^-$$

2. From the first addition of NaOH until immediately before the equivalence point, there is a mixture of unreacted HA plus the A^- produced by Reaction 10-2. *Aha! A buffer!* We can use the Henderson-Hasselbalch equation to find the pH.
3. At the equivalence point, "all" HA has been converted into A^-. The same solution could have been made by dissolving A^- in water. We have a weak base whose pH is determined by the reaction

$$A^- + H_2O \overset{K_b}{\rightleftharpoons} HA + OH^-$$

4. Beyond the equivalence point, excess NaOH is being added to a solution of A^-. To a good approximation, pH is determined by the strong base. We calculate the pH as if we had simply added excess NaOH to water. We neglect the tiny effect of A^-.

Region 1: Before Base Is Added

Before adding any base, we have a solution of 0.020 00 M HA with $pK_a = 6.27$. This is simply a weak-acid problem.

The initial solution contains just the *weak acid* HA.

$$\underset{F-x}{HA} \rightleftharpoons \underset{x}{H^+} + \underset{x}{A^-} \qquad K_a = 10^{-6.27}$$

$$\frac{x^2}{0.020\,00 - x} = K_a \Rightarrow x = 1.03 \times 10^{-4} \Rightarrow pH = 3.99$$

Region 2: Before the Equivalence Point

Adding OH^- creates a mixture of HA and A^-. This mixture is a buffer whose pH can be calculated with the Henderson-Hasselbalch equation (8-16) from the quotient $[A^-]/[HA]$.

Before the equivalence point, there is a mixture of HA and A^-, which is a *buffer*.

Suppose we wish to calculate $[A^-]/[HA]$ when 3.00 mL of OH^- have been added. Because $V_e = 10.00$ mL, we have added enough base to react with three-tenths of the HA. We can make a table showing the relative concentrations before and after the reaction:

We only need *relative* concentrations because pH depends on the quotient $[A^-]/[HA]$.

Titration reaction:	HA	$+ OH^-$	$\rightarrow A^-$	$+ H_2O$
Relative initial quantities (HA ≡ 1)	1	$\frac{3}{10}$	—	—
Relative final quantities	$\frac{7}{10}$	—	$\frac{3}{10}$	—

Once we know the *quotient* $[A^-]/[HA]$ in any solution, we know its pH:

$$pH = pK_a + \log\left(\frac{[A^-]}{[HA]}\right) = 6.27 + \log\left(\frac{3/10}{7/10}\right) = 5.90$$

The point at which the volume of titrant is $\frac{1}{2}V_e$ is a special one in any titration.

Titration reaction:	HA	$+ OH^-$	$\rightarrow A^-$	$+ H_2O$
Relative initial quantities	1	$\frac{1}{2}$	—	—
Relative final quantities	$\frac{1}{2}$	—	$\frac{1}{2}$	—

$$pH = pK_a + \log\left(\frac{1/2}{1/2}\right) = pK_a$$

When $V_b = \frac{1}{2}V_e$, $pH = pK_a$. This is a landmark in any titration.

When the volume of titrant is $\frac{1}{2}V_e$, $pH = pK_a$ for the acid HA (neglecting activity coefficients). From an experimental titration curve, you can find the approximate value of pK_a by reading the pH when $V_b = \frac{1}{2}V_e$, where V_b is the volume of added base. (To find the true value of pK_a requires activity coefficients.)

Advice As soon as you recognize a mixture of HA and A^- in any solution, *you have a buffer!* You can calculate the pH from the quotient $[A^-]/[HA]$.

$$pH = pK_a + \log\left(\frac{[A^-]}{[HA]}\right)$$

Learn to recognize buffers! They lurk in every corner of acid-base chemistry.

Region 3: At the Equivalence Point

At the equivalence point, there is exactly enough NaOH to consume HA.

At the equivalence point, HA has been converted into A^-, a *weak base*.

Titration reaction:	HA	$+ OH^-$	$\rightarrow A^-$	$+ H_2O$
Relative initial quantities	1	1	—	—
Relative initial quantities	—	—	1	—

The solution contains "just" A^-. We could have prepared the same solution by dissolving the salt Na^+A^- in distilled water. *A solution of Na^+A^- is merely a solution of a weak base.*

To compute the pH of a weak base, we write the reaction of the weak base with water:

$$\underset{F-x}{A^-} + H_2O \rightleftharpoons \underset{x}{HA} + \underset{x}{OH^-} \qquad K_b = \frac{K_w}{K_a}$$

The only tricky point is that the formal concentration of A^- is no longer 0.020 00 M, which was the initial concentration of HA. A^- has been diluted by NaOH from the buret:

$$F' = \underbrace{(0.020\,00\text{ M})}_{\substack{\text{Initial}\\\text{concentration}\\\text{of HA}}}\underbrace{\left(\frac{\overset{\text{Initial volume of HA}}{50.00}}{\underset{\text{Total volume of solution}}{50.00 + 10.00}}\right)}_{\substack{\text{Dilution}\\\text{factor}}} = 0.016\,7\text{ M}$$

With this value of F′, we can solve the problem:

$$\frac{x^2}{F' - x} = K_b = \frac{K_w}{K_a} = 1.86 \times 10^{-8} \Rightarrow x = 1.76 \times 10^{-5}\text{ M}$$

$$pH = -\log[H^+] = -\log\left(\frac{K_w}{x}\right) = 9.25$$

The pH is always higher than 7 at the equivalence point in the titration of a weak acid with a strong base.

The pH at the equivalence point in this titration is 9.25. **It is not 7.00.** The equivalence-point pH will *always* be above 7 for the titration of a weak acid, because the acid is converted into its conjugate base at the equivalence point.

Region 4: After the Equivalence Point

Here we assume that the pH is governed by the excess OH^-.

Now we are adding NaOH to a solution of A^-. The base NaOH is so much stronger than the base A^- that it is fair to say that the pH is determined by the excess OH^-.

Let's calculate the pH when $V_b = 10.10$ mL, which is just 0.10 mL past V_e. The concentration of excess OH^- is

$$[OH^-] = \underbrace{(0.100\,0\text{ M})}_{\substack{\text{Initial}\\\text{concentration}\\\text{of OH}^-}}\underbrace{\left(\frac{\overset{\text{Volume of excess OH}^-}{0.10}}{\underset{\text{Total volume of solution}}{50.00 + 10.10}}\right)}_{\substack{\text{Dilution}\\\text{factor}}} = 1.66 \times 10^{-4}\text{ M}$$

$$pH = -\log\left(\frac{K_w}{[OH^-]}\right) = 10.22$$

Challenge Compare the concentration of OH^- from excess titrant at $V_b = 10.10$ mL to the concentration of OH^- from hydrolysis of A^-. Satisfy yourself that it is fair to neglect the contribution of A^- to the pH after the equivalence point.

The Titration Curve

Landmarks in a titration:

At $V_b = V_e$, the curve is steepest.

At $V_b = \frac{1}{2}V_e$, pH = pK_a and the slope is minimal.

The *buffer capacity* measures the ability of the solution to resist changes in pH.

Calculations for the titration of MES with NaOH are shown in Table 10-2. The calculated titration curve in Figure 10-2 has two easily identified points. One is the equivalence point, which is the steepest part of the curve. The other landmark is the point where $V_b = \frac{1}{2}V_e$ and pH = pK_a. This latter point is also an inflection point, having the minimum slope.

If you look back at Figure 8-4b, you will note that the maximum *buffer capacity* occurs when pH = pK_a. That is, the solution is most resistant to pH changes when pH = pK_a (and $V_b = \frac{1}{2}V_e$); the slope (dpH/dV_b) is therefore at its minimum.

Figure 10-3 shows how the titration curve depends on the acid dissociation constant of HA and on the concentrations of reactants. As HA becomes a weaker acid, or as the concentrations of analyte and titrant decrease, the inflection near the equivalence point decreases, until the equivalence point becomes too shallow to detect. *It is not practical to titrate an acid or a base when its strength is too weak or its concentration too dilute.*

10-3 Titration of Weak Base with Strong Acid

The titration of a weak base with a strong acid is the reverse of the titration of a weak acid with a strong base. The *titration reaction* is

$$B + H^+ \rightarrow BH^+$$

TABLE 10-2 Calculation of the titration curve for 50.00 mL of 0.020 00 M MES treated with 0.100 0 M NaOH

	mL base added (V_b)	pH
Region 1	0.00	3.99
(weak acid)	0.50	4.99
	1.00	5.32
	2.00	5.67
	3.00	5.90
	4.00	6.09
Region 2	5.00	6.27
(buffer)	6.00	6.45
	7.00	6.64
	8.00	6.87
	9.00	7.22
	9.50	7.55
	9.90	8.27
Region 3	10.00	9.25
(weak base)	10.10	10.22
	10.50	10.91
	11.00	11.21
Region 4	12.00	11.50
(excess OH^-)	13.00	11.67
	14.00	11.79
	15.00	11.88
	16.00	11.95

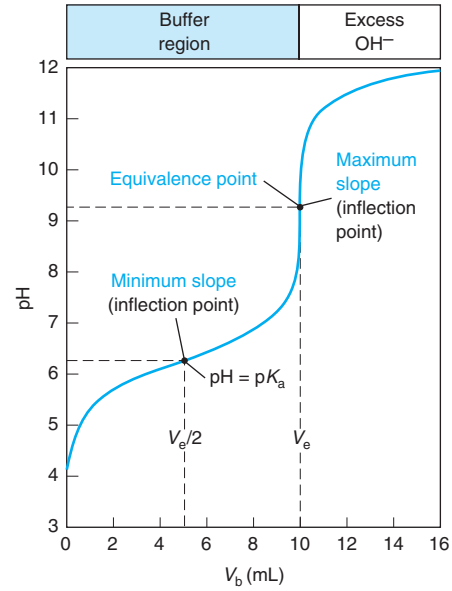


FIGURE 10-2 Calculated titration curve for the reaction of 50.00 mL of 0.020 00 M MES with 0.100 0 M NaOH. Landmarks occur at half of the equivalence volume (pH = pK_a) and at the equivalence point, which is the steepest part of the curve.

Because the reactants are a weak base and a strong acid, the reaction goes essentially to completion after each addition of acid. There are four distinct regions of the titration curve:

1. Before acid is added, the solution contains just the weak base, B, in water. The pH is determined by the K_b reaction.

$$\underset{F-x}{B} + H_2O \overset{K_b}{\rightleftharpoons} \underset{x}{BH^+} + \underset{x}{OH^-}$$

When V_a (= volume of added acid) = 0, we have a *weak-base* problem.

2. Between the initial point and the equivalence point, there is a mixture of B and BH^+—*Aha! A buffer!* The pH is computed by using

$$pH = pK_a\,(\text{for } BH^+) + \log\left(\frac{[B]}{[BH^+]}\right)$$

When $0 < V_a < V_e$, we have a *buffer*.

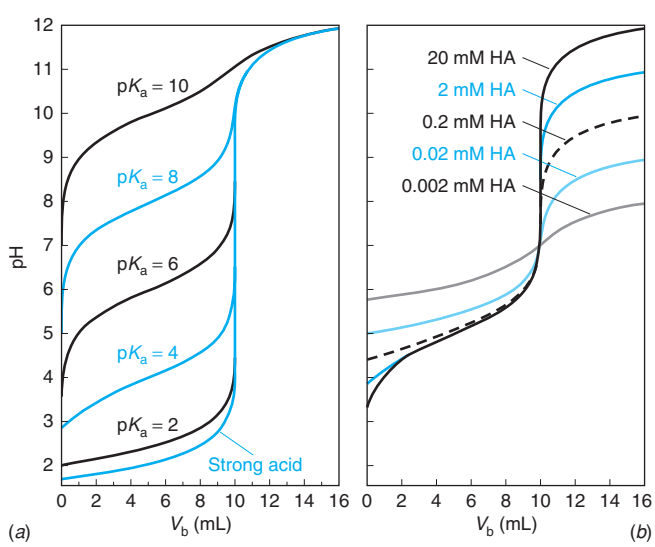


FIGURE 10-3 (*a*) Calculated curves showing the titration of 50.0 mL of 0.020 0 M HA with 0.100 M NaOH. (*b*) Calculated curves showing the titration of 50.0 mL of HA (pK_a = 5) with NaOH whose concentration is five times greater than that of HA. As the acid becomes weaker or more dilute, the end point becomes less distinct.

In adding acid (increasing V_a), we reach the special point where $V_a = \frac{1}{2}V_e$ and $pH = pK_a$ (for BH^+). As before, pK_a can be determined easily from the titration curve.

3. At the equivalence point, B has been converted into BH^+, a weak acid. The pH is calculated by considering the acid dissociation reaction of BH^+.

When $V_a = V_e$, the solution contains the *weak acid* BH^+.

$$\underset{F' - x}{BH^+} \rightleftharpoons \underset{x}{B} + \underset{x}{H^+} \qquad K_a = \frac{K_w}{K_b}$$

The formal concentration of BH^+, F′, is not the original formal concentration of B because some dilution has occurred. The solution contains BH^+ at the equivalence point, so it is acidic. *The pH at the equivalence point must be below 7.*

For $V_a > V_e$, there is excess *strong acid*.

4. After the equivalence point, the excess strong acid determines the pH. We neglect the contribution of weak acid, BH^+.

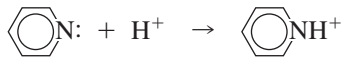
EXAMPLE **Titration of Pyridine with HCl**

Consider the titration of 25.00 mL of 0.083 64 M pyridine with 0.106 7 M HCl.

Pyridine

$$K_b = 1.59 \times 10^{-9} \Rightarrow K_a = \frac{K_w}{K_b} = 6.31 \times 10^{-6} \qquad pK_a = 5.20$$

The titration reaction is



and the equivalence point occurs at 19.60 mL:

$$\underbrace{(V_e\,(\text{mL}))(0.106\,7\text{ M})}_{\text{mmol of HCl}} = \underbrace{(25.00\text{ mL})(0.083\,64\text{ M})}_{\text{mmol of pyridine}} \Rightarrow V_e = 19.60\text{ mL}$$

Find the pH when $V_a = 4.63$ mL.

Solution Part of the pyridine has been neutralized, so there is a mixture of pyridine and pyridinium ion—*Aha! A buffer!* The fraction of pyridine that has been titrated is 4.63/19.60 = 0.236, because it takes 19.60 mL to titrate the whole sample. The fraction of pyridine remaining is 1 − 0.236 = 0.764. The pH is

$$pH = pK_a + \log\left(\frac{[B]}{[BH^+]}\right)$$

$$= 5.20 + \log\frac{0.764}{0.236} = 5.71$$

Test Yourself Find the pH when $V_a = 14.63$ mL. (***Answer:*** 4.73)

10-4 Titrations in Diprotic Systems

The principles developed for titrations of monoprotic acids and bases are readily extended to titrations of polyprotic acids and bases. We will examine two cases.

A Typical Case

The upper curve in Figure 10-4 is calculated for the titration of 10.0 mL of 0.100 M base (B) with 0.100 M HCl. The base is dibasic, with $pK_{b1} = 4.00$ and $pK_{b2} = 9.00$. The titration curve has reasonably sharp breaks at both equivalence points, corresponding to the reactions

$$B + H^+ \rightarrow BH^+$$

$$BH^+ + H^+ \rightarrow BH_2^{2+}$$

The volume at the first equivalence point is 10.00 mL because

$$\underbrace{(V_e\,(\text{mL}))(0.100\text{ M})}_{\text{mmol of HCl}} = \underbrace{(10.00\text{ mL})(0.100\,0\text{ M})}_{\text{mmol of B}} \Rightarrow V_e = 10.00\text{ mL}$$

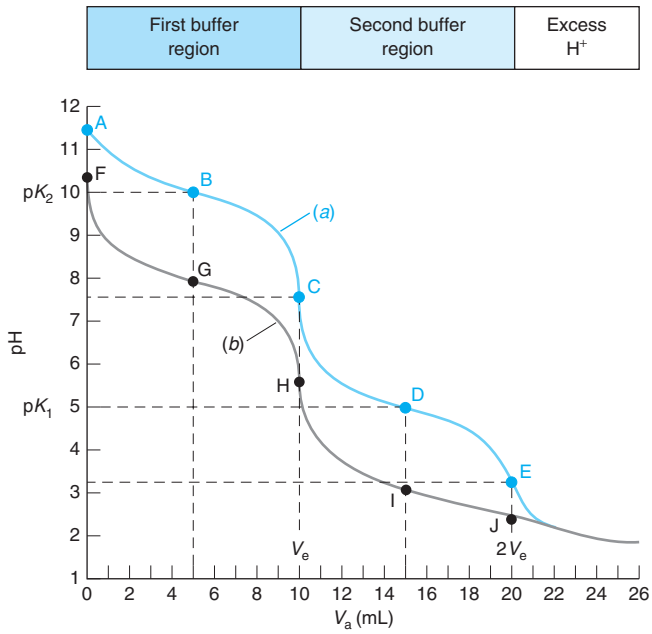


FIGURE 10-4 (*a*) Titration of 10.0 mL of 0.100 M base (pK_{b1} = 4.00, pK_{b2} = 9.00) with 0.100 M HCl. The two equivalence points are C and E. Points B and D are the half-neutralization points, whose pH values equal pK_{a2} and pK_{a1}, respectively. (*b*) Titration of 10.0 mL of 0.100 M nicotine (pK_{b1} = 6.15, pK_{b2} = 10.85) with 0.100 M HCl. There is no sharp break at the second equivalence point, J, because the pH is too low.

The volume at the second equivalence point must be $2V_e$, because the second reaction requires the same number of moles of HCl as the first reaction.

$V_{e2} = 2V_{e1}$, always.

The pH calculations are similar to those for corresponding points in the titration of a monobasic compound. Let's examine points A through E in Figure 10-4.

Point A

Before acid is added, the solution contains just weak base, B, whose pH is governed by the reaction

The fully basic form of a dibasic compound can be treated as if it were monobasic. (The K_{b2} reaction can be neglected.)

$$\underset{0.100 - x}{B} + H_2O \overset{K_{b1}}{\rightleftharpoons} \underset{x}{BH^+} + \underset{x}{OH^-}$$

$$\frac{x^2}{0.100 - x} = 1.00 \times 10^{-4} \Rightarrow x = 3.11 \times 10^{-3}$$

$$[H^+] = \frac{K_w}{x} \Rightarrow pH = 11.49$$

Point B

At any point between A (the initial point) and C (the first equivalence point), we have a buffer containing B and BH^+. Point B is halfway to the equivalence point, so $[B] = [BH^+]$. The pH is calculated from the Henderson-Hasselbalch equation *for the weak acid*, BH^+, whose acid dissociation constant is K_{a2} (for BH_2^{2+}) $= K_w/K_{b1} = 10^{-10.00}$.

Of course, you remember that

$$K_{a2} = \frac{K_w}{K_{b1}} \qquad K_{a1} = \frac{K_w}{K_{b2}}$$

$$pH = pK_{a2} + \log\frac{[B]}{[BH^+]} = 10.00 + \log 1 = 10.00$$

So the pH at point B is just pK_{a2}.

To calculate the quotient $[B]/[BH^+]$ at any point in the buffer region, just find what fraction of the way from point A to point C the titration has progressed. For example, if V_a = 1.5 mL, then

$$\frac{[B]}{[BH^+]} = \frac{8.5}{1.5}$$

because 10.0 mL are required to reach the equivalence point and we have added just 1.5 mL. The pH at V_a = 1.5 mL is

$$pH = 10.00 + \log\frac{8.5}{1.5} = 10.75$$

Point C

At the first equivalence point, *B has been converted into BH^+, the intermediate form of the diprotic acid, BH_2^{2+}. BH^+ is both an acid and a base*. From Equation 9-11, we know that

BH^+ is the *intermediate form* of a diprotic acid.

$$pH \approx \frac{1}{2}(pK_1 + pK_2)$$

$$[H^+] \approx \sqrt{\frac{K_1K_2F + K_1K_w}{K_1 + F}} \qquad \textbf{(10-3)}$$

where K_1 and K_2 are the acid dissociation constants of BH_2^{2+}.

The formal concentration of BH^+ is calculated by considering dilution of the original solution of B.

$$F = \underbrace{(0.100\ M)}_{\text{Original concentration of B}}\underbrace{\left(\frac{10.0}{20.0}\right)}_{\text{Dilution factor}} = 0.050\,0\ M$$

Initial volume of B

Total volume of solution

Plugging all the numbers into Equation 10-3 gives

$$[H^+] = \sqrt{\frac{(10^{-5})(10^{-10})(0.050\,0) + (10^{-5})(10^{-14})}{10^{-5} + 0.050\,0}} = 3.16 \times 10^{-8}$$

$$pH = 7.50$$

Note that, in this example, $pH = \frac{1}{2}(pK_{a1} + pK_{a2})$.

The intermediate form of a polyprotic acid is the worst possible choice for a buffer.

Point C in Figure 10-4 shows where the intermediate form of a diprotic acid lies on a titration curve. This is the *least-buffered* point on the whole curve, because the pH changes most rapidly if small amounts of acid or base are added. There is a misconception that the intermediate form of a diprotic acid behaves as a buffer when, in fact, it is the *worst choice* for a buffer.

Point D

At any point between C and E, there is a buffer containing BH^+ (the base) and BH_2^{2+} (the acid). When $V_a = 15.0$ mL, $[BH^+] = [BH_2^{2+}]$ and

$$pH = pK_{a1} + \log\frac{[BH^+]}{[BH_2^{2+}]} = 5.00 + \log 1 = 5.00$$

Challenge Show that, if V_a were 17.2 mL, the ratio in the log term would be

$$\frac{[BH^+]}{[BH_2^{2+}]} = \frac{20.0 - 17.2}{17.2 - 10.0} = \frac{2.8}{7.2}$$

Point E

Point E is the second equivalence point, at which the solution is formally the same as one prepared by dissolving BH_2Cl_2 in water. The formal concentration of BH_2^{2+} is

$$F = (0.100\ M)\left(\frac{10.0}{30.0}\right) = 0.033\,3\ M$$

Original volume of B

Total volume of solution

The pH is determined by the acid dissociation reaction of BH_2^{2+}.

At the second equivalence point, we have made BH_2^{2+}, which can be treated as a monoprotic weak acid.

$$\underset{F - x}{BH_2^{2+}} \rightleftharpoons \underset{x}{BH^+} + \underset{x}{H^+} \qquad K_{a1} = \frac{K_w}{K_{b2}}$$

$$\frac{x^2}{0.033\,3 - x} = 1.0 \times 10^{-5} \Rightarrow x = 5.72 \times 10^{-4} \Rightarrow pH = 3.24$$

Beyond the second equivalence point ($V_a > 20.0$ mL), the pH of the solution can be calculated from the volume of strong acid added to the solution. For example, at $V_a = 25.00$ mL, there is an excess of 5.00 mL of 0.100 M HCl in a total volume of 10.00 + 25.00 = 35.00 mL. The pH is found by writing

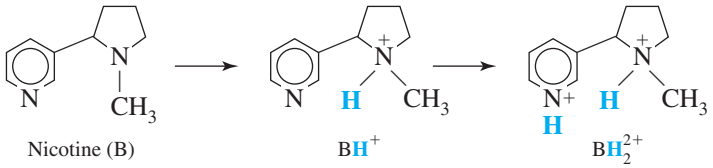
$$[H^+] = (0.100\ M)\left(\frac{5.00}{35.00}\right) = 1.43 \times 10^{-2}\ M \Rightarrow pH = 1.85$$

Blurred End Points

When the pH is too low or too high or when pK_a values are too close together, end points are obscured.

Titrations of many diprotic acids or bases show two clear end points, as in curve *a* in Figure 10-4. Some titrations do not show both end points, as illustrated by curve *b*, which is calculated

for the titration of 10.0 mL of 0.100 M nicotine ($pK_{b1} = 6.15$, $pK_{b2} = 10.85$) with 0.100 M HCl. The two reactions are



There is no perceptible break at the second equivalence point (J), because BH_2^{2+} is too strong an acid (or, equivalently, BH^+ is too weak a base). As the titration approaches low pH ($\lesssim 3$), the approximation that HCl reacts completely with BH^+ to give BH_2^{2+} breaks down. To calculate pH between points I and J requires the systematic treatment of equilibrium. Later in this chapter, we describe how to calculate the whole curve with a spreadsheet.

In the titration of ribonuclease at the beginning of this chapter, there is a continuous change in pH, with no clear breaks. The reason why there are no breaks is that 29 groups are titrated in the pH interval shown. The 29 end points are so close together that a nearly uniform rise results. The curve can be analyzed to find the many pK_a values, but the individual pK_a values will not be determined very precisely.

10-5 Finding the End Point with a pH Electrode

Titrations are commonly performed to find out how much analyte is present or to measure equilibrium constants. We can obtain the information necessary for both purposes by monitoring pH during the titration. Figure 2-12 showed an *autotitrator*, which performs the entire operation automatically.[6] The instrument waits for pH to stabilize after each addition of titrant, before adding the next increment. The end point is computed automatically by finding the maximum slope in the titration curve.

Box 10-1 illustrates an important application of acid-base titrations in environmental analysis.

Figure 10-5a shows experimental results for the manual titration of a hexaprotic weak acid, H_6A, with NaOH. Because the compound is difficult to purify, only a tiny amount was available for titration. Just 1.430 mg was dissolved in 1.000 mL of aqueous solution and titrated with microliter quantities of 0.065 92 M NaOH, delivered with a Hamilton syringe.

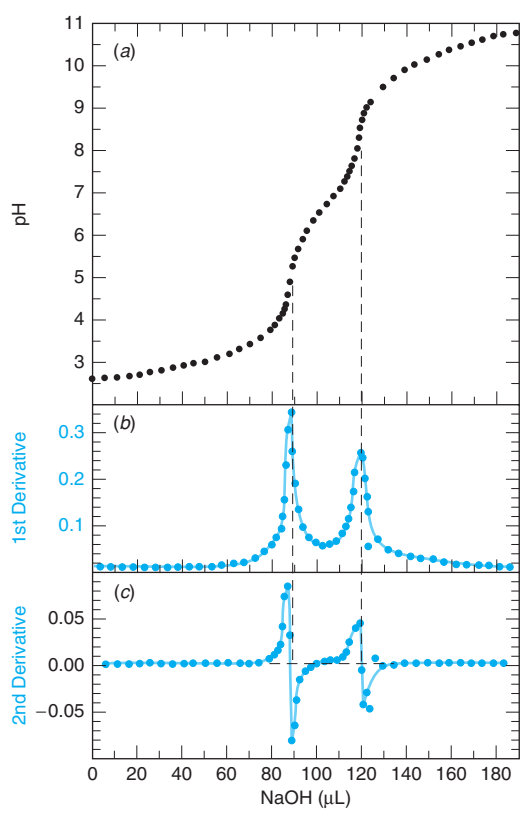


FIGURE 10-5 (*a*) Experimental points in the titration of 1.430 mg of xylenol orange, a hexaprotic acid, dissolved in 1.000 mL of aqueous 0.10 M $NaNO_3$. The titrant was 0.065 92 M NaOH. (*b*) The first derivative, $\Delta pH/\Delta V$, of the titration curve. (*c*) The second derivative, $\Delta(\Delta pH/\Delta V)/\Delta V$, which is the derivative of the curve in panel *b*. Derivatives for the first end point are calculated in Figure 10-6. End points are taken as maxima in the derivative curve and zero crossings of the second derivative.

BOX 10-1 Alkalinity and Acidity

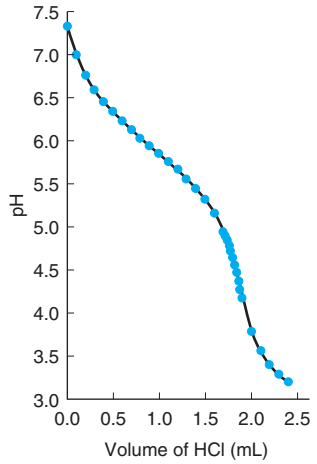
The *alkalinity* of a sample of natural water is defined as the moles of HCl equivalent to the excess moles of basic species in the sample from weak acids with $pK_a > 4.5$ at 25°C and zero ionic strength.[4] Alkalinity is approximately equal to the moles of HCl needed to bring 1 kg of water to pH 4.5, which is the second equivalence point in the titration of CO_3^{2-}. To a good approximation,

$$\text{Alkalinity} \approx [OH^-] + 2[CO_3^{2-}] + [HCO_3^-]$$

When water is titrated with HCl to pH 4.5, OH^-, CO_3^{2-}, and HCO_3^- will have reacted. Minor species that could contribute to alkalinity in natural waters include phosphate, borate, silicate, fluoride, ammonia, sulfide, and organic compounds. In oceanography, alkalinity is used to estimate anthropogenic (man-made) CO_2 penetration into the ocean and in measuring the marine $CaCO_3$ budget (sources and sinks for $CaCO_3$).[5] Oceanographers must account for salinity (ionic strength) and temperature in the measurement of alkalinity.[4]

Alkalinity and *hardness* (dissolved Ca^{2+} and Mg^{2+}, Box 11-3) are important characteristics of irrigation water. Alkalinity in excess of the $Ca^{2+} + Mg^{2+}$ content is called "residual sodium carbonate." Water with a residual sodium carbonate content equivalent to ≥2.5 mmol H^+/kg is not suitable for irrigation. Residual sodium carbonate between 1.25 and 2.5 mmol H^+/kg is marginal, whereas ≤1.25 mmol H^+/kg is suitable for irrigation.

Acidity of natural waters refers to the total acid content that can be titrated to pH 8.3 with NaOH. This pH is the second equivalence point for titration of carbonic acid (H_2CO_3) with OH^-. Almost all weak acids in the water also will be titrated in this procedure. Acidity is expressed as millimoles of OH^- needed to bring 1 kg of water to pH 8.3.



Alkalinity titration of 165.4 mL of saltwater at 20.05°C with 0.209 5 M HCl in a closed cell to prevent escape of CO_2. HCl contains NaCl, so ionic strength remains constant. [Data from Dickson.[4]]

Figure 10-5a shows two clear breaks, near 90 and 120 μL, which correspond to titration of the *third* and *fourth* protons of H_6A.

$$H_4A^{2-} + OH^- \rightarrow H_3A^{3-} + H_2O \qquad (\sim 90\ \mu L \text{ equivalence point})$$

$$H_3A^{3-} + OH^- \rightarrow H_2A^{4-} + H_2O \qquad (\sim 120\ \mu L \text{ equivalence point})$$

The first two and last two equivalence points are unrecognizable, because they occur at too low or too high a pH.

Using Derivatives to Find the End Point

End point: maximum slope second derivative = 0.

The end point is taken as the volume where the slope (dpH/dV) of the titration curve is greatest. The slope (first derivative) in Figure 10-5b is calculated in the spreadsheet in Figure 10-6.

	A	B	C	D	E	F
1	Derivatives of a Titration Curve					
2	Data		1st derivative		2nd derivative	
3	μL NaOH	pH	μL	ΔpH/ΔμL		Δ(ΔpH/ΔμL)
4	85.0	4.245			μL	ΔμL
5			85.5	0.155		
6	86.0	4.400			86.0	0.0710
7			86.5	0.226		
8	87.0	4.626			87.0	0.0810
9			87.5	0.307		
10	88.0	4.933			88.0	0.0330
11			88.5	0.340		
12	89.0	5.273			89.0	−0.0830
13			89.0	0.257		
14	90.0	5.530			90.0	−0.0680
15			90.5	0.189		
16	91.0	5.719			91.25	−0.0390
17			92.0	0.131		
18	93.0	5.980				
19	Representative formulas:					
20	C5 = (A6+A4)/2			E6 = (C7+C5)/2		
21	D5 = (B6−B4)/(A6−A4)			F6 = (D7−D5)/(C7−C5)		

FIGURE 10-6 Spreadsheet for computing first and second derivatives near 90 μL in Figure 10-5.

The first two columns contain experimental volume and pH. (The pH meter was precise to three digits, even though accuracy ends in the second decimal place.) To compute the first derivative, each pair of volumes is averaged and the quantity $\Delta pH/\Delta V$ is calculated. ΔpH is the change in pH between consecutive readings and ΔV is the change in volume between consecutive additions. Figure 10-5c and the last two columns of the spreadsheet give the second derivative, computed in an analogous manner. The end point is the volume at which the second derivative is 0. Figure 10-7 allows us to make good estimates of the end points.

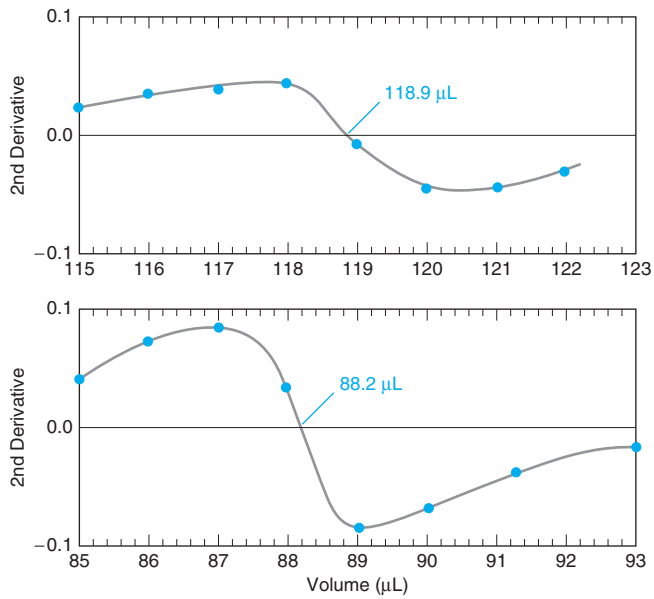


FIGURE 10-7 Enlargement of the end-point regions in the second derivative curve shown in Figure 10-5c.

EXAMPLE **Computing Derivatives of a Titration Curve**

Let's see how the first and second derivatives in Figure 10-6 are calculated.

Solution The first number in the third column, 85.5, is the average of the first two volumes (85.0 and 86.0) in the first column. The derivative $\Delta pH/\Delta V$ is calculated from the first two pH values and the first two volumes:

$$\frac{\Delta pH}{\Delta V} = \frac{4.400 - 4.245}{86.0 - 85.0} = 0.155$$

The coordinates ($x = 85.5$, $y = 0.155$) are one point in the graph of the first derivative in Figure 10-5b.

The second derivative is computed from the first derivative. The first entry in the fifth column of Figure 10-6 is 86.0, which is the average of 85.5 and 86.5. The second derivative is

$$\frac{\Delta(\Delta pH/\Delta V)}{\Delta V} = \frac{0.226 - 0.155}{86.5 - 85.5} = 0.071$$

The coordinates ($x = 86.0$, $y = 0.071$) are plotted in the second derivative graph in Figure 10-6c.

Test Yourself Verify the derivative in cell D7 of Figure 10-6.

Using a Gran Plot to Find the End Point[7,8]

A problem with using derivatives to find the end point is that titration data are least accurate right near the end point, because buffering is minimal and electrode response is sluggish. A **Gran plot** uses data from before the end point (typically from 0.8 V_e or 0.9 V_e up to V_e) to locate the end point.

A related method uses data from the middle of the titration (not near the equivalence point) to deduce V_e and K_a.[9]

Consider the titration of a weak acid, HA:

$$HA \rightleftharpoons H^+ + A^- \qquad K_a = \frac{[H^+]\gamma_{H^+}[A^-]\gamma_{A^-}}{[HA]\gamma_{HA}}$$

It will be necessary to include activity coefficients in this discussion because a pH electrode responds to hydrogen ion *activity*, not concentration.

Strong plus weak react completely.

Prior to the equivalence point, it is a good approximation to say that each mole of NaOH converts 1 mol of HA into 1 mol of A^-. If we titrate V_a mL of HA (whose formal concentration is F_a) with V_b mL of NaOH (whose formal concentration is F_b), we can write

$$[A^-] = \frac{\text{moles of } OH^- \text{ delivered}}{\text{total volume}} = \frac{V_bF_b}{V_b + V_a}$$

$$[HA] = \frac{\text{original moles of HA} - \text{moles of } OH^-}{\text{total volume}} = \frac{V_aF_a - V_bF_b}{V_a + V_b}$$

Substitution of these values of $[A^-]$ and [HA] into the equilibrium expression gives

$$K_a = \frac{[H^+]\gamma_{H^+}V_bF_b\gamma_{A^-}}{(V_aF_a - V_bF_b)\gamma_{HA}}$$

which can be rearranged to

$\mathcal{A}_{H^+} = [H^+]\gamma_{H^+} = 10^{-pH}$

$$V_b\underbrace{[H^+]\gamma_{H^+}}_{10^{-pH}} = \frac{\gamma_{HA}}{\gamma_{A^-}}K_a\left(\frac{V_aF_a - V_bF_b}{F_b}\right) \qquad \textbf{(10-4)}$$

The term on the left is $V_b \cdot 10^{-pH}$, because $[H^+]\gamma_{H^+} = 10^{-pH}$. The term in parentheses on the right is

$V_aF_a = V_eF_b \Rightarrow V_e = \dfrac{V_aF_a}{F_b}$

$$\frac{V_aF_a - V_bF_b}{F_b} = \frac{V_aF_a}{F_b} - V_b = V_e - V_b$$

Equation 10-4 can, therefore, be written in the form

Gran plot equation:

$$V_b \cdot 10^{-pH} = \frac{\gamma_{HA}}{\gamma_{A^-}}K_a(V_e - V_b) \qquad \textbf{(10-5)}$$

Gran plot:

Plot $V_b \cdot 10^{-pH}$ versus V_b

x-intercept = V_e

Slope = $-K_a\gamma_{HA}/\gamma_{A^-}$

A graph of $V_b \cdot 10^{-pH}$ versus V_b is called a *Gran plot*. If γ_{HA}/γ_{A^-} is constant, the graph is a straight line with a slope of $-K_a\gamma_{HA}/\gamma_{A^-}$ and an x-intercept of V_e. Figure 10-8 shows a Gran plot for the titration in Figure 10-5. Any units can be used for V_b, but the same units must be used on both axes. In Figure 10-8, V_b is expressed in microliters on both axes.

The beauty of a Gran plot is that it enables us to use data taken *before* the end point to find the end point. The slope of the Gran plot enables us to find K_a. Although we derived the Gran function for a monoprotic acid, the same plot (V_b10^{-pH} versus V_b) applies to polyprotic acids (such as H_6A in Figure 10-5).

The Gran function, $V_b \cdot 10^{-pH}$, does not actually go to 0, because 10^{-pH} is never 0. The curve must be extrapolated to find V_e. The reason the function does not reach 0 is that we have used the approximation that every mole of OH^- generates 1 mol of A^-, which is not true as V_b approaches V_e. Only the linear portion of the Gran plot is used.

Another source of curvature in the Gran plot is changing ionic strength, which causes γ_{HA}/γ_{A^-} to vary. In Figure 10-8, this variation was avoided by maintaining nearly constant ionic strength with $NaNO_3$. Even without added salt, the last 10–20% of data before V_e gives a fairly straight line because the quotient γ_{HA}/γ_{A^-} does not change very much. The Gran plot in the acidic region gives accurate results even if CO_2 is dissolved in the strong-base titrant. The Gran plot in the basic region can be used to measure CO_2 in the strong base.[7]

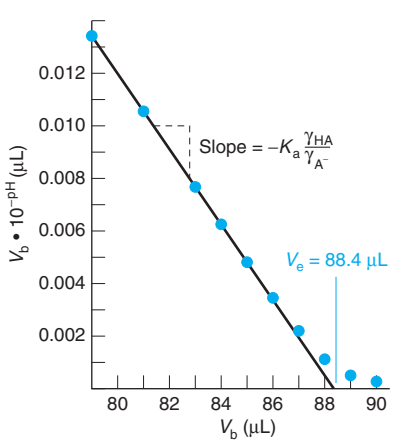


FIGURE 10-8 Gran plot for the first equivalence point of Figure 10-5. This plot gives an estimate of V_e that differs from that in Figure 10-7 by 0.2 μL (88.4 versus 88.2 μL). The last 10–20% of volume prior to V_e is normally used for a Gran plot.

Challenge Show that, when weak base, B, is titrated with a strong acid, the Gran function is

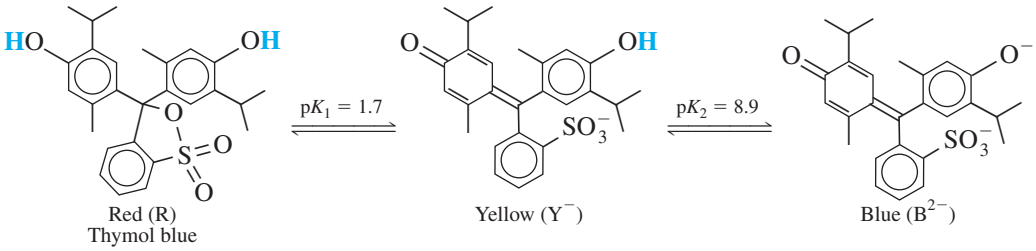
$$V_a \cdot 10^{+pH} = \left(\frac{1}{K_a} \cdot \frac{\gamma_B}{\gamma_{BH^+}}\right)(V_e - V_a) \qquad \textbf{(10-6)}$$

where V_a is the volume of strong acid and K_a is the acid dissociation constant of BH^+. A graph of V_a10^{+pH} versus V_a should be a straight line with a slope of $-\gamma_B/(\gamma_{BH^+}K_a)$ and an x-intercept of V_e.

10-6 Finding the End Point with Indicators

An acid-base **indicator** is itself an acid or base whose various protonated species have different colors. An example is thymol blue.

An indicator is an acid or a base whose various protonated forms have different colors.



Below pH 1.7, the predominant species is red; between pH 1.7 and pH 8.9, the predominant species is yellow; and above pH 8.9, the predominant species is blue (Color Plate 3). For simplicity, we designate the three species R, Y^-, and B^{2-}.

The equilibrium between R and Y^- can be written

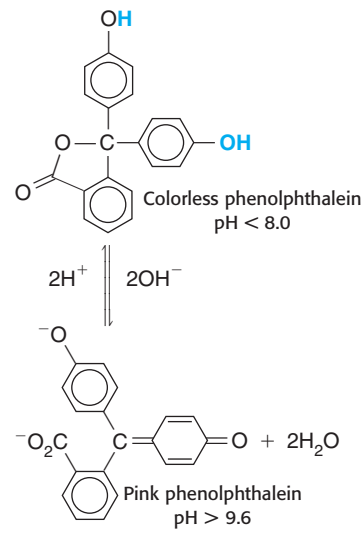
$$R \underset{}{\overset{K_1}{\rightleftharpoons}} Y^- + H^+ \qquad pH = pK_1 + \log \frac{[Y^-]}{[R]} \tag{10-7}$$

pH	$[Y^-]$:[R]	Color
0.7	1:10	red
1.7	1:1	orange
2.7	10:1	yellow

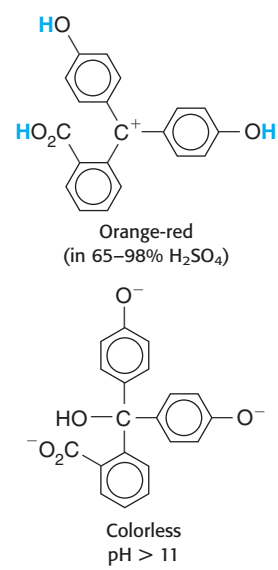
At pH 1.7 (= pK_1), there will be a 1:1 mixture of the yellow and red species, which appears orange. As a crude rule of thumb, we can say that the solution will appear red when $[Y^-]/[R] \lesssim 1/10$ and yellow when $[Y^-]/[R] \gtrsim 10/1$. From Equation 10-7, we see that the solution will be red when $pH \approx pK_1 - 1$ and yellow when $pH \approx pK_1 + 1$. In tables of indicator colors, thymol blue is listed as red below pH 1.2 and yellow above pH 2.8. The pH values predicted by our rule of thumb are 0.7 and 2.7. Between pH 1.2 and 2.8, the indicator exhibits various shades of orange. The pH range (1.2 to 2.8) over which the color changes is called the **transition range.** Whereas most indicators have a single color change, thymol blue has another transition, from yellow to blue, between pH 8.0 and pH 9.6. In this range, various shades of green are seen.

Acid-base indicator color changes are featured in Demonstration 10-1. Box 10-2 shows how optical absorption by indicators allows us to measure pH.

One of the most common indicators is phenolphthalein, usually used for its colorless-to-pink transition at pH 8.0–9.6.



In strong acid, the colorless form of phenolphthalein turns orange-red. In strong base, the red species loses its color.[10]



Choosing an Indicator

A titration curve for which pH = 5.54 at the equivalence point is shown in Figure 10-9. An indicator with a color change near this pH would be useful for an end point. In Figure 10-9,

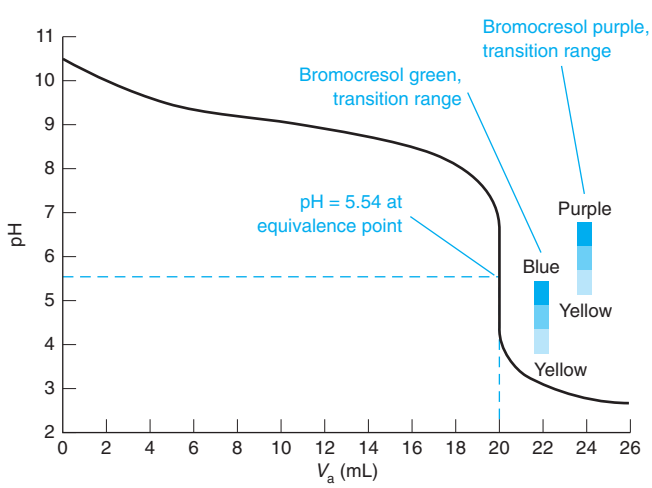
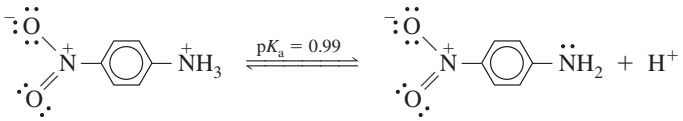


FIGURE 10-9 Calculated titration curve for the reaction of 100 mL of 0.010 0 M base (pK_b = 5.00) with 0.050 0 M HCl.

BOX 10-2 What Does a Negative pH Mean?

In the 1930s, Louis Hammett and his students measured the strengths of very weak acids and bases, using a weak reference base (B), such as *p*-nitroaniline ($pK_a = 0.99$), whose base strength could be measured in aqueous solution.



p-Nitroanilinium ion BH^+ — *p*-Nitroaniline B

Suppose that some *p*-nitroaniline and a second base, C, are dissolved in a strong acid, such as 2 M HCl. The pK_a of CH^+ can be measured relative to that of BH^+ by first writing a Henderson-Hasselbalch equation for each acid:

$$pH = pK_a\,(\text{for } BH^+) + \log\frac{[B]\gamma_B}{[BH^+]\gamma_{BH^+}}$$

$$pH = pK_a\,(\text{for } CH^+) + \log\frac{[C]\gamma_C}{[CH^+]\gamma_{CH^+}}$$

Setting the two equations equal (because there is only one pH) gives

$$\underbrace{pK_a(\text{for } CH^+) - pK_a(\text{for } BH^+)}_{\Delta pK_a} = \log\frac{[B][CH^+]}{[C][BH^+]} + \log\frac{\gamma_B\gamma_{CH^+}}{\gamma_C\gamma_{BH^+}}$$

The ratio of activity coefficients is close to unity, so the second term on the right is close to 0. Neglecting this last term gives an operationally useful result:

$$\Delta pK_a \approx \log\frac{[B][CH^+]}{[C][BH^+]}$$

That is, if you have a way to find the concentrations of B, BH^+, C, and CH^+ and if you know pK_a for BH^+, then you can find pK_a for CH^+.

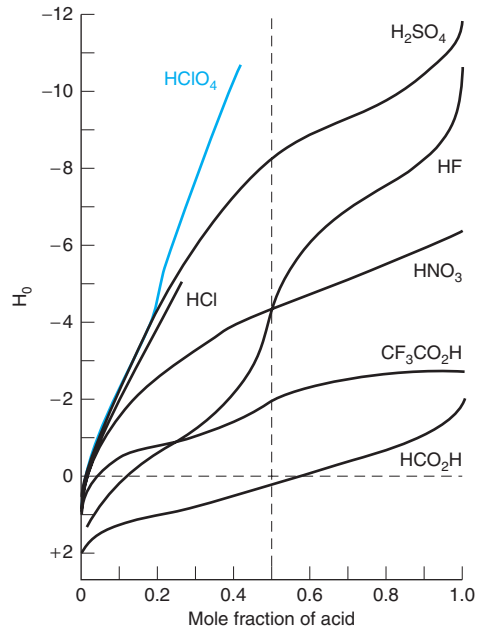
Concentrations can be measured with a spectrophotometer[12] or by nuclear magnetic resonance,[13] so pK_a for CH^+ can be determined. Then, with CH^+ as the reference, the pK_a for another compound, DH^+, can be measured. This procedure can be extended to measure the strengths of successively weaker bases (such as nitrobenzene, $pK_a = -11.38$), far too weak to be protonated in water.

The acidity of a solvent that protonates the weak base, B, is defined as the **Hammett acidity function:**

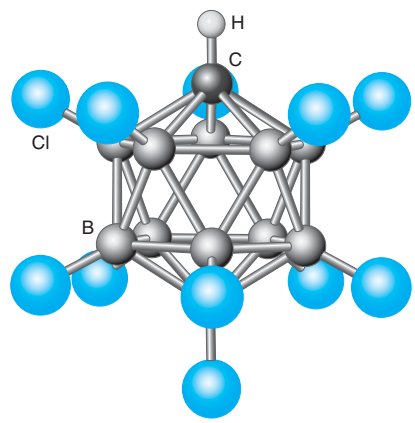
Hammett acidity function:

$$H_0 = pK_a(\text{for } BH^+) + \log\frac{[B]}{[BH^+]}$$

For dilute aqueous solutions, H_0 approaches pH. For concentrated acids, H_0 is a measure of the acid strength. The weaker a base, B, the stronger the acidity of the solvent must be to protonate the base. Acidity of strongly acidic solvents is now measured more conveniently by electrochemical methods.[14]



Hammett acidity function, H_0, for aqueous solutions of acids. [Data from R. A. Cox and K. Yates, "Acidity Functions," *Can. J. Chem.* **1983**, *61*, 2225.]



Icosahedral carborane anion of $[CHB_{11}Cl_{11}]^-H^+$, the strongest known acid.[15] Icosahedral $H_2[B_{12}Cl_{12}]$ is the strongest known diprotic acid.

When we refer to *negative* pH, we usually mean H_0 values. For example, as measured by its ability to protonate very weak bases, 8 M $HClO_4$ has a "pH" close to −4. The graph shows that $HClO_4$ is a stronger acid than other mineral acids. Values of H_0 for several powerfully acidic solvents are shown in the table. The strongest known acid is $[CHB_{11}Cl_{11}]^-H^+$, in which the icosahedral carborane cage has no significant affinity for H^+.

Acid	Name	H_0
H_2SO_4 (100%)	sulfuric acid	−11.93
$H_2SO_4 \cdot SO_3$	fuming sulfuric acid (oleum)	−14.14
HSO_3F	fluorosulfuric acid	−15.07
HSO_3F + 10% SbF_5	"super acid"	−18.94
HSO_3F + 7% $SbF_5 \cdot 3SO_3$	—	−19.35

DEMONSTRATION 10-1 Indicators and the Acidity of CO_2

This one is just plain fun.[11] Place 900 mL of water and a magnetic stirring bar in each of two 1-L graduated cylinders. Add 10 mL of 1 M NH_3 to each. Then put 2 mL of phenolphthalein indicator solution in one and 2 mL of bromothymol blue indicator solution in the other. Both indicators will have the color of their basic species.

Drop a few chunks of Dry Ice (solid CO_2) into each cylinder. As the CO_2 bubbles through each cylinder, the solutions become more acidic. First the pink phenolphthalein color disappears. After some time, the pH drops low enough for bromothymol blue to change from blue to green, but not all the way to yellow.

Add 20 mL of 6 M HCl to *the bottom* of each cylinder, using a length of Tygon tubing attached to a funnel. Then stir each solution for a few seconds on a magnetic stirrer. Explain what happens. The sequence of events is shown in Color Plate 4.

the pH drops steeply (from 7 to 4) over a small volume interval. Therefore, any indicator with a color change in this pH interval would provide a fair approximation to the equivalence point. The closer the point of color change is to pH 5.54, the more accurate will be the end point. The difference between the observed end point (color change) and the true equivalence point is called the **indicator error.**

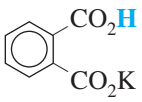
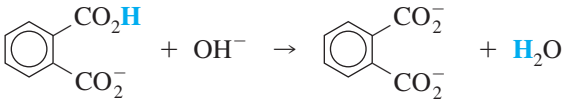
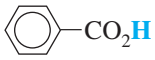
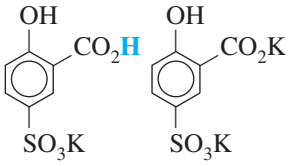
If you dump half a bottle of indicator into your reaction, you will introduce a different indicator error. Because indicators are acids or bases, they react with analyte or titrant. The moles of indicator must be negligible relative to the moles of analyte. Never use more than a few drops of dilute indicator solution.

Several of the indicators in Table 10-3 would be useful for the titration in Figure 10-9. If bromocresol purple were used, we would use the purple-to-yellow color change as the end point. The last trace of purple should disappear near pH 5.2, which is quite close to the true equivalence point in Figure 10-9. If bromocresol green were used as the indicator, a color change from blue to green (= yellow + blue) would mark the end point.

TABLE 10-3 Common indicators

Indicator	Transition range (pH)	Acid color	Base color	Preparation
Methyl violet	0.0–1.6	Yellow	Violet	0.05 wt% in H_2O
Cresol red	0.2–1.8	Red	Yellow	0.1 g in 26.2 mL 0.01 M NaOH. Then add ~225 mL H_2O.
Thymol blue	1.2–2.8	Red	Yellow	0.1 g in 21.5 mL 0.01 M NaOH. Then add ~225 mL H_2O.
Cresol purple	1.2–2.8	Red	Yellow	0.1 g in 26.2 mL 0.01 M NaOH. Then add ~225 mL H_2O.
Erythrosine, disodium	2.2–3.6	Orange	Red	0.1 wt% in H_2O
Methyl orange	3.1–4.4	Red	Yellow	0.01 wt% in H_2O
Congo red	3.0–5.0	Violet	Red	0.1 wt% in H_2O
Ethyl orange	3.4–4.8	Red	Yellow	0.1 wt% in H_2O
Bromocresol green	3.8–5.4	Yellow	Blue	0.1 g in 14.3 mL 0.01 M NaOH. Then add ~225 mL H_2O.
Methyl red	4.8–6.0	Red	Yellow	0.02 g in 60 mL ethanol. Then add 40 mL H_2O.
Chlorophenol red	4.8–6.4	Yellow	Red	0.1 g in 23.6 mL 0.01 M NaOH. Then add ~225 mL H_2O.
Bromocresol purple	5.2–6.8	Yellow	Purple	0.1 g in 18.5 mL 0.01 M NaOH. Then add ~225 mL H_2O.
p-Nitrophenol	5.6–7.6	Colorless	Yellow	0.1 wt% in H_2O
Litmus	5.0–8.0	Red	Blue	0.1 wt% in H_2O
Bromothymol blue	6.0–7.6	Yellow	Blue	0.1 g in 16.0 mL 0.01 M NaOH. Then add ~225 mL H_2O.
Phenol red	6.4–8.0	Yellow	Red	0.1 g in 28.2 mL 0.01 M NaOH. Then add ~225 mL H_2O.
Neutral red	6.8–8.0	Red	Yellow	0.01 g in 50 mL ethanol. Then add 50 mL H_2O.
Cresol red	7.2–8.8	Yellow	Red	See above.
α-Naphtholphthalein	7.3–8.7	Pink	Green	0.1 g in 50 mL ethanol. Then add 50 mL H_2O.
Cresol purple	7.6–9.2	Yellow	Purple	See above.
Thymol blue	8.0–9.6	Yellow	Blue	See above.
Phenolphthalein	8.0–9.6	Colorless	Pink	0.05 g in 50 mL ethanol. Then add 50 mL H_2O.
Thymolphthalein	8.3–10.5	Colorless	Blue	0.04 g in 50 mL ethanol. Then add 50 mL H_2O.
Alizarin yellow	10.1–12.0	Yellow	Orange-red	0.01 wt% in H_2O
Nitramine	10.8–13.0	Colorless	Orange-brown	0.1 g in 70 mL ethanol. Then add 30 mL H_2O.
Tropaeolin O	11.1–12.7	Yellow	Orange	0.1 wt% in H_2O

TABLE 10-4 Primary standards

Compound	Density (g/mL) for buoyancy corrections	Notes
ACIDS		
 Potassium hydrogen phthalate FM 204.221	1.64	The pure commercial material is dried at 105°C and used to standardize base. A phenolphthalein end point is satisfactory. 
HCl Hydrochloric acid FM 36.461	—	HCl and water distill as an *azeotrope* (a mixture), whose composition (~6 M) depends on pressure and is tabulated as a function of the pressure during distillation. See Problem 10-56 for more information.
K**H**$(IO_3)_2$ Potassium hydrogen iodate FM 389.912	—	This is a strong acid, so any indicator with an end point between ~5 and ~9 is adequate.
 Benzoic acid FM 122.121	1.27	Primary standard for nonaqueous titrations in solvents such as ethanol. A glass electrode is used to find the end point.
 Sulfosalicylic acid double salt FM 550.639	—	1 mol of commercial grade sulfosalicylic acid is combined with 0.75 mol of reagent-grade $KHCO_3$, recrystallized several times from water, and dried at 110°C to produce the double salt with 3 K^+ ions and one titratable H^+.[16] Phenolphthalein is used as the indicator for titration with NaOH.
$\mathbf{H}_3\overset{+}{N}SO_3^-$ Sulfamic acid FM 97.094	2.15	Sulfamic acid is a strong acid with one acidic proton, so any indicator with an end point between ~5 and ~9 is suitable.
BASES		
$H_2NC(CH_2OH)_3$ Tris(hydroxymethyl)aminomethane (also called tris or tham) FM 121.135	1.33	The pure commercial material is dried at 100°–103°C and titrated with strong acid. The end point is in the range pH 4.5–5. $H_2NC(CH_2OH)_3 + H^+ \rightarrow H_3\overset{+}{N}C(CH_2OH)_3$
HgO Mercuric oxide FM 216.59	11.1	Pure HgO is dissolved in a large excess of I^- or Br^-, whereupon 2 OH^- are liberated: $HgO + 4I^- + H_2O \rightarrow HgI_4^{2-} + 2OH^-$ The base is titrated, using an indicator end point.
Na_2CO_3 Sodium carbonate FM 105.988	2.53	Primary-standard-grade Na_2CO_3 is commercially available. Alternatively, recrystallized $NaHCO_3$ can be heated for 1 h at 260°–270°C to produce pure Na_2CO_3. Sodium carbonate is titrated with acid to an end point of pH 4–5. Just before the end point, the solution is boiled to expel CO_2.
$Na_2B_4O_7 \cdot 10H_2O$ Borax FM 381.372	1.73	The recrystallized material is dried in a chamber containing an aqueous solution saturated with NaCl and sucrose. This procedure gives the decahydrate in pure form.[17] The standard is titrated with acid to a methyl red end point. "$B_4O_7 \cdot 10H_2O^{2-}$" $+ 2H^+ \rightarrow 4B(OH)_3 + 5H_2O$

In general, *we seek an indicator whose transition range overlaps the steepest part of the titration curve as closely as possible*. The steepness of the titration curve near the equivalence point in Figure 10-9 ensures that the indicator error caused by the noncoincidence of the end point and equivalence point will be small. If the indicator end point were at pH 6.4 (instead of 5.54), the error in V_e would be only 0.25% in this particular case. You can estimate the indicator error by calculating the volume of titrant required to attain pH 6.4 instead of pH 5.54.

Choose an indicator whose transition range overlaps the steepest part of the titration curve.

10-7 Practical Notes

Acids and bases in Table 10-4 can be obtained pure enough to be *primary standards*.[18] NaOH and KOH are not primary standards because they contain carbonate (from reaction with atmospheric CO_2) and adsorbed water. Solutions of NaOH and KOH must be standardized against a primary standard such as potassium hydrogen phthalate. Solutions of NaOH for titrations are prepared by diluting a stock solution of 50 wt% aqueous NaOH. Sodium carbonate is insoluble in this stock solution and settles to the bottom.

Procedures for preparing standard acid and base are given at the end of this chapter.

Alkaline solutions (for example, 0.1 M NaOH) must be protected from the atmosphere; otherwise, they absorb CO_2:

$$OH^- + CO_2 \rightarrow HCO_3^-$$

CO_2 changes the concentration of strong base over a period of time and decreases the extent of reaction near the end point in the titration of weak acids. If solutions are kept in tightly capped polyethylene bottles, they can be used for about a week with little change.

Standard solutions are commonly stored in high-density polyethylene bottles with screw caps. Evaporation from the bottle slowly changes the reagent concentration. The chemical supplier Sigma-Aldrich reports that an aqueous solution stored in a tightly capped bottle became 0.2% more concentrated in 2 years at 23°C and 0.5% more concentrated in 2 years at 30°C. Enclosing the bottle in a sealed, aluminized bag reduced evaporation by a factor of 10. The lesson is that a standard solution has a finite shelf life.

Strongly basic solutions attack glass and are best stored in plastic containers. Such solutions should not be kept in a buret longer than necessary. Boiling 0.01 M NaOH in a flask for 1 h decreases the molarity by 10% because OH^- reacts with glass.[19]

10-8 Kjeldahl Nitrogen Analysis

Developed in 1883, the **Kjeldahl nitrogen analysis** is one of the most widely used methods for determining nitrogen in organic substances. Protein is the main nitrogen-containing constituent of food. Most proteins contain close to 16 wt% nitrogen, so measuring nitrogen is a surrogate for measuring protein (Box 10-3). The other common way to measure nitrogen in food is by combustion analysis (Section 26-4).

In the Kjeldahl method, a sample is first *digested* (decomposed and dissolved) in boiling sulfuric acid, which converts amine and amide nitrogen into ammonium ion, NH_4^+, and oxidizes other elements present:[23]

Kjeldahl digestion:
$$\text{organic C, H, N} \xrightarrow[H_2SO_4]{\text{boiling}} NH_4^+ + CO_2 + H_2O \qquad \textbf{(10-8)}$$

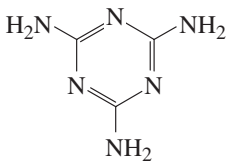
Each atom of nitrogen in starting material is converted into one NH_4^+ ion.

Mercury, copper, and selenium compounds catalyze the digestion. To speed the reaction, the boiling point of concentrated (98 wt%) sulfuric acid (338°C) is raised by adding K_2SO_4. Digestion is carried out in a long-neck *Kjeldahl flask* (Figure 10-10) that prevents loss of sample from spattering. Alternative digestion procedures employ H_2SO_4 plus H_2O_2 or $K_2S_2O_8$ plus NaOH[24] in a microwave bomb (a pressurized vessel shown in Figure 27-7).

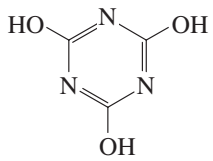
After digestion is complete, the solution containing NH_4^+ is made basic, and the liberated NH_3 is steam distilled (with a large excess of steam) into a receiver containing a known amount of HCl[25] (Figure 10-11). Excess, unreacted HCl is then titrated with standard NaOH to determine how much HCl was consumed by NH_3.

BOX 10-3 Kjeldahl Nitrogen Analysis Behind the Headlines

In 2007, dogs and cats in North America suddenly began to die from kidney failure. The illness was traced to animal food containing ingredients from China. Melamine, used to make plastics, had been deliberately added to food ingredients "in a bid to meet the contractual demand for the amount of protein in the products."[20] Cyanuric acid, used to disinfect swimming pools, was also found in the food. Melamine alone does not cause kidney failure, but the combination of melamine and cyanuric acid does.



Melamine
(66.6 wt% nitrogen)



Cyanuric acid
(32.6 wt% nitrogen)

What do these compounds have to do with protein? Nothing—except that they are high in nitrogen. Protein, which contains ~16 wt% nitrogen, is the main source of nitrogen in food. Kjeldahl nitrogen analysis is a surrogate measurement for protein in food. For example, if food contains 10 wt% protein, it will contain ~16% of 10% = 1.6 wt% N. If you measure 1.6 wt% N in food, you could conclude that the food contains ~10 wt% protein. Melamine contains 66.6 wt% N, which is four times more than protein. Adding 1 wt% melamine to food makes it appear that the food contains an additional 4 wt% protein.

Protein source	Weight % nitrogen
Meat	16.0
Blood plasma	15.3
Milk	15.6
Flour	17.5
Egg	14.9

SOURCE: D. J. Holme and H. Peck, Analytical Biochemistry, 3rd ed. (New York: Addison Wesley Longman, 1998), p. 388.

Incredibly, in the summer of 2008, approximately 300 000 Chinese babies became sick and some suffered kidney failure.[21] Many Chinese companies had diluted milk with water and added melamine to make the protein content appear normal. Poisoned milk products were sold in the domestic and export markets. In a response to the appearance of melamine in food, at least one company developed a colorimetric assay that distinguishes protein nitrogen from nonprotein nitrogen.[22]

Another means to measure nitrogen in food is the *Dumas method*. Organic material mixed with CuO is heated in CO_2 at 650°–700°C to produce CO_2, H_2O, N_2, and nitrogen oxides. Products are carried by a stream of CO_2 through hot Cu to convert nitrogen oxides to N_2. The gases are bubbled through concentrated KOH(*aq*) to capture CO_2. The volume of N_2 is measured in a gas buret. This method does not distinguish protein from melamine.

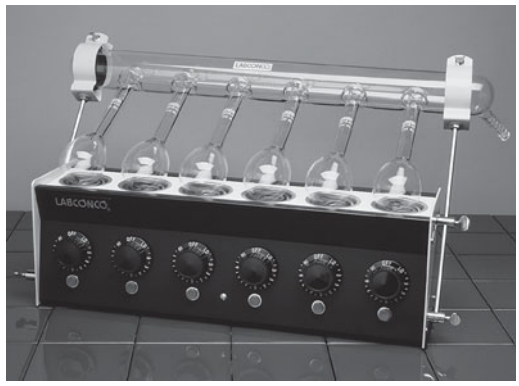
Neutralization of NH_4^+: $$NH_4^+ + OH^- \rightarrow NH_3(g) + H_2O \quad \textbf{(10-9)}$$

Distillation of NH_3 into standard HCl: $$NH_3 + H^+ \rightarrow NH_4^+ \quad \textbf{(10-10)}$$

Titration of unreacted HCl with NaOH: $$H^+ + OH^- \rightarrow H_2O \quad \textbf{(10-11)}$$

An alternative to a titration is to neutralize the acid and raise the pH with a buffer, followed by addition of reagents that form a colored product with NH_3.[26] The absorbance of the colored product gives the concentration of NH_3 from the digestion.

(*a*)



(*b*)

FIGURE 10-10 (*a*) Kjeldahl digestion flask with long neck to minimize loss from spattering. (*b*) Six-port manifold for multiple samples provides for exhaust of fumes. [Courtesy Labconco Corp.]

EXAMPLE Kjeldahl Analysis

A typical protein contains 16.2 wt% nitrogen. A 0.500-mL aliquot of protein solution was digested, and the liberated NH_3 was distilled into 10.00 mL of 0.021 40 M HCl. Unreacted HCl required 3.26 mL of 0.019 8 M NaOH for complete titration. Find the concentration of protein (mg protein/mL) in the original sample.

Solution The initial amount of HCl in the receiver was (10.00 mL)(0.021 40 mmol/mL) = 0.214 0 mmol. The NaOH required for titration of unreacted HCl in Reaction 10-11 was (3.26 mL)(0.019 8 mmol/mL) = 0.064 5 mmol. The difference, 0.214 0 − 0.064 5 = 0.149 5 mmol, must be the quantity of NH_3 produced in Reaction 10-9 and distilled into the HCl.

Because 1 mol of N in the protein produces 1 mol of NH_3, there must have been 0.149 5 mmol of N in the protein, corresponding to

$$(0.149\ 5\ \text{mmol})\left(14.006\ 74\ \frac{\text{mg N}}{\text{mmol}}\right) = 2.093\ \text{mg N}$$

If the protein contains 16.2 wt% N, there must be

$$\frac{2.093\ \text{mg N}}{0.162\ \text{mg N/mg protein}} = 12.9\ \text{mg protein} \Rightarrow \frac{12.9\ \text{mg protein}}{0.500\ \text{mL}} = 25.8\ \frac{\text{mg protein}}{\text{mL}}$$

Test Yourself Find mg protein/mL if 3.00 mL of NaOH were required. (***Answer:*** 26.7 mg/mL)

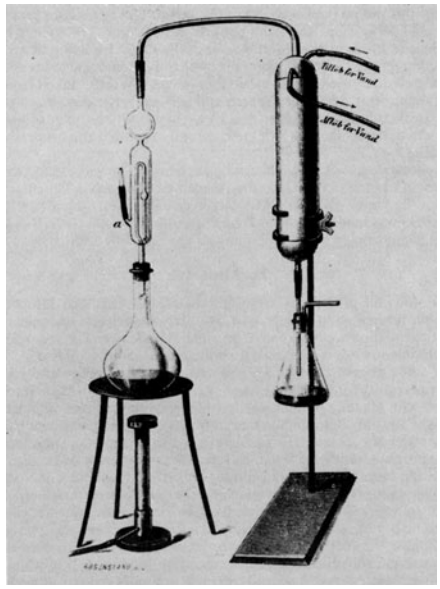


FIGURE 10-11 Original apparatus used by Dutch chemist J. Kjeldahl (1849–1900). [From D. T. Burns, "Kjeldahl, the Man, the Method and the Carlsberg Laboratory," *Anal. Proc.* (Royal Society of Chemistry) **1984,** *21*, 210.]

10-9 The Leveling Effect

The strongest acid that can exist in water is H_3O^+ and the strongest base is OH^-. If an acid stronger than H_3O^+ is dissolved in water, it protonates H_2O to make H_3O^+. If a base stronger than OH^- is dissolved in water, it deprotonates H_2O to make OH^-. Because of this **leveling effect,** $HClO_4$ and HCl behave as if they had the same acid strength; both are *leveled* to H_3O^+:

$$HClO_4 + H_2O \rightarrow H_3O^+ + ClO_4^-$$
$$HCl + H_2O \rightarrow H_3O^+ + Cl^-$$

In acetic acid solvent, which is less basic than H_2O, $HClO_4$ and HCl are not leveled to the same strength:

$$HClO_4 + \underset{\text{Acetic acid solvent}}{CH_3CO_2H} \rightleftharpoons CH_3CO_2H_2^+ + ClO_4^- \qquad K = 1.3 \times 10^{-5}$$
$$HCl + CH_3CO_2H \rightleftharpoons CH_3CO_2H_2^+ + Cl^- \qquad K = 2.8 \times 10^{-9}$$

In acetic acid solution, $HClO_4$ is a stronger acid than HCl; but, in aqueous solution, both are leveled to the strength of H_3O^+.

The equilibrium constants show that $HClO_4$ is a stronger acid than HCl in acetic acid solvent.

Figure 10-12 shows a titration curve for a mixture of five acids titrated with 0.2 M tetrabutylammonium hydroxide in methyl isobutyl ketone solvent. This solvent is not protonated

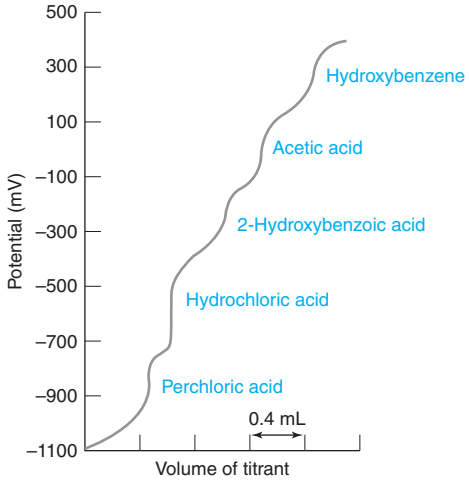


FIGURE 10-12 Titration of a mixture of acids with tetrabutylammonium hydroxide in methyl isobutyl ketone solvent shows that the order of acid strength is $HClO_4$ > HCl > 2-hydroxybenzoic acid > acetic acid > hydroxybenzene. Measurements were made with a glass electrode and a platinum reference electrode. The ordinate is proportional to pH, with increasing pH as the potential becomes more positive. [From D. B. Bruss and G. E. A. Wyld, "Methyl Isobutyl Ketone as a Wide-Range Solvent for Titration of Acid Mixtures and Nitrogen Bases," *Anal. Chem.* **1957,** *29*, 232.]

Question Where do you think the end point for the acid $H_3O^+ClO_4^-$ would come in Figure 10-12?

to a great extent by any of the acids. We see that perchloric acid is a stronger acid than HCl in this solvent as well.

Now consider a base such as urea, $(H_2N)_2C{=}O$ ($K_b = 1.3 \times 10^{-14}$), that is too weak to give a distinct end point when titrated with a strong acid in water.

Titration with $HClO_4$ in H_2O: $$B + H_3O^+ \rightleftharpoons BH^+ + H_2O$$

The end point cannot be recognized because the equilibrium constant for the titration reaction is not large enough. If an acid stronger than H_3O^+ were available, the titration reaction might have an equilibrium constant large enough to give a distinct end point. If the same base were dissolved in acetic acid and titrated with $HClO_4$ in acetic acid, a clear end point might be observed. The reaction

A base too weak to be titrated by H_3O^+ in water might be titrated by $HClO_4$ in acetic acid solvent.

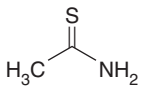
Titration with $HClO_4$ in CH_3CO_2H: $$B + HClO_4 \rightleftharpoons \underbrace{BH^+ClO_4^-}_{\text{An ion pair}}$$

might have a large equilibrium constant, because $HClO_4$ is a much stronger acid than H_3O^+. (The product in this reaction is written as an ion pair because the *dielectric constant* of acetic acid is too low to allow ions to separate extensively.) Titrations that are not feasible in water might be feasible in other solvents.[27]

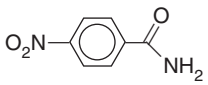
Dielectric constant is discussed in Problem 7-13.

In *electrophoresis* (Chapter 25), ions are separated by their different mobilities in an electric field. Compounds shown in the margin are such weak bases that they cannot be protonated in aqueous solution and, therefore, cannot be made into charged species for aqueous electrophoresis. However, in anhydrous acetonitrile solvent, they are protonated by $HClO_4$ in anhydrous acetic acid and can be separated as cations.[28]

Compounds that can be protonated in acetonitrile by perchloric acid plus acetic acid, $CH_3C(OH)_2^+ClO_4^-$:



Thioacetamide



4-Nitrobenzamide

10-10 Calculating Titration Curves with Spreadsheets

This chapter has been critical for developing your understanding of the chemistry that occurs during titrations. However, the approximations we used are of limited value when concentrations are too dilute or equilibrium constants are not of the right magnitude or K_a values are too closely spaced, like those in a protein. This section develops equations to deal with titrations in a general manner, using spreadsheets.[29]

Experiment 10, "Fitting a Titration Curve with Excel Solver," at www.whfreeman.com/qca, applies equations developed in this section.

Titrating a Weak Acid with a Strong Base

Consider the titration of a volume V_a of acid HA (initial concentration C_a) with a volume V_b of NaOH of concentration C_b. The charge balance for this solution is

Charge balance: $$[H^+] + [Na^+] = [A^-] + [OH^-]$$

and the concentration of Na^+ is just

$$[Na^+] = \frac{C_bV_b}{V_a + V_b}$$

because we have diluted C_bV_b moles of NaOH to a total volume of $V_a + V_b$. Similarly, the formal concentration of the weak acid is

$$F_{HA} = [HA] + [A^-] = \frac{C_aV_a}{V_a + V_b}$$

because we have diluted C_aV_a moles of HA to a total volume of $V_a + V_b$.

Now we use the fractional composition equations from Section 9-5. The concentration of A^- can be written in terms of α_{A^-} defined in Equation 9-18:

α_{A^-} = fraction of acid in the form A^-:
$$\alpha_{A^-} = \frac{[A^-]}{F_{HA}}$$

$$[A^-] = \alpha_{A^-} \cdot F_{HA} = \frac{\alpha_{A^-} \cdot C_aV_a}{V_a + V_b} \qquad \textbf{(10-12)}$$

where $\alpha_{A^-} = K_a/([H^+] + K_a)$ and K_a is the acid dissociation constant of HA. Substituting for $[Na^+]$ and $[A^-]$ in the charge balance gives

$$[H^+] + \frac{C_bV_b}{V_a + V_b} = \frac{\alpha_{A^-} \cdot C_aV_a}{V_a + V_b} + [OH^-]$$

which you can rearrange to the form

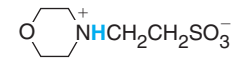
Fraction of titration for weak acid by strong base:

$$\phi \equiv \frac{C_b V_b}{C_a V_a} = \frac{\alpha_{A^-} - \dfrac{[H^+] - [OH^-]}{C_a}}{1 + \dfrac{[H^+] - [OH^-]}{C_b}} \qquad \textbf{(10-13)}$$

$\phi = C_b V_b / C_a V_a$ is the fraction of the way to the equivalence point:

ϕ	Volume of base
0.5	$V_b = \frac{1}{2} V_e$
1	$V_b = V_e$
2	$V_b = 2V_e$

At last! Equation 10-13 is really useful. It relates the volume of titrant (V_b) to the pH and a bunch of constants. The quantity ϕ, which is the quotient $C_b V_b / C_a V_a$, is the fraction of the way to the equivalence point, V_e. When $\phi = 1$, the volume of base added, V_b, is equal to V_e. Equation 10-13 works backward from the way you are accustomed to thinking, because you need to put in pH on the right to get out volume on the left. Let me say that again: We *put in a concentration* of H^+ and *get out the volume of titrant* that produces that concentration.



2-(*N*-Morpholino)ethanesulfonic acid
MES, $pK_a = 6.27$

Let's use Equation 10-13 to calculate the titration curve for 50.00 mL of the weak acid 0.020 00 M MES with 0.100 0 M NaOH, which was shown in Figure 10-2 and Table 10-2. The equivalence volume is $V_e = 10.00$ mL. Quantities in Equation 10-13 are

$$C_b = 0.1 \text{ M} \qquad [H^+] = 10^{-pH}$$

$$C_a = 0.02 \text{ M} \qquad [OH^-] = K_w/[H^+]$$

$$V_a = 50 \text{ mL}$$

$$K_a = 5.3_7 \times 10^{-7} \qquad \alpha_{A^-} = \frac{K_a}{[H^+] + K_a}$$

$$K_w = 10^{-14}$$

pH is the input

$$V_b = \frac{\phi C_a V_a}{C_b} \text{ is the output}$$

The input to the spreadsheet in Figure 10-13 is pH in column B and the output is V_b in column G. From the pH, the values of $[H^+]$, $[OH^-]$, and α_{A^-} are computed in columns C, D, and E. Equation 10-13 is used in column F to find the fraction of titration, ϕ. From this value, we calculate the volume of titrant, V_b, in column G.

How do we know what pH values to put in? Trial-and-error allows us to find the starting pH, by putting in a pH and seeing whether V_b is positive or negative. In a few tries, it is easy to home in on the pH at which $V_b = 0$. In Figure 10-13, a pH of 3.90 is too low, because ϕ and V are both negative. Input values of pH are spaced as closely as you like, so that you can generate a smooth titration curve. To save space, we show only a few points in Figure 10-13, including the

In Figure 10-13, you could use Excel Goal Seek (page 158) to vary pH in cell B5 until V_b in cell G5 is 0.

	A	B	C	D	E	F	G
1	Titration of weak acid with strong base						
2							
3	C_b =	pH	$[H^+]$	$[OH^-]$	$\alpha(A^-)$	ϕ	V_b (mL)
4	0.1	3.90	1.26E-04	7.94E-11	0.004	-0.002	-0.020
5	C_a =	3.99	1.02E-04	9.77E-11	0.005	0.000	0.001
6	0.02	5.00	1.00E-05	1.00E-09	0.051	0.050	0.505
7	V_a =	6.00	1.00E-06	1.00E-08	0.349	0.349	3.493
8	50	6.27	5.37E-07	1.86E-08	0.500	0.500	5.000
9	K_a =	7.00	1.00E-07	1.00E-07	0.843	0.843	8.430
10	5.37E-07	8.00	1.00E-08	1.00E-06	0.982	0.982	9.818
11	K_w =	9.00	1.00E-09	1.00E-05	0.998	0.999	9.987
12	1.E-14	9.25	5.62E-10	1.78E-05	0.999	1.000	10.000
13		10.00	1.00E-10	1.00E-04	1.000	1.006	10.058
14		11.00	1.00E-11	1.00E-03	1.000	1.061	10.606
15		12.00	1.00E-12	1.00E-02	1.000	1.667	16.667
16							
17	C4 = 10^-B4			F4 = (E4-(C4-D4)/$A$6)/(1+(C4-D4)/$A$4)			
18	D4 = $A$12/C4			G4 = F4*$A$6*$A$8/$A$4			
19	E4 = $A$10/(C4+$A$10)						

FIGURE 10-13 Spreadsheet uses Equation 10-13 to calculate the titration curve for 50 mL of the weak acid, 0.02 M MES (pK_a = 6.27) treated with 0.1 M NaOH. We provide pH as input in column B, and the spreadsheet tells us what volume of base is required to generate that pH.

TABLE 10-5 Titration equations for spreadsheets

Calculation of ϕ

Titrating strong acid with strong base

$$\phi = \frac{C_bV_b}{C_aV_a} = \frac{1 - \dfrac{[H^+] - [OH^-]}{C_a}}{1 + \dfrac{[H^+] - [OH^-]}{C_b}}$$

Titrating weak acid (HA) with strong base

$$\phi = \frac{C_bV_b}{C_aV_a} = \frac{\alpha_{A^-} - \dfrac{[H^+] - [OH^-]}{C_a}}{1 + \dfrac{[H^+] - [OH^-]}{C_b}}$$

Titrating strong base with strong acid

$$\phi = \frac{C_aV_a}{C_bV_b} = \frac{1 + \dfrac{[H^+] - [OH^-]}{C_b}}{1 - \dfrac{[H^+] - [OH^-]}{C_a}}$$

Titrating weak base (B) with strong acid

$$\phi = \frac{C_aV_a}{C_bV_b} = \frac{\alpha_{BH^+} + \dfrac{[H^+] - [OH^-]}{C_b}}{1 - \dfrac{[H^+] - [OH^-]}{C_a}}$$

Titrating weak acid (HA) with weak base (B)

$$\phi = \frac{C_bV_b}{C_aV_a} = \frac{\alpha_{A^-} - \dfrac{[H^+] - [OH^-]}{C_a}}{\alpha_{BH^+} + \dfrac{[H^+] - [OH^-]}{C_b}}$$

Titrating weak base (B) with weak acid (HA)

$$\phi = \frac{C_aV_a}{C_bV_b} = \frac{\alpha_{BH^+} + \dfrac{[H^+] - [OH^-]}{C_b}}{\alpha_{A^-} - \dfrac{[H^+] - [OH^-]}{C_a}}$$

Titrating H_2A with strong base ($\rightarrow\rightarrow A^{2-}$)

$$\phi = \frac{C_bV_b}{C_aV_a} = \frac{\alpha_{HA^-} + 2\alpha_{A^{2-}} - \dfrac{[H^+] - [OH^-]}{C_a}}{1 + \dfrac{[H^+] - [OH^-]}{C_b}}$$

Titrating H_3A with strong base ($\rightarrow\rightarrow\rightarrow A^{3-}$)

$$\phi = \frac{C_bV_b}{C_aV_a} = \frac{\alpha_{H_2A^-} + 2\alpha_{HA^{2-}} + 3\alpha_{A^{3-}} - \dfrac{[H^+] - [OH^-]}{C_a}}{1 + \dfrac{[H^+] - [OH^-]}{C_b}}$$

Titrating dibasic B with strong acid ($\rightarrow\rightarrow BH_2^{2+}$)

$$\phi = \frac{C_aV_a}{C_bV_b} = \frac{\alpha_{BH^+} + 2\alpha_{BH_2^{2+}} + \dfrac{[H^+] - [OH^-]}{C_b}}{1 - \dfrac{[H^+] - [OH^-]}{C_a}}$$

Titrating tribasic B with strong acid ($\rightarrow\rightarrow\rightarrow BH_3^{3+}$)

$$\phi = \frac{C_aV_a}{C_bV_b} = \frac{\alpha_{BH^+} + 2\alpha_{BH_2^{2+}} + 3\alpha_{BH_3^{3+}} + \dfrac{[H^+] - [OH^-]}{C_b}}{1 - \dfrac{[H^+] - [OH^-]}{C_a}}$$

Symbols

ϕ = fraction of the way to the first equivalence point
C_a = initial concentration of acid
C_b = initial concentration of base
α = fraction of dissociation of acid or fraction of association of base
V_a = volume of acid
V_b = volume of base

Calculation of α

Monoprotic systems

$$\alpha_{HA} = \frac{[H^+]}{[H^+] + K_a} \qquad \alpha_{A^-} = \frac{K_a}{[H^+] + K_a}$$

$$\alpha_{BH^+} = \frac{[H^+]}{[H^+] + K_{BH^+}} \qquad \alpha_B = \frac{K_{BH^+}}{[H^+] + K_{BH^+}}$$

Symbols

K_a = acid dissociation constant of HA
K_{BH^+} = acid dissociation constant of BH^+ ($= K_w/K_b$)

Diprotic systems

$$\alpha_{H_2A} = \alpha_{BH_2^{2+}} = \frac{[H^+]^2}{[H^+]^2 + [H^+]K_1 + K_1K_2} \qquad \alpha_{HA^-} = \alpha_{BH^+} = \frac{[H^+]K_1}{[H^+]^2 + [H^+]K_1 + K_1K_2} \qquad \alpha_{A^{2-}} = \alpha_B = \frac{K_1K_2}{[H^+]^2 + [H^+]K_1 + K_1K_2}$$

Symbols

K_1 and K_2 for the acid are the acid dissociation constants of H_2A and HA^-, respectively.
K_1 and K_2 for the base are the acid dissociation constants of BH_2^{2+} and BH^+, respectively: $K_1 = K_w/K_{b2}$; $K_2 = K_w/K_{b1}$.

Triprotic systems

$$\alpha_{H_3A} = \frac{[H^+]^3}{[H^+]^3 + [H^+]^2K_1 + [H^+]K_1K_2 + K_1K_2K_3} \qquad \alpha_{H_2A^-} = \frac{[H^+]^2K_1}{[H^+]^3 + [H^+]^2K_1 + [H^+]K_1K_2 + K_1K_2K_3}$$

$$\alpha_{HA^{2-}} = \frac{[H^+]K_1K_2}{[H^+]^3 + [H^+]^2K_1 + [H^+]K_1K_2 + K_1K_2K_3} \qquad \alpha_{A^{3-}} = \frac{K_1K_2K_3}{[H^+]^3 + [H^+]^2K_1 + [H^+]K_1K_2 + K_1K_2K_3}$$

midpoint (pH 6.27 $\Rightarrow V_b = 5.00$ mL) and the end point (pH 9.25 $\Rightarrow V_b = 10.00$ mL). This spreadsheet reproduces Table 10-2 without approximations other than neglecting activity coefficients. It gives correct results even when the approximations used in Table 10-2 fail.

Titrating a Weak Acid with a Weak Base

Now consider the titration of V_a mL of acid HA (initial concentration C_a) with V_b mL of base B whose concentration is C_b. Let the acid dissociation constant of HA be K_a and the acid dissociation constant of BH^+ be K_{BH^+}. The charge balance is

Charge balance: $$[H^+] + [BH^+] = [A^-] + [OH^-]$$

As before, we can say that $[A^-] = \alpha_{A^-} \cdot F_{HA}$, where $\alpha_{A^-} = K_a/([H^+] + K_a)$ and $F_{HA} = C_aV_a/(V_a + V_b)$.

We can write an analogous expression for $[BH^+]$, which is a monoprotic weak acid. If the acid were HA, we would use Equation 9-17 to say

$$[HA] = \alpha_{HA} \cdot F_{HA} \qquad \alpha_{HA} = \frac{[H^+]}{[H^+] + K_a}$$

α_{HA} = fraction of acid in the form HA:

$$\alpha_{HA} = \frac{[HA]}{F_{HA}}$$

where K_a applies to the acid HA. For the weak acid BH^+, we write

$$[BH^+] = \alpha_{BH^+} \cdot F_B \qquad \alpha_{BH^+} = \frac{[H^+]}{[H^+] + K_{BH^+}}$$

α_{BH^+} = fraction of base in the form BH^+:

$$\alpha_{BH^+} = \frac{[BH^+]}{F_B}$$

where the formal concentration of base is $F_B = C_bV_b/(V_a + V_b)$.

Substituting for $[BH^+]$ and $[A^-]$ in the charge balance gives

$$[H^+] + \frac{\alpha_{BH^+} \cdot C_bV_b}{V_a + V_b} = \frac{\alpha_{A^-} \cdot C_aV_a}{V_a + V_b} + [OH^-]$$

which can be rearranged to the useful result

Fraction of titration for weak acid by weak base: $$\phi = \frac{C_bV_b}{C_aV_a} = \frac{\alpha_{A^-} - \dfrac{[H^+] - [OH^-]}{C_a}}{\alpha_{BH^+} + \dfrac{[H^+] - [OH^-]}{C_b}} \qquad \textbf{(10-14)}$$

Equation 10-14 for a weak base looks just like Equation 10-13 for a strong base, except that α_{BH^+} replaces 1 in the denominator.

Table 10-5 gives useful equations derived by writing a charge balance and substituting fractional compositions for various concentrations. For titration of the diprotic acid, H_2A, ϕ is the fraction of the way to the first equivalence point. When $\phi = 2$, we are at the second equivalence point. It should not surprise you that, when $\phi = 0.5$, pH $\approx$ pK_1, and when $\phi = 1.5$, pH $\approx$ pK_2. When $\phi = 1$, we have the intermediate HA^- and pH $\approx \frac{1}{2}$(pK_1 + pK_2).

Terms to Understand

Gran plot	indicator	Kjeldahl nitrogen analysis	transition range
Hammett acidity function	indicator error	leveling effect	

Summary

Key equations used to calculate titration curves:

Strong acid/strong base titration

$H^+ + OH^- \rightarrow H_2O$

pH is determined by the concentration of excess unreacted H^+ or OH^-

Weak acid titrated with OH^-

$HA + OH^- \rightarrow A^- + H_2O$ (V_e = equivalence volume)

(V_b = volume of added base)

$V_b = 0$: pH determined by K_a ($HA \overset{K_a}{\rightleftharpoons} H^+ + A^-$)

$0 < V_b < V_e$: $pH = pK_a + \log([A^-]/[HA])$

$pH = pK_a$ when $V_b = \frac{1}{2}V_e$ (neglecting activity)

At V_e: pH governed by K_b ($A^- + H_2O \overset{K_b}{\rightleftharpoons} HA + OH^-$)

After V_e: pH is determined by excess OH^-

Weak base titrated with H^+

$B + H^+ \rightarrow BH^+$ (V_e = equivalence volume)

(V_a = volume of added acid)

$V_a = 0$: pH determined by K_b ($B + H_2O \overset{K_b}{\rightleftharpoons} BH^+ + OH^-$)

$0 < V_a < V_e$: $pH = pK_{BH^+} + \log([B]/[BH^+])$

$pH = pK_{BH^+}$ when $V_a = \frac{1}{2}V_e$

At V_e: pH governed by K_{BH^+} ($BH^+ \overset{K_{BH^+}}{\rightleftharpoons} B + H^+$)

After V_e: pH is determined by excess H^+

H_2A titrated with OH^-

$H_2A \xrightarrow{OH^-} HA^- \xrightarrow{OH^-} A^{2-}$

Equivalence volumes: $V_{e2} = 2V_{e1}$

$V_b = 0$: pH determined by K_1 ($H_2A \overset{K_1}{\rightleftharpoons} H^+ + HA^-$)

$0 < V_b < V_{e1}$: $pH = pK_1 + \log([HA^-]/[H_2A])$

$pH = pK_1$ when $V_b = \frac{1}{2}V_{e1}$

At V_{e1}: $[H^+] = \sqrt{\dfrac{K_1K_2F' + K_1K_w}{K_1 + F'}}$

$\Rightarrow pH \approx \frac{1}{2}(pK_1 + pK_2)$

F' = formal concentration of HA^-

$V_{e1} < V_b < V_{e2}$: $pH = pK_2 + \log([A^{2-}]/[HA^-])$

$pH = pK_2$ when $V_b = \frac{3}{2}V_{e1}$

At V_{e2}: pH governed by K_{b1}

($A^{2-} + H_2O \overset{K_{b1}}{\rightleftharpoons} HA^- + OH^-$)

After V_{e2}: pH is determined by excess OH^-

Behavior of derivatives at the equivalence point

First derivative: $\Delta pH/\Delta V$ has greatest magnitude

Second derivative: $\Delta(\Delta pH/\Delta V))/\Delta V = 0$

Gran plot

Plot $V_b \cdot 10^{-pH}$ versus V_b

x-intercept = V_e; slope = $-K_a\gamma_{HA}/\gamma_{A^-}$

K_a = acid dissociation constant

γ = activity coefficient

Choosing an indicator: Color transition range should match pH at V_e. Preferably the color change should occur entirely within the steep portion of the titration curve.

Kjeldahl nitrogen analysis: A nitrogen-containing organic compound is digested with a catalyst in boiling H_2SO_4. Nitrogen is converted into NH_4^+, which is converted into NH_3 with base and distilled into standard HCl. The excess, unreacted HCl tells us how much nitrogen was present in the original analyte.

Exercises

10-A. Calculate the pH at each of the following points in the titration of 50.00 mL of 0.010 0 M NaOH with 0.100 M HCl. Volume of acid added: 0.00, 1.00, 2.00, 3.00, 4.00, 4.50, 4.90, 4.99, 5.00, 5.01, 5.10, 5.50, 6.00, 8.00, and 10.00 mL. Make a graph of pH versus volume of HCl added.

10-B. Calculate the pH at each point listed for the titration of 50.0 mL of 0.050 0 M formic acid with 0.050 0 M KOH. The points to calculate are V_b = 0.0, 10.0, 20.0, 25.0, 30.0, 40.0, 45.0, 48.0, 49.0, 49.5, 50.0, 50.5, 51.0, 52.0, 55.0, and 60.0 mL. Draw a graph of pH versus V_b.

10-C. Calculate the pH at each point listed for the titration of 100.0 mL of 0.100 M cocaine (Section 8-4, $K_b = 2.6 \times 10^{-6}$) with 0.200 M HNO_3. The points to calculate are V_a = 0.0, 10.0, 20.0, 25.0, 30.0, 40.0, 49.0, 49.9, 50.0, 50.1, 51.0, and 60.0 mL. Draw a graph of pH versus V_a.

10-D. Consider the titration of 50.0 mL of 0.050 0 M malonic acid with 0.100 M NaOH. Calculate the pH at each point listed and sketch the titration curve: V_b = 0.0, 8.0, 12.5, 19.3, 25.0, 37.5, 50.0, and 56.3 mL.

10-E. Write the chemical reactions (including structures of reactants and products) that occur when the amino acid histidine is titrated with perchloric acid. (Histidine is a molecule with no net charge.) A solution containing 25.0 mL of 0.050 0 M histidine was titrated with 0.050 0 M $HClO_4$. Calculate the pH at the following values of V_a: 0, 4.0, 12.5, 25.0, 26.0, and 50.0 mL.

10-F. Select indicators from Table 10-3 that would be useful for the titrations in Figures 10-1 and 10-2 and the $pK_a = 8$ curve in Figure 10-3. Select a different indicator for each titration and state what color change you would use as the end point.

10-G. When 100.0 mL of a weak acid were titrated with 0.093 81 M NaOH, 27.63 mL were required to reach the equivalence point. The pH at the equivalence point was 10.99. What was the pH when only 19.47 mL of NaOH had been added?

10-H. A 0.100 M solution of the weak acid HA was titrated with 0.100 M NaOH. The pH measured when $V_b = \frac{1}{2}V_e$ was 4.62. Using activity coefficients, calculate pK_a. The size of the A^- anion is 450 pm.

10-I. *Finding the end point from pH measurements.* Here are data points around the second apparent end point in Figure 10-5:

V_b (μL)	pH	V_b (μL)	pH
107.0	6.921	117.0	7.878
110.0	7.117	118.0	8.090
113.0	7.359	119.0	8.343
114.0	7.457	120.0	8.591
115.0	7.569	121.0	8.794
116.0	7.705	122.0	8.952

(a) Prepare a spreadsheet or table analogous to Figure 10-6, showing the first and second derivatives. Plot both derivatives versus V_b and locate the end point in each plot.

(b) Prepare a Gran plot analogous to Figure 10-8. Use the least-squares procedure to find the best straight line and find the end point. You will have to use your judgment as to which points lie on the "straight" line.

10-J. *Indicator error*. Consider the titration in Figure 10-2 in which the equivalence-point pH in Table 10-2 is 9.25 at a volume of 10.00 mL.

(a) Suppose you used the yellow-to-blue transition of thymol blue indicator to find the end point. According to Table 10-3, the last trace of green disappears near pH 9.6. What volume of base is required to reach pH 9.6? The difference between this volume and 10 mL is the indicator error.

(b) If you used cresol red, with a color change at pH 8.8, what would be the indicator error?

10-K. *Spectrophotometry with indicators*.† Acid-base indicators are themselves acids or bases. Consider an indicator, HIn, which dissociates according to the equation

$$HIn \overset{K_a}{\rightleftharpoons} H^+ + In^-$$

The molar absorptivity, ε, is 2 080 $M^{-1}\,cm^{-1}$ for HIn and 14 200 $M^{-1}\,cm^{-1}$ for In^-, at a wavelength of 440 nm.

(a) Write an expression for the absorbance of a solution containing HIn at a concentration [HIn] and In^- at a concentration [In^-] in a cell of pathlength 1.00 cm. The total absorbance is the sum of absorbances of each component.

(b) A solution containing indicator at a formal concentration of 1.84 $\times 10^{-4}$ M is adjusted to pH 6.23 and found to exhibit an absorbance of 0.868 at 440 nm. Calculate pK_a for this indicator.

†This problem is based on Beer's law in Section 17-2.

Problems

Titration of Strong Acid with Strong Base

10-1. Distinguish the terms *end point* and *equivalence point*.

10-2. Consider the titration of 100.0 mL of 0.100 M NaOH with 1.00 M HBr. Find the pH at the following volumes of acid added and make a graph of pH versus V_a: V_a = 0, 1, 5, 9, 9.9, 10, 10.1, and 12 mL.

10-3. Why does an acid-base titration curve (pH versus volume of titrant) have an abrupt change at the equivalence point?

Titration of Weak Acid with Strong Base

10-4. Sketch the general appearance of the curve for the titration of a weak acid with a strong base. Explain (in words) what chemistry governs the pH in each of the four distinct regions of the curve.

10-5. Why is it not practical to titrate an acid or a base that is too weak or too dilute?

10-6. A weak acid HA (pK_a = 5.00) was titrated with 1.00 M KOH. The acid solution had a volume of 100.0 mL and a molarity of 0.100 M. Find the pH at the following volumes of base added and make a graph of pH versus V_b: V_b = 0, 1, 5, 9, 9.9, 10, 10.1, and 12 mL.

10-7. Consider the titration of the weak acid HA with NaOH. At what fraction of V_e does pH = $pK_a - 1$? At what fraction of V_e does pH = $pK_a + 1$? Use these two points, plus $V_b = 0, \frac{1}{2}V_e, V_e$, and $1.2V_e$ to sketch the titration curve for the reaction of 100 mL of 0.100 M anilinium bromide ("aminobenzene · HBr") with 0.100 M NaOH.

10-8. What is the pH at the equivalence point when 0.100 M hydroxyacetic acid is titrated with 0.050 0 M KOH?

10-9. Find the equilibrium constant for the reaction of MES (Table 8-2) with NaOH.

10-10. When 22.63 mL of aqueous NaOH were added to 1.214 g of cyclohexylaminoethanesulfonic acid (FM 207.29, structure in Table 8-2) dissolved in 41.37 mL of water, the pH was 9.24. Calculate the molarity of the NaOH.

10-11. *Use activity coefficients* to calculate the pH after 10.0 mL of 0.100 M trimethylammonium bromide were titrated with 4.0 mL of 0.100 M NaOH.

Titration of Weak Base with Strong Acid

10-12. Sketch the general appearance of the curve for the titration of a weak base with a strong acid. Explain (in words) what chemistry governs the pH in each of the four distinct regions of the curve.

10-13. Why is the equivalence-point pH necessarily below 7 when a weak base is titrated with strong acid?

10-14. A 100.0-mL aliquot of 0.100 M weak base B (pK_b = 5.00) was titrated with 1.00 M $HClO_4$. Find the pH at the following volumes of acid added and make a graph of pH versus V_a: V_a = 0, 1, 5, 9, 9.9, 10, 10.1, and 12 mL.

10-15. At what point in the titration of a weak base with a strong acid is the maximum buffer capacity reached? This is the point at which a given small addition of acid causes the least pH change.

10-16. What is the equilibrium constant for the reaction between benzylamine and HCl?

10-17. A 50.0-mL solution of 0.031 9 M benzylamine was titrated with 0.050 0 M HCl. Calculate the pH at the following volumes of added acid: V_a = 0, 12.0, $\frac{1}{2}V_e$, 30.0, V_e, and 35.0 mL.

10-18. Calculate the pH of a solution made by mixing 50.00 mL of 0.100 M NaCN with

(a) 4.20 mL of 0.438 M $HClO_4$

(b) 11.82 mL of 0.438 M $HClO_4$

(c) What is the pH at the equivalence point with 0.438 M $HClO_4$?

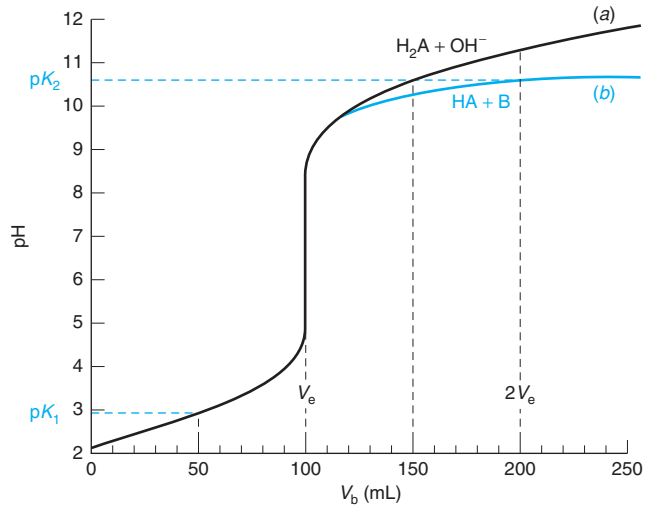
Titrations in Diprotic Systems

10-19. Sketch the general appearance of the curve for the titration of a weak diprotic acid with NaOH. Explain (in words) what chemistry governs the pH in each distinct region of the curve.

10-20. The opening page of this chapter shows the titration curve for an enzyme. Is the average charge of the protein positive, negative, or neutral at its isoionic point? How do you know?

10-21. The base Na^+A^-, whose anion is dibasic, was titrated with HCl to give curve *b* in Figure 10-4. Is the first equivalence point (H) the isoelectric point or the isoionic point?

10-22. The figure compares the titration of a monoprotic weak acid with a monoprotic weak base and the titration of a diprotic acid with strong base.



(*a*) Titration of 100 mL of 0.050 M H_2A (pK_1 = 2.86, pK_2 = 10.64) with 0.050 M NaOH. (*b*) Titration of 100 mL of the weak acid HA (0.050 M, pK_a = 2.86) with the weak base B (0.050 M, pK_b = 3.36).

(a) Write the reaction between the weak acid and the weak base and show that the equilibrium constant is $10^{7.78}$. This large value means that the reaction goes "to completion" after each addition of reagent.

(b) Why does pK_2 intersect the upper curve at $\frac{3}{2}V_e$ and the lower curve at $2V_e$? On the lower curve, "pK_2" is pK_a for the acid, BH^+.

10-23. The dibasic compound B (pK_{b1} = 4.00, pK_{b2} = 8.00) was titrated with 1.00 M HCl. The initial solution of B was 0.100 M and had a volume of 100.0 mL. Find the pH at the following volumes of acid added and make a graph of pH versus V_a: V_a = 0, 1, 5, 9, 10, 11, 15, 19, 20, and 22 mL.

10-24. A 100.0-mL aliquot of 0.100 M diprotic acid H_2A (pK_1 = 4.00, pK_2 = 8.00) was titrated with 1.00 M NaOH. Find the pH at the following volumes of base added and make a graph of pH versus V_b: V_b = 0, 1, 5, 9, 10, 11, 15, 19, 20, and 22 mL.

10-25. Calculate the pH at 10.0-mL intervals (from 0 to 100 mL) in the titration of 40.0 mL of 0.100 M piperazine with 0.100 M HCl. Make a graph of pH versus V_a.

10-26. Calculate the pH when 25.0 mL of 0.020 0 M 2-aminophenol have been titrated with 10.9 mL of 0.015 0 M $HClO_4$.

10-27. Consider the titration of 50.0 mL of 0.100 M sodium glycinate, $H_2NCH_2CO_2Na$, with 0.100 M HCl.

(a) Calculate the pH at the second equivalence point.

(b) Show that our approximate method of calculations gives incorrect (physically unreasonable) values of pH at V_a = 90.0 and V_a = 101.0 mL.

10-28. A solution containing 0.100 M glutamic acid (the molecule with no net charge) was titrated to its first equivalence point with 0.025 0 M RbOH.

(a) Draw the structures of reactants and products.

(b) Calculate the pH at the first equivalence point.

10-29. Find the pH of the solution when 0.010 0 M tyrosine is titrated to the equivalence point with 0.004 00 M $HClO_4$.

10-30. This problem deals with the amino acid cysteine, which we will abbreviate H_2C.

(a) A 0.030 0 M solution was prepared by dissolving dipotassium cysteine, K_2C, in water. Then 40.0 mL of this solution were titrated with 0.060 0 M $HClO_4$. Calculate the pH at the first equivalence point.

(b) Calculate the quotient $[C^{2-}]/[HC^-]$ in a solution of 0.050 0 M cysteinium bromide (the salt $H_3C^+Br^-$).

10-31. How many grams of dipotassium oxalate (FM 166.22) should be added to 20.0 mL of 0.800 M $HClO_4$ to give a pH of 4.40 when the solution is diluted to 500 mL?

10-32. When 5.00 mL of 0.103 2 M NaOH were added to 0.112 3 g of alanine (FM 89.093) in 100.0 mL of 0.10 M KNO_3, the measured pH was 9.57. *Use activity coefficients* to find pK_2 for alanine. Consider the ionic strength of the solution to be 0.10 M and consider each ionic form of alanine to have an activity coefficient of 0.77.

Finding the End Point with a pH Electrode

10-33. What is a Gran plot used for?

10-34. Data for the titration of 100.00 mL of a weak acid by NaOH are given below. Find the end point by preparing a Gran plot, using the last 10% of the volume prior to V_e.

mL NaOH	pH	mL NaOH	pH	mL NaOH	pH
0.00	4.14	20.75	6.09	22.70	6.70
1.31	4.30	21.01	6.14	22.76	6.74
2.34	4.44	21.10	6.15	22.80	6.78
3.91	4.61	21.13	6.16	22.85	6.82
5.93	4.79	21.20	6.17	22.91	6.86
7.90	4.95	21.30	6.19	22.97	6.92
11.35	5.19	21.41	6.22	23.01	6.98
13.46	5.35	21.51	6.25	23.11	7.11
15.50	5.50	21.61	6.27	23.17	7.20
16.92	5.63	21.77	6.32	23.21	7.30
18.00	5.71	21.93	6.37	23.30	7.49
18.35	5.77	22.10	6.42	23.32	7.74
18.95	5.82	22.27	6.48	23.40	8.30
19.43	5.89	22.37	6.53	23.46	9.21
19.93	5.95	22.48	6.58	23.55	9.86
20.48	6.04	22.57	6.63		

10-35. Prepare a second derivative graph to find the end point from the following titration data.

mL NaOH	pH	mL NaOH	pH	mL NaOH	pH
10.679	7.643	10.725	6.222	10.750	4.444
10.696	7.447	10.729	5.402	10.765	4.227
10.713	7.091	10.733	4.993		
10.721	6.700	10.738	4.761		

Finding the End Point with Indicators

10-36. Explain the origin of the rule of thumb that indicator color changes occur at $pK_{HIn} \pm 1$.

10-37. Why does a properly chosen indicator change color near the equivalence point in a titration?

10-38. The pH of microscopic vesicles (compartments) in living cells can be estimated by infusing an indicator (HIn) into the compartment and measuring the quotient $[In^-]/[HIn]$ from the spectrum of the indicator inside the vesicle. Explain how this tells us the pH.

10-39. Write the formula of a compound with a negative pK_a.

10-40. Consider the titration in Figure 10-2, for which the pH at the equivalence point is calculated to be 9.25. If thymol blue is used as an indicator, what color will be observed through most of the titration prior to the equivalence point? At the equivalence point? After the equivalence point?

10-41. What color do you expect to observe for cresol purple indicator (Table 10-3) at the following pH values? **(a)** 1.0; **(b)** 2.0; **(c)** 3.0

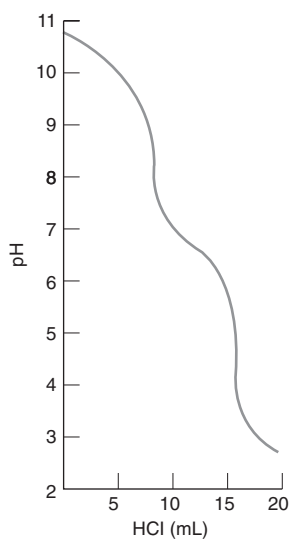
10-42. Cresol red has *two* transition ranges listed in Table 10-3. What color would you expect it to be at the following pH values? **(a)** 0; **(b)** 1; **(c)** 6; **(d)** 9

10-43. Would the indicator bromocresol green, with a transition range of pH 3.8–5.4, ever be useful in the titration of a weak acid with a strong base?

10-44. **(a)** What is the pH at the equivalence point when 0.030 0 M NaF is titrated with 0.060 0 M $HClO_4$?

(b) Why would an indicator end point probably not be useful in this titration?

10-45. A titration curve for $NaCO_3$ titrated with HCl is shown here. Suppose that *both* phenolphthalein and bromocresol green are present in the titration solution. State what colors you expect to observe at the following volumes of added HCl: **(a)** 2 mL; **(b)** 10 mL; **(c)** 19 mL.



10-46. In the Kjeldahl nitrogen determination, the final product is a solution of NH_4^+ in HCl solution. It is necessary to titrate the HCl without titrating NH_4^+.

(a) Calculate the pH of pure 0.010 M NH_4Cl.

(b) Select an indicator that would allow you to titrate HCl but not NH_4^+.

10-47. A 10.231-g sample of window cleaner containing ammonia was diluted with 39.466 g of water. Then 4.373 g of solution were titrated with 14.22 mL of 0.106 3 M HCl to reach a bromocresol green end point. Find the weight percent of NH_3 (FM 17.031) in the cleaner.

10-48. A procedure to measure the alkalinity (Box 10-1) of home swimming pool water is to titrate a fixed volume of pool water by counting the number of drops of standard H_2SO_4 to reach the bromocresol green end point.[30] Explain what is measured in this titration and why bromocresol green was chosen.

Practical Notes, Kjeldahl Analysis, and Leveling Effect

10-49. Give the name and formula of a primary standard used to standardize **(a)** HCl and **(b)** NaOH.

10-50. Why is it more accurate to use a primary standard with a high equivalent mass (the mass required to provide or consume 1 mol of H^+) than one with a low equivalent mass?

10-51. Explain how to use potassium hydrogen phthalate to standardize a solution of NaOH.

10-52. A solution was prepared from 1.023 g of the primary standard tris (Table 10-4) plus 99.367 g of water; 4.963 g of the solution were titrated with 5.262 g of aqueous HNO_3 to reach the methyl red end point. Calculate the concentration of the HNO_3 (expressed as mol HNO_3/kg solution).

10-53. The balance says that you have weighed out 1.023 g of tris to standardize a solution of HCl. Use the buoyancy correction in Section 2-3 and the density in Table 10-4 to determine how many grams you have really weighed out. The volume of HCl required to react with the tris was 28.37 mL. Does the buoyancy correction introduce a random or a systematic error into the calculated molarity of HCl? What is the magnitude of the error expressed as a percentage? Is the calculated molarity of HCl higher or lower than the true molarity?

10-54. A solution was prepared by dissolving 0.194 7 g of HgO (Table 10-4) in 20 mL of water containing 4 g of KBr. Titration with HCl required 17.98 mL to reach a phenolphthalein end point. Calculate the molarity of the HCl.

10-55. How many grams of potassium hydrogen phthalate should be weighed into a flask to standardize ~0.05 M NaOH if you wish to use ~30 mL of base for the titration?

10-56. Constant-boiling aqueous HCl can be used as a primary standard for acid-base titrations. When ~20 wt% HCl (FM 36.461) is distilled, the composition of the distillate varies in a regular manner with the barometric pressure:

P (Torr)	HCl[a] (g/100 g solution)
770	20.196
760	20.220
750	20.244
740	20.268
730	20.292

a. The composition of distillate is from C. W. Foulk and M. Hollingsworth, J. Am. Chem. Soc. ***1923,*** *45, 1223, with numbers corrected for the current values of atomic masses.*

(a) Make a graph of the data in the table to find the weight percent of HCl collected at 746 Torr.

(b) What mass of distillate (weighed in air, using weights whose density is 8.0 g/mL) should be dissolved in 1.000 0 L to give 0.100 00 M HCl? The density of distillate over the whole range in the table is close to 1.096 g/mL. You will need this density to change the mass measured in vacuum to mass measured in air. See Section 2-3 for buoyancy corrections.

10-57. (a) *Uncertainty in formula mass.* In an extremely-high-precision gravimetric titration, the uncertainty in formula mass of the primary standard could contribute to the uncertainty of the result. Review Section 3-5 and express the formula mass of potassium hydrogen phthalate, $C_8H_5O_4K$, with its proper uncertainty based on a rectangular distribution of uncertainty of atomic mass.

(b) *Systematic uncertainty in reagent purity.* The manufacturer of potassium hydrogen phthalate states that the purity is 1.000 00 ± 0.000 05. In the absence of further information, we assume that the distribution of uncertainty is rectangular. What standard uncertainty would you use for the purity of this reagent?

10-58. The Kjeldahl procedure was used to analyze 256 μL of a solution containing 37.9 mg protein/mL. The liberated NH_3 was collected in 5.00 mL of 0.033 6 M HCl, and the remaining acid required 6.34 mL of 0.010 M NaOH for complete titration. What is the weight percent of nitrogen in the protein?

10-59. What is meant by the leveling effect?

10-60. Considering the following pK_a values,[31] explain why dilute sodium methoxide ($NaOCH_3$) and sodium ethoxide ($NaOCH_2CH_3$) are leveled to the same base strength in aqueous solution. Write the chemical reactions that occur when these bases are added to water.

CH_3OH	pK_a = 15.54
CH_3CH_2OH	pK_a = 16.0
HOH	pK_a = 15.74 (for $K_a = [H^+][OH^-]/[H_2O]$)

10-61. The base B is too weak to titrate in aqueous solution.

(a) Which solvent, pyridine or acetic acid, would be more suitable for the titration of B with $HClO_4$? Why?

(b) Which solvent would be more suitable for the titration of a very weak acid with tetrabutylammonium hydroxide? Why?

10-62. Explain why sodium amide ($NaNH_2$) and phenyl lithium (C_6H_5Li) are leveled to the same base strength in aqueous solution. Write the chemical reactions that occur when these reagents are added to water.

10-63. Pyridine is half protonated in aqueous phosphate buffer at pH 5.2. If you mix 45 mL of phosphate buffer with 55 mL of methanol, the buffer must have a pH of 3.2 to half protonate pyridine. Suggest a reason why.

Calculating Titration Curves with Spreadsheets

10-64. Derive the following equation for the titration of potassium hydrogen phthalate (K^+HP^-) with NaOH:

$$\phi = \frac{C_bV_b}{C_aV_a} = \frac{\alpha_{HP^-} + 2\alpha_{P^{2-}} - 1 - \dfrac{[H^+] - [OH^-]}{C_a}}{1 + \dfrac{[H^+] - [OH^-]}{C_b}}$$

10-65. *Effect of pK_a in the titration of weak acid with strong base.* Use Equation 10-13 to compute and plot the family of curves at the left side of Figure 10-3. For a strong acid, choose a large K_a, such as $K_a = 10^2$ or p$K_a = -2$.

10-66. *Effect of concentration in the titration of weak acid with strong base.* Use your spreadsheet from Problem 10-65 to prepare a family of titration curves for pK_a = 6, with the following combinations of concentrations: **(a)** C_a = 20 mM, C_b = 100 mM; **(b)** C_a = 2 mM, C_b = 10 mM; **(c)** C_a = 0.2 mM, C_b = 1 mM.

10-67. *Effect of pK_b in the titration of weak base with strong acid.* Using the appropriate equation in Table 10-5, compute and plot a family of curves analogous to the left part of Figure 10-3 for the titration of 50.0 mL of 0.020 0 M B (pK_b = −2.00, 2.00, 4.00, 6.00, 8.00, and 10.00) with 0.100 M HCl. (The value pK_b = −2.00 represents a strong base.) In the expression for α_{BH^+}, $K_{BH^+} = K_w/K_b$.

10-68. *Titrating weak acid with weak base.*

(a) Prepare a family of graphs for the titration of 50.0 mL of 0.020 0 M HA (pK_a = 4.00) with 0.100 M B (pK_b = 3.00, 6.00, and 9.00).

(b) Write the acid-base reaction that occurs when acetic acid and sodium benzoate (the salt of benzoic acid) are mixed, and find the equilibrium constant for the reaction. Find the pH of a solution prepared by mixing 212 mL of 0.200 M acetic acid with 325 mL of 0.050 0 M sodium benzoate.

10-69. *Titrating diprotic acid with strong base.* Prepare a family of graphs for the titration of 50.0 mL of 0.020 0 M H_2A with 0.100 M NaOH. Consider the following cases: **(a)** pK_1 = 4.00, pK_2 = 8.00; **(b)** pK_1 = 4.00, pK_2 = 6.00; **(c)** pK_1 = 4.00, pK_2 = 5.00.

10-70. *Titrating nicotine with strong acid.* Prepare a spreadsheet to reproduce the lower curve in Figure 10-4.

10-71. *Titrating triprotic acid with strong base.* Prepare a spreadsheet to graph the titration of 50.0 mL of 0.020 0 M histidine · 2HCl with 0.100 M NaOH. Treat histidine · 2HCl with the triprotic acid equation in Table 10-5.

10-72. *A tetraprotic system.* Write an equation for the titration of tetrabasic base with strong acid ($B + H^+ \rightarrow\rightarrow\rightarrow\rightarrow BH_4^{4+}$. You can do this by inspection of Table 10-5 or you can derive it from the charge balance for the titration reaction. Graph the titration of 50.0 mL of 0.020 0 M sodium pyrophosphate ($Na_4P_2O_7$) with 0.100 M $HClO_4$. Pyrophosphate is the anion of pyrophosphoric acid.

Using Beer's Law with Indicators†

10-73. Spectrophotometric properties of a particular indicator are given below:

$$\underset{\substack{\lambda_{max} = 395\text{ nm} \\ \varepsilon_{395} = 1.80 \times 10^4\text{ M}^{-1}\text{ cm}^{-1} \\ \varepsilon_{604} = 0}}{HIn} \xrightleftharpoons{pK_a = 7.95} \underset{\substack{\lambda_{max} = 604\text{ nm} \\ \varepsilon_{604} = 4.97 \times 10^4\text{ M}^{-1}\text{ cm}^{-1}}}{In^-} + H^+$$

A solution with a volume of 20.0 mL containing 1.40×10^{-5} M indicator plus 0.050 0 M benzene-1,2,3-tricarboxylic acid was treated with 20.0 mL of aqueous KOH. The resulting solution had an absorbance at 604 nm of 0.118 in a 1.00-cm cell. Calculate the molarity of the KOH solution.

†These problems are based on Beer's law in Section 17-2.

10-74. A certain acid-base indicator exists in three colored forms:

H_2In	$\xrightleftharpoons{pK_1 = 1.00}$	HIn^-	$\xrightleftharpoons{pK_2 = 7.95}$	In^{2-}
$\lambda_{max} = 520$ nm		$\lambda_{max} = 435$ nm		$\lambda_{max} = 572$ nm
$\varepsilon_{520} = 5.00 \times 10^4$		$\varepsilon_{435} = 1.80 \times 10^4$		$\varepsilon_{572} = 4.97 \times 10^4$
Red		Yellow		Red
$\varepsilon_{435} = 1.67 \times 10^4$		$\varepsilon_{520} = 2.13 \times 10^3$		$\varepsilon_{520} = 2.50 \times 10^4$
$\varepsilon_{572} = 2.03 \times 10^4$		$\varepsilon_{572} = 2.00 \times 10^2$		$\varepsilon_{435} = 1.15 \times 10^4$

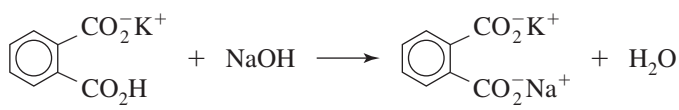
The units of molar absorptivity, ε, are $M^{-1}\ cm^{-1}$. A solution containing 10.0 mL of 5.00×10^{-4} M indicator was mixed with 90.0 mL of 0.1 M phosphate buffer (pH 7.50). Calculate the absorbance of this solution at 435 nm in a 1.00-cm cell.

Reference Procedure: Preparing Standard Acid and Base

Standard 0.1 M NaOH

1. Prepare 50 wt% aqueous NaOH solution in advance and allow the Na_2CO_3 precipitate to settle overnight. (Na_2CO_3 is insoluble in this solution.) Store the solution in a tightly sealed polyethylene bottle and avoid disturbing the precipitate when supernate is taken. The density is close to 1.50 g of solution per milliliter.

2. Dry primary-standard-grade potassium hydrogen phthalate for 1 h at 110°C and store it in a desiccator.



Potassium hydrogen phthalate FM 204.221

3. Boil 1 L of water for 5 min to expel CO_2. Pour the water into a polyethylene bottle, which should be tightly capped whenever possible. Calculate the volume of 50 wt% NaOH needed (~5.3 mL) to produce 1 L of ~0.1 M NaOH. Use a graduated cylinder to transfer this much NaOH to the bottle of water. Mix well and allow the solution to cool to room temperature (preferably overnight).

4. Weigh out four ~0.51-g portions of potassium hydrogen phthalate and dissolve each in ~25 mL of distilled water in a 125-mL flask. Each sample should require ~25 mL of 0.1 M NaOH. Add 3 drops of phenolphthalein indicator (Table 10-3) to each, and titrate one of them rapidly to find the approximate end point. The buret should have a loosely fitted cap to minimize entry of CO_2.

5. Calculate the volume of NaOH required for each of the other three samples and titrate them carefully. During each titration, periodically tilt and rotate the flask to wash liquid from the walls into the solution. When very near the end, deliver less than 1 drop of titrant at a time. To do this, carefully suspend a fraction of a drop from the buret tip, touch it to the inside wall of the flask, wash it into the bulk solution by careful tilting, and swirl the solution. The end point is the first appearance of pink color that persists for 15 s. The color will slowly fade as CO_2 from air dissolves in the solution.

6. Calculate the average molarity ($\bar{x}$), the standard deviation (s), and the relative standard deviation ($s/\bar{x}$). If you have used some care, the relative standard deviation should be <0.2%.

Standard 0.1 M HCl

1. The inside cover of this book tells us that 8.2 mL of ~37 wt% HCl should be added to 1 L of water to produce ~0.1 M HCl. Prepare this solution in a capped polyethylene bottle, using a graduated cylinder to deliver the HCl.

2. Dry primary-standard-grade Na_2CO_3 for 1 h at 110°C and cool it in a desiccator.

3. Weigh four samples containing enough Na_2CO_3 to react with ~25 mL of 0.1 M HCl from a buret and place each in a 125-mL flask. When ready to titrate each one, dissolve it in ~25 mL of distilled water.

$$2HCl + Na_2CO_3 \rightarrow CO_2 + 2NaCl + H_2O$$

FM 105.988

Add 3 drops of bromocresol green indicator (Table 10-3) and titrate one sample rapidly to a green color to find the approximate end point.

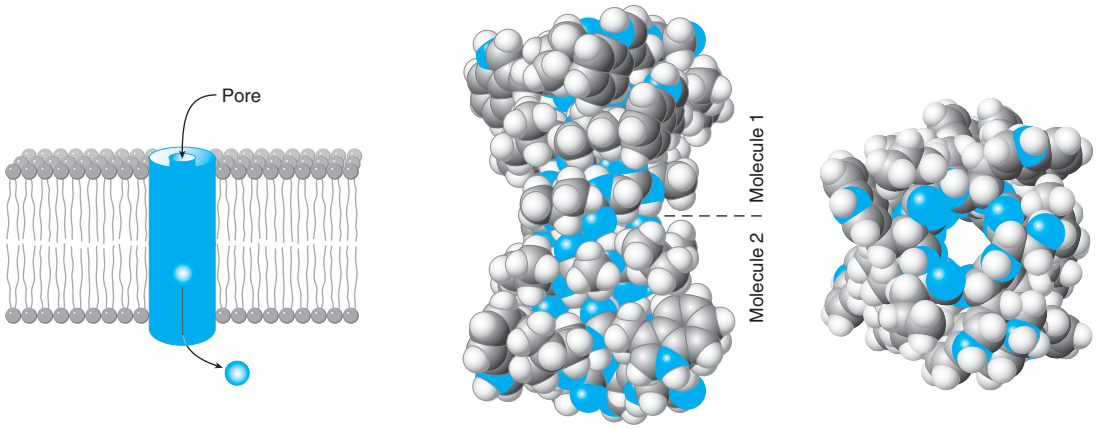
4. Carefully titrate each of the other samples until it just turns from blue to green. Then boil the solution to expel CO_2. The solution should return to a blue color. Carefully add HCl from the buret until the solution turns green again.

5. Titrate one blank prepared from 3 drops of indicator plus 50 mL of 0.05 M NaCl. Subtract the blank volume of HCl from that required to titrate Na_2CO_3.

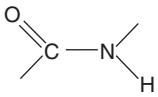
6. Calculate the mean HCl molarity, standard deviation, and relative standard deviation.

11 EDTA Titrations

ION CHANNELS IN CELL MEMBRANES



Left and center: Two gramicidin A molecules associate to span a cell membrane. *Right:* Axial view showing ion channel. [Structure from B. Roux, "Computational Studies of the Gramicidin Channel," *Acc. Chem. Res.* **2002**, *35*, 366, based on solid-state nuclear magnetic resonance. Schematic at left from L. Stryer, *Biochemistry*, 4th ed. (New York: W. H. Freeman and Company, 1995).]



Amide group

Gramicidin A is an antibiotic that kills cells by making their membranes permeable to Na^+ and K^+. Gramicidin A is made of 15 amino acids wound into a helix with a 0.4-nm-diameter channel through the middle. The channel is lined by polar amide groups, and the outside of gramicidin is covered by nonpolar hydrocarbon substituents (Table 9-1). *Polar* groups have positive and negative regions that attract neighboring molecules by electrostatic forces. *Nonpolar* groups have little charge separation and are soluble inside the nonpolar cell membrane.

Metal cations dissolve in water and are said to be *hydrophilic* ("water loving"). Cell membranes exclude water and are described as *hydrophobic* ("water hating"). Gramicidin A lodges in the cell membrane because the outside of the molecule is hydrophobic. Na^+ and K^+ pass through each hydrophilic pore at a rate of 10^7 ions/s. The pore is selective for monovalent cations; it excludes anions and more highly charged cations.

Part of the Nobel Prize in Chemistry in 2003 was awarded to Roderick MacKinnon for elucidating the structure of potassium channels that selectively permit K^+ to pass through membranes of cells such as nerves.[1] Unlike gramicidin A channels, the potassium channels are selective for K^+ over Na^+. Amide oxygen atoms of the protein backbone in the channel are spaced just right to replace waters of hydration from $K(H_2O)_6^+$. There is little change in energy when hydrated K^+ sheds H_2O and binds inside the channel. The spacing of amide oxygens is too great by 0.04 nm to displace H_2O from $Na(H_2O)_6^+$. Hydrated Na^+ remains outside the channel, whereas hydrated K^+ sheds H_2O and binds inside the channel. K^+ passes at a rate of 10^8 ions/s per channel—100 times faster than Na^+.

EDTA is a merciful abbreviation for *ethylenediaminetetraacetic acid,* a compound that forms strong 1:1 complexes with most metal ions (Figure 11-1) and finds wide use in quantitative analysis. EDTA plays a larger role as a strong metal-binding agent in industrial processes and in products such as detergents, cleaning agents, and food additives that prevent metal-catalyzed oxidation of food. EDTA is an emerging player in environmental chemistry.[2] For example, the majority of nickel discharged into San Francisco Bay and a significant fraction of the iron, lead, copper, and zinc are EDTA complexes that pass unscathed through wastewater treatment plants.

Dissolved nickel in the south San Francisco Bay reaches 110 nM in the summer.

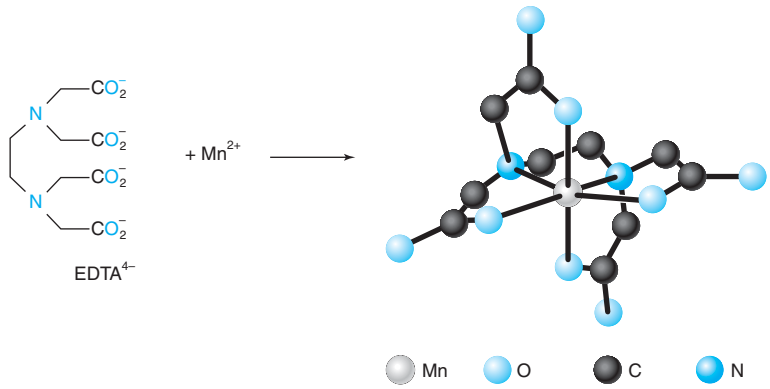
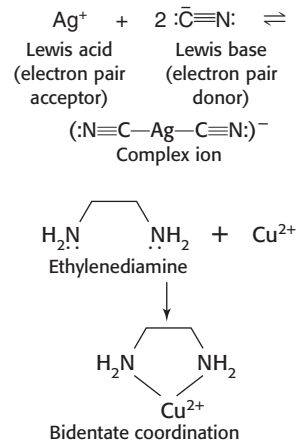


FIGURE 11-1 EDTA forms strong 1:1 complexes with most metal ions, binding through four oxygen and two nitrogen atoms. The six-coordinate geometry of Mn^{2+}-EDTA found in the compound KMnEDTA · $2H_2O$ was deduced from X-ray crystallography. [From J. Stein, J. P. Fackler, Jr., G. J. McClune, J. A. Fee, and L. T. Chan, "Reactions of Mn-EDTA and MnCyDTA Complexes with O_2^-: X-Ray Structure of KMnEDTA · $2H_2O$," *Inorg. Chem.* **1979**, *18*, 3511.]

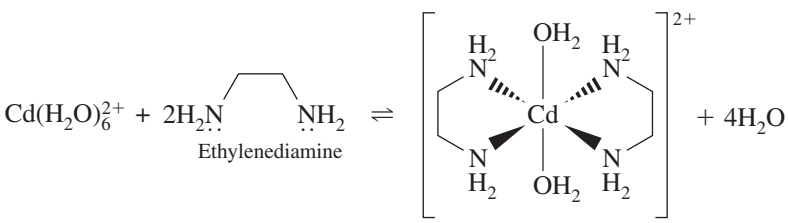
11-1 Metal-Chelate Complexes

Metal ions are **Lewis acids,** accepting electron pairs from electron-donating ligands that are **Lewis bases.** Cyanide (CN^-) is called a **monodentate** ligand because it binds to a metal ion through only one atom (the carbon atom). Most transition metal ions bind six ligand atoms. A ligand that attaches to a metal ion through more than one ligand atom is said to be **multidentate** ("many toothed"), or a **chelating ligand** (pronounced KEE-late-ing).[3]



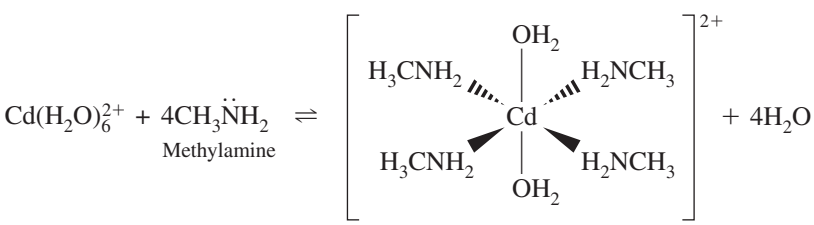
A simple chelating ligand is 1,2-diaminoethane $H_2\ddot{N}CH_2CH_2\ddot{N}H_2$, also called ethylenediamine), whose binding to a metal ion is shown in the margin. We say that ethylenediamine is *bidentate* because it binds to the metal through two ligand atoms.

The **chelate effect** is the ability of multidentate ligands to form more stable metal complexes than those formed by similar monodentate ligands.[4,5] For example, the reaction of $Cd(H_2O)_6^{2+}$ with two molecules of ethylenediamine is more favorable than its reaction with four molecules of methylamine:



$$K \equiv \beta_2 = 8 \times 10^9 \qquad \textbf{(11-1)}$$

Nomenclature for formation constants (K and β) was discussed in Box 6-2.



$$K \equiv \beta_4 = 4 \times 10^6 \qquad \textbf{(11-2)}$$

We have drawn *trans* isomers of the octahedral complexes (with H_2O ligands at opposite poles), but *cis* isomers are also possible (with H_2O ligands adjacent to each other).

At pH 12 in the presence of 2 M ethylenediamine and 4 M methylamine, the quotient $[Cd(\text{ethylenediamine})_2^{2+}]/[Cd(\text{methylamine})_4^{2+}]$ is 30.

An important *tetradentate* ligand is adenosine triphosphate (ATP), which binds to divalent metal ions (such as Mg^{2+}, Mn^{2+}, Co^{2+}, and Ni^{2+}) through four of their six coordination positions (Figure 11-2). The fifth and sixth positions are occupied by water molecules. The biologically active form of ATP is generally the Mg^{2+} complex.

Metal-chelate complexes are ubiquitous in biology. Bacteria such as *Escherichia coli* and *Salmonella enterica* in your gut excrete a powerful iron chelator called enterobactin (Figure 11-3) to scavenge iron that is essential for bacterial growth. The iron-enterobactin complex is recognized at specific sites on the bacterial cell surface and taken into the cell. Iron is then released inside the bacterium by enzymatic disassembly of the chelator. To fight bacterial infection, your immune system produces a protein called siderocalin to sequester and inactivate enterobactin.[9] An important medical application of chelates is described in Box 11-1.

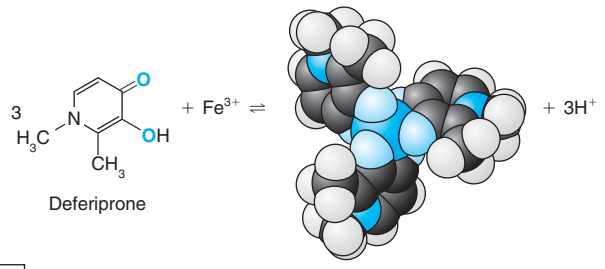
BOX 11-1 Chelation Therapy and Thalassemia

Oxygen is carried in blood by the iron-containing protein hemoglobin, which consists of two pairs of subunits, designated α and β. β-Thalassemia major is a genetic disease in which the β subunits of hemoglobin are not synthesized in adequate quantities. Children afflicted with this disease survive only with frequent transfusions of normal red blood cells. The problem with this treatment is that patients accumulate 4–8 g of iron per year from the hemoglobin in the transfused cells. The body has no mechanism for excreting large quantities of iron, and patients eventually die from the toxic effects of iron overload.

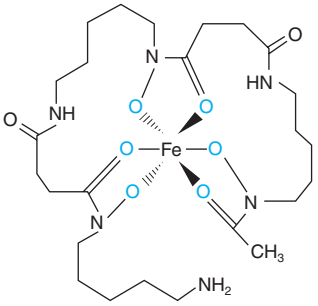
To enhance iron excretion, intensive chelation therapy is used. The most successful drug is *desferrioxamine B*, a powerful Fe^{3+} chelator produced by the microbe *Streptomyces pilosus*.[6] The formation constant for the Fe(III) complex, called ferrioxamine B, is $10^{30.6}$. Used in conjunction with ascorbic acid—vitamin C, a reducing agent that reduces Fe^{3+} to the more soluble Fe^{2+}—desferrioxamine clears several grams of iron per year from an overloaded patient. The ferrioxamine complex is excreted in the urine.

Desferrioxamine reduces the incidence of heart and liver disease in thalassemia patients. In patients for whom desferrioxamine effectively controls iron overload, there is a 91% rate of cardiac disease-free survival after 15 years of therapy.[7] There are negative effects of desferrioxamine treatment; for example, too high a dose stunts a child's growth.

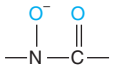
Desferrioxamine is expensive and must be taken by overnight subcutaneous infusion five to seven nights per week. It is not absorbed through the intestine. Many potent iron chelators have been tested to find an effective one that can be taken orally, but few have entered clinical practice.[8] The orally administered chelator deferiprone, introduced in 1987, is used with positive effect in more than 50 countries (but is not licensed in the United States and Canada). Combined use of desferrioxamine and deferiprone increases survival and reduces the incidence of cardiac disease, in comparison with desferrioxamine treatment only. An orally administered chelator called deferasirox was approved for use in the United States in 2005. The continued search for new chelators indicates that no current treatment is fully effective. In the long term, bone marrow transplants or gene therapy might cure the disease.



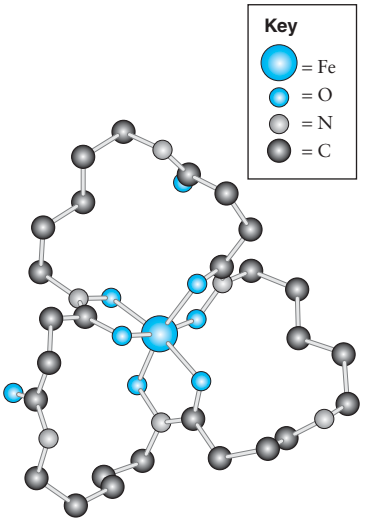
Deferiprone



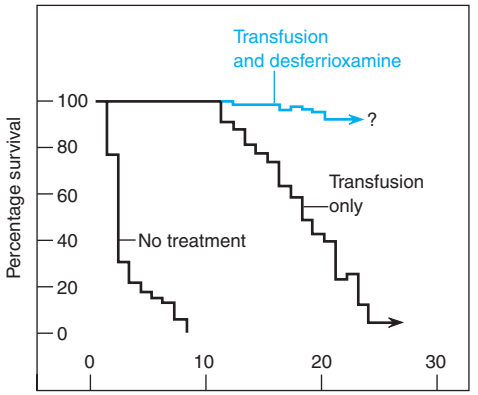
Ferrioxamine B



Hydroxamate group



Crystal structure of ferrioxamine E



Structure of the iron complex ferrioxamine B and crystal structure of a related compound, ferrioxamine E, in which the chelate has a cyclic structure. Graph shows success of transfusions and transfusions plus chelation therapy. [Crystal structure kindly provided by M. Neu, Los Alamos National Laboratory, based on D. Van der Helm and M. Poling, *J. Am. Chem. Soc.* **1976**, *98*, 82. Graph from P. S. Dobbin and R. C. Hider, "Iron Chelation Therapy," *Chem. Br.* **1990**, *26*, 565.]

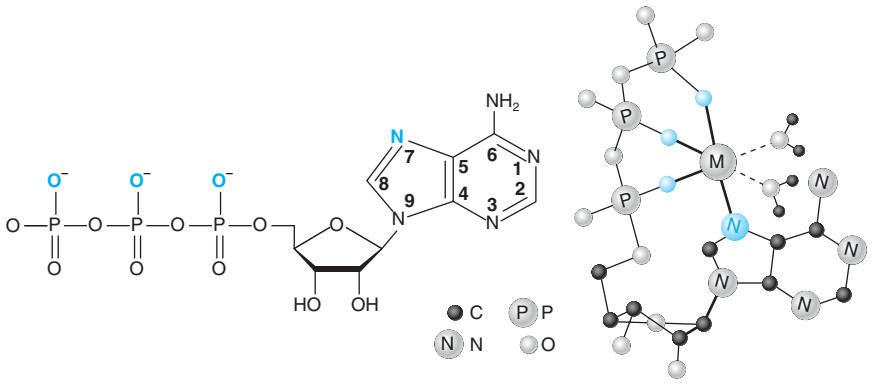


FIGURE 11-2 (*a*) Structure of adenosine triphosphate (ATP), with ligand atoms shown in color. (*b*) Possible structure of a metal-ATP complex; the metal, M, has four bonds to ATP and two bonds to H_2O ligands.

Aminocarboxylic acids in Figure 11-4 are synthetic chelating agents. Amine N atoms and carboxylate O atoms are potential ligand atoms in these molecules (Figures 11-5 and 11-6). When these molecules bind to a metal ion, the ligand atoms lose their protons. A medical application of the ligand DTPA in Figure 11-4 is illustrated by the tightly bound complex Gd^{3+}-DTPA, which is injected into humans at a concentration of ~0.5 mM to provide contrast in magnetic resonance imaging.[10]

A titration based on complex formation is called a **complexometric titration.** Ligands other than NTA in Figure 11-4 form strong 1:1 complexes with all metal ions except univalent ions such as Li^+, Na^+, and K^+. *The stoichiometry is 1:1 regardless of the charge on the ion.*

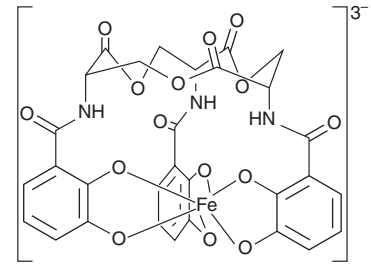


FIGURE 11-3 Iron(III)-enterobactin complex. Certain bacteria secrete enterobactin to capture iron and bring it into the cell. Enterobactin is one of several known chelates—designated *siderophores*—released by microbes to capture iron to be used by the cell. [From R. J. Abergel, J. A. Warner, D. K. Shuh, and K. N. Raymond, "Enterobactin Protonation and Iron Release," *J. Am. Chem. Soc.* **2006**, *128*, 8920.]

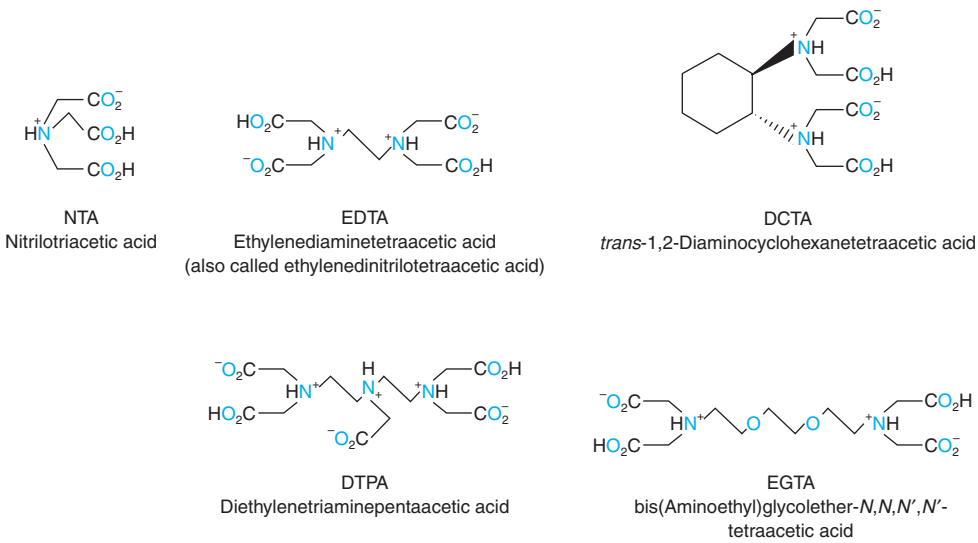


FIGURE 11-4 Structures of analytically useful chelating agents. Nitrilotriacetic acid (NTA) tends to form 2:1 (ligand:metal) complexes with metal ions, whereas the others form 1:1 complexes.

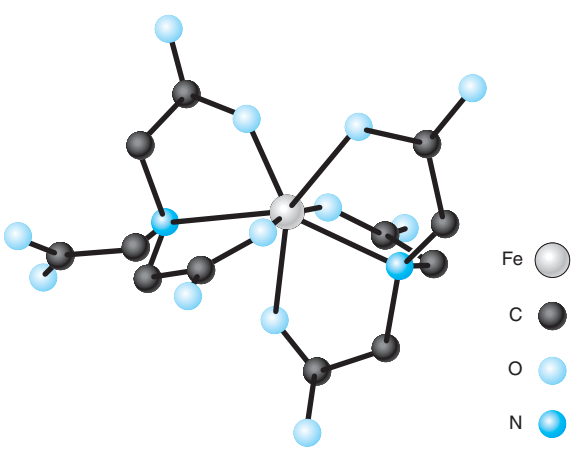


FIGURE 11-5 Structure of $Fe(NTA)_2^{3-}$ in the salt $Na_3[Fe(NTA)_2] \cdot 5H_2O$. The ligand at the right binds to Fe through three O atoms and one N atom. The other ligand uses two O atoms and one N atom. Its third carboxylate group is uncoordinated. The Fe atom is seven coordinate. [From W. Clegg, A. K. Powell, and M. J. Ware, "Structure of $Na_3[Fe(NTA)_2] \cdot 5H_2O$," *Acta Crystallogr.* **1984**, *C40*, 1822.]

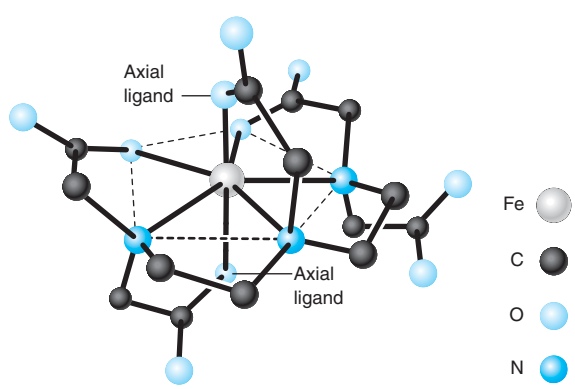


FIGURE 11-6 Structure of $Fe(DTPA)^{2-}$ found in the salt $Na_2[Fe(DTPA)] \cdot 2H_2O$. The seven-coordinate pentagonal bipyramidal coordination environment of the iron atom features 3 N and 2 O ligands in the equatorial plane (dashed lines) and two axial O ligands. The axial Fe—O bond lengths are 11 to 19 pm shorter than those of the more crowded equatorial Fe—O bonds. One carboxyl group of the ligand is uncoordinated. [From D. C. Finnen, A. A. Pinkerton, W. R. Dunham, R. H. Sands, and M. O. Funk, Jr., "Structures and Spectroscopic Characterization of Fe(III)-DTPA Complexes," *Inorg. Chem.* **1991**, *30*, 3960.]

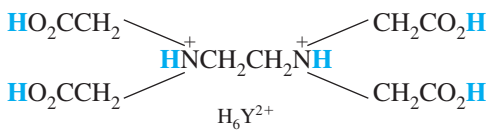
11-2 EDTA

One mole of EDTA reacts with *one* mole of metal ion.

EDTA is, by far, the most widely used chelator in analytical chemistry. By direct titration or through an indirect sequence of reactions, virtually every element of the periodic table can be measured with EDTA.

Acid-Base Properties

EDTA is a hexaprotic system, designated H_6Y^{2+}. The highlighted, acidic hydrogen atoms are the ones that are lost upon metal-complex formation.



$pK_1 = 0.0$ ($CO_2\mathbf{H}$)	$pK_4 = 2.69$ ($CO_2\mathbf{H}$)
$pK_2 = 1.5$ ($CO_2\mathbf{H}$)	$pK_5 = 6.13$ ($N\mathbf{H}^+$)
$pK_3 = 2.00$ ($CO_2\mathbf{H}$)	$pK_6 = 10.37$ ($N\mathbf{H}^+$)

pK applies at 25°C and $\mu = 0.1$ M, except pK_1 applies at $\mu = 1$ M

The first four pK values apply to carboxyl protons, and the last two are for the ammonium protons. The neutral acid is tetraprotic, with the formula H_4Y.

H_4Y can be dried at 140°C for 2 h and used as a primary standard. It can be dissolved by adding NaOH solution from a plastic container. NaOH solution from a glass bottle should not be used because it contains alkaline earth metals leached from the glass. Reagent-grade $Na_2H_2Y \cdot 2H_2O$ contains ~0.3% excess water. It may be used in this form with suitable correction for the mass of excess water or dried to the composition $Na_2H_2Y \cdot 2H_2O$ at 80°C.[11] The certified reference material $CaCO_3$ can be used to standardize EDTA or to verify the composition of standard EDTA.

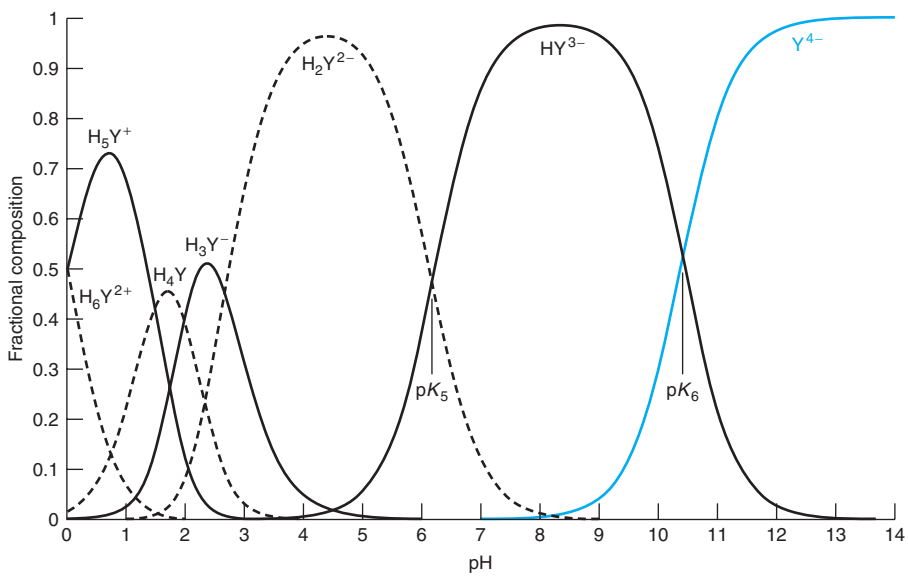


FIGURE 11-7 Fractional composition diagram for EDTA.

The fraction of EDTA in each of its protonated forms is plotted in Figure 11-7. As in Section 9-5, we can define α for each species as the fraction of EDTA in that form. For example, $\alpha_{Y^{4-}}$ is defined as

Fraction of EDTA in the form Y^{4-}:

$$\alpha_{Y^{4-}} = \frac{[Y^{4-}]}{[H_6Y^{2+}] + [H_5Y^+] + [H_4Y] + [H_3Y^-] + [H_2Y^{2-}] + [HY^{3-}] + [Y^{4-}]}$$

$$\alpha_{Y^{4-}} = \frac{[Y^{4-}]}{[\text{EDTA}]} \qquad (11\text{-}3)$$

where [EDTA] is the total concentration of all *free* EDTA species in the solution. By "free," we mean EDTA not complexed to metal ions. Following the derivation in Section 9-5, we can show that $\alpha_{Y^{4-}}$ is given by

$$\alpha_{Y^{4-}} = \frac{K_1K_2K_3K_4K_5K_6}{D} \tag{11-4}$$

where $D = [H^+]^6 + [H^+]^5K_1 + [H^+]^4K_1K_2 + [H^+]^3K_1K_2K_3 + [H^+]^2K_1K_2K_3K_4 + [H^+]K_1K_2K_3K_4K_5 + K_1K_2K_3K_4K_5K_6$. Table 11-1 gives values for $\alpha_{Y^{4-}}$ as a function of pH.

TABLE 11-1 Values of $\alpha_{Y^{4-}}$ for EDTA at 25°C and $\mu = 0.10$ M

pH	$\alpha_{Y^{4-}}$
0	1.3×10^{-23}
1	1.4×10^{-18}
2	2.6×10^{-14}
3	2.1×10^{-11}
4	3.0×10^{-9}
5	2.9×10^{-7}
6	1.8×10^{-5}
7	3.8×10^{-4}
8	4.2×10^{-3}
9	0.041
10	0.30
11	0.81
12	0.98
13	1.00
14	1.00

EXAMPLE What does $\alpha_{Y^{4-}}$ mean?

The fraction of all free EDTA in the form Y^{4-} is called $\alpha_{Y^{4-}}$. At pH 6.00 and a formal concentration of 0.10 M, the composition of an EDTA solution is

$[H_6Y^{2+}] = 8.9 \times 10^{-20}$ M $\quad [H_5Y^+] = 8.9 \times 10^{-14}$ M $\quad [H_4Y] = 2.8 \times 10^{-7}$ M

$[H_3Y^-] = 2.8 \times 10^{-5}$ M $\quad [H_2Y^{2-}] = 0.057$ M $\quad [HY^{3-}] = 0.043$ M

$[Y^{4-}] = 1.8 \times 10^{-6}$ M

Find $\alpha_{Y^{4-}}$.

Solution $\alpha_{Y^{4-}}$ is the fraction in the form Y^{4-}:

$$\alpha_{Y^{4-}} = \frac{[Y^{4-}]}{[H_6Y^{2+}] + [H_5Y^+] + [H_4Y] + [H_3Y^-] + [H_2Y^{2-}] + [HY^{3-}] + [Y^{4-}]}$$

$$= \frac{1.8 \times 10^{-6}}{(8.9 \times 10^{-20}) + (8.9 \times 10^{-14}) + (2.8 \times 10^{-7}) + (2.8 \times 10^{-5}) + (0.057) + (0.043) + (1.8 \times 10^{-6})}$$

$$= 1.8 \times 10^{-5}$$

Question From Figure 11-7, which species has the greatest concentration at pH 6? At pH 7? At pH 11?

Test Yourself At what pH does $\alpha_{Y^{4-}} = 0.50$? (***Answer:*** pH = pK_6 = 10.37)

EDTA Complexes

The equilibrium constant for the reaction of a metal with a ligand is called the **formation constant,** K_f, or the **stability constant:**

Formation constant:

$$M^{n+} + Y^{4-} \rightleftharpoons MY^{n-4} \qquad K_f = \frac{[MY^{n-4}]}{[M^{n+}][Y^{4-}]} \tag{11-5}$$

Note that K_f for EDTA is defined in terms of the species Y^{4-} reacting with the metal ion. The equilibrium constant could have been defined for any of the other six forms of EDTA in the solution. Equation 11-5 should not be interpreted to mean that only Y^{4-} reacts with metal ions. Table 11-2 shows that formation constants for most EDTA complexes are large and tend to be larger for more positively charged cations.

In many transition metal complexes, EDTA engulfs the metal ion, forming the six-coordinate species in Figure 11-1. If you try to build a space-filling model of a six-coordinate metal-EDTA complex, you will find strain in the chelate rings. This strain is relieved when the O ligands are drawn back toward the N atoms. Such distortion opens up a seventh coordination position, which can be occupied by H_2O, as in Figure 11-8. In some complexes, such as $Ca(EDTA)(H_2O)_2^{2-}$, the metal ion is so large that it accommodates eight ligand atoms.[12] Larger metal ions require more ligand atoms. Even if H_2O is attached to the metal ion, the formation constant is still given by Equation 11-5. The relation remains true because solvent (H_2O) is omitted from the reaction quotient.

Lanthanide and actinide elements typically have a coordination number of 9, with the shape of a tricapped trigonal prism (Figure 11-9).[13] Pu(IV) forms a complex with one EDTA plus three H_2O molecules to complete the coordination sphere with nine ligand atoms.[14] Eu(III) forms mixed complexes of the type Eu(EDTA)(NTA) in which EDTA provides six ligand atoms and NTA provides three ligand atoms (Figure 11-4).[15]

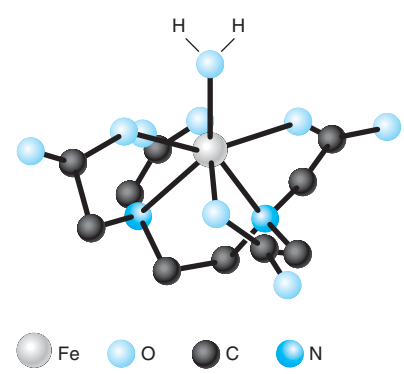


FIGURE 11-8 Seven-coordinate geometry of $Fe(EDTA)(H_2O)^-$. Other metal ions that form seven-coordinate EDTA complexes include Fe^{2+}, Mg^{2+}, Cd^{2+}, Co^{2+}, Mn^{2+}, Ru^{3+}, Cr^{3+}, Co^{3+}, V^{3+}, Ti^{3+}, In^{3+}, Sn^{4+}, Os^{4+}, and Ti^{4+}. Some of these same ions also form six-coordinate EDTA complexes. Eight-coordinate complexes are formed by Ca^{2+}, Er^{3+}, Yb^{3+}, and Zr^{4+}. [From T. Mizuta, J. Wang, and K. Miyoshi, "A 7-Coordinate Structure of Fe(III)-EDTA," *Bull. Chem. Soc. Japan* **1993**, *66*, 2547.]

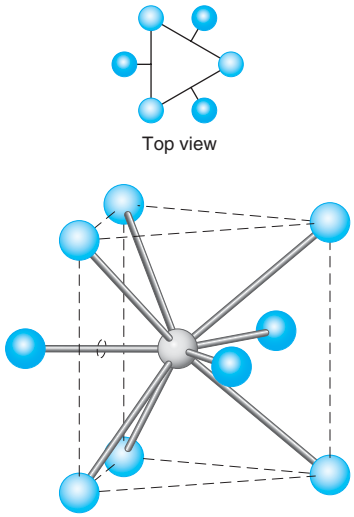


FIGURE 11-9 Tricapped trigonal prismatic structure of many Ln(III) and An(III) complexes, where Ln is a lanthanide element and An is an actinide element. In $M(H_2O)_9^{3+}$, bonds from the metal to the 6 O atoms at the corners of the prism are shorter than bonds from the metal to the 3 O atoms projecting out from the rectangular faces.

TABLE 11-2 Formation constants for metal-EDTA complexes

Ion	log K_f	Ion	log K_f	Ion	log K_f
Li^+	2.95	V^{3+}	25.9[a]	Tl^{3+}	35.3
Na^+	1.86	Cr^{3+}	23.4[a]	Bi^{3+}	27.8[a]
K^+	0.8	Mn^{3+}	25.2	Ce^{3+}	15.93
Be^{2+}	9.7	Fe^{3+}	25.1	Pr^{3+}	16.30
Mg^{2+}	8.79	Co^{3+}	41.4	Nd^{3+}	16.51
Ca^{2+}	10.65	Zr^{4+}	29.3	Pm^{3+}	16.9
Sr^{2+}	8.72	Hf^{4+}	29.5	Sm^{3+}	17.06
Ba^{2+}	7.88	VO^{2+}	18.7	Eu^{3+}	17.25
Ra^{2+}	7.4	VO_2^+	15.5	Gd^{3+}	17.35
Sc^{3+}	23.1[a]	Ag^+	7.20	Tb^{3+}	17.87
Y^{3+}	18.08	Tl^+	6.41	Dy^{3+}	18.30
La^{3+}	15.36	Pd^{2+}	25.6[a]	Ho^{3+}	18.56
V^{2+}	12.7[a]	Zn^{2+}	16.5	Er^{3+}	18.89
Cr^{2+}	13.6[a]	Cd^{2+}	16.5	Tm^{3+}	19.32
Mn^{2+}	13.89	Hg^{2+}	21.5	Yb^{3+}	19.49
Fe^{2+}	14.30	Sn^{2+}	18.3[b]	Lu^{3+}	19.74
Co^{2+}	16.45	Pb^{2+}	18.0	Th^{4+}	23.2
Ni^{2+}	18.4	Al^{3+}	16.4	U^{4+}	25.7
Cu^{2+}	18.78	Ga^{3+}	21.7		
Ti^{3+}	21.3	In^{3+}	24.9		

NOTE: The stability constant is the equilibrium constant for the reaction $M^{n+} + Y^{4-} \rightleftharpoons MY^{n-4}$. Values in table apply at 25°C and ionic strength 0.1 M unless otherwise indicated.

a. 20°C, ionic strength = 0.1 M. b. 20°C, ionic strength = 1 M.

SOURCE: A. E. Martell, R. M. Smith, and R. J. Motekaitis, NIST Critically Selected Stability Constants of Metal Complexes, NIST Standard Reference Database 46, Gaithersburg, MD, 2001.

Conditional Formation Constant

The formation constant $K_f = [MY^{n-4}]/[M^{n+}][Y^{4-}]$ describes the reaction between Y^{4-} and a metal ion. As you see in Figure 11-7, most EDTA is not Y^{4-} below pH 10.37. The species HY^{3-}, H_2Y^{2-}, and so on, predominate at lower pH. From the definition $\alpha_{Y^{4-}} = [Y^{4-}]/[\text{EDTA}]$, we can express the concentration of Y^{4-} as

$$[Y^{4-}] = \alpha_{Y^{4-}}[\text{EDTA}]$$

where [EDTA] is the total concentration of all EDTA species not bound to metal ion.

The formation constant can now be rewritten as

Only some of the free EDTA is in the form Y^{4-}.

$$K_f = \frac{[MY^{n-4}]}{[M^{n+}][Y^{4-}]} = \frac{[MY^{n-4}]}{[M^{n+}]\alpha_{Y^{4-}}[\text{EDTA}]}$$

If the pH is fixed by a buffer, then $\alpha_{Y^{4-}}$ is a constant that can be combined with K_f:

Conditional formation constant:

$$K_f' = \alpha_{Y^{4-}}K_f = \frac{[MY^{n-4}]}{[M^{n+}][\text{EDTA}]} \qquad (11\text{-}6)$$

The number $K_f' = \alpha_{Y^{4-}}K_f$ is called the **conditional formation constant,** or the *effective formation constant.* It describes the formation of MY^{n-4} at any particular pH. After we learn to use Equation 11-6, we will modify it to allow for the possibility that not all metal ion is in the form M^{n+}.

With the conditional formation constant, we can treat EDTA complex formation as if all free EDTA were in one form.

The conditional formation constant allows us to look at EDTA complex formation as if the uncomplexed EDTA were all in one form:

$$M^{n+} + \text{EDTA} \rightleftharpoons MY^{n-4} \qquad K_f' = \alpha_{Y^{4-}}K_f$$

At any given pH, we can find $\alpha_{Y^{4-}}$ and evaluate K_f'.

EXAMPLE Using the Conditional Formation Constant

The formation constant in Table 11-2 for CaY^{2-} is $10^{10.65}$. Calculate the concentration of free Ca^{2+} in a solution of 0.10 M CaY^{2-} at pH 10.00 and at pH 6.00.

Solution The complex formation reaction is

$$Ca^{2+} + EDTA \rightleftharpoons CaY^{2-} \qquad K_f' = \alpha_{Y^{4-}} K_f$$

where EDTA on the left side of the equation refers to all forms of unbound EDTA (Y^{4-}, HY^{3-}, H_2Y^{2-}, H_3Y^-, and so on). Using $\alpha_{Y^{4-}}$ from Table 11-1, we find

$$\text{At pH 10.00:} \qquad K_f' = (0.30)(10^{10.65}) = 1.3_4 \times 10^{10}$$
$$\text{At pH 6.00:} \qquad K_f' = (1.8 \times 10^{-5})(10^{10.65}) = 8.0 \times 10^5$$

Dissociation of CaY^{2-} must produce equal quantities of Ca^{2+} and EDTA, so we can write

	Ca^{2+}	+ EDTA	$\rightleftharpoons$ CaY^{2-}
Initial concentration (M)	0	0	0.10
Final concentration (M)	x	x	$0.10 - x$

$$\frac{[CaY^{2-}]}{[Ca^{2+}][EDTA]} = \frac{0.10 - x}{x^2} = K_f' = 1.3_4 \times 10^{10} \quad \text{at pH 10.00}$$
$$= 8.0 \times 10^5 \quad \text{at pH 6.00}$$

Solving for x (= $[Ca^{2+}]$), we find $[Ca^{2+}] = 2.7 \times 10^{-6}$ M at pH 10.00 and 3.5×10^{-4} M at pH 6.00. *Using the conditional formation constant at a fixed pH, we treat the dissociated EDTA as if it were a single species.*

Test Yourself Find $[Ca^{2+}]$ in 0.10 M CaY^{2-} at pH 8.00. (***Answer:*** 2.3×10^{-5} M)

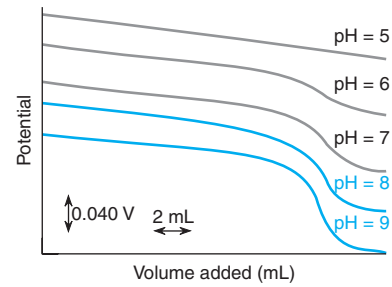


FIGURE 11-10 Titration of Ca^{2+} with EDTA as a function of pH. As the pH is lowered, the end point becomes less distinct. The potential was measured with mercury and calomel electrodes, as described in Exercise 14-B. [From C. N. Reilley and R. W. Schmid, "Chelometric Titration with Potentiometric End Point Detection. Mercury as a pM Indicator Electrode," *Anal. Chem.* **1958**, *30*, 947.]

You can see from the example that a metal-EDTA complex becomes less stable at lower pH. For a titration reaction to be effective, it must go "to completion" (say, 99.9%), which means that the equilibrium constant is large—the analyte and titrant are essentially completely reacted at the equivalence point. Figure 11-10 shows how pH affects the titration of Ca^{2+} with EDTA. Below pH ≈ 8, the end point is not sharp enough to allow accurate determination. The conditional formation constant for CaY^{2-} is just too small for "complete" reaction at low pH.

pH can be used to select which metals will be titrated by EDTA and which will not. Metals with higher formation constants can be titrated at lower pH. If a solution containing both Fe^{3+} and Ca^{2+} is titrated at pH 4, Fe^{3+} is titrated without interference from Ca^{2+}.

11-3 EDTA Titration Curves

In this section, we calculate the concentration of free M^{n+} during its titration with EDTA.[16] The titration reaction is

$$M^{n+} + EDTA \rightleftharpoons MY^{n-4} \qquad K_f' = \alpha_{Y^{4-}} K_f \tag{11-7}$$

If K_f' is large, we can consider the reaction to be complete at each point in the titration.

The titration curve is a graph of pM (= $-\log[M^{n+}]$) versus the volume of added EDTA. The curve is analogous to plotting pH versus volume of titrant in an acid-base titration. There are three natural regions of the titration curve in Figure 11-11.

K_f' is the effective formation constant at the fixed pH of the solution.

Region 1: Before the Equivalence Point

In this region, there is excess M^{n+} left in solution after the EDTA has been consumed. The concentration of free metal ion is equal to the concentration of excess, unreacted M^{n+}. The dissociation of MY^{n-4} is negligible.

Region 2: At the Equivalence Point

There is exactly as much EDTA as metal in the solution. We can treat the solution as if it had been made by dissolving pure MY^{n-4}. Some free M^{n+} is generated by the slight dissociation of MY^{n-4}:

$$MY^{n-4} \rightleftharpoons M^{n+} + EDTA$$

In this reaction, EDTA represents free EDTA in all its forms. At the equivalence point, $[M^{n+}]$ = [EDTA].

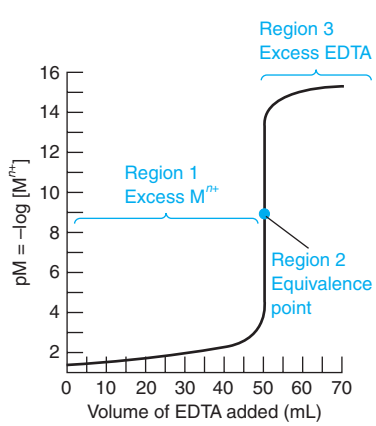


FIGURE 11-11 Three regions in an EDTA titration illustrated for reaction of 50.0 mL of 0.050 0 M M^{n+} with 0.050 0 M EDTA, assuming $K_f' = 1.15 \times 10^{16}$. The concentration of free M^{n+} decreases as the titration proceeds.

Region 3: After the Equivalence Point

Now there is excess EDTA, and virtually all the metal ion is in the form MY^{n-4}. The concentration of free EDTA can be equated to the concentration of excess EDTA added after the equivalence point.

Titration Calculations

Let's calculate the shape of the titration curve for the reaction of 50.0 mL of 0.040 0 M Ca^{2+} (buffered to pH 10.00) with 0.080 0 M EDTA:

$$Ca^{2+} + EDTA \rightarrow CaY^{2-}$$

The value of $\alpha_{Y^{4-}}$ comes from Table 11-1.

$$K_f' = \alpha_{Y^{4-}} K_f = (0.30)(10^{10.65}) = 1.3_4 \times 10^{10}$$

Because K_f' is large, it is reasonable to say that the reaction goes to completion with each addition of titrant. We want to make a graph in which pCa^{2+} ($= -\log[Ca^{2+}]$) is plotted versus milliliters of added EDTA. The equivalence volume is 25.0 mL.

Region 1: Before the Equivalence Point

Before the equivalence point, there is excess unreacted Ca^{2+}.

Consider the addition of 5.0 mL of EDTA. Because the equivalence point requires 25.0 mL of EDTA, one-fifth of the Ca^{2+} will be consumed and four-fifths remains.

$$[Ca^{2+}] = \underbrace{\left(\frac{25.0 - 5.0}{25.0}\right)}_{\substack{\text{Fraction}\\ \text{remaining}\\ (=4/5)}} \underbrace{(0.040\ 0\ \text{M})}_{\substack{\text{Original}\\ \text{concentration}\\ \text{of } Ca^{2+}}} \underbrace{\left(\frac{\overset{\text{Initial volume of } Ca^{2+}}{50.0}}{\underset{\text{Total volume of solution}}{55.0}}\right)}_{\text{Dilution factor}}$$

$$= 0.029\ 1\ \text{M} \Rightarrow pCa^{2+} = -\log[Ca^{2+}] = 1.54$$

In a similar manner, we could calculate pCa^{2+} for any volume of EDTA less than 25.0 mL.

Region 2: At the Equivalence Point

At the equivalence point, the major species is CaY^{2-}, in equilibrium with small, equal amounts of free Ca^{2+} and EDTA.

Virtually all the metal is in the form CaY^{2-}. With negligible dissociation, the concentration of CaY^{2-} is equal to the original concentration of Ca^{2+}, with a correction for dilution.

$$[CaY^{2-}] = \underbrace{(0.040\ 0\ \text{M})}_{\substack{\text{Original}\\ \text{concentration}\\ \text{of } Ca^{2+}}} \underbrace{\left(\frac{\overset{\text{Initial volume of } Ca^{2+}}{50.0}}{\underset{\text{Total volume of solution}}{75.0}}\right)}_{\text{Dilution factor}} = 0.026\ 7\ \text{M}$$

The concentration of free Ca^{2+} is small and unknown. We can write

	Ca^{2+}	+	EDTA	$\rightleftharpoons$	CaY^{2-}
Initial concentration (M)	—		—		0.026 7
Final concentration (M)	x		x		$0.026\ 7 - x$

[EDTA] refers to the total concentration of all forms of EDTA not bound to metal.

$$\frac{[CaY^{2-}]}{[Ca^{2+}][EDTA]} = K_f' = 1.3_4 \times 10^{10}$$

$$\frac{0.026\ 7 - x}{x^2} = 1.3_4 \times 10^{10} \Rightarrow x = 1.4 \times 10^{-6}\ \text{M}$$

$$pCa^{2+} = -\log[Ca^{2+}] = -\log x = 5.85$$

Region 3: After the Equivalence Point

After the equivalence point, virtually all the metal is in the form CaY^{2-}. There is a known excess of EDTA. A small amount of free Ca^{2+} exists in equilibrium with CaY^{2-} and EDTA.

In this region, virtually all the metal is in the form CaY^{2-}, and there is excess, unreacted EDTA. The concentrations of CaY^{2-} and excess EDTA are easily calculated. For example, at 26.0 mL, there is 1.0 mL of excess EDTA.

$$[EDTA] = \underbrace{(0.080\ 0\ \text{M})}_{\substack{\text{Original}\\ \text{concentration}\\ \text{of EDTA}}} \underbrace{\left(\frac{\overset{\text{Volume of excess EDTA}}{1.0}}{\underset{\text{Total volume of solution}}{76.0}}\right)}_{\text{Dilution factor}} = 1.05 \times 10^{-3}\ \text{M}$$

$$[CaY^{2-}] = \underbrace{(0.040\,0\text{ M})}_{\text{Original concentration of } Ca^{2+}}\underbrace{\left(\frac{50.0}{76.0}\right)}_{\text{Dilution factor}} = 2.63 \times 10^{-2}\text{ M}$$

Original volume of Ca^{2+} → 50.0; Total volume of solution → 76.0

The concentration of Ca^{2+} is governed by

$$\frac{[CaY^{2-}]}{[Ca^{2+}][EDTA]} = K_f' = 1.3_4 \times 10^{10}$$

$$\frac{[2.63 \times 10^{-2}]}{[Ca^{2+}](1.05 \times 10^{-3})} = 1.3_4 \times 10^{10}$$

$$[Ca^{2+}] = 1.9 \times 10^{-9}\text{ M} \Rightarrow pCa^{2+} = 8.73$$

The same sort of calculation can be used for any volume past the equivalence point.

The Titration Curve

Calculated titration curves for Ca^{2+} and Sr^{2+} in Figure 11-12 show a distinct break at the equivalence point, where the slope is greatest. The Ca^{2+} end point is more distinct than the Sr^{2+} end point because the conditional formation constant, $\alpha_{Y^{4-}}K_f$, for CaY^{2-} is greater than that of SrY^{2-}. If the pH is lowered, the conditional formation constant decreases (because $\alpha_{Y^{4-}}$ decreases), and the end point becomes less distinct, as we saw in Figure 11-10. The pH cannot be raised arbitrarily high, because metal hydroxide might precipitate.

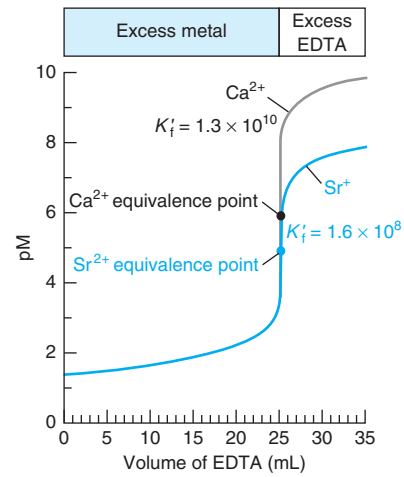


FIGURE 11-12 Theoretical titration curves for the reaction of 50.0 mL of 0.040 0 M metal ion with 0.080 0 M EDTA at pH 10.00.

11-4 Do It with a Spreadsheet

Let's see how to reproduce the EDTA titration curves in Figure 11-12 by using one equation that applies to the entire titration. Because the reactions are carried out at fixed pH, the equilibria and mass balances are sufficient to solve for all unknowns.

Consider the titration of metal ion M (initial concentration = C_M, volume = V_M) with a solution of ligand L (concentration = C_L, volume added = V_L) to form a 1:1 complex:

$$M + L \rightleftharpoons ML \qquad K_f = \frac{[ML]}{[M][L]} \Rightarrow [ML] = K_f[M][L] \tag{11-8}$$

Total metal concentration $= \dfrac{\text{initial moles of metal}}{\text{total volume}} = \dfrac{C_M V_M}{V_M + V_L}$

Total ligand concentration $= \dfrac{\text{moles of ligand added}}{\text{total volume}} = \dfrac{C_L V_L}{V_M + V_L}$

The mass balances for metal and ligand are

Mass balance for M: $$[M] + [ML] = \frac{C_M V_M}{V_M + V_L}$$

Mass balance for L: $$[L] + [ML] = \frac{C_L V_L}{V_M + V_L}$$

Substituting $K_f[M][L]$ (from Equation 11-8) for [ML] in the mass balances gives

$$[M](1 + K_f[L]) = \frac{C_M V_M}{V_M + V_L} \tag{11-9}$$

$$[L](1 + K_f[M]) = \frac{C_L V_L}{V_M + V_L} \Rightarrow [L] = \frac{\dfrac{C_L V_L}{V_M + V_L}}{1 + K_f[M]} \tag{11-10}$$

Now substitute the expression for [L] from Equation 11-10 back into Equation 11-9

$$[M]\left(1 + K_f \frac{\dfrac{C_L V_L}{V_M + V_L}}{1 + K_f[M]}\right) = \frac{C_M V_M}{V_M + V_L}$$

and do about five lines of algebra to solve for the fraction of titration, ϕ:

Spreadsheet equation for titration of M with L:

$$\phi = \frac{C_L V_L}{C_M V_M} = \frac{1 + K_f[M] - \dfrac{[M] + K_f[M]^2}{C_M}}{K_f[M] + \dfrac{[M] + K_f[M]^2}{C_L}} \tag{11-11}$$

Replace K_f by K_f' if L = EDTA.

As in acid-base titrations in Table 10-5, ϕ is the fraction of the way to the equivalence point. When $\phi = 1$, $V_L = V_e$. When $\phi = \frac{1}{2}$, $V_L = \frac{1}{2}V_e$. And so on.

FIGURE 11-13 Spreadsheet for the titration of 50.0 mL of 0.040 0 M Ca^{2+} with 0.080 0 M EDTA at pH 10.00. This spreadsheet reproduces calculations of Section 11-3. pM was varied by trial and error to find volumes of 5.00, 25.00, and 26.00 mL used in the preceding section. Better yet, use Goal Seek (page 158) to vary pM in cell B9 until the volume in cell E9 is 25.000 mL.

	A	B	C	D	E
1	Titration of 50 mL of 0.04 M Ca^{2+} with 0.08 M EDTA				
2					
3	C_M =	pM	M	Phi	V(ligand)
4	0.04	1.398	4.00E-02	0.000	0.002
5	V_M =	1.537	2.90E-02	0.201	5.026
6	50	2.00	1.00E-02	0.667	16.667
7	C(ligand) =	3.00	1.00E-03	0.963	24.074
8	0.08	4.00	1.00E-04	0.996	24.906
9	K_f' =	5.85	1.41E-06	1.000	25.0000
10	1.34E+10	7.00	1.00E-07	1.001	25.019
11		8.00	1.00E-08	1.007	25.187
12		8.73	1.86E-09	1.040	26.002
13	C4 = 10^-B4				
14	Equation 11-11:				
15	D4 = (1+$A$10*C4-(C4+C4*C4*$A$10)/$A$4)/				
16		(C4*$A$10+(C4+C4*C4*$A$10)/$A$8)			
17	E4 = D4*$A$4*$A$6/$A$8				

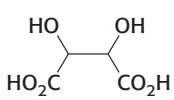
For a titration with EDTA, you can follow the derivation through and find that the formation constant, K_f, should be replaced in Equation 11-11 by the conditional formation constant, K_f', which applies at the fixed pH of the titration. Figure 11-13 shows a spreadsheet in which Equation 11-11 is used to calculate the Ca^{2+} titration curve in Figure 11-12. As in acid-base titrations, your input in column B is pM = –log[Ca^{2+}] and the output in column E is volume of titrant. To find the initial point, vary pM until V_1 is close to 0.

If you reverse the process and titrate ligand with metal ion, the fraction of the way to the equivalence point is the inverse of the fraction in Equation 11-11:

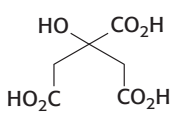
Replace K_f by K_f' if L = EDTA.

Spreadsheet equation for titration of L with M:

$$\phi = \frac{C_M V_M}{C_L V_L} = \frac{K_f[M] + \dfrac{[M] + K_f[M]^2}{C_L}}{1 + K_f[M] - \dfrac{[M] + K_f[M]^2}{C_M}} \qquad \textbf{(11-12)}$$



Tartaric acid



Citric acid

$N(CH_2CH_2OH)_3$
Triethanolamine

11-5 Auxiliary Complexing Agents

EDTA titration conditions in this chapter were selected to prevent metal hydroxide precipitation at the chosen pH. To permit many metals to be titrated in alkaline solutions with EDTA, we use an **auxiliary complexing agent.** This reagent is a ligand, such as ammonia, tartrate, citrate, or triethanolamine, that binds the metal strongly enough to prevent metal hydroxide from precipitating but weakly enough to give up the metal when EDTA is added. Zn^{2+} is usually titrated in ammonia buffer, which fixes the pH and complexes the metal ion to keep it in solution. Let's see how this works.

Metal-Ligand Equilibria[17]

Consider a metal ion that forms two complexes with the auxiliary complexing ligand L:

$$M + L \rightleftharpoons ML \qquad \beta_1 = \frac{[ML]}{[M][L]} \qquad \textbf{(11-13)}$$

$$M + 2L \rightleftharpoons ML_2 \qquad \beta_2 = \frac{[ML_2]}{[M][L]^2} \qquad \textbf{(11-14)}$$

The equilibrium constants, β_i, are called *overall* or **cumulative formation constants.** The fraction of metal ion in the uncomplexed state, M, can be expressed as

$$\alpha_M = \frac{[M]}{M_{tot}} \qquad \textbf{(11-15)}$$

where M_{tot} is the total concentration of all forms of M (= M, ML, and ML_2 in this case).

Now let's find a useful expression for α_M. The mass balance for metal is

$$M_{tot} = [M] + [ML] + [ML_2]$$

Equations 11-13 and 11-14 allow us to say $[ML] = \beta_1[M][L]$ and $[ML_2] = \beta_2[M][L]^2$. Therefore,

$$M_{tot} = [M] + \beta_1[M][L] + \beta_2[M][L]^2$$
$$= [M]\{1 + \beta_1[L] + \beta_2[L]^2\}$$

Substituting this last result into Equation 11-15 gives the desired result.

Fraction of free metal ion:

$$\alpha_M = \frac{[M]}{[M]\{1 + \beta_1[L] + \beta_2[L]^2\}} = \frac{1}{1 + \beta_1[L] + \beta_2[L]^2} \quad \textbf{(11-16)}$$

If the metal forms more than two complexes, Equation 11-16 takes the form

$$\alpha_M = \frac{1}{1 + \beta_1[L] + \beta_2[L]^2 + \cdots + \beta_n[L]^n}$$

EXAMPLE Ammonia Complexes of Zinc

Zn^{2+} and NH_3 form the complexes $Zn(NH_3)^{2+}$, $Zn(NH_3)_2^{2+}$, $Zn(NH_3)_3^{2+}$, and $Zn(NH_3)_4^{2+}$. If the concentration of free, *unprotonated* NH_3 is 0.10 M, find the fraction of zinc in the form Zn^{2+}. (At any pH, there will also be some NH_4^+ in equilibrium with NH_3.)

Solution Appendix I gives formation constants for the complexes $Zn(NH_3)^{2+}$ ($\beta_1 = 10^{2.18}$), $Zn(NH_3)_2^{2+}$ ($\beta_2 = 10^{4.43}$), $Zn(NH_3)_3^{2+}$ ($\beta_3 = 10^{6.74}$), and $Zn(NH_3)_4^{2+}$ ($\beta_4 = 10^{8.70}$). The appropriate form of Equation 11-16 is

$$\alpha_{Zn^{2+}} = \frac{1}{1 + \beta_1[L] + \beta_2[L]^2 + \beta_3[L]^3 + \beta_4[L]^4} \quad \textbf{(11-17)}$$

Equation 11-17 gives the fraction of zinc in the form Zn^{2+}. Putting in [L] = 0.10 M and the four values of β_i gives $\alpha_{Zn^{2+}} = 1.8 \times 10^{-5}$, which means there is very little free Zn^{2+} in the presence of 0.10 M NH_3.

Test Yourself Find $\alpha_{Zn^{2+}}$ if free, unprotonated $[NH_3] = 0.02$ M. (***Answer:*** 0.007 2)

BOX 11-2 Metal Ion Hydrolysis Decreases the Effective Formation Constant for EDTA Complexes

Equation 11-18 states that the effective (conditional) formation constant for an EDTA complex is the product of the formation constant, K_f, times the fraction of metal in the form M^{m+} times the fraction of EDTA in the form Y^{4-}: $K_f'' = \alpha_{M^{m+}}\alpha_{Y^{4-}}K_f$. Table 11-1 told us that $\alpha_{Y^{4-}}$ increases with pH until it levels off at 1 near pH 11.

In Section 11-3, we had no auxiliary complexing ligand and we implicitly assumed that $\alpha_{M^{m+}} = 1$. In fact, metal ions react with water to form $M(OH)_n$ species. Combinations of pH and metal ion in Section 11-3 were selected so that hydrolysis to $M(OH)_n$ is negligible. We can find such conditions for most M^{2+} ions, but not for M^{3+} or M^{4+}. Even in acidic solution, Fe^{3+} hydrolyzes to $Fe(OH)^{2+}$ and $Fe(OH)_2^+$.[18] (Appendix I gives formation constants for hydroxide complexes.) The graph shows that $\alpha_{Fe^{3+}}$ is close to 1 between pH 1 and 2 ($\log \alpha_{Fe^{3+}} \approx 0$), but then drops as hydrolysis occurs. At pH 5, the fraction of Fe(III) in the form Fe^{3+} is $\sim 10^{-5}$.

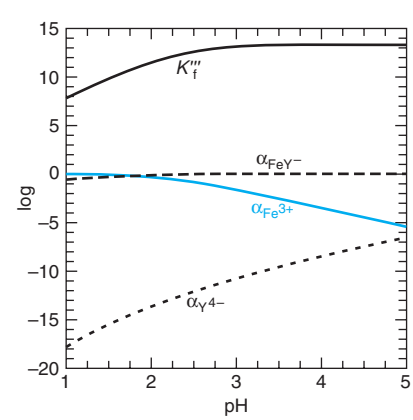
The effective formation constant for FeY^- in the graph has three contributions:

$$K_f''' = \frac{\alpha_{Fe^{3+}}\alpha_{Y^{4-}}}{\alpha_{FeY^-}}K_f$$

As pH increases, $\alpha_{Y^{4-}}$ increases, so K_f''' increases. As pH increases, metal hydrolysis occurs, so $\alpha_{Fe^{3+}}$ decreases. The increase in $\alpha_{Y^{4-}}$ is canceled by the decrease in $\alpha_{Fe^{3+}}$, so K_f''' is nearly constant above pH 3. The third contribution to K_f''' is α_{FeY^-}, which is the fraction of the EDTA complex in the form FeY^-. At low pH, some of the complex gains a proton to form FeHY, which decreases α_{FeY^-} near pH 1.

In the pH range 2 to 5, α_{FeY^-} is nearly constant at 1. In neutral and basic solution, complexes such as $Fe(OH)Y^{2-}$ and $[Fe(OH)Y]_2^{4-}$ are formed and α_{FeY^-} decreases.

Take-home message: In this book, we restrict ourselves to cases in which there is no hydrolysis and $\alpha_{M^{m+}}$ is controlled by a deliberately added auxiliary ligand. In reality, hydrolysis of M^{m+} and MY influences most EDTA titrations and makes the theoretical analysis more complicated than we pretend in this chapter.



Contributions of $\alpha_{Y^{4-}}$, $\alpha_{Fe^{3+}}$, and α_{FeY^-} to the effective formation constant, K_f''', for FeY^-. Curves were calculated by considering the species H_6Y^{2+}, H_5Y^+, H_4Y, H_3Y^-, H_2Y^{2-}, HY^{3-}, Y^{4-}, Fe^{3+}, $Fe(OH)^{2+}$, $Fe(OH)_2^+$, FeY^-, and FeHY.

EDTA Titration with an Auxiliary Complexing Agent

Now consider a titration of Zn^{2+} by EDTA in the presence of NH_3. The extension of Equation 11-6 requires a new conditional formation constant to account for the fact that only some of the EDTA is in the form Y^{4-} and only some of the zinc not bound to EDTA is in the form Zn^{2+}:

K_f'' is the effective formation constant at a fixed pH and fixed concentration of auxiliary complexing agent. Box 11-2 describes the influence of metal ion hydrolysis on the effective formation constant.

$$K_f'' = \alpha_{Zn^{2+}}\alpha_{Y^{4-}}K_f \tag{11-18}$$

In this expression, $\alpha_{Zn^{2+}}$ is given by Equation 11-17 and $\alpha_{Y^{4-}}$ is given by Equation 11-4. For particular values of pH and $[NH_3]$, we can compute K_f'' and proceed with titration calculations as in Section 11-3, substituting K_f'' for K_f'. An assumption in this process is that EDTA is a much stronger complexing agent than ammonia, so essentially all EDTA binds Zn^{2+} until the metal ion is consumed.

EXAMPLE EDTA Titration in the Presence of Ammonia

Consider the titration of 50.0 mL of 1.00×10^{-3} M Zn^{2+} with 1.00×10^{-3} M EDTA at pH 10.00 in the presence of 0.10 M NH_3. (This is the concentration of NH_3. There is also NH_4^+ in the solution.) The equivalence point is at 50.0 mL. Find pZn^{2+} after addition of 20.0, 50.0, and 60.0 mL of EDTA.

Solution In Equation 11-17, we found that $\alpha_{Zn^{2+}} = 1.8 \times 10^{-5}$. Table 11-1 tells us that $\alpha_{Y^{4-}} = 0.30$. With K_f from Table 11-2, the conditional formation constant is

$$K_f'' = \alpha_{Zn^{2+}}\alpha_{Y^{4-}}K_f = (1.8 \times 10^{-5})(0.30)(10^{16.5}) = 1.7 \times 10^{11}$$

(a) *Before the equivalence point—20.0 mL:* Because the equivalence point is 50.0 mL, the fraction of Zn^{2+} remaining is 30.0/50.0. The dilution factor is 50.0/70.0. Therefore, the concentration of zinc not bound to EDTA is

$$C_{Zn^{2+}} = \left(\frac{30.0}{50.0}\right)(1.00 \times 10^{-3}\text{ M})\left(\frac{50.0}{70.0}\right) = 4.3 \times 10^{-4}\text{ M}$$

However, nearly all zinc not bound to EDTA is bound to NH_3. The concentration of free Zn^{2+} is

The relation $[Zn^{2+}] = \alpha_{Zn^{2+}} C_{Zn^{2+}}$ follows from Equation 11-15.

$$[Zn^{2+}] = \alpha_{Zn^{2+}}C_{Zn^{2+}} = (1.8 \times 10^{-5})(4.3 \times 10^{-4}) = 7.7 \times 10^{-9}\text{ M}$$
$$\Rightarrow pZn^{2+} = -\log[Zn^{2+}] = 8.11$$

Let's try a reality check. The product $[Zn^{2+}][OH^-]^2$ is $[10^{-8.11}][10^{-4.00}]^2 = 10^{-16.11}$, which does not exceed the solubility product of $Zn(OH)_2$ ($K_{sp} = 10^{-15.52}$).

(b) *At the equivalence point—50.0 mL:* At the equivalence point, the dilution factor is 50.0/100.0, so $[ZnY^{2-}] = (50.0/100.0)(1.00 \times 10^{-3}\text{ M}) = 5.00 \times 10^{-4}$ M. We then create a table of concentrations:

	$C_{Zn^{2+}}$	+ EDTA	$\rightleftharpoons$ ZnY^{2-}
Initial concentration (M)	0	0	5.00×10^{-4}
Final concentration (M)	x	x	$5.00 \times 10^{-4} - x$

$$K_f'' = 1.7 \times 10^{11} = \frac{[ZnY^{2-}]}{[C_{Zn^{2+}}][EDTA]} = \frac{5.00 \times 10^{-4} - x}{x^2}$$
$$\Rightarrow x = C_{Zn^{2+}} = 5.4 \times 10^{-8}\text{ M}$$
$$[Zn^{2+}] = \alpha_{Zn^{2+}}C_{Zn^{2+}} = (1.8 \times 10^{-5})(5.4 \times 10^{-8}) = 9.7 \times 10^{-13}\text{ M}$$
$$\Rightarrow pZn^{2+} = -\log[Zn^{2+}] = 12.01$$

(c) *After the equivalence point—60.0 mL:* Almost all zinc is in the form ZnY^{2-}. With a dilution factor of 50.0/110.0 for zinc, we find

$$[ZnY^{2-}] = \left(\frac{50.0}{110.0}\right)(1.00 \times 10^{-3}\text{ M}) = 4.5 \times 10^{-4}\text{ M}$$

We also know the concentration of excess EDTA, whose dilution factor is 10.0/110.0:

$$[EDTA] = \left(\frac{10.0}{110.0}\right)(1.00 \times 10^{-3}\text{ M}) = 9.1 \times 10^{-5}\text{ M}$$

Once we know $[ZnY^{2-}]$ and [EDTA], we can use the equilibrium constant to find $[Zn^{2+}]$:

$$\frac{[ZnY^{2-}]}{[Zn^{2+}][EDTA]} = \alpha_{Y^{4-}}K_f = K_f' = (0.30)(10^{16.5}) = 9.5 \times 10^{15}$$

$$\frac{[4.5 \times 10^{-4}]}{[Zn^{2+}][9.1 \times 10^{-5}]} = 9.5 \times 10^{15} \Rightarrow [Zn^{2+}] = 5.3 \times 10^{-16}\ M$$

$$\Rightarrow pZn^{2+} = 15.28$$

After the equivalence point, the problem does not depend on the presence of NH_3, because we know both $[ZnY^{2-}]$ and [EDTA].

Test Yourself Find pZn^{2+} after adding 30.0 and 51.0 mL of EDTA. (***Answer:*** 8.35, 14.28)

Figure 11-14 compares the calculated titration curves for Zn^{2+} in the presence of different concentrations of auxiliary complexing agent. The greater the concentration of NH_3, the smaller the change of pZn^{2+} near the equivalence point. The auxiliary ligand must be kept below the level that would obliterate the end point of the titration. Color Plate 5 shows the appearance of a Cu^{2+}-ammonia solution during an EDTA titration.

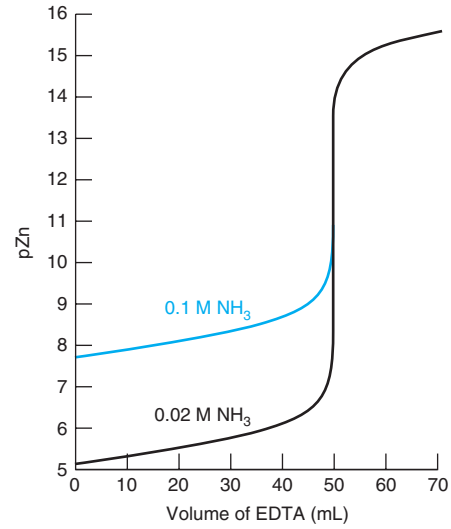


FIGURE 11-14 Titration curves for the reaction of 50.0 mL of 1.00×10^{-3} M Zn^{2+} with 1.00×10^{-3} M EDTA at pH 10.00 in the presence of two different concentrations of NH_3.

11-6 Metal Ion Indicators

The most common way to detect the end point in EDTA titrations is with a metal ion indicator. Alternatives include a mercury electrode (Figure 11-10 and Exercise 14-B) and an ion-selective electrode (Section 14-6). A pH electrode will follow the course of the titration in unbuffered solution, because H_2Y^{2-} releases $2H^+$ when it forms a metal complex.

End-point detection methods:

1. Metal ion indicators
2. Mercury electrode
3. Ion-selective electrode
4. Glass (pH) electrode

Metal ion indicators (Table 11-3) are compounds that change color when they bind to a metal ion. *Useful indicators must bind metal less strongly than EDTA does.*

A typical titration is illustrated by the reaction of Mg^{2+} with EDTA at pH 10 with Calmagite indicator.

$$\underset{\text{Red}}{MgIn} + \underset{\text{Colorless}}{EDTA} \rightarrow \underset{\text{Colorless}}{MgEDTA} + \underset{\text{Blue}}{In} \qquad (11\text{-}19)$$

The indicator must release its metal to EDTA.

At the start of the experiment, a small amount of indicator (In) is added to the colorless solution of Mg^{2+} to form a red complex. As EDTA is added, it reacts first with free, colorless Mg^{2+}. When free Mg^{2+} is used up, the last EDTA added before the equivalence point displaces indicator from the red MgIn complex. The change from the red MgIn to blue unbound In signals the end point of the titration (Demonstration 11-1).

DEMONSTRATION 11-1 Metal Ion Indicator Color Changes

This demonstration illustrates the color change associated with Reaction 11-19 and shows how a second dye can be added to produce a more easily detected color change.

STOCK SOLUTIONS

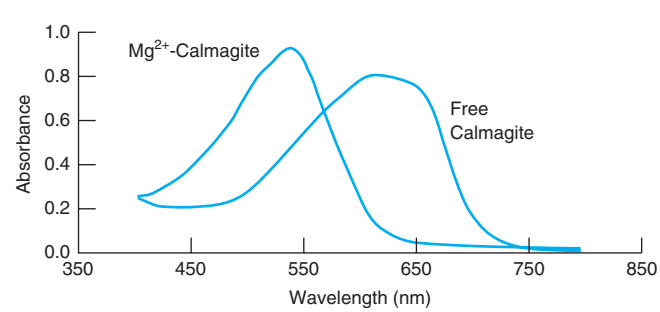
Buffer (pH 10.0): Add 142 mL of concentrated (14.5 M) aqueous ammonia to 17.5 g of ammonium chloride and dilute to 250 mL with water.

$MgCl_2$: 0.05 M

EDTA: 0.05 M $Na_2H_2EDTA \cdot 2H_2O$

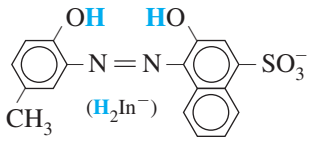
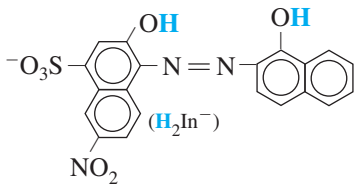
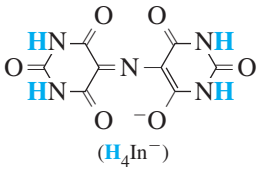
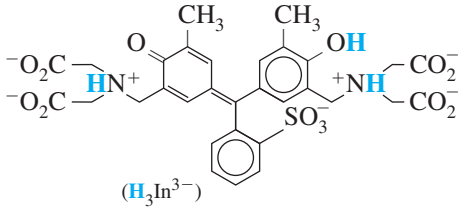
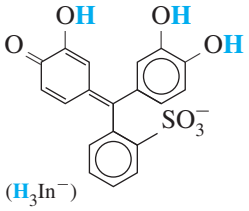
Prepare a solution containing 25 mL of $MgCl_2$, 5 mL of buffer, and 300 mL of water. Add six drops of Eriochrome black T or Calmagite indicator (Table 11-3) and titrate with EDTA. Note the color change from wine red to pale blue at the end point (Color Plate 6a). The spectroscopic change accompanying the color change is shown in the figure.

For some observers, the change of indicator color is not as sharp as desired. The colors can be affected by adding an "inert" dye whose color alters the appearance of the solution before and after the titration. Adding 3 mL of methyl red (Table 10-3) (or many other yellow dyes) produces an orange color prior to the end point and a green color after it. This sequence of colors is shown in Color Plate 6b.



Visible spectra of Mg^{2+}-Calmagite and free Calmagite at pH 10 in ammonia buffer. [From C. E. Dahm, J. W. Hall, and B. E. Mattioni, "A Laser Pointer-Based Spectrometer for Endpoint Detection of EDTA Titrations," *J. Chem. Ed.* **2004**, *81*, 1787.]

TABLE 11-3 Common metal ion indicators

Name	Structure	pK_a	Color of free indicator	Color of metal ion complex
Calmagite		$pK_2 = 8.1$ $pK_3 = 12.4$	H_2In^- red HIn^{2-} blue In^{3-} orange	Wine red
Eriochrome black T		$pK_2 = 6.3$ $pK_3 = 11.6$	H_2In^- red HIn^{2-} blue In^{3-} orange	Wine red
Murexide		$pK_2 = 9.2$ $pK_3 = 10.9$	H_4In^- red-violet H_3In^{2-} violet H_2In^{3-} blue	Yellow (with Co^{2+}, Ni^{2+}, Cu^{2+}); red with Ca^{2+}
Xylenol orange		$pK_2 = 2.32$ $pK_3 = 2.85$ $pK_4 = 6.70$ $pK_5 = 10.47$ $pK_6 = 12.23$	H_5In^- yellow H_4In^{2-} yellow H_3In^{3-} yellow H_2In^{4-} violet HIn^{5-} violet In^{6-} violet	Red
Pyrocatechol violet		$pK_1 = 0.2$ $pK_2 = 7.8$ $pK_3 = 9.8$ $pK_4 = 11.7$	H_4In red H_3In^- yellow H_2In^{2-} violet HIn^{3-} red-purple	Blue

PREPARATION AND STABILITY:

Calmagite: 0.05 g/100 mL H_2O; solution is stable for a year in the dark.

Eriochrome black T: Dissolve 0.1 g of the solid in 7.5 mL of triethanolamine plus 2.5 mL of absolute ethanol; solution is stable for months; best used for titrations above pH 6.5.

Murexide: Grind 10 mg of murexide with 5 g of reagent NaCl in a clean mortar; use 0.2–0.4 g of the mixture for each titration.

Xylenol orange: 0.5 g/100 mL H_2O; solution is stable indefinitely.

Pyrocatechol violet: 0.1 g/100 mL; solution is stable for several weeks.

Most metal ion indicators are also acid-base indicators, with pK_a values listed in Table 11-3. Because the color of free indicator is pH dependent, most indicators can be used only in certain pH ranges. For example, xylenol orange (pronounced ZY-leen-ol) changes from yellow to red when it binds to a metal ion at pH 5.5. This color change is easy to observe. At pH 7.5, the change is from violet to red and difficult to see. A spectrophotometer can measure the color change, but it is more convenient if we can see it. Figure 11-15 shows pH ranges in which many metals can be titrated and indicators that are useful in different ranges.

The indicator must give up its metal ion to the EDTA. If a metal does not freely dissociate from an indicator, the metal is said to **block** the indicator. Eriochrome black T is blocked by Cu^{2+}, Ni^{2+}, Co^{2+}, Cr^{3+}, Fe^{3+}, and Al^{3+}. It cannot be used for the *direct titration* of any of these metals. It can be used for a *back titration*, however. For example, excess standard EDTA can be added to Cu^{2+}. Then indicator is added and the excess EDTA is back-titrated with Mg^{2+}.

Question What color change occurs when the back titration is performed?

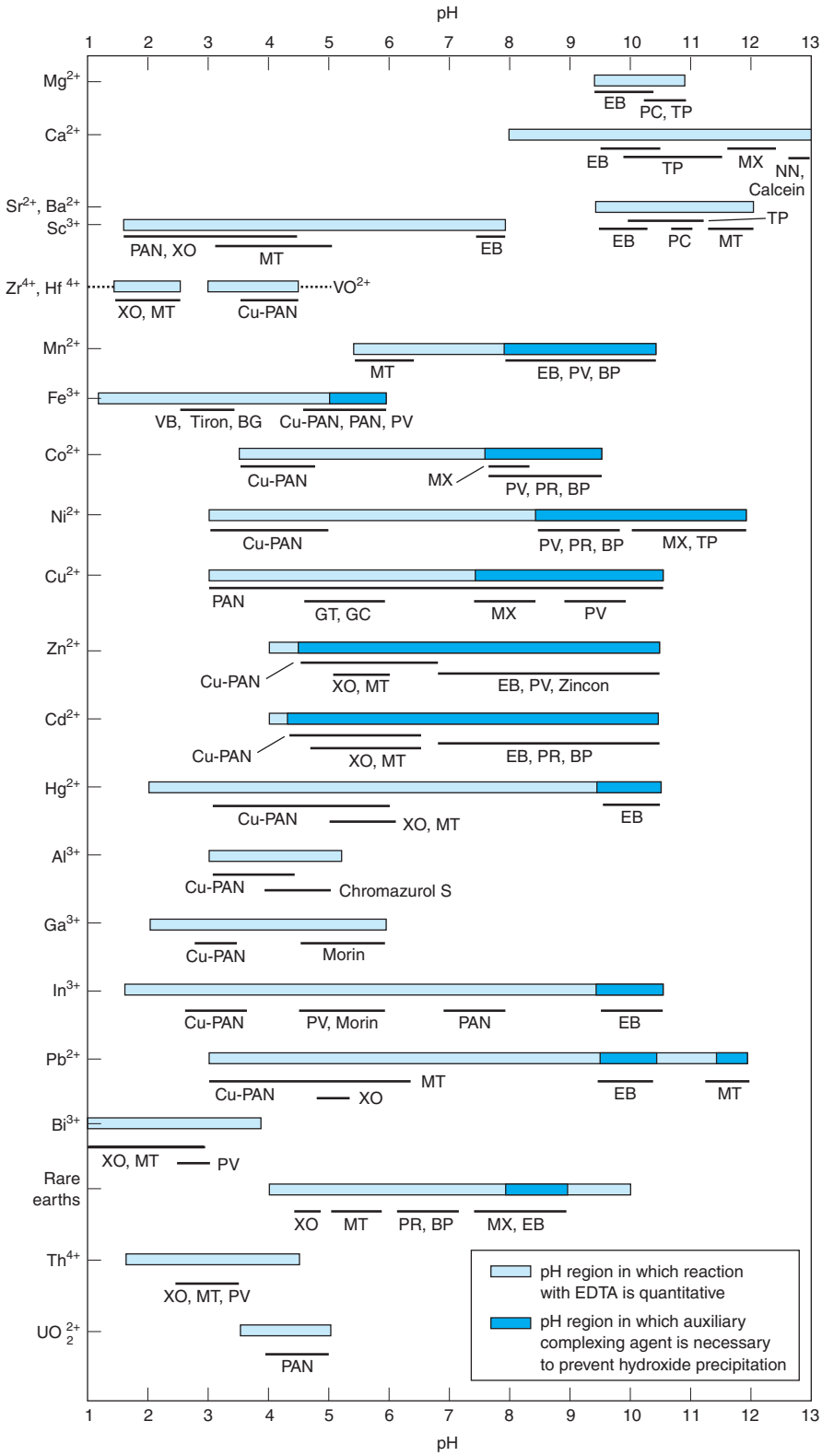
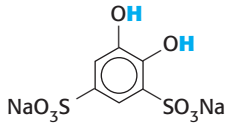


FIGURE 11-15 Guide to EDTA titrations of common metals. Light color shows pH region in which reaction with EDTA is quantitative. Dark color shows pH region in which auxiliary complexing agent is required to prevent metal from precipitating. Calmagite is more stable than Eriochrome black T (EB) and can be substituted for EB. [Adapted from K. Ueno, "Guide for Selecting Conditions of EDTA Titrations," *J. Chem. Ed.* **1965**, *42*, 432.]

Abbreviations for indicators:

BG, Bindschedler's green leuco base
BP, Bromopyrogallol red
EB, Eriochrome black T
GC, Glycinecresol red
GT, Glycinethymol blue
MT, Methylthymol blue
MX, Murexide
NN, Patton & Reeder's dye
PAN, Pyridylazonaphthol
Cu-PAN, PAN plus Cu-EDTA
PC, *o*-Cresolphthalein complexone
PR, Pyrogallol red
PV, Pyrocatechol violet
TP, Thymolphthalein complexone
VB, Variamine blue B base
XO, Xylenol orange



"Tiron"
1,2-dihydroxybenzene-3,5-disulfonic acid, disodium salt

$pK_4(OH) = 12.5$
$pK_3(OH) = 7.6$

Tiron is an indicator for EDTA titration of Fe(III) at pH 2–3 at 40°C. Color change is from blue to pale yellow.

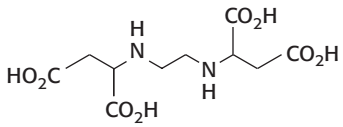
11-7 EDTA Titration Techniques

Because so many elements can be analyzed with EDTA, there is extensive literature dealing with many variations of the basic procedure.[16,21]

Direct Titration

In a **direct titration,** analyte is titrated with standard EDTA. Analyte is buffered to a pH at which the conditional formation constant for the metal-EDTA complex is large and the color of the free indicator is distinctly different from that of the metal-indicator complex.

Phytoremediation.[19,20] An approach to removing toxic metals from contaminated soil is to grow plants that accumulate 1–15 g metal/g dry mass of plant. The plant is harvested to recover metals such as Pb, Cd, and Ni. Phytoremediation is enhanced by adding EDTA to mobilize insoluble metals. Unfortunately, rain spreads soluble metal-EDTA complexes through the soil, so phytoremediation is limited to locations where the connection with groundwater is blocked or where leaching is not important. The natural chelate, EDDS mobilizes metal and biodegrades before it can spread very far.



S,S-Ethylenediaminedisuccinic acid (EDDS)

Auxiliary complexing agents such as NH_3, tartrate, citrate, or triethanolamine may be employed to prevent metal ion from precipitating in the absence of EDTA. For example, Pb^{2+} is titrated in NH_3 buffer at pH 10 in the presence of tartrate, which complexes Pb^{2+} and does not allow $Pb(OH)_2$ to precipitate. The lead-tartrate complex must be less stable than the lead-EDTA complex, or the titration would not be feasible.

Back Titration

In a **back titration,** a known excess of EDTA is added to the analyte. Excess EDTA is then titrated with a standard solution of a second metal ion. A back titration is necessary if analyte precipitates in the absence of EDTA, if it reacts too slowly with EDTA, or if it blocks the indicator. The metal ion for the back titration must not displace analyte from EDTA.

EXAMPLE A Back Titration

Ni^{2+} can be analyzed by a back titration using standard Zn^{2+} at pH 5.5 with xylenol orange indicator. A solution containing 25.00 mL of Ni^{2+} in dilute HCl is treated with 25.00 mL of 0.052 83 M Na_2EDTA. The solution is neutralized with NaOH, and the pH is adjusted to 5.5 with acetate buffer. The solution turns yellow when a few drops of indicator are added. Titration with 0.022 99 M Zn^{2+} requires 17.61 mL to reach the red end point. What is the molarity of Ni^{2+} in the unknown?

Solution The unknown was treated with 25.00 mL of 0.052 83 M EDTA, which contains (25.00 mL)(0.052 83 M) = 1.320 8 mmol of EDTA. Back titration required (17.61 mL) × (0.022 99 M) = 0.404 9 mmol of Zn^{2+}. Because 1 mol of EDTA reacts with 1 mol of any metal ion, there must have been

$$1.320\ 8 \text{ mmol EDTA} - 0.404\ 9 \text{ mmol } Zn^{2+} = 0.915\ 9 \text{ mmol } Ni^{2+}$$

The concentration of Ni^{2+} is 0.915 9 mmol/25.00 mL = 0.036 64 M.

Test Yourself If back titration required 13.00 mL Zn^{2+}, what was the original concentration of Ni^{2+}? (***Answer:*** 0.040 88 M)

Back titration prevents precipitation of analyte. For example, $Al(OH)_3$ precipitates at pH 7 in the absence of EDTA. An acidic solution of Al^{3+} can be treated with excess EDTA, adjusted to pH 7–8 with sodium acetate, and boiled to ensure complete formation of stable, soluble $Al(EDTA)^-$. The solution is then cooled; Calmagite indicator is added; and back titration with standard Zn^{2+} is performed.

Displacement Titration

Hg^{2+} does not have a satisfactory indicator, but a **displacement titration** is feasible. Hg^{2+} is treated with excess $Mg(EDTA)^{2-}$ to displace Mg^{2+}, which is titrated with standard EDTA.

$$M^{n+} + MgY^{2-} \rightarrow MY^{n-4} + Mg^{2+} \qquad \textbf{(11-20)}$$

The conditional formation constant for $Hg(EDTA)^{2-}$ must be greater than K_f' for $Mg(EDTA)^{2-}$, or else Mg^{2+} will not be displaced from $Mg(EDTA)^{2-}$.

There is no suitable indicator for Ag^+. However, Ag^+ will displace Ni^{2+} from tetracyanonickelate(II) ion:

$$2Ag^+ + Ni(CN)_4^{2-} \rightarrow 2Ag(CN)_2^- + Ni^{2+}$$

The liberated Ni^{2+} can then be titrated with EDTA to find out how much Ag^+ was added.

Indirect Titration

Anions that precipitate with certain metal ions can be analyzed with EDTA by **indirect titration.** For example, sulfate can be analyzed by precipitation with excess Ba^{2+} at pH 1. The $BaSO_4(s)$ is washed and then boiled with excess EDTA at pH 10 to bring Ba^{2+} back into solution as $Ba(EDTA)^{2-}$. Excess EDTA is back-titrated with Mg^{2+}.

BOX 11-3 Water Hardness

Hardness is the total concentration of alkaline earth (Group 2) ions, which are mainly Ca^{2+} and Mg^{2+}, in water. Hardness is commonly expressed as the equivalent number of milligrams of $CaCO_3$ per liter. Thus, if $[Ca^{2+}] + [Mg^{2+}] = 1$ mM, we would say that the hardness is 100 mg $CaCO_3$ per liter because 100 mg $CaCO_3$ = 1 mmol $CaCO_3$. Water of hardness less than 60 mg $CaCO_3$ per liter is considered to be "soft." If the hardness is above 270 mg/L, the water is considered to be "hard."

Hard water reacts with soap to form insoluble curds:

$$\underset{\text{Soap}}{Ca^{2+} + 2RCO_2^-} \rightarrow \underset{\text{Precipitate}}{Ca(RCO_2)_2(s)} \qquad \textbf{(A)}$$

R is a long-chain hydrocarbon such as $C_{17}H_{35}$—

Enough soap to consume Ca^{2+} and Mg^{2+} must be used before soap is available for cleaning. Hard water leaves solid deposits called *scale* on pipes when it evaporates, but hard water is not known to be unhealthy. Hardness is beneficial in irrigation water because alkaline earth ions tend to *flocculate* (cause to aggregate) colloidal particles in soil and thereby increase the permeability of the soil to water. Soft water etches concrete, plaster, and grout.

To measure hardness, the sample is treated with ascorbic acid (or hydroxylamine) to reduce Fe^{3+} to Fe^{2+} and Cu^{2+} to Cu^+ and then with cyanide to mask Fe^{2+}, Cu^+, and several other minor metal ions. Titration with EDTA at pH 10 in NH_3 buffer then gives the total concentrations of Ca^{2+} and Mg^{2+}. Ca^{2+} can be determined separately if the titration is carried out at pH 13 without ammonia. At this pH, $Mg(OH)_2$ precipitates and is inaccessible to EDTA. Interference by many metal ions can be reduced by the right choice of indicators.[23]

Insoluble carbonates are converted into soluble bicarbonates by excess carbon dioxide:

$$CaCO_3(s) + CO_2 + H_2O \rightarrow Ca(HCO_3)_2(aq) \qquad \textbf{(B)}$$

Heat converts bicarbonate into carbonate (driving off CO_2) and precipitates $CaCO_3$ scale that clogs boiler pipes. The fraction of hardness due to $Ca(HCO_3)_2(aq)$ is called *temporary hardness* because this calcium is lost (by precipitation of $CaCO_3$) upon heating. Hardness arising from other salts (mainly dissolved $CaSO_4$) is called *permanent hardness* because it is not removed by heating.

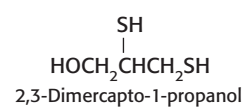
Alternatively, an anion can be precipitated with excess standard metal ion. The precipitate is filtered and washed, and excess metal in the filtrate is titrated with EDTA. Anions such as CO_3^{2-}, CrO_4^{2-}, S^{2-}, and SO_4^{2-} can be determined by indirect titration with EDTA.[22]

Masking

A **masking agent** is a reagent that protects some component of the analyte from reaction with EDTA. For example, Al^{3+} in a mixture of Mg^{2+} and Al^{3+} can be measured by first masking the Al^{3+} with F^-, thereby leaving only the Mg^{2+} to react with EDTA.

Masking prevents one species from interfering in the analysis of another. Masking is not restricted to EDTA titrations. Box 11-3 gives an important application of masking.

Cyanide masks Cd^{2+}, Zn^{2+}, Hg^{2+}, Co^{2+}, Cu^+, Ag^+, Ni^{2+}, Pd^{2+}, Pt^{2+}, Fe^{2+}, and Fe^{3+}, but not Mg^{2+}, Ca^{2+}, Mn^{2+}, or Pb^{2+}. When cyanide is added to a solution containing Cd^{2+} and Pb^{2+}, only Pb^{2+} reacts with EDTA. (*Caution:* Cyanide forms toxic gaseous HCN below pH 11. Cyanide solutions should be strongly basic and only handled in a hood.) Fluoride masks Al^{3+}, Fe^{3+}, Ti^{4+}, and Be^{2+}. (*Caution:* HF formed by F^- in acidic solution is extremely hazardous and should not contact skin and eyes. It may not be immediately painful, but the affected area should be flooded with water and then treated with calcium gluconate gel that you have on hand *before* the accident. First aid providers must wear rubber gloves to protect themselves.) Triethanolamine masks Al^{3+}, Fe^{3+}, and Mn^{2+}; 2,3-dimercapto-1-propanol masks Bi^{3+}, Cd^{2+}, Cu^{2+}, Hg^{2+}, and Pb^{2+}.



2,3-Dimercapto-1-propanol

Demasking releases metal ion from a masking agent. Cyanide complexes can be demasked with formaldehyde:

$$M(CN)_m^{n-m} + \underset{\text{Formaldehyde}}{mH_2CO} + mH^+ \rightarrow mH_2C\begin{matrix}OH\\ \diagup \\ \diagdown \\ CN\end{matrix} + M^{n+}$$

Thiourea masks Cu^{2+} by reducing it to Cu^+ and complexing the Cu^+. Copper can be liberated from thiourea by oxidation with H_2O_2. Selectivity afforded by masking, demasking, and pH control allows individual components of complex mixtures of metal ions to be analyzed by EDTA titration.

Terms to Understand

auxiliary complexing agent
back titration
blocking
chelate effect
chelating ligand
complexometric titration
conditional formation constant
cumulative formation constant
demasking
direct titration
displacement titration
formation constant
indirect titration
Lewis acid
Lewis base
masking agent
metal ion indicator
monodentate
multidentate
stability constant

Summary

In a complexometric titration, analyte and titrant form a complex ion, and the equilibrium constant is called the formation constant, K_f. Chelating (multidentate) ligands form more stable complexes than do monodentate ligands. Synthetic aminocarboxylic acids such as EDTA have large metal-binding constants.

Formation constants for EDTA are expressed in terms of $[Y^{4-}]$, even though there are six protonated forms of EDTA. Because the fraction ($\alpha_{Y^{4-}}$) of free EDTA in the form Y^{4-} depends on pH, we define a conditional (or effective) formation constant as $K_f' = \alpha_{Y^{4-}} K_f = [MY^{n-4}]/[M^{n+}][EDTA]$. This constant describes the hypothetical reaction $M^{n+} + EDTA \rightleftharpoons MY^{n-4}$, where EDTA refers to all forms of EDTA not bound to metal ion. Titration calculations fall into three categories. When excess unreacted M^{n+} is present, pM is calculated directly from $pM = -\log[M^{n+}]$. When excess EDTA is present, we know both $[MY^{n-4}]$ and [EDTA], so $[M^{n+}]$ can be calculated from the conditional formation constant. At the equivalence point, the condition $[M^{n+}] = [EDTA]$ allows us to solve for $[M^{n+}]$. A single spreadsheet equation applies in all three regions of the titration curve.

The greater the effective formation constant, the sharper is the EDTA titration curve. Addition of auxiliary complexing agents, which compete with EDTA for the metal ion and thereby limit the sharpness of the titration curve, is often necessary to keep the metal in solution. Calculations for a solution containing EDTA and an auxiliary complexing agent utilize the conditional formation constant $K_f'' = \alpha_M \alpha_{Y^{4-}} K_f$, where α_M is the fraction of free metal ion not complexed by the auxiliary ligand.

For end-point detection, we commonly use metal ion indicators, a glass electrode, an ion-selective electrode, or a mercury electrode. When a direct titration is not suitable, because the analyte is unstable, reacts slowly with EDTA, or has no suitable indicator, a back titration of excess EDTA or a displacement titration of $Mg(EDTA)^{2-}$ may be feasible. Masking prevents interference by unwanted species. Indirect EDTA titrations are available for many anions and other species that do not react directly with the reagent.

Exercises

11-A. Potassium ion in a 250.0 (±0.1) mL water sample was precipitated with sodium tetraphenylborate:

$$K^+ + (C_6H_5)_4B^- \rightarrow KB(C_6H_5)_4(s)$$

The precipitate was filtered, washed, dissolved in an organic solvent, and treated with excess $Hg(EDTA)^{2-}$:

$$4HgY^{2-} + (C_6H_5)_4B^- + 4H_2O \rightarrow H_3BO_3 + 4C_6H_5Hg^+ + 4HY^{3-} + OH^-$$

The liberated EDTA was titrated with 28.73 (±0.03) mL of 0.043 7 (±0.000 1) M Zn^{2+}. Find $[K^+]$ (and its absolute uncertainty) in the original sample.

11-B. A 25.00-mL sample containing Fe^{3+} and Cu^{2+} required 16.06 mL of 0.050 83 M EDTA for complete titration. A 50.00-mL sample of the unknown was treated with NH_4F to protect the Fe^{3+}. Then Cu^{2+} was reduced and masked by thiourea. Addition of 25.00 mL of 0.050 83 M EDTA liberated Fe^{3+} from its fluoride complex to form an EDTA complex. The excess EDTA required 19.77 mL of 0.018 83 M Pb^{2+} to reach a xylenol orange end point. Find $[Cu^{2+}]$ in the unknown.

11-C. Calculate pCu^{2+} (to the 0.01 decimal place) at each of the following points in the titration of 50.0 mL of 0.040 0 M EDTA with 0.080 0 M $Cu(NO_3)_2$ at pH 5.00: 0.1, 5.0, 10.0, 15.0, 20.0, 24.0, 25.0, 26.0, and 30.0 mL. Make a graph of pCu^{2+} versus volume of titrant.

11-D. Calculate the concentration of H_2Y^{2-} at the equivalence point in Exercise 11-C.

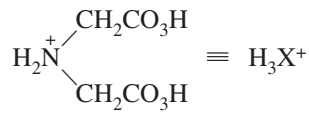
11-E. Suppose that 0.010 0 M Mn^{2+} is titrated with 0.005 00 M EDTA at pH 7.00.

(a) What is the concentration of free Mn^{2+} at the equivalence point?

(b) What is the quotient $[H_3Y^-]/[H_2Y^{2-}]$ in the solution when the titration is just 63.7% of the way to the equivalence point?

11-F. A solution containing 20.0 mL of 1.00×10^{-3} M Co^{2+} in the presence of 0.10 M $C_2O_4^{2-}$ at pH 9.00 was titrated with 1.00×10^{-2} M EDTA. Using formation constants from Appendix I for $Co(C_2O_4)$ and $Co(C_2O_4)_2^{2-}$, calculate pCo^{2+} for the following volumes of added EDTA: 0, 1.00, 2.00, and 3.00 mL. Consider the concentration of $C_2O_4^{2-}$ to be fixed at 0.10 M. Sketch a graph of pCo^{2+} versus milliliters of added EDTA.

11-G. Iminodiacetic acid forms 2:1 complexes with many metal ions:



$$\equiv H_3X^+$$

$$\alpha_{X^{2-}} = \frac{[X^{2-}]}{[H_3X^+] + [H_2X] + [HX^-] + [X^{2-}]}$$

$$Cu^{2+} + 2X^{2-} \rightleftharpoons CuX_2^{2-} \qquad K = \beta_2 = 3.5 \times 10^{16}$$

A 25.0 mL solution containing 0.120 M iminodiacetic acid buffered to pH 7.00 was titrated with 25.0 mL of 0.050 0 M Cu^{2+}. Given that $\alpha_{X^{2-}} = 4.6 \times 10^{-3}$ at pH 7.00, calculate $[Cu^{2+}]$ in the resulting solution.

Problems

EDTA

11-1. What is the chelate effect?

11-2. State (in words) what $\alpha_{Y^{4-}}$ means. Calculate $\alpha_{Y^{4-}}$ for EDTA at **(a)** pH 3.50 and **(b)** pH 10.50.

11-3. **(a)** Find the conditional formation constant for $Mg(EDTA)^{2-}$ at pH 9.00.

(b) Find the concentration of free Mg^{2+} in 0.050 M $Na_2[Mg(EDTA)]$ at pH 9.00.

11-4. *Metal ion buffers.* By analogy to a hydrogen ion buffer, a metal ion buffer tends to maintain a particular metal ion concentration in solution. A mixture of the acid HA and its conjugate base A^- maintains $[H^+]$ defined by the equation $K_a = [A^-][H^+]/[HA]$. A mixture of CaY^{2-} and Y^{4-} serves as a Ca^{2+} buffer governed by the equation $1/K_f' = [EDTA][Ca^{2+}]/[CaY^{2-}]$. How many grams of $Na_2EDTA \cdot 2H_2O$ (FM 372.23) should be mixed with 1.95 g of $Ca(NO_3)_2 \cdot 2H_2O$ (FM 200.12) in a 500-mL volumetric flask to give a buffer with $pCa^{2+} = 9.00$ at pH 9.00?

11-5. *Purification by reprecipitation and predominant species of polyprotic acids.* To measure oxygen isotopes in SO_4^{2-} for geologic studies, SO_4^{2-} was precipitated with excess Ba^{2+}.[24] In the presence of HNO_3, $BaSO_4$ precipitate is contaminated by NO_3^-. The solid can be purified by washing, redissolving in the absence of HNO_3, and reprecipitating. For purification, 30 mg of $BaSO_4$ were dissolved in 15 mL of 0.05 M DTPA (Figure 11-4) in 1 M NaOH with vigorous shaking at 70°C. $BaSO_4$ was reprecipitated by adding 10 M HCl dropwise to obtain pH 3–4 and allowing the mixture to stand for 1 h. The solid was washed twice by centrifuging, removing the liquid, and resuspending in deionized water. The molar ratio NO_3^-/SO_4^{2-} was reduced from 0.25 in the original precipitate to 0.001 after two cycles of dissolution and reprecipitation. What are the predominant species of sulfate and DTPA at pH 14 and pH 3? Explain why $BaSO_4$ dissolves in DTPA in 1 M NaOH and then reprecipitates when the pH is lowered to 3–4.

EDTA Titration Curves

11-6. A 100.0 mL solution of 0.050 0 M M^{n+} buffered to pH 9.00 was titrated with 0.050 0 M EDTA.

(a) What is the equivalence volume, V_e, in milliliters?

(b) Calculate the concentration of M^{n+} at $V = \frac{1}{2}V_e$.

(c) What fraction ($\alpha_{Y^{4-}}$) of free EDTA is in the form Y^{4-} at pH 9.00?

(d) The formation constant (K_f) is $10^{12.00}$. Calculate the value of the conditional formation constant K_f' ($= \alpha_{Y^{4-}}K_f$)

(e) Calculate the concentration of M^{n+} at $V = V_e$.

(f) What is the concentration of M^{n+} at $V = 1.100\ V_e$?

11-7. Calculate pCo^{2+} at each of the following points in the titration of 25.00 mL of 0.020 26 M Co^{2+} by 0.038 55 M EDTA at pH 6.00: **(a)** 12.00 mL; **(b)** V_e; **(c)** 14.00 mL.

11-8. Consider the titration of 25.0 mL of 0.020 0 M $MnSO_4$ with 0.010 0 M EDTA in a solution buffered to pH 8.00. Calculate pMn^{2+} at the following volumes of added EDTA and sketch the titration curve:

(a) 0 mL **(d)** 49.0 mL **(g)** 50.1 mL
(b) 20.0 mL **(e)** 49.9 mL **(h)** 55.0 mL
(c) 40.0 mL **(f)** 50.0 mL **(i)** 60.0 mL

11-9. For the same volumes used in Problem 11-8, calculate pCa^{2+} for the titration of 25.00 mL of 0.020 00 M EDTA with 0.010 00 M $CaSO_4$ at pH 10.00.

11-10. Calculate $[HY^{3-}]$ in a solution prepared by mixing 10.00 mL of 0.010 0 M $VOSO_4$, 9.90 mL of 0.010 0 M EDTA, and 10.0 mL of buffer with a pH of 4.00.

11-11. *Titration of metal ion with EDTA.* Use Equation 11-11 to compute curves (pM versus mL of EDTA added) for the titration of 10.00 mL of 1.00 mM M^{2+} (= Cd^{2+} or Cu^{2+}) with 10.0 mM EDTA at pH 5.00. Plot both curves on one graph.

11-12. *Effect of pH on the EDTA titration.* Use Equation 11-11 to compute curves (pCa^{2+} versus mL of EDTA added) for the titration of 10.00 mL of 1.00 mM Ca^{2+} with 1.00 mM EDTA at pH 5.00, 6.00, 7.00, 8.00, and 9.00. Plot all curves on one graph and compare your results with Figure 11-10.

11-13. *Titration of EDTA with metal ion.* Use Equation 11-12 to reproduce the results of Exercise 11-C.

Auxiliary Complexing Agents

11-14. State the purpose of an auxiliary complexing agent and give an example of its use.

11-15. According to Appendix I, Cu^{2+} forms two complexes with acetate:

$$Cu^{2+} + CH_3CO_2^- \rightleftharpoons Cu(CH_3CO_2)^+ \qquad \beta_1(=K_1)$$
$$Cu^{2+} + 2CH_3CO_2^- \rightleftharpoons Cu(CH_3CO_2)_2(aq) \qquad \beta_2$$

(a) Referring to Box 6-2, find K_2 for the reaction

$$Cu(CH_3CO_2)^+ + CH_3CO_2^- \rightleftharpoons Cu(CH_3CO_2)_2(aq) \qquad K_2$$

(b) Consider 1.00 L of solution prepared by mixing 1.00×10^{-4} mol $Cu(ClO_4)_2$ and 0.100 mol CH_3CO_2Na. Use Equation 11-16 to find the fraction of copper in the form Cu^{2+}.

11-16. Calculate pCu^{2+} at each of the following points in the titration of 50.00 mL of 0.001 00 M Cu^{2+} with 0.001 00 M EDTA at pH 11.00 in a solution with $[NH_3]$ *fixed* at 1.00 M:

(a) 0 mL **(c)** 45.00 mL **(e)** 55.00 mL
(b) 1.00 mL **(d)** 50.00 mL

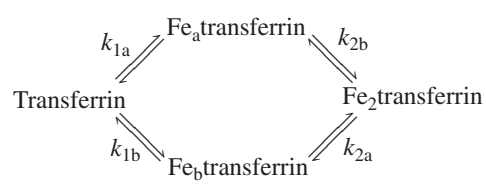
11-17. Consider the derivation of the fraction α_M in Equation 11-16.

(a) Derive the following expressions for the fractions α_{ML} and α_{ML_2}:

$$\alpha_{ML} = \frac{\beta_1[L]}{1 + \beta_1[L] + \beta_2[L]^2} \qquad \alpha_{ML_2} = \frac{\beta_2[L]^2}{1 + \beta_1[L] + \beta_2[L]^2}$$

(b) Calculate the values of α_{ML} and α_{ML_2} for the conditions in Problem 11-15.

11-18. *Microequilibrium constants for binding of metal to a protein.* The iron-transport protein, transferrin, has two distinguishable metal-binding sites, designated a and b. The *microequilibrium* formation constants for each site are defined as follows:



For example, the formation constant k_{1a} refers to the reaction Fe^{3+} + transferrin $\rightleftharpoons$ Fe_atransferrin, in which the metal ion binds to site a:

$$k_{1a} = \frac{[Fe_a\text{transferrin}]}{[Fe^{3+}][\text{transferrin}]}$$

(a) Write the chemical reactions corresponding to the conventional macroscopic formation constants, K_1 and K_2.

(b) Show that $K_1 = k_{1a} + k_{1b}$ and $K_2^{-1} = k_{2a}^{-1} + k_{2b}^{-1}$.

(c) Show that $k_{1a}k_{2b} = k_{1b}k_{2a}$. This expression means that, if you know any three of the microequilibrium constants, you automatically know the fourth one.

(d) *A challenge to your sanity*. From the equilibrium constants below, *find the equilibrium fraction of each of the four species in the diagram above in circulating blood that is 40% saturated with iron* (that is, Fe/transferrin = 0.80, because each protein can bind 2 Fe).

Effective formation constants for blood plasma at pH 7.4

$k_{1a} = 6.0 \times 10^{22}$	$k_{2a} = 2.4 \times 10^{22}$
$k_{1b} = 1.0 \times 10^{22}$	$k_{2b} = 4.2 \times 10^{21}$
$K_1 = 7.0 \times 10^{22}$	$K_2 = 3.6 \times 10^{21}$

The binding constants are so large that you may assume that there is negligible free Fe^{3+}. To get started, let's use the abbreviations [T] = [transferrin], [FeT] = [Fe_aT] + [Fe_bT], and [Fe_2T] = [Fe_2transferrin]. Now we can write

Mass balance for protein: $[T] + [FeT] + [Fe_2T] = 1$ **(A)**

Mass balance for iron:

$$\frac{[FeT] + 2[Fe_2T]}{[T] + [FeT] + [Fe_2T]} = [FeT] + 2[Fe_2T] = 0.8 \quad \textbf{(B)}$$

Combined equilibria: $$\frac{K_1}{K_2} = 19_{.44} = \frac{[FeT]^2}{[T][Fe_2T]} \quad \textbf{(C)}$$

Now you have three equations with three unknowns and should be able to tackle this problem.

11-19. *Spreadsheet equation for auxiliary complexing agent.* Consider the titration of metal M (initial concentration = C_M, initial volume = V_M) with EDTA (concentration = C_{EDTA}, volume added = V_{EDTA}) in the presence of an auxiliary complexing ligand (such as ammonia). Follow the derivation in Section 11-4 to show that the master equation for the titration is

$$\phi = \frac{C_{EDTA}V_{EDTA}}{C_M V_M} = \frac{1 + K_f''[M]_{free} - \dfrac{[M]_{free} + K_f''[M]_{free}^2}{C_M}}{K_f''[M]_{free} + \dfrac{[M]_{free} + K_f''[M]_{free}^2}{C_{EDTA}}}$$

where K_f'' is the conditional formation constant in the presence of auxiliary complexing agent at the fixed pH of the titration (Equation 11-18) and $[M]_{free}$ is the total concentration of metal not bound to EDTA. $[M]_{free}$ is the same as M_{tot} in Equation 11-15. The result is equivalent to Equation 11-11, with [M] replaced by $[M]_{free}$ and K_f replaced by K_f''.

11-20. *Auxiliary complexing agent.* Use the equation derived in Problem 11-19.

(a) Prepare a spreadsheet to reproduce the 20-, 50-, and 60-mL points in the EDTA titration of Zn^{2+} in the presence of NH_3 in the example on pages 248–249.

(b) Use your spreadsheet to plot the curve for the titration of 50.00 mL of 5.00 mM Ni^{2+} by 10.00 mM EDTA at pH 11.00 in the presence of a fixed oxalate concentration of 0.100 M.

11-21. *Spreadsheet equation for formation of the complexes ML and ML_2.* Consider the titration of metal M (initial concentration = C_M, initial volume = V_M) with ligand L (concentration = C_L, volume added = V_L), which can form 1:1 and 2:1 complexes:

$$M + L \rightleftharpoons ML \qquad \beta_1 = \frac{[ML]}{[M][L]}$$

$$M + 2L \rightleftharpoons ML_2 \qquad \beta_2 = \frac{[ML_2]}{[M][L]^2}$$

Let α_M be the fraction of metal in the form M, α_{ML} be the fraction in the form ML, and α_{ML_2} be the fraction in the form ML_2. Following the derivation in Section 11-5, you could show that these fractions are given by

$$\alpha_M = \frac{1}{1 + \beta_1[L] + \beta_2[L]^2} \qquad \alpha_{ML} = \frac{\beta_1[L]}{1 + \beta_1[L] + \beta_2[L]^2}$$

$$\alpha_{ML_2} = \frac{\beta_2[L]^2}{1 + \beta_1[L] + \beta_2[L]^2}$$

The concentrations of ML and ML_2 are

$$[ML] = \alpha_{ML}\frac{C_M V_M}{V_M + V_L} \qquad [ML_2] = \alpha_{ML_2}\frac{C_M V_M}{V_M + V_L}$$

because $C_M V_M/(V_M + V_L)$ is the total concentration of all metal in the solution. The mass balance for ligand is

$$[L] + [ML] + 2[ML_2] = \frac{C_L V_L}{V_M + V_L}$$

By substituting expressions for [ML] and $[ML_2]$ into the mass balance, show that the master equation for a titration of metal by ligand is

$$\phi = \frac{C_L V_L}{C_M V_M} = \frac{\alpha_{ML} + 2\alpha_{ML_2} + ([L]/C_M)}{1 - ([L]/C_L)}$$

11-22. *Titration of M with L to form ML and ML_2.* Use the equation from Problem 11-21, where M is Cu^{2+} and L is acetate. Consider adding 0.500 M acetate to 10.00 mL of 0.050 0 M Cu^{2+} at pH 7.00 (so that all ligand is present as $CH_3CO_2^-$, not CH_3CO_2H). Formation constants for $Cu(CH_3CO_2)^+$ and $Cu(CH_3CO_2)_2$ are given in Appendix I. Construct a spreadsheet in which the input is pL and the output is **(a)** [L]; **(b)** V_L; **(c)** [M]; **(d)** [ML]; **(e)** $[ML_2]$. Prepare a graph showing concentrations of L, M, ML, and ML_2 as V_L ranges from 0 to 3 mL.

Metal Ion Indicators

11-23. Explain why the change from red to blue in Reaction 11-19 occurs suddenly at the equivalence point instead of gradually throughout the entire titration.

11-24. List four methods for detecting the end point of an EDTA titration.

11-25. Calcium ion was titrated with EDTA at pH 11, using Calmagite as indicator (Table 11-3). Which is the principal species of Calmagite at pH 11? What color was observed before the equivalence point? After the equivalence point?

11-26. Pyrocatechol violet (Table 11-3) is to be used as a metal ion indicator in an EDTA titration. The procedure is as follows:

1. Add a known excess of EDTA to the unknown metal ion.
2. Adjust the pH with a suitable buffer.
3. Back-titrate the excess chelate with standard Al^{3+}.

From the following available buffers, select the best buffer, and then state what color change will be observed at the end point. Explain your answer.

(a) pH 6–7 **(b)** pH 7–8 **(c)** pH 8–9 **(d)** pH 9–10

EDTA Titration Techniques

11-27. Give three circumstances in which an EDTA back titration might be necessary.

11-28. Describe what is done in a displacement titration and give an example.

11-29. Give an example of the use of a masking agent.

11-30. What is meant by water hardness? Explain the difference between temporary and permanent hardness.

11-31. How many milliliters of 0.050 0 M EDTA are required to react with 50.0 mL of 0.010 0 M Ca^{2+}? With 50.0 mL of 0.010 0 M Al^{3+}?

11-32. A 50.0-mL sample containing Ni^{2+} was treated with 25.0 mL of 0.050 0 M EDTA to complex all the Ni^{2+} and leave excess EDTA in solution. The excess EDTA was then back-titrated, requiring 5.00 mL of 0.050 0 M Zn^{2+}. What was the concentration of Ni^{2+} in the original solution?

11-33. A 50.0-mL aliquot of solution containing 0.450 g of $MgSO_4$ (FM 120.37) in 0.500 L required 37.6 mL of EDTA solution for titration. How many milligrams of $CaCO_3$ (FM 100.09) will react with 1.00 mL of this EDTA solution?

11-34. Cyanide solution (12.73 mL) was treated with 25.00 mL of Ni^{2+} solution (containing excess Ni^{2+}) to convert the cyanide into tetracyanonickelate(II):

$$4CN^- + Ni^{2+} \rightarrow Ni(CN)_4^{2-}$$

Excess Ni^{2+} was then titrated with 10.15 mL of 0.013 07 M EDTA. $Ni(CN)_4^{2-}$ does not react with EDTA. If 39.35 mL of EDTA were required to react with 30.10 mL of the original Ni^{2+} solution, calculate the molarity of CN^- in the 12.73-mL sample.

11-35. A 1.000-mL sample of unknown containing Co^{2+} and Ni^{2+} was treated with 25.00 mL of 0.038 72 M EDTA. Back titration with 0.021 27 M Zn^{2+} at pH 5 required 23.54 mL to reach the xylenol orange end point. A 2.000-mL sample of unknown was passed through an ion-exchange column that retards Co^{2+} more than Ni^{2+}. The Ni^{2+} that passed through the column was treated with 25.00 mL of 0.038 72 M EDTA and required 25.63 mL of 0.021 27 M Zn^{2+} for back titration. The Co^{2+} emerged from the column later. It, too, was treated with 25.00 mL of 0.038 72 M EDTA. How many milliliters of 0.021 27 M Zn^{2+} will be required for back titration?

11-36. A 50.0-mL solution containing Ni^{2+} and Zn^{2+} was treated with 25.0 mL of 0.045 2 M EDTA to bind all the metal. The excess unreacted EDTA required 12.4 mL of 0.012 3 M Mg^{2+} for complete reaction. An excess of the reagent 2,3-dimercapto-1-propanol was then added to displace the EDTA from zinc. Another 29.2 mL of Mg^{2+} were required for reaction with the liberated EDTA. Calculate the molarity of Ni^{2+} and Zn^{2+} in the original solution.

11-37. Sulfide ion was determined by indirect titration with EDTA. To a solution containing 25.00 mL of 0.043 32 M $Cu(ClO_4)_2$ plus 15 mL of 1 M acetate buffer (pH 4.5) were added 25.00 mL of unknown sulfide solution with vigorous stirring. The CuS precipitate was filtered and washed with hot water. Then ammonia was added to the filtrate (which contained excess Cu^{2+}) until the blue color of $Cu(NH_3)_4^{2+}$ was observed. Titration of the filtrate with 0.039 27 M EDTA required 12.11 mL to reach the murexide end point. Calculate the molarity of sulfide in the unknown.

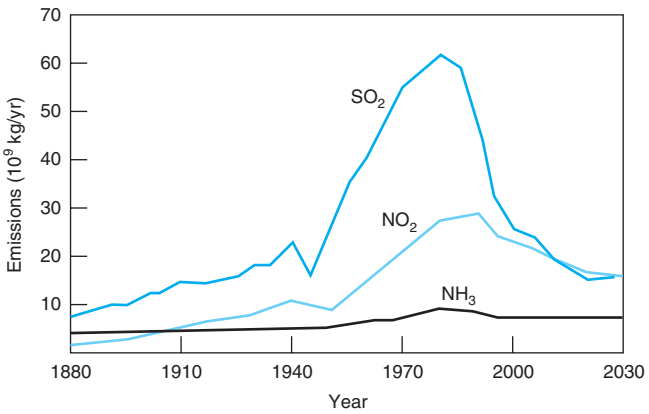
11-38. *Indirect EDTA determination of cesium.* Cesium ion does not form a strong EDTA complex, but it can be analyzed by adding a known excess of $NaBiI_4$ in cold concentrated acetic acid containing excess NaI. Solid $Cs_3Bi_2I_9$ is precipitated, filtered, and removed. The excess yellow BiI_4^- is then titrated with EDTA. The end point occurs when the yellow color disappears. (Sodium thiosulfate is used in the reaction to prevent the liberated I^- from being oxidized to yellow aqueous I_2 by O_2 from the air.) The precipitation is fairly selective for Cs^+. The ions Li^+, Na^+, K^+, and low concentrations of Rb^+ do not interfere, although Tl^+ does. Suppose that 25.00 mL of unknown containing Cs^+ were treated with 25.00 mL of 0.086 40 M $NaBiI_4$ and the unreacted BiI_4^- required 14.24 mL of 0.043 7 M EDTA for complete titration. Find the concentration of Cs^+ in the unknown.

11-39. The sulfur content of insoluble sulfides that do not readily dissolve in acid can be measured by oxidation with Br_2 to SO_4^{2-}.[25] Metal ions are then replaced with H^+ by an ion-exchange column, and sulfate is precipitated as $BaSO_4$ with a known excess of $BaCl_2$. The excess Ba^{2+} is then titrated with EDTA to determine how much was present. (To make the indicator end point clearer, a small, known quantity of Zn^{2+} also is added. The EDTA titrates both the Ba^{2+} and the Zn^{2+}.) Knowing the excess Ba^{2+}, we can calculate how much sulfur was in the original material. To analyze the mineral sphalerite (ZnS, FM 97.46), 5.89 mg of powdered solid were suspended in a mixture of CCl_4 and H_2O containing 1.5 mmol Br_2. After 1 h at 20°C and 2 h at 50°C, the powder dissolved and the solvent and excess Br_2 were removed by heating. The residue was dissolved in 3 mL of water and passed through an ion-exchange column to replace Zn^{2+} with H^+. Then 5.000 mL of 0.014 63 M $BaCl_2$ were added to precipitate all sulfate as $BaSO_4$. After the addition of 1.000 mL of 0.010 00 M $ZnCl_2$ and 3 mL of ammonia buffer, pH 10, the excess Ba^{2+} and Zn^{2+} required 2.39 mL of 0.009 63 M EDTA to reach the Calmagite end point. Find the weight percent of sulfur in the sphalerite. What is the theoretical value?

12 Advanced Topics in Equilibrium

ACID RAIN

St. Paul's Cathedral, London. [Pictor International/ Picture Quest.]



Estimated emissions over Europe. [From R. F. Wright, T. Larssen, L. Camarero, B. J. Crosby, R. C. Ferrier, R. Helliwell, M. Forsius, A. Jenkins, J. Kopáček, V. Majer, F. Moldan, M. Posch, M. Rogora, and W. Schöpp, "Recovery of Acidified European Surface Waters," *Environ. Sci. Technol.* **2005**, *39*, 64A.]

Limestone and marble are building materials whose main constituent is calcite, the common crystalline form of calcium carbonate. This mineral is not very soluble in neutral or basic solution ($K_{sp} = 4.5 \times 10^{-9}$), but it dissolves in acid by virtue of two **coupled equilibria,** in which the reactions have a species in common—carbonate, in this case:

$$\underset{\text{Calcite}}{CaCO_3(s)} \rightleftharpoons Ca^{2+} + \underset{\text{Carbonate}}{CO_3^{2-}}$$

$$CO_3^{2-} + H^+ \rightleftharpoons \underset{\text{Bicarbonate}}{HCO_3^-}$$

Carbonate produced in the first reaction is protonated to form bicarbonate in the second reaction. Le Châtelier's principle tells us that, if we remove a product of the first reaction, we will draw the reaction to the right, making calcite more soluble. This chapter deals with coupled equilibria in chemical systems.

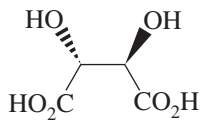
Between 1980 and 1990, half a millimeter of the thickness of the external stone walls of St. Paul's Cathedral in London was dissolved by acidic rainfall. A corner of the building facing a power station dissolved at 10 times the rate of the rest of the building until the station was closed. The power station and other industries that burn coal emit SO_2, which is a major source of acid rain (described in Box 14-1). Loss of heavy industry and laws limiting emissions decreased atmospheric SO_2 from as high as 100 ppb in the 1970s to 10 ppb in 2000. Only a quarter of a millimeter of St. Paul's external stone disappeared between 1990 and 2000.[1,2]

This optional chapter provides tools to compute the concentrations of species in systems with many simultaneous equilibria.[3] The most important tool is the systematic treatment of equilibrium from Chapter 7. The other tool is a spreadsheet for numerical solution of the equilibrium equations. We will also see how to incorporate activity coefficients into equilibrium calculations. Later chapters in this book do not depend on Chapter 12.

12-1 General Approach to Acid-Base Systems

We first illustrate a general approach to find the concentrations of species in mixtures of acids and bases. Consider a solution made by dissolving 20.0 mmol sodium tartrate (Na^+HT^-), 15.0 mmol pyridinium chloride (PyH^+Cl^-), and 10.0 mmol KOH in a volume of 1.00 L. The problem is to find the pH and concentrations of all species in the solution.

The approach to equilibrium problems in this chapter is adapted from Julian Roberts, University of Redlands.



D-Tartaric acid
H_2T
$pK_1 = 3.036$, $pK_2 = 4.366$

Pyridinium chloride
PyH^+Cl^-
$pK_a = 5.20$

For this example, we designate the two acid dissociation constants of H_2T as K_1 and K_2. We designate the acid dissociation constant of PyH^+ as K_a.

The chemical reactions and equilibrium constants at 0 ionic strength are

$$H_2T \rightleftharpoons HT^- + H^+ \qquad K_1 = 10^{-3.036} \tag{12-1}$$

$$HT^- \rightleftharpoons T^{2-} + H^+ \qquad K_2 = 10^{-4.366} \tag{12-2}$$

$$PyH^+ \rightleftharpoons Py + H^+ \qquad K_a = 10^{-5.20} \tag{12-3}$$

$$H_2O \rightleftharpoons H^+ + OH^- \qquad K_w = 10^{-14.00} \tag{12-4}$$

The charge balance is

$$[H^+] + [PyH^+] + [Na^+] + [K^+] = [OH^-] + [HT^-] + 2[T^{2-}] + [Cl^-] \tag{12-5}$$

There is a factor of 2 in front of $[T^{2-}]$ because the ion has a charge −2. 1 M T^{2-} contributes a charge of 2 M.

and there are several mass balances:

$$[Na^+] = 0.020\,0\ M \qquad [K^+] = 0.010\,0\ M \qquad [Cl^-] = 0.015\,0\ M$$

$$[H_2T] + [HT^-] + [T^{2-}] = 0.020\,0\ M \qquad [PyH^+] + [Py] = 0.015\,0\ M$$

There are 10 independent equations and 10 species, so we have enough information to solve for all the concentrations.

"Independent" equations cannot be derived from one another. As a trivial example, the equations $a = b + c$ and $2a = 2b + 2c$ are not independent. The three equilibrium expressions for K_a, K_b, and K_w for a weak acid and its conjugate base provide only two independent equations because we can derive K_b from K_a and K_w: $K_b = K_w/K_a$.

There is a systematic way to handle this problem without algebraic gymnastics.

Step 1 Write a *fractional composition equation* from Section 9-5 for each acid or base that appears in the charge balance.

Step 2 Substitute the fractional composition expressions into the charge balance and enter known values for $[Na^+]$, $[K^+]$, and $[Cl^-]$. Also, write $[OH^-] = K_w/[H^+]$. At this point, you will have a complicated equation in which the only variable is $[H^+]$.

Step 3 Use your trusty spreadsheet to solve for $[H^+]$.

Here is a recap of the fractional composition equations from Section 9-5 for *any* monoprotic acid HA and *any* diprotic acid H_2A.

Monoprotic system:

$$[HA] = \alpha_{HA}F_{HA} = \frac{[H^+]F_{HA}}{[H^+] + K_a} \tag{12-6a}$$

$F_{HA} = [HA] + [A^-]$

$$[A^-] = \alpha_{A^-}F_{HA} = \frac{K_aF_{HA}}{[H^+] + K_a} \tag{12-6b}$$

Diprotic system:

$$[H_2A] = \alpha_{H_2A}F_{H_2A} = \frac{[H^+]^2F_{H_2A}}{[H^+]^2 + [H^+]K_1 + K_1K_2} \tag{12-7a}$$

$F_{H_2A} = [H_2A] + [HA^-] + [A^{2-}]$

$$[HA^-] = \alpha_{HA^-}F_{H_2A} = \frac{K_1[H^+]F_{H_2A}}{[H^+]^2 + [H^+]K_1 + K_1K_2} \tag{12-7b}$$

$$[A^{2-}] = \alpha_{A^{2-}}F_{H_2A} = \frac{K_1K_2F_{H_2A}}{[H^+]^2 + [H^+]K_1 + K_1K_2} \tag{12-7c}$$

Table 10-5 gave fractional composition equations for H_3A.

In each equation, α_i is the fraction in each form. For example, $\alpha_{A^{2-}}$ is the fraction of diprotic acid in the form A^{2-}. When we multiply $\alpha_{A^{2-}}$ times F_{H_2A} (the total or formal concentration of H_2A), the product is the concentration of A^{2-}.

Applying the General Procedure

Now let's apply the general procedure to the mixture of 0.020 0 M sodium tartrate (Na^+HT^-), 0.015 0 M pyridinium chloride (PyH^+Cl^-), and 0.010 0 M KOH. We designate the formal concentrations as $F_{H_2T} = 0.020\,0$ M and $F_{PyH^+} = 0.015\,0$ M.

Step 1 Write a *fractional composition equation* for each acid or base that appears in the charge balance.

$$[PyH^+] = \alpha_{PyH^+}F_{PyH^+} = \frac{[H^+]F_{PyH^+}}{[H^+] + K_a} \tag{12-8}$$

$$[HT^-] = \alpha_{HT^-}F_{H_2T} = \frac{K_1[H^+]F_{H_2T}}{[H^+]^2 + [H^+]K_1 + K_1K_2} \tag{12-9}$$

$$[T^{2-}] = \alpha_{T^{2-}}F_{H_2T} = \frac{K_1K_2F_{H_2T}}{[H^+]^2 + [H^+]K_1 + K_1K_2} \tag{12-10}$$

All quantities on the right side of these expressions are known, except for $[H^+]$.

Step 2 Substitute the fractional composition expressions into the charge balance 12-5. Enter values for $[Na^+]$, $[K^+]$, and $[Cl^-]$, and write $[OH^-] = K_w/[H^+]$.

$$[H^+] + [PyH^+] + [Na^+] + [K^+] = [OH^-] + [HT^-] + 2[T^{2-}] + [Cl^-] \tag{12-5}$$

K_a, K_1, K_2, and $[H^+]$ are contained in the α expressions. The only variable in Equation 12-11 is $[H^+]$.

$$[H^+] + \alpha_{PyH^+}F_{PyH^+} + [0.020\,0] + [0.010\,0] = \frac{K_w}{[H^+]} + \alpha_{HT^-}F_{H_2T} + 2\alpha_{T^{2-}}F_{H_2T} + [0.015\,0] \tag{12-11}$$

Step 3 The spreadsheet in Figure 12-1 solves Equation 12-11 for $[H^+]$.

Key step: *Guess* a value for $[H^+]$ and use Excel Solver to vary $[H^+]$ until it satisfies the charge balance.

In Figure 12-1, shaded boxes contain input. Everything else is computed by the spreadsheet. Values for F_{H_2T}, pK_1, pK_2, F_{PyH^+}, pK_a, and $[K^+]$ were given in the problem. The initial value of pH in cell H13 is a *guess*. We will use Excel Solver to vary pH until the sum of charges in cell E15 is 0. Species in the charge balance are in cells B10:E13. $[H^+]$ in cell B10 is

	A	B	C	D	E	F	G	H	I
1	Mixture of 0.020 M Na^+HT^-, 0.015 M PyH^+Cl^-, and 0.010 M KOH								
2									
3	F_{H2T} =	0.020		F_{PyH+} =	0.015		$[K^+]$ =	0.010	
4	pK_1 =	3.036		pK_a =	5.20		K_w =	1.00E-14	
5	pK_2 =	4.366		K_a =	6.31E-06				
6	K_1 =	9.20E-04							
7	K_2 =	4.31E-05							
8									
9	Species in charge balance:						Other concentrations:		
10	$[H^+]$ =	1.00E-06		$[OH^-]$ =	1.00E-08		$[H_2T]$ =	4.93E-07	
11	$[PyH^+]$ =	2.05E-03		$[HT^-]$ =	4.54E-04		[Py] =	1.29E-02	
12	$[Na^+]$ =	0.020		$[T^{2-}]$ =	1.95E-02				
13	$[K^+]$ =	0.010		$[Cl^-]$ =	0.015		pH =	6.000	← initial value
14									is a guess
15	Positive charge minus negative charge =				-2.25E-02	← vary pH in H13 with Solver to make this 0			
16					E15 = B10+B11+B12+B13-E10-E11-2*E12-E13				
17	Check: $[PyH^+]$ + [Py] =			0.01500	(= B11+H11)				
18	Check: $[H_2T]$ + $[HT^-]$ + $[T^{2-}]$ =			0.02000	(= H10+E11+E12)				
19									
20	Formulas:								
21	B6 = 10^-B4		B7 = 10^-B5		E5 = 10^-E4		E10 = H4/B10		
22	B10 = 10^-H13		B12 = B3		B13 = H3		E13 = E3		
23	E11 = B6*B10*B3/(B10^2+B10*B6+B6*B7)						B11 = B10*E3/(B10+E5)		
24	E12 = B6*B7*B3/(B10^2+B10*B6+B6*B7)						H11 = E5*E3/(B10+E5)		
25	H10 = B10^2*B3/(B10^2+B10*B6+B6*B7)								

FIGURE 12-1 Spreadsheet for mixture of acids and bases uses Solver to find the value of pH in cell H13 that satisfies the charge balance in cell E15. The sums $[PyH^+]$ + [Py] in cell D17 and $[H_2T]$ + $[HT^-]$ + $[T^{2-}]$ in cell D18 are computed to verify that the formulas for each of the species do not have mistakes. These sums are independent of pH.

computed from the pH we guessed in cell H13. $[PyH^+]$ in cell B11 is computed with Equation 12-8. Known values are entered for $[Na^+]$, $[K^+]$, and $[Cl^-]$. $[OH^-]$ is computed from $K_w/[H^+]$. $[HT^-]$ and $[T^{2-}]$ in cells E11 and E12 are computed with Equations 12-9 and 12-10.

The sum of charges, $[H^+] + [PyH^+] + [Na^+] + [K^+] - [OH^-] - [HT^-] - 2[T^{2-}] - [Cl^-]$, is computed in cell E15. If we had guessed the correct pH in cell H13, the sum of the charges would be 0. Instead, the sum is -2.25×10^{-2} M. We use Excel Solver to vary pH in cell H13 until the sum of charges in cell E15 is 0.

Using Excel Solver

In Excel 2007, in the Data ribbon, select Solver, and a window similar to Figure 18-4 appears. (If you don't see Solver in the Analysis section of the ribbon, click the Microsoft Office button at the top left of the spreadsheet. Click Excel Options and select Add-Ins. Highlight Solver Add-In, click OK, and Solver is loaded.) In the Data ribbon, click on Solver. In the Solver window, Set Target Cell E15 Equal To Value of 0 By Changing Cells H13. Then click Solve. Solver will vary the pH in cell H13 to make the net charge in cell E15 equal to 0. Starting with a pH of 6 in cell H13, Solver returns a net charge of ~10^{-6} in cell E15 by adjusting the pH in cell H13 to 4.298. (In earlier versions of Excel, select Solver in the Tools menu and proceed as described above. If you don't see Solver in the Tools menu, select Add-Ins and click on Solver in the Add-Ins window. Click OK and Solver appears in the Tools menu.)

The reason the charge is 10^{-6} instead of 0 is that the default precision of Solver is 10^{-6}. To get a charge closer to 0, click on Options in the Solver window. Precision will probably have the default setting of 0.000 001. Enter 1e-16 for Precision and click OK. Run Solver again. This time, the charge in cell E15 is reduced to ~10^{-16}. The pH in cell H13 is still 4.298 (to three decimal places). The difference in pH required to reduce the net charge from 10^{-6} to 10^{-16} is not perceptible in the third decimal place of pH. Many chemistry problems involve very large or very small numbers for which you might need to adjust the precision of Solver. The concentrations after executing Solver are

	A	B	C	D	E	F	G	H
9	Species in charge balance:						Other concentrations:	
10	$[H^+]$ =	5.04E-05		$[OH^-]$ =	1.99E-10		$[H_2T]$ =	5.73E-04
11	$[PyH^+]$ =	1.33E-02		$[HT^-]$ =	1.05E-02		[Py] =	1.67E-03
12	$[Na^+]$ =	0.020		$[T^{2-}]$ =	8.95E-03			
13	$[K^+]$ =	0.010		$[Cl^-]$ =	0.015		pH =	4.298
14								
15	Positive charge minus negative charge =				9.71E-17			

Ignorance Is Bliss: A Complication of Ion Pairing

We should not get too cocky with our newfound power to handle complex problems, because we have oversimplified the actual situation. For one thing, we have not included activity coefficients, which ordinarily affect the answer by a few tenths of a pH unit. In Section 12-2, we will show how to incorporate activity coefficients.

Even with activity coefficients, we are always limited by chemistry that we do not know. In the mixture of sodium hydrogen tartrate (Na^+HT^-), pyridinium chloride (PyH^+Cl^-), and KOH, several possible ion-pair equilibria are

$$Na^+ + T^{2-} \rightleftharpoons NaT^- \qquad K_{NaT^-} = \frac{[NaT^-]}{[Na^+][T^{2-}]} = 8 \qquad \textbf{(12-12)}$$

$$Na^+ + HT^- \rightleftharpoons NaHT \qquad K_{NaHT} = \frac{[NaHT]}{[Na^+][[HT^-]} = 1.6 \qquad \textbf{(12-13)}$$

$$Na^+ + Py \rightleftharpoons PyNa^+ \qquad K_{PyNa^+} = 1.0 \qquad \textbf{(12-14)}$$

$$K^+ + T^{2-} \rightleftharpoons KT^- \qquad K_{KT^-} = 3$$

$$K^+ + HT^- \rightleftharpoons KHT \qquad K_{KHT} = ?$$

$$PyH^+ + Cl^- \rightleftharpoons PyH^+Cl^- \qquad K_{PyHCl} = ?$$

$$PyH^+ + T^{2-} \rightleftharpoons PyHT^- \qquad K_{PyHT^-} = ?$$

Equilibrium constants from A. E. Martell, R. M. Smith, and R. J. Motekaitis, *NIST Standard Reference Database 46*, Version 6.0, 2001.

Some equilibrium constants at 0 ionic strength are listed above. Values for the other reactions are not available, but there is no reason to believe that the reactions do not occur.

How could we add ion pairing to our spreadsheet? For simplicity, we outline how to add just Reactions 12-12 and 12-13. With these reactions, the mass balance for sodium is

$$[Na^+] + [NaT^-] + [NaHT] = F_{Na} = F_{H_2T} = 0.020\,0\ M \tag{12-15}$$

From the ion-pair equilibria, we write $[NaT^-] = K_{NaT^-}[Na^+][T^{2-}]$ and $[NaHT] = K_{NaHT}[Na^+][HT^-]$. With these substitutions for $[NaT^-]$ and $[NaHT]$ in the mass balance for sodium, we find an expression for $[Na^+]$:

$$[Na^+] = \frac{F_{H_2T}}{1 + K_{NaT^-}[T^{2-}] + K_{NaHT}[HT^-]} \tag{12-16}$$

A bigger nuisance when considering ion pairs is that the fractional composition equations for $[H_2T]$, $[HT^-]$, and $[T^{2-}]$ also are changed because the mass balance for H_2T now has five species in it instead of three:

$$F_{H_2T} = [H_2T] + [HT^-] + [T^{2-}] + [NaT^-] + [NaHT] \tag{12-17}$$

We must derive new equations analogous to 12-9 and 12-10 from the mass balance 12-17.

The new fractional composition equations are messy, so we reserve this case for Problem 12-19. The end result is that ion-pair equilibria 12-12 and 12-13 change the calculated pH from 4.30 to 4.26. This change is not large, so neglecting ion pairs with small equilibrium constants does not lead to serious error. We find that 7% of sodium is tied up in ion pairs. *Our ability to compute the distribution of species in a solution is limited by our knowledge of relevant equilibria.*

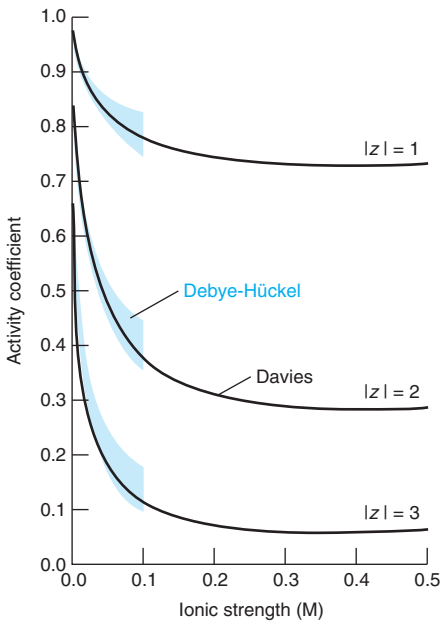


FIGURE 12-2 Activity coefficients from extended Debye-Hückel and Davies equations. Shaded areas give Debye-Hückel activity coefficients for the range of ion sizes in Table 7-1.

12-2 Activity Coefficients

Even if we know all reactions and equilibrium constants for a given system, we cannot compute concentrations accurately without activity coefficients. Chapter 7 gave the extended Debye-Hückel equation 7-6 for activity coefficients with size parameters in Table 7-1. Many ions of interest are not in Table 7-1, and we do not know their size parameter. Therefore, we introduce the *Davies equation*, which has no size parameter:

Davies equation:

$$\log \gamma = -0.51z^2\left(\frac{\sqrt{\mu}}{1 + \sqrt{\mu}} - 0.3\mu\right) \quad \text{(at 25°C)} \tag{12-18}$$

where γ is the activity coefficient for an ion of charge z at ionic strength μ. Equation 12-18 is used up to $\mu \approx 0.5$ M (Figure 12-2) but is more accurate at lower ionic strength. For best accuracy, Pitzer's equations are used (Chapter 7, reference 7).

Now consider a primary standard buffer containing 0.025 0 *m* KH_2PO_4 and 0.025 0 *m* Na_2HPO_4. Its pH at 25°C is 6.865 ± 0.006.[4] The concentration unit, *m*, is *molality*, which means moles of solute per kilogram of solvent. For precise chemical measurements, concentrations are expressed in molality, rather than molarity, because molality is independent of temperature. Tabulated equilibrium constants usually apply to molality, not molarity. Uncertainties in equilibrium constants are usually sufficiently great to render the ~0.3% difference between molality and molarity of dilute solutions unimportant.

A 0.5 wt% solution of K_2HPO_4 has a *molarity* of 0.028 13 mol/L and a *molality* of 0.028 20 mol/kg. The difference is 0.25%.

Acid-base equilibrium constants for H_3PO_4 at $\mu = 0$ at 25°C are

$$H_3PO_4 \rightleftharpoons H_2PO_4^- + H^+ \qquad K_1 = \frac{[H_2PO_4^-]\gamma_{H_2PO_4^-}[H^+]\gamma_{H^+}}{[H_3PO_4]\gamma_{H_3PO_4}} = 10^{-2.148} \tag{12-19}$$

$$H_2PO_4^- \rightleftharpoons HPO_4^{2-} + H^+ \qquad K_2 = \frac{[HPO_4^{2-}]\gamma_{HPO_4^{2-}}[H^+]\gamma_{H^+}}{[H_2PO_4^-]\gamma_{H_2PO_4^-}} = 10^{-7.198} \tag{12-20}$$

$$HPO_4^{2-} \rightleftharpoons PO_4^{3-} + H^+ \qquad K_3 = \frac{[PO_4^{3-}]\gamma_{PO_4^{3-}}[H^+]\gamma_{H^+}}{[HPO_4^{2-}]\gamma_{HPO_4^{2-}}} = 10^{-12.375} \tag{12-21}$$

Equilibrium constants can be determined by measuring concentration quotients at several low ionic strengths and extrapolating to 0 ionic strength.

For $\mu \neq 0$, we rearrange the equilibrium constant expression to incorporate activity coefficients into an effective equilibrium constant, K' at the given ionic strength.

$$K_1' = K_1\left(\frac{\gamma_{H_3PO_4}}{\gamma_{H_2PO_4^-}\gamma_{H^+}}\right) = \frac{[H_2PO_4^-][H^+]}{H_3PO_4} \tag{12-22}$$

$$K_2' = K_2\left(\frac{\gamma_{H_2PO_4^-}}{\gamma_{HPO_4^{2-}}\gamma_{H^+}}\right) = \frac{[HPO_4^{2-}][H^+]}{H_2PO_4^-} \quad (12\text{-}23)$$

$$K_3' = K_3\left(\frac{\gamma_{HPO_4^{2-}}}{\gamma_{PO_4^{3-}}\gamma_{H^+}}\right) = \frac{[PO_4^{3-}][H^+]}{[HPO_4^{2-}]} \quad (12\text{-}24)$$

K_2' gives the *concentration quotient* $\frac{[HPO_4^{2-}][H^+]}{[H_2PO_4^-]}$ at a specified ionic strength.

For ionic species, we compute activity coefficients with the Davies equation 12-18. For the neutral species H_3PO_4, we assume that $\gamma \approx 1.00$.

Now we remind ourselves of the equations for water ionization

$$H_2O \rightleftharpoons H^+ + OH^- \qquad K_w = [H^+]\gamma_{H^+}[OH^-]\gamma_{OH^-} = 10^{-13.995}$$

Values of K_w are found in Table 6-1.

$$K_w' = \frac{K_w}{\gamma_{H^+}\gamma_{OH^-}} = [H^+][OH^-] \Rightarrow [OH^-] = K_w'/[H^+] \quad (12\text{-}25)$$

$$pH = -\log([H^+]\gamma_{H^+}) \quad (12\text{-}26)$$

Here is how we use effective equilibrium constants:

Step 1 Solve the acid-base problem with the constants K_1, K_2, and K_3, which apply at $\mu = 0$. Activity coefficients are considered to be unity in this first step.

Step 2 From the results of step 1, compute the ionic strength. Then use the Davies equation to compute activity coefficients. With these activity coefficients, compute the effective equilibrium constants, K_1', K_2', and K_3', and K_w'.

Step 3 Solve the acid-base problem again, this time with K_1', K_2', and K_3', and K_w'.

Step 4 From the results of step 3, compute a new ionic strength and a new set of K' values. Repeat the process several times until the ionic strength is constant.

Let's find the pH of 0.025 0 *m* KH_2PO_4 plus 0.025 0 *m* Na_2HPO_4. The chemical reactions are 12-19 through 12-21 plus water ionization. Mass balances are $[K^+] = 0.025\,0\ m$, $[Na^+] = 0.050\,0\ m$, and total phosphate $\equiv F_{H_3P} = 0.050\,0\ m$. The charge balance is

$$[Na^+] + [K^+] + [H^+] = [H_2PO_4^-] + 2[HPO_4^{2-}] + 3[PO_4^{3-}] + [OH^-] \quad (12\text{-}27)$$

Our strategy is to substitute expressions into the charge balance to obtain an equation in which the only variable is $[H^+]$. For this purpose, we use the fractional composition equations for the triprotic acid, H_3PO_4, which we abbreviate as H_3P:

$$[P^{3-}] = \alpha_{P^{3-}}F_{H_3P} = \frac{K_1'K_2'K_3'F_{H_3P}}{[H^+]^3 + [H^+]^2K_1' + [H^+]K_1'K_2' + K_1'K_2'K_3'} \quad (12\text{-}28)$$

$$[HP^{2-}] = \alpha_{HP^{2-}}F_{H_3P} = \frac{[H^+]K_1'K_2'F_{H_3P}}{[H^+]^3 + [H^+]^2K_1' + [H^+]K_1'K_2' + K_1'K_2'K_3'} \quad (12\text{-}29)$$

$$[H_2P^-] = \alpha_{H_2P^-}F_{H_3P} = \frac{[H^+]^2K_1'F_{H_3P}}{[H^+]^3 + [H^+]^2K_1' + [H^+]K_1'K_2' + K_1'K_2'K_3'} \quad (12\text{-}30)$$

$$[H_3P] = \alpha_{H_3P}F_{H_3P} = \frac{[H^+]^3F_{H_3P}}{[H^+]^3 + [H^+]^2K_1' + [H^+]K_1'K_2' + K_1'K_2'K_3'} \quad (12\text{-}31)$$

Figure 12-3 puts everything together in a spreadsheet. Input values for $F_{KH_2PO_4}$, $F_{Na_2HPO_4}$, pK_1, pK_2, pK_3, and pK_w are in the shaded cells. We *guess* a value for pH in cell H15 and write the initial ionic strength of 0 in cell C19. Cells A9:H10 compute activities with the Davies equation. With $\mu = 0$, all activity coefficients are 1. Cells A13:H16 compute concentrations. $[H^+]$ in cell B13 is $(10^{-pH})/\gamma_{H^+}$ = (10^-H15)/B9. Cell E18 computes the sum of charges.

An initial guess of pH = 7 in cell H15 gives a net charge of 0.005 6 *m* in cell E18, which is not shown in Figure 12-3. Excel Solver was then used to vary pH in cell H15 to produce a net charge near 0 in cell E18. For this purpose, the precision was set to 1e-16 in Solver Options. Figure 12-3 shows that executing Solver gives pH = 7.198 in cell H15 and a net charge of -2×10^{-17} *m* in cell E18. The calculated ionic strength in cell C20 is 0.100 *m*.

For the second iteration, we write the ionic strength 0.100 *m* in cell C19 of Figure 12-4. This ionic strength automatically gives new activity coefficients in cells A9:H10 and new effective equilibrium constants in cells H3:H6. The sum of charges in cell E18 is no longer near zero. Application of Solver to vary pH in cell H15 to try to get 0 net charge produces a net charge of 9×10^{-17} *m* in cell E18. The new ionic strength in Cell C20 remains 0.100 *m*, so

	A	B	C	D	E	F	G	H
1	Mixture of KH_2PO_4 and Na_2HPO_4 including activity coefficients from Davies equation							
2								
3	F_{KH2PO4} =	0.0250		pK_1 =	2.148		K_1' =	7.11E-03
4	$F_{Na2HPO4}$ =	0.0250		pK_2 =	7.198		K_2' =	6.34E-08
5	F_{H3P} =	0.0500	(=B3+B4)	pK_3 =	12.375		K_3' =	4.22E-13
6				pK_w =	13.995		K_w' =	1.01E-14
7								
8	Activity coefficients:							
9	H^+ =	1.00		H_3P =	1.00	(fixed at 1)	HP^{2-} =	1.00
10	OH^- =	1.00		H_2P^-=	1.00		P^{3-} =	1.00
11								
12	Species in charge balance:						Other concentrations:	
13	$[H^+]$ =	6.34E-08		$[OH^-]$ =	1.60E-07		$[H_3P]$ =	2.23E-07
14	$[Na^+]$ =	0.050000		$[H_2P^-]$ =	2.50E-02			
15	$[K^+]$ =	0.025000		$[HP^{2-}]$ =	2.50E-02		pH =	7.198
16				$[P^{3-}]$ =	1.66E-07		↑ initial value is a guess	
17								
18	Positive charge minus negative charge =				-2.27E-17			
19	Ionic strength =		0.0000	←initial value is 0				
20	New ionic strength =		0.1000	←substitute this value into cell C19 for next iteration				
21								
22	Formulas:							
23	H3 = 10^-E3*E9/(E10*B9)				H4 = 10^-E4*E10/(H9*B9)			
24	H5 = 10^-E5*H9/(H10*B9)				H6 = 10^-E6/(B9*B10)			
25	B9 = B10 = E10 = 10^(-0.51*1^2*(SQRT($C$19)/(1+SQRT($C$19))-0.3*$C$19))							
26	H9 = 10^(-0.51*2^2*(SQRT($C$19)/(1+SQRT($C$19))-0.3*$C$19))							
27	H10 = 10^(-0.51*3^2*(SQRT($C$19)/(1+SQRT($C$19))-0.3*$C$19))							
28	B13 = (10^-H15)/B9		B14 = 2*B4		B15 = B3		E13 = H6/(B13)	
29	E14 = B13^2*H3*B5/(B13^3+B13^2*H3+B13*H3*H4+H3*H4*H5)							
30	E15 = B13*H3*H4*B5/(B13^3+B13^2*H3+B13*H3*H4+H3*H4*H5)							
31	E16 = H3*H4*H5*B5/(B13^3+B13^2*H3+B13*H3*H4+H3*H4*H5)							
32	H13 = B13^3*B5/(B13^3+B13^2*H3+B13*H3*H4+H3*H4*H5)							
33	E18 = B13+B14+B15-E13-E14-2*E15-3*E16							
34	C20 = 0.5*(B13+B14+B15+E13+E14+4*E15+9*E16)							

FIGURE 12-3 Spreadsheet solved for the system 0.025 0 *m* KH_2PO_4 plus 0.025 0 *m* Na_2HPO_4 with initial ionic strength = 0 and activity coefficients = 1.

	A	B	C	D	E	F	G	H
1	Mixture of KH_2PO_4 and Na_2HPO_4 including activity coefficients from Davies equation							
2								
3	F_{KH2PO4} =	0.0250		pK_1 =	2.148		K_1' =	1.17E-02
4	$F_{Na2HPO4}$ =	0.0250		pK_2 =	7.198		K_2' =	1.70E-07
5	F_{H3P} =	0.0500	(=B3+B4)	pK_3 =	12.375		K_3' =	1.86E-12
6				pK_w =	13.995		K_w' =	1.66E-14
7								
8	Activity coefficients:							
9	H^+ =	0.78		H_3P =	1.00	(fixed at 1)	HP^{2-} =	0.37
10	OH^-=	0.78		H_2P^- =	0.78		P^{3-} =	0.11
11								
12	Species in charge balance:						Other concentrations:	
13	$[H^+]$ =	1.70E-07		$[OH^-]$ =	9.74E-08		$[H_3P]$ =	3.65E-07
14	$[Na^+]$ =	0.050000		$[H_2P^-]$ =	2.50E-02			
15	$[K^+]$ =	0.025000		$[HP^{2-}]$ =	2.50E-02		pH =	6.876
16				$[P^{3-}]$ =	2.73E-07		↑ initial value is a guess	
17								
18	Positive charge minus negative charge =				8.56E-17			
19	Ionic strength =		0.1000	← initial value is 0				
20	New ionic strength =		0.1000	← substitute this value into cell C19 for next iteration				

FIGURE 12-4 Second iteration of spreadsheet solved for the system 0.025 0 *m* KH_2PO_4 plus 0.025 0 *m* Na_2HPO_4 with ionic strength = 0.100 from the first iteration.

we are done. When the new ionic strength in cell C20 equals the old ionic strength in cell C19 (to three decimal places), there is no need for further iteration.

The final pH in cell H15 of Figure 12-4 is 6.876, which differs from the certified pH of 6.865 by 0.011. This difference is about as close an agreement between a measured and computed pH as you will encounter. If we had used extended Debye-Hückel activity coefficients for $\mu = 0.1\ m$ in Table 7-1, the computed pH would be 6.859, differing from the stated pH by just 0.006.

Sometimes Solver cannot find a solution if Precision is set too small in the Options window. You can make the Precision larger and see if Solver can find a solution. You can also try a different initial guess for pH.

Back to Basics

A spreadsheet operating on the charge balance to reduce the net charge to zero is an excellent, general method for solving complex equilibrium problems. However, we did learn how to find the pH of a mixture of KH_2PO_4 plus Na_2HPO_4 back in Chapter 8 by a simple, less rigorous method. Recall that, when we mix a weak acid ($H_2PO_4^-$) and its conjugate base (HPO_4^{2-}), *what we mix is what we get*. The pH is estimated from the Henderson-Hasselbalch equation 8-18 with activity coefficients:

$$\text{pH} = \text{p}K_a + \log\frac{[A^-]\gamma_{A^-}}{[HA]\gamma_{HA}} = \text{p}K_2 + \log\frac{[HPO_4^{2-}]\gamma_{HPO_4^{2-}}}{[H_2PO_4^-]\gamma_{H_2PO_4^-}} \qquad \textbf{(8-18)}$$

For 0.025 m KH_2PO_4 plus 0.025 m Na_2HPO_4, the ionic strength is

$$\mu = \frac{1}{2}\sum_i c_i z_i^2 = \frac{1}{2}([K^+]\cdot(+1)^2 + [H_2PO_4^-]\cdot(-1)^2 + [Na^+]\cdot(+1)^2 + [HPO_4^{2-}]\cdot(-2)^2)$$

$$= \frac{1}{2}([0.025]\cdot 1 + [0.025]\cdot 1 + [0.050]\cdot 1 + [0.025]\cdot 4) = 0.100\ m$$

In Table 7-1, the activity coefficients at $\mu = 0.1\ m$ are 0.775 for $H_2PO_4^-$ and 0.355 for HPO_4^{2-}. Inserting these values into Equation 8-18 gives

$$\text{pH} = 7.198 + \log\frac{[0.025]0.355}{[0.025]0.775} = 6.859$$

$\text{p}K_a = \text{p}K_2$ in Equation 8-18 applies at $\mu = 0$.

The answer is the same that we generate with the spreadsheet because the approximation that what we mix is what we get is excellent in this case.

So you already knew how to find the pH of this buffer by a simple calculation. The value of the general method with the charge balance in the spreadsheet is that it applies even when what you mix is not what you get, because the concentrations are very low or K_2 is not so small or there are additional equilibria.

Ignorance Is Still Bliss

Even in such a simple solution as KH_2PO_4 plus Na_2HPO_4, for which we were justifiably proud of computing an accurate pH, we have overlooked numerous ion-pair equilibria:

$$PO_4^{3-} + Na^+ \rightleftharpoons NaPO_4^{2-} \quad K = 27 \qquad HPO_4^{2-} + Na^+ \rightleftharpoons NaHPO_4^- \quad K = 12$$

$$H_2PO_4^- + Na^+ \rightleftharpoons NaH_2PO_4 \quad K = 2 \qquad NaPO_4^{2-} + Na^+ \rightleftharpoons Na_2PO_4^- \quad K = 14$$

$$Na_2PO_4^- + H^+ \rightleftharpoons Na_2HPO_4 \qquad K = 5.4 \times 10^{10}$$

There is an analogous set of reactions for K^+, whose equilibrium constants are similar to those for Na^+.

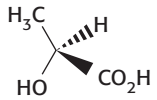
The reliability of the calculated concentrations depends on knowing all relevant equilibria and having the fortitude to include them all in the computation, which is by no means trivial.

The effective $\text{p}K_2$ for H_3PO_4 listed in the *NIST Critically Selected Stability Constants Database 46* (2001) for an ionic strength of 0.1 M has the following values: 6.71 for Na^+ background ions, 6.75 for K^+ background ions, and 6.92 for unspecified tetraalkylammonium background ions. The dependence of the effective pK on the nature of the background ions strongly suggests that ion-pairing reactions play an observable role in the solution chemistry.

12-3 Dependence of Solubility on pH

An important example of the effect of pH on solubility is tooth decay. Tooth enamel contains the mineral hydroxyapatite, which is insoluble near neutral pH, but dissolves in acid because both phosphate and hydroxide in the hydroxyapatite react with H^+:

$$\underset{\text{Calcium hydroxyapatite}}{Ca_{10}(PO_4)_6(OH)_2(s)} + 14H^+ \rightleftharpoons 10Ca^{2+} + 6H_2PO_4^- + 2H_2O$$



L-Lactic acid

Bacteria on the surface of our teeth metabolize sugars to produce lactic acid, which lowers the pH enough to slowly dissolve tooth enamel. Fluoride inhibits tooth decay because it forms fluorapatite, $Ca_{10}(PO_4)_6F_2$, which is more acid resistant than hydroxyapatite.

Solubility of CaF_2

The mineral *fluorite*, CaF_2, in Figure 12-5 has a cubic crystal structure and often cleaves to form nearly perfect octahedra (eight-sided solids with equilateral triangular faces). Depending on impurities, the mineral takes on a variety of colors and may fluoresce when irradiated with an ultraviolet lamp.

The solubility of CaF_2 is governed by K_{sp} for the salt, hydrolysis of F^- and of Ca^{2+}, and by ion pairing between Ca^{2+} and F^-:

Solubility products are in Appendix F. The acid dissociation constant of HF is from Appendix G. The hydrolysis constant for Ca is the inverse of the formation constant of $CaOH^+$ in Appendix I. The ion-pair formation constant for CaF^+ is listed in Appendix J.

$$CaF_2(s) \rightleftharpoons Ca^{2+} + 2F^- \qquad K_{sp} = [Ca^{2+}][F^-]^2 = 3.2 \times 10^{-11} \qquad \textbf{(12-32)}$$

$$HF \rightleftharpoons H^+ + F^- \qquad K_{HF} = \frac{[H^+][F^-]}{[HF]} = 6.8 \times 10^{-4} \qquad \textbf{(12-33)}$$

$$Ca^{2+} + H_2O \rightleftharpoons CaOH^+ + H^+ \qquad K_a = \frac{[CaOH^+][H^+]}{[Ca^{2+}]} = 2 \times 10^{-13} \qquad \textbf{(12-34)}$$

$$Ca^{2+} + F^- \rightleftharpoons CaF^+ \qquad K_{ip} = \frac{[CaF^+]}{[Ca^{2+}][F^-]} = 4.3 \qquad \textbf{(12-35)}$$

$$H_2O \rightleftharpoons H^+ + OH^- \qquad K_w = [H^+][OH^-] = 1.0 \times 10^{-14} \qquad \textbf{(12-36)}$$

The charge balance is

$$\textit{Charge balance:} \quad [H^+] + 2[Ca^{2+}] + [CaOH^+] + [CaF^+] = [OH^-] + [F^-] \qquad \textbf{(12-37)}$$

To find the mass balance, we need to realize that all calcium and fluoride species come from CaF_2. Therefore, the total fluoride equals two times the total calcium:

$$2[\text{total calcium species}] = [\text{total fluoride species}]$$

$$2\{[Ca^{2+}] + [CaOH^+] + [CaF^+]\} = [F^-] + [HF] + [CaF^+]$$

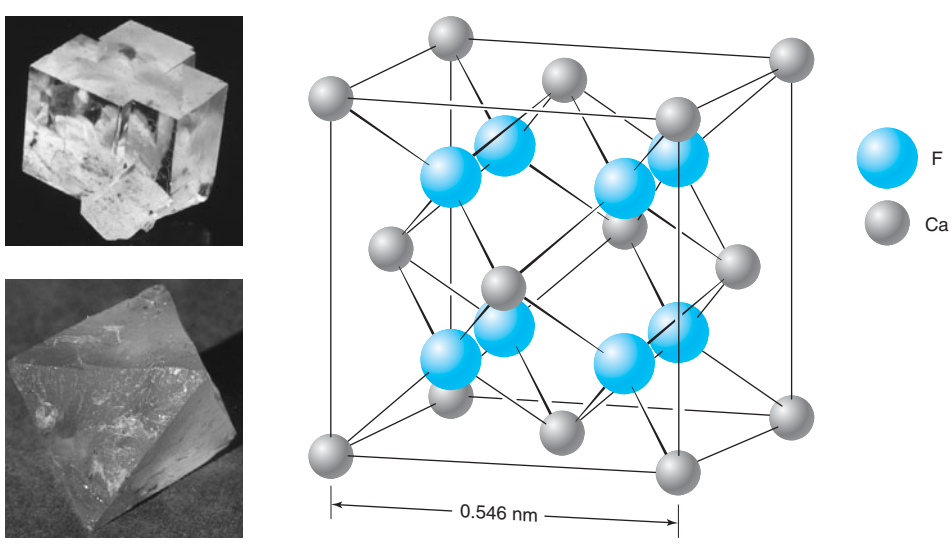
$$\textit{Mass balance:} \quad 2[Ca^{2+}] + 2[CaOH^+] + [CaF^+] = [F^-] + [HF] \qquad \textbf{(12-38)}$$

There are seven independent equations and seven unknowns, so we have enough information.

How to use activity coefficients

We omit activity coefficients here, but you do know how to use them. You would solve the problem with activity coefficients equal to 1, find the ionic strength, and then compute activity coefficients with the Davies equation. Then you would compute effective equilibrium constants incorporating activity coefficients and solve the problem again. After each iteration, you would find a new ionic strength and a new set of activity coefficients. Repeat the process until ionic strength is constant. Wow! You are smart!

We want to reduce seven equations with seven unknowns to one equation with one unknown—but this is not easy. However, we can express all concentrations in terms of $[H^+]$



(*a*) (*b*)

FIGURE 12-5 Crystals of the mineral fluorite, CaF_2. Each Ca^{2+} ion is surrounded by eight F^- ions at the corners of a cube. Each F^- ion is surrounded by four Ca^{2+} ions at the corners of a tetrahedron. If you imagine the next unit cell above this one, you should see that the Ca^{2+} ion at the center of the top face of the cell shown here is adjacent to four F^- ions in this cell and four F^- ions in the next cell above it.

and $[F^-]$, so we can reduce the mass and charge balance to two equations with two unknowns. Here are the substitutions from the equilibrium expressions:

$$[Ca^{2+}] = K_{sp}/[F^-]^2 \qquad [HF] = [H^+][F^-]/K_{HF}$$

$$[CaOH^+] = \frac{K_a[Ca^{2+}]}{[H^+]} = \frac{K_aK_{sp}}{[H^+][F^-]^2} \qquad [CaF^+] = K_{ip}[Ca^{2+}][F^-] = \frac{K_{ip}K_{sp}}{[F^-]}$$

The first expression for $[CaOH^+]$ is from Equation 12-34. The second expression is obtained by substituting $[Ca^{2+}] = K_{sp}/[F^-]^2$ into the first equation.

Putting these expressions into the charge balance gives

$$[H^+] + 2[Ca^{2+}] + [CaOH^+] + [CaF^+] - [OH^-] - [F^-] = 0 \qquad \textbf{(12-39a)}$$

$$[H^+] + \frac{2K_{sp}}{[F^-]^2} + \frac{K_aK_{sp}}{[H^+][F^-]^2} + \frac{K_{ip}K_{sp}}{[F^-]} - \frac{K_w}{[H^+]} - [F^-] = 0 \qquad \textbf{(12-39b)}$$

Substitution in the mass balance gives

$$2[Ca^{2+}] + 2[CaOH^+] + [CaF^+] - [F^-] - [HF] = 0$$

$$\frac{2K_{sp}}{[F^-]^2} + \frac{2K_aK_{sp}}{[H^+][F^-]^2} + \frac{K_{ip}K_{sp}}{[F^-]} - [F^-] - \frac{[H^+][F^-]}{K_{HF}} = 0 \qquad \textbf{(12-40)}$$

We could do some messy algebra to solve Equation 12-39b for $[H^+]$ and substitute this expression for $[H^+]$ into Equation 12-40 to get an equation with $[F^-]$ as the only unknown.[5]

Instead, we will use a spreadsheet for a numerical solution. *Suppose that the pH is somehow fixed by a buffer.* The mass balance relating calcium to fluoride is still correct. However, the charge balance is no longer valid, because the buffer introduces additional ions into the solution. We will find a way around the loss of the charge balance shortly.

When buffer is added, the mass balance still applies but the original charge balance is no longer correct.

In the spreadsheet in Figure 12-6, enter pH in column A. Compute $[H^+] = 10^{-pH}$ in column B and *guess* a value for $[F^-]$ in column C. With these values of $[H^+]$ and $[F^-]$,

	A	B	C	D	E	F	G	H	I	J
1	Finding the concentrations of species in saturated calcium fluoride solution									
2										
3	K_{sp} =	3.2E-11		Mass balance:						
4	K_{HF} =	6.8E-04		$\frac{2K_{sp}}{[F^-]^2}+\frac{2K_aK_{sp}}{[H^+][F^-]^2}+\frac{K_{ip}K_{sp}}{[F^-]}-[F^-]-\frac{[H^+][F^-]}{K_{HF}}=0$						
5	K_a =	2.E-13								
6	K_{ip} =	4.3								
7	K_w =	1.0E-14		Mass						
8	Input		$[F^-]$ found by	balance						Sum of
9	pH	$[H^+]$	SOLVER	sum	$[Ca^{2+}]$	$[CaOH^+]$	$[CaF^+]$	[HF]	$[OH^-]$	charges
10	0	1.E+00	3.517E-05	5.6E-17	2.6E-02	5.17E-15	3.9E-06	5.17E-02	1.0E-14	1.1E+00
11	1	1.E-01	7.561E-05	0.0E+00	5.6E-03	1.12E-14	1.8E-06	1.11E-02	1.0E-13	1.1E-01
12	2	1.E-02	1.597E-04	-7.6E-17	1.3E-03	2.51E-14	8.6E-07	2.35E-03	1.0E-12	1.2E-02
13	3	1.E-03	2.960E-04	-2.8E-17	3.7E-04	7.31E-14	4.6E-07	4.35E-04	1.0E-11	1.4E-03
14	4	1.E-04	3.822E-04	-1.2E-17	2.2E-04	4.38E-13	3.6E-07	5.62E-05	1.0E-10	1.6E-04
15	5	1.E-05	3.982E-04	-1.5E-17	2.0E-04	4.04E-12	3.5E-07	5.86E-06	1.0E-09	1.6E-05
16	6	1.E-06	3.999E-04	-7.8E-18	2.0E-04	4.00E-11	3.4E-07	5.88E-07	1.0E-08	1.6E-06
17	7	1.E-07	4.001E-04	-1.0E-17	2.0E-04	4.00E-10	3.4E-07	5.88E-08	1.0E-07	5.8E-08
18	8	1.E-08	4.001E-04	-1.0E-17	2.0E-04	4.00E-09	3.4E-07	5.88E-09	1.0E-06	-9.9E-07
19	9	1.E-09	4.001E-04	-1.1E-17	2.0E-04	4.00E-08	3.4E-07	5.88E-10	1.0E-05	-1.0E-05
20	10	1.E-10	4.004E-04	-2.5E-17	2.0E-04	3.99E-07	3.4E-07	5.89E-11	1.0E-04	-1.0E-04
21	11	1.E-11	4.028E-04	-8.7E-18	2.0E-04	3.95E-06	3.4E-07	5.92E-12	1.0E-03	-1.0E-03
22	12	1.E-12	4.252E-04	-2.5E-17	1.8E-04	3.54E-05	3.2E-07	6.25E-13	1.0E-02	-1.0E-02
23	13	1.E-13	5.770E-04	-5.5E-17	9.6E-05	1.92E-04	2.4E-07	8.48E-14	1.0E-01	-1.0E-01
24	14	1.E-14	1.104E-03	-2.0E-17	2.6E-05	5.25E-04	1.2E-07	1.62E-14	1.0E+00	-1.0E+00
25										
26	B10 = 10^-A10			E10 = $B$3/C10^2			F10 = $B$5*$B$3/(B10*C10^2)			
27	G10 = $B$6*$B$3/C10			H10 = B10*C10/$B$4			I10 = $B$7/B10			
28	D10 = 2*$B$3/C10^2+2*$B$5*$B$3/(B10*C10^2)+$B$6*$B$3/C10-C10-B10*C10/$B$4									
29	J10 = B10+2*E10+F10+G10-I10-C10									

FIGURE 12-6 Spreadsheet using Solver for saturated CaF_2 at fixed pH values.

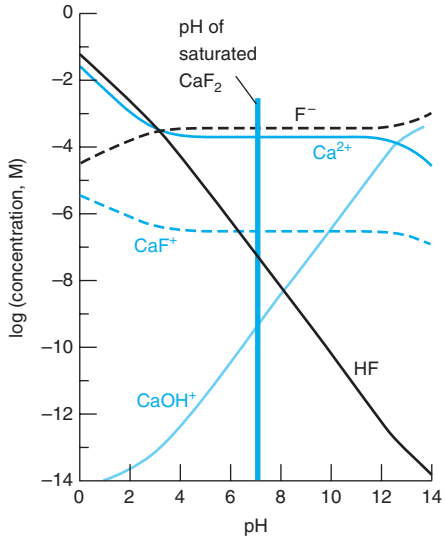


FIGURE 12-7 pH dependence of species in a saturated solution of CaF_2. As pH is lowered, H^+ reacts with F^- to make HF, and $[Ca^{2+}]$ increases. Note the logarithmic ordinate.

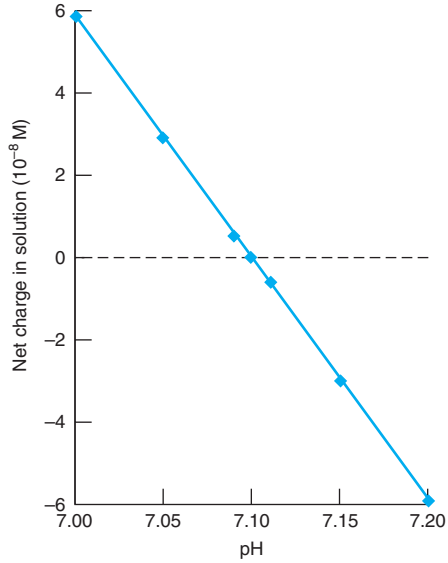


FIGURE 12-8 Net charge in a saturated solution of CaF_2 due to H^+, Ca^{2+}, $CaOH^+$, CaF^+, OH^-, and F^- as a function of pH. The net charge is 0 in unbuffered solution at pH 7.10.

compute the mass balance 12-40 in column D. Then use Solver to vary $[F^-]$ in column C to make the mass balance 0 in column D.

Each row of the spreadsheet must be dealt with separately. For example, in row 10, the pH was set to 0 in cell A10 and the initial *guessed* value of $[F^-]$ in cell C10 was 0.000 1 M. Before executing Solver, Precision was set to 1e-16 in Solver Options. In Solver, Set Target Cell D10 Equal To Value of 0 By Changing Cells C10. Solver changes the value of $[F^-]$ in cell C10 to 3.517E-5 to satisfy the mass balance in cell D10. With the correct value of $[F^-]$ in cell C10, the concentrations of $[Ca^{2+}]$, $[CaOH^+]$, $[CaF^+]$, [HF], and $[OH^-]$ in columns E through I must be correct.

Figure 12-7 shows how the concentrations vary with pH. At low pH, H^+ reacts with F^- to produce HF and increases the solubility of CaF_2. The species CaF^+ and $CaOH^+$ are minor at most pH values, but $CaOH^+$ becomes the major form of calcium above pH 12.7, which is pK_a for Reaction 12-34. A reaction that we did not consider was precipitation of $Ca(OH)_2(s)$. Comparison of the product $[Ca^{2+}][OH^-]^2$ with K_{sp} for $Ca(OH)_2$ indicates that $Ca(OH)_2$ should precipitate at a pH between 13 and 14.

What would be the pH if we had not added buffer? Column J in Figure 12-6 gives the net charge from Equation 12-39a, which includes all ions other than buffer. The pH of unbuffered solution is the pH at which column J is 0. The net charge goes through 0 near pH 7. Finer computations in Figure 12-8 show that the net charge is 0 at pH 7.10. A saturated solution of CaF_2 is predicted to have a pH of 7.10 (ignoring activity coefficients).

Acid Rain Dissolves Minerals and Creates Environmental Hazards

In general, salts of basic ions such as F^-, OH^-, S^{2-}, CO_3^{2-}, $C_2O_4^{2-}$, and PO_4^{3-} have increased solubility at low pH, because the anions react with H^+. Figure 12-9 shows that marble, which is largely $CaCO_3$, dissolves more readily as the acidity of rain increases. Much of the acid in rain comes from SO_2 emissions from combustion of fuels containing sulfur and from nitrogen oxides produced by all types of combustion. SO_2, for example, reacts in the air to make sulfuric acid ($SO_2 + H_2O \rightarrow H_2SO_3 \xrightarrow{\text{oxidation}} H_2SO_4$), which finds its way back to the ground in rainfall.

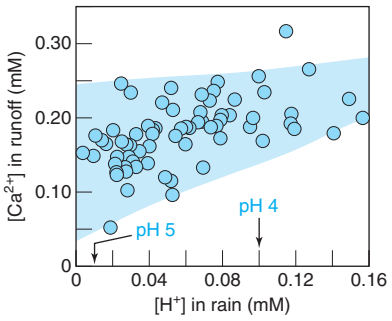


FIGURE 12-9 Measured calcium in acid rain runoff from marble stone (which is largely $CaCO_3$) roughly increases as $[H^+]$ in the rain increases. [Data from P. A. Baedecker and M. M. Reddy, "The Erosion of Carbonate Stone by Acid Rain," *J. Chem. Ed.* **1993**, *70*, 104.]

Aluminum is the third most abundant element on Earth (after oxygen and silicon), but it is tightly locked into insoluble minerals such as kaolinite ($Al_2(OH)_4Si_2O_5$) and bauxite (AlOOH). Acid rain from human activities is a recent change for our planet, and it is introducing soluble forms of aluminum (and lead and mercury) into the environment.[6] Figure 12-10 shows that, below pH 5, aluminum is mobilized from minerals and its concentration in lake water rises rapidly. At a concentration of 130 μg/L, aluminum kills fish. In humans, high concentrations of aluminum cause dementia, softening of bones, and anemia. Aluminum is suspected

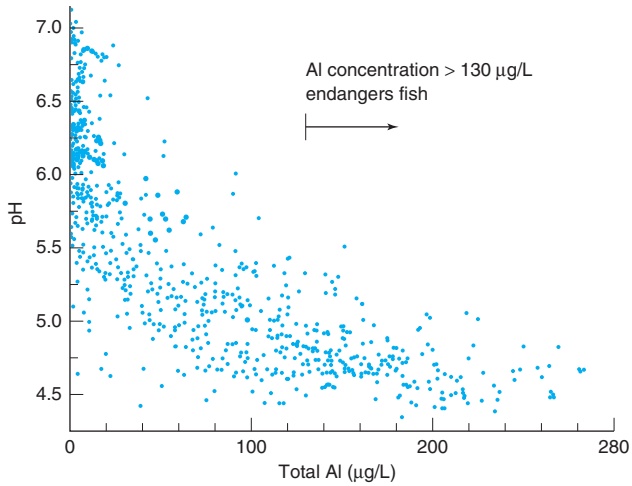


FIGURE 12-10 Relation of total aluminum (including dissolved and suspended species) in 1 000 Norwegian lakes as a function of the pH of the lake water. The more acidic the water, the greater the aluminum concentration. [From G. Howells, *Acid Rain and Acid Waters*, 2nd ed. (Hertfordshire: Ellis Horwood, 1995).]

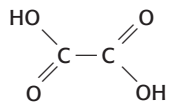
as a possible cause of Alzheimer's disease. Although metallic elements from minerals are liberated by acid, the concentration and availability of metal ions in the environment tend to be regulated by organic matter that binds metal ions.[7]

Solubility of Barium Oxalate

Now consider the dissolution of $Ba(C_2O_4)$, whose anion is *dibasic* and whose cation is a weak acid.[8] The chemistry in this system is

$$Ba(C_2O_4)(s) \rightleftharpoons Ba^{2+} + \underset{\text{Oxalate}}{C_2O_4^{2-}} \qquad K_{sp} = [Ba^{2+}][C_2O_4^{2-}] = 1.0 \times 10^{-6} \qquad \textbf{(12-41)}$$

$$H_2C_2O_4 \rightleftharpoons HC_2O_4^- + H^+ \qquad K_1 = \frac{[H^+][HC_2O_4^-]}{[H_2C_2O_4]} = 5.4 \times 10^{-2} \qquad \textbf{(12-42)}$$



Oxalic acid

$$HC_2O_4^- \rightleftharpoons C_2O_4^{2-} + H^+ \qquad K_2 = \frac{[H^+][C_2O_4^{2-}]}{[HC_2O_4^-]} = 5.42 \times 10^{-5} \qquad \textbf{(12-43)}$$

$$Ba^{2+} + H_2O \rightleftharpoons BaOH^+ + H^+ \qquad K_a = \frac{[H^+][BaOH^+]}{[Ba^{2+}]} = 4.4 \times 10^{-14} \qquad \textbf{(12-44)}$$

Ba^{2+} is a weak acid.

$$Ba^{2+} + C_2O_4^{2-} \rightleftharpoons Ba(C_2O_4)(aq) \qquad K_{ip} = \frac{[Ba(C_2O_4)(aq)]}{[Ba^{2+}][C_2O_4^{2-}]} = 2.1 \times 10^2 \qquad \textbf{(12-45)}$$

Ion pairing

The value of K_{sp} applies at $\mu = 0.1$ M and 20°C. K_{ip} is for $\mu = 0$ and 18°C. K_1, K_2, and K_a apply at $\mu = 0$ and 25°C. For lack of better information, we will use this mixed set of equilibrium constants.

The charge balance is

$$\textit{Charge balance: } [H^+] + 2[Ba^{2+}] + [BaOH^+] = [OH^-] + [HC_2O_4^-] + 2[C_2O_4^{2-}] \qquad \textbf{(12-46)}$$

The mass balance states that the total moles of barium equal the total moles of oxalate:

$$[\text{Total barium}] = [\text{total oxalate}]$$

$$[Ba^{2+}] + [BaOH^+] + \cancel{[Ba(C_2O_4)(aq)]} = [H_2C_2O_4] + [HC_2O_4^-] + [C_2O_4^{2-}] + \cancel{[Ba(C_2O_4)(aq)]}$$

$$\textit{Mass balance: } \underbrace{[Ba^{2+}] + [BaOH^+]}_{F_{Ba}} = \underbrace{[H_2C_2O_4] + [HC_2O_4^-] + [C_2O_4^{2-}]}_{F_{H_2Ox}} \qquad \textbf{(12-47)}$$

We are defining F_{Ba} and F_{H_2O} to *exclude* the ion pair $Ba(C_2O_4)(aq)$.

There are eight unknowns and eight independent equations (including $[OH^-] = K_w/[H^+]$), so we have enough information to find the concentrations of all species.

We deal with ion pairing by adding Reactions 12-41 and 12-45 to find

$$Ba(C_2O_4)(s) \rightleftharpoons Ba(C_2O_4)(aq) \qquad K = [Ba(C_2O_4)(aq)] = K_{sp}K_{ip} = 2.1 \times 10^{-4} \qquad \textbf{(12-48)}$$

Therefore, $[Ba(C_2O_4)(aq)] = 2.1 \times 10^{-4}$ M as long as undissolved $Ba(C_2O_4)(s)$ is present.

The ion pair $Ba(C_2O_4)(aq)$ has a constant concentration in this system.

Now for our old friends, the fractional composition equations. Abbreviating oxalic acid as H_2Ox, we can write

$F_{H_2Ox} = [H_2C_2O_4] + [HC_2O_4^-] + [C_2O_4^{2-}]$

$$[H_2Ox] = \alpha_{H_2Ox}F_{H_2Ox} = \frac{[H^+]^2F_{H_2Ox}}{[H^+]^2 + [H^+]K_1 + K_1K_2} \quad \textbf{(12-49)}$$

$$[HOx^-] = \alpha_{HOx^-}F_{H_2Ox} = \frac{K_1[H^+]F_{H_2Ox}}{[H^+]^2 + [H^+]K_1 + K_1K_2} \quad \textbf{(12-50)}$$

$$[Ox^{2-}] = \alpha_{Ox^{2-}}F_{H_2Ox} = \frac{K_1K_2F_{H_2Ox}}{[H^+]^2 + [H^+]K_1 + K_1K_2} \quad \textbf{(12-51)}$$

Also, Ba^{2+} and $BaOH^+$ are a conjugate acid-base pair. Ba^{2+} behaves as a monoprotic acid HA, and $BaOH^+$ is the conjujate base A^-.

$F_{Ba} = [Ba^{2+}] + [BaOH^+]$

$$[Ba^{2+}] = \alpha_{Ba^{2+}}F_{Ba} = \frac{[H^+]F_{Ba}}{[H^+] + K_a} \quad \textbf{(12-52)}$$

$$[BaOH^+] = \alpha_{BaOH^+}F_{Ba} = \frac{K_aF_{Ba}}{[H^+] + K_a} \quad \textbf{(12-53)}$$

Suppose that the pH is fixed by adding a buffer (and therefore the charge balance 12-46 is no longer valid). From K_{sp}, we can write

$$K_{sp} = [Ba^{2+}][C_2O_4^{2-}] = \alpha_{Ba^{2+}}F_{Ba}\alpha_{Ox^{2-}}F_{H_2Ox}$$

But the mass balance 12-47 told us that $F_{Ba} = F_{H_2Ox}$. Therefore,

$$K_{sp} = \alpha_{Ba^{2+}}F_{Ba}\alpha_{Ox^{2-}}F_{H_2Ox} = \alpha_{Ba^{2+}}F_{Ba}\alpha_{Ox^{2-}}F_{Ba}$$

$$\Rightarrow F_{Ba} = \sqrt{\frac{K_{sp}}{\alpha_{Ba^{2+}}\alpha_{Ox^{2-}}}} \quad \textbf{(12-54)}$$

In the spreadsheet in Figure 12-11, pH is specified in column A. From this pH, plus K_1 and K_2, the fractions α_{H_2Ox}, α_{HOx^-}, and $\alpha_{Ox^{2-}}$ are computed with Equations 12-49 through 12-51 in columns C, D, and E. From the pH and K_a, the fractions $\alpha_{Ba^{2+}}$ and α_{BaOH^+} are computed with Equations 12-52 and 12-53 in columns F and G. The total concentrations of barium and oxalate, F_{Ba} and F_{H_2Ox} are equal and calculated in column H from Equation 12-54. In a real spreadsheet, we would have continued to the right with column I. To fit on this page, the spreadsheet was continued in row 18. In this lower section, the concentrations of $[Ba^{2+}]$ and $[BaOH^+]$ are computed with Equations 12-52 and 12-53. $[H_2C_2O_4]$, $[HC_2O_4^-]$, and $[C_2O_4^{2-}]$ are found with Equations 12-49 through 12-51.

The net charge ($= [H^+] + 2[Ba^{2+}] + [BaOH^+] - [OH^-] - [HC_2O_4^-] - 2[C_2O_4^{2-}]$) is computed beginning in cell H19. If we had not added buffer to fix the pH, the net charge would be 0. Net charge goes from positive to negative between pH 6 and 8. By using Solver, we find the pH in cell A11 that makes the net charge 0 in cell H23 (with Solver Precision = 1e-16). This pH, 7.64, is the pH of unbuffered solution.

Results in Figure 12-12 show that the solubility of barium oxalate is steady at 10^{-3} M in the middle pH range. Solubility increases below pH 5 because $C_2O_4^{2-}$ reacts with H^+ to make $HC_2O_4^-$. Solubility increases above pH 13 because Ba^{2+} reacts with OH^- to make $BaOH^+$.

A final point is to see that the solubility of $Ba(OH)_2(s)$ is not exceeded. Evaluation of the product $[Ba^{2+}][OH^-]^2$ shows that $K_{sp} = 3 \times 10^{-4}$ is not exceeded below pH 13.9. We predict that $Ba(OH)_2(s)$ will begin to precipitate at pH 13.9.

12-4 Analyzing Acid-Base Titrations with Difference Plots[9]

Niels Bjerrum (1879–1958) was a Danish physical chemist who made fundamental contributions to inorganic coordination chemistry and is responsible for much of our understanding of acids and bases and titration curves.[10]

A *difference plot*, also called a *Bjerrum plot*, is an excellent means to extract metal-ligand formation constants or acid dissociation constants from titration data obtained with electrodes. We will apply the difference plot to an acid-base titration curve.

We derive the key equation for a diprotic acid, H_2A, and extend it to a general acid, H_nA. The mean fraction of protons bound to H_2A ranges from 0 to 2 and is defined as

$$\bar{n}_H = \frac{\text{moles of bound } H^+}{\text{total moles of weak acid}} = \frac{2[H_2A] + [HA^-]}{[H_2A] + [HA^-] + [A^{2-}]} \quad \textbf{(12-55)}$$

	A	B	C	D	E	F	G	H
1	Finding the concentrations of species in saturated barium oxalate solution							
2								
3	K_{sp} =	1.0E-06		K_1 =	5.4E-02		K_{ip} =	2.1E+02
4	K_a =	4.4E-14		K_2 =	5.42E-05		K_w =	1.0E-14
5								F_{Ba}
6	pH	$[H^+]$	$\alpha(H_2Ox)$	$\alpha(HOx^-)$	$\alpha(Ox^{2-})$	$\alpha(Ba^{2+})$	$\alpha(BaOH^+)$	$= F_{H2Ox}$
7	0	1.E+00	9.5E-01	5.1E-02	2.8E-06	1.0E+00	4.4E-14	6.0E-01
8	2	1.E-02	1.6E-01	8.4E-01	4.6E-03	1.0E+00	4.4E-12	1.5E-02
9	4	1.E-04	1.2E-03	6.5E-01	3.5E-01	1.0E+00	4.4E-10	1.7E-03
10	6	1.E-06	3.4E-07	1.8E-02	9.8E-01	1.0E+00	4.4E-08	1.0E-03
11	7.643	2.E-08	1.8E-10	4.2E-04	1.0E+00	1.0E+00	1.9E-06	1.0E-03
12	8	1.E-08	3.4E-11	1.8E-04	1.0E+00	1.0E+00	4.4E-06	1.0E-03
13	10	1.E-10	3.4E-15	1.8E-06	1.0E+00	1.0E+00	4.4E-04	1.0E-03
14	12	1.E-12	3.4E-19	1.8E-08	1.0E+00	9.6E-01	4.2E-02	1.0E-03
15	14	1.E-14	3.4E-23	1.8E-10	1.0E+00	1.9E-01	8.1E-01	2.3E-03
16								
17								net
18	pH	$[Ba^{2+}]$	$[BaOH^+]$	$[H_2Ox]$	$[HOx^-]$	$[Ox^{2-}]$	$[OH^-]$	charge
19	0	6.0E-01	2.6E-14	5.7E-01	3.1E-02	1.7E-06	1.0E-14	2.2E+00
20	2	1.5E-02	6.5E-14	2.3E-03	1.2E-02	6.7E-05	1.0E-12	2.7E-02
21	4	1.7E-03	7.4E-13	2.0E-06	1.1E-03	5.9E-04	1.0E-10	1.2E-03
22	6	1.0E-03	4.4E-11	3.4E-10	1.8E-05	9.9E-04	1.0E-08	1.9E-05
23	7.643	1.0E-03	1.9E-09	1.8E-13	4.2E-07	1.0E-03	4.4E-07	6.9E-18
24	8	1.0E-03	4.4E-09	3.4E-14	1.8E-07	1.0E-03	1.0E-06	-8.1E-07
25	10	1.0E-03	4.4E-07	3.4E-18	1.8E-09	1.0E-03	1.0E-04	-1.0E-04
26	12	9.8E-04	4.3E-05	3.5E-22	1.9E-11	1.0E-03	1.0E-02	-1.0E-02
27	14	4.3E-04	1.9E-03	7.9E-26	4.3E-13	2.3E-03	1.0E+00	-1.0E+00
28								
29	B7 = 10^-A7						B19 = F7*H7	
30	C7 = $B7^2/($B7^2+$B7*$E$3+$E$3*$E$4)						C19 = G7*H7	
31	D7 = $B7*$E$3/($B7^2+$B7*$E$3+$E$3*$E$4)						D19 = C7*H7	
32	E7 $E$3*$E$4/($B7^2+$B7*$E$3+$E$3*$E$4)						E19 = D7*H7	
33	F7 = B7/(B7+$B$4)						F19 = E7*H7	
34	G7 = $B$4/(B7+$B$4)						G19 = $H$4/B7	
35	H7 = SQRT($B$3/(E7*F7))				H19 = B7+2*B19+C19-G19-E19-2*F19			

FIGURE 12-11 Spreadsheet for saturated BaC_2O_4. Solver was used to find the pH in cell A11 necessary to make the net charge 0 in cell H23.

We can measure $\bar{n}_H$ by a titration beginning with a mixture of A mmol of H_2A and C mmol of HCl in V_0 mL. We add HCl to increase the degree of protonation of H_2A, which is partially dissociated in the absence of HCl. We titrate the solution with standard NaOH at a concentration of C_b mol/L. After adding v mL of NaOH, the number of mmol of Na^+ in the solution is $C_b v$.

To maintain a nearly constant ionic strength, the solution of H_2A plus HCl contains 0.10 M KCl, and the concentrations of H_2A and HCl are much less than 0.10 M. NaOH is sufficiently concentrated so that the added volume is small relative to V_0.

The charge balance for the titration solution is

$$[H^+] + [Na^+] + [K^+] = [OH^-] + [Cl^-]_{HCl} + [Cl^-]_{KCl} + [HA^-] + 2[A^{2-}]$$

where $[Cl^-]_{HCl}$ is from HCl and $[Cl^-]_{KCl}$ is from KCl. But $[K^+] = [Cl^-]_{KCl}$, so we cancel these terms. The net charge balance is

$$[H^+] + [Na^+] = [OH^-] + [Cl^-]_{HCl} + [HA^-] + 2[A^{2-}] \tag{12-56}$$

The denominator of Equation 12-55 is $F_{H_2A} = [H_2A] + [HA^-] + [A^{2-}]$. The numerator can be written as $2F_{H_2A} - [HA^-] - 2[A^{2-}]$. Therefore

$$\bar{n}_H = \frac{2F_{H_2A} - [HA^-] - 2[A^{2-}]}{F_{H_2A}} \tag{12-57}$$

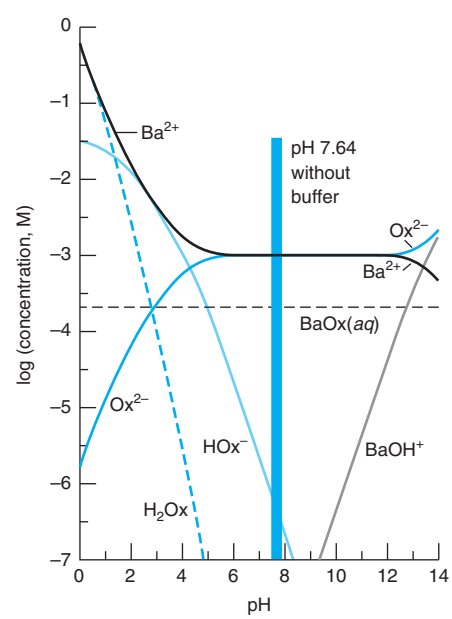


FIGURE 12-12 pH dependence of the concentrations of species in saturated BaC_2O_4. As pH is lowered, H^+ reacts with $C_2O_4^{2-}$ to make $HC_2O_4^-$ and $H_2C_2O_4$, and the concentration of Ba^{2+} increases.

From Equation 12-56, we can write: $-[HA^-] - 2[A^{2-}] = [OH^-] + [Cl^-]_{HCl} - [H^+] - [Na^+]$. Substituting this expression into the numerator of Equation 12-57 gives

$$\bar{n}_H = \frac{2F_{H_2A} + [OH^-] + [Cl^-]_{HCl} - [H^+] - [Na^+]}{F_{H_2A}} = 2 + \frac{[OH^-] + [Cl^-]_{HCl} - [H^+] - [Na^+]}{F_{H_2A}}$$

For the general polyprotic acid H_nA, the mean fraction of bound protons turns out to be

$$\bar{n}_H = n + \frac{[OH^-] + [Cl^-]_{HCl} - [H^+] - [Na^+]}{F_{H_nA}} \tag{12-58}$$

Each term on the right side of Equation 12-58 is known during the titration. From the reagents that were mixed, we can say

$$F_{H_2A} = \frac{\text{mmol } H_2A}{\text{total volume}} = \frac{A}{V_0 + v} \qquad [Cl^-]_{HCl} = \frac{\text{mmol HCl}}{\text{total volume}} = \frac{C}{V_0 + v}$$

$$[Na^+] = \frac{\text{mmol NaOH}}{\text{total volume}} = \frac{C_b v}{V_0 + v}$$

$[H^+]$ and $[OH^-]$ are measured with a pH electrode and calculated as follows: Let the effective value of K_w that applies at $\mu = 0.10$ M be $K'_w = K_w/(\gamma_{H^+}\gamma_{OH^-}) = [H^+][OH^-]$ (Equation 12-25). Remembering that $pH = -\log([H^+]\gamma_{H^+})$, we write

$$[H^+] = \frac{10^{-pH}}{\gamma_{H^+}} \qquad [OH^-] = \frac{K'_w}{[H^+]} = 10^{(pH - pK'_w)} \cdot \gamma_{H^+}$$

Substituting into Equation 12-58 gives the measured fraction of bound protons:

Experimental fraction of protons bound to polyprotic acid

$$\bar{n}_H(\text{measured}) = n + \frac{10^{(pH - pK'_w)} \cdot \gamma_{H^+} + C/(V_0 + v) - (10^{-pH})/\gamma_{H^+} - C_b v/(V_0 + v)}{A/(V_0 + v)} \tag{12-59}$$

In acid-base titrations, a **difference plot,** or *Bjerrum plot*, is a graph of the mean fraction of protons bound to an acid versus pH. The mean fraction is $\bar{n}_H$ calculated with Equation 12-59. For complex formation, the difference plot gives the mean number of ligands bound to a metal versus pL ($= -\log[\text{ligand}]$).

Equation 12-59 gives the measured value of $\bar{n}_H$. What is the theoretical value? For a diprotic acid, the theoretical mean fraction of bound protons is

If Equation 12-60 is not obvious, you can derive it from Equation12-55 by writing the right-hand side as

$$\frac{2[H_2A] + [HA^-]}{[H_2A] + [HA^-] + [A^{2-}]} = \frac{2[H_2A] + [HA^-]}{F_{H_2A}} = \frac{2[H_2A]}{F_{H_2A}} + \frac{[HA^-]}{F_{H_2A}} = 2\alpha_{H_2A} + \alpha_{HA^-}$$

$$\bar{n}_H(\text{theoretical}) = 2\alpha_{H_2A} + \alpha_{HA^-} \tag{12-60}$$

where α_{H_2A} is the fraction of acid in the form H_2A and α_{HA^-} is the fraction in the form HA^-. You should be able to write expressions for α_{H_2A} and α_{HA^-} in your sleep by now.

$$\alpha_{H_2A} = \frac{[H^+]^2}{[H^+]^2 + [H^+]K_1 + K_1K_2} \qquad \alpha_{HA^-} = \frac{[H^+]K_1}{[H^+]^2 + [H^+]K_1 + K_1K_2} \tag{12-61}$$

We extract K_1 and K_2 from an experimental titration by constructing a difference plot with Equation 12-59. This plot is a graph of $\bar{n}_H$(measured) versus pH. We then fit the theoretical curve (Equation 12-60) to the experimental curve by the method of least squares to find the values of K_1 and K_2 that minimize the sum of the squares of the residuals:

Best values of K_1 and K_2 minimize the sum of the squares of the residuals.

$$\sum(\text{residuals})^2 = \sum[\bar{n}_H(\text{measured}) - \bar{n}_H(\text{theoretical})]^2 \tag{12-62}$$

Experimental data for a titration of the amino acid glycine are given in Figure 12-13. The initial 40.0-mL solution contained 0.190 mmol of glycine plus 0.232 mmol of HCl to increase the fraction of fully protonated $^+H_3NCH_2CO_2H$. Aliquots of 0.490 5 M NaOH were added and the pH was measured after each addition. Volumes and pH are listed in columns A and B beginning in row 16. pH was precise to the 0.001 decimal place, but the accuracy of pH measurement is, at best, ±0.02.

$H_3NCH_2CO_2H$
Glycine

$pK_1 = 2.35$ at $\mu = 0$

$pK_2 = 9.78$ at $\mu = 0$

Input values of concentration, volume, and moles are in cells B3:B6 in Figure 12-13. Cell B7 has the value 2 to indicate that glycine is a diprotic acid. Cell B8 has the activity coefficient of H^+ computed with the Davies equation, 12-18. Cell B9 begins with the effective value of $pK'_w = 13.797$ in 0.1 M KCl.[11] We allowed the spreadsheet to vary pK'_w for best fit of the experimental data, giving 13.807 in cell B9. Cells B10 and B11 began with estimates of pK_1 and pK_2 for glycine. We used the values 2.35 and 9.78 from Table 9-1, which apply at $\mu = 0$. As explained in the next section, we use Solver to vary pK_1, pK_2, and pK'_w for best fit of the experimental data, giving 2.312 and 9.625 in cells B10 and B11.

	A	B	C	D	E	F	G	H	I
1	Difference plot for glycine								
2				C16 = 10^-B16/$B$8					
3	Titrant NaOH =	0.4905	C_b (M)	D16 = 10^-$B$9/C16					
4	Initial volume =	40	V_0 (mL)	E16 = $B$7+($B$6-$B$3*A16-(C16-D16)*($B$4+A16))/$B$5					
5	Glycine =	0.190	L (mmol)	F16 + $C16^2/($C16^2+$C16*$E$10+$E$10*$E$11)					
6	HCl added =	0.232	A (mmol)	G16 = $C16*$E$10/($C16^2+$C16*$E$10+$E$10*$E$11)					
7	Number of H^+ =	2	n	H16 = 2*F16+G16					
8	Activity coeff =	0.78	γ_H	I16 = (E16-H16)^2					
9	pK_w' =	13.807							
10	pK_1 =	2.312		K_1 =	0.0048713	= 10^-B10			
11	pK_2 =	9.625		K_2 =	2.371E-10	= 10^-B11			
12	$\Sigma(resid)^2$ =	0.0048	= sum of column I						
13									
14	v	pH	$[H^+]$ =	$[OH^-]$ =	Measured			Theoretical	$(residuals)^2$ =
15	mL NaOH		$(10^{-pH})/\gamma_H$	$(10^{-pKw})/[H^+]$	n_H	α_{H2A}	α_{HA^-}	n_H	$(n_{meas} - n_{theor})^2$
16	0.00	2.234	7.48E-03	2.08E-12	1.646	0.606	0.394	1.606	0.001656
17	0.02	2.244	7.31E-03	2.13E-12	1.630	0.600	0.400	1.600	0.000879
18	0.04	2.254	7.14E-03	2.18E-12	1.612	0.595	0.405	1.595	0.000319
19	0.06	2.266	6.95E-03	2.24E-12	1.601	0.588	0.412	1.588	0.000174
20	0.08	2.278	6.76E-03	2.30E-12	1.589	0.581	0.419	1.581	0.000056
21	0.10	2.291	6.56E-03	2.38E-12	1.578	0.574	0.426	1.574	0.000020
22	:								
23	0.50	2.675	2.71E-03	5.75E-12	1.353	0.357	0.643	1.357	0.000022
24	:								
25	1.56	11.492	4.13E-12	3.77E-03	0.016	0.000	0.017	0.017	0.000000
26	1.58	11.519	3.88E-12	4.01E-03	0.018	0.000	0.016	0.016	0.000004
27	1.60	11.541	3.69E-12	4.22E-03	0.015	0.000	0.015	0.015	0.000000

FIGURE 12-13 Spreadsheet for difference plot of the titration of 0.190 mmol glycine plus 0.232 mmol HCl in 40.0 mL with 0.490 5 M NaOH. Cells A16:B27 give only a fraction of the experimental data. [Complete data listed in Problem 12-16 provided by A. Kraft, Heriot-Watt University.]

The spreadsheet in Figure 12-13 computes $[H^+]$ and $[OH^-]$ in columns C and D beginning in row 16. The mean fraction of protonation, $\bar{n}_H$(measured) from Equation 12-59, is in column E. The Bjerrum difference plot in Figure 12-14 shows $\bar{n}_H$(measured) versus pH. Values of α_{H_2A} and α_{HA^-} from Equations 12-61 are computed in columns F and G and $\bar{n}_H$(theoretical) was computed with Equation 12-60 in column H. Column I contains the squares of the residuals, $[\bar{n}_H(\text{measured}) - \bar{n}_H(\text{theoretical})]^2$. The sum of the squares of the residuals is in cell B12.

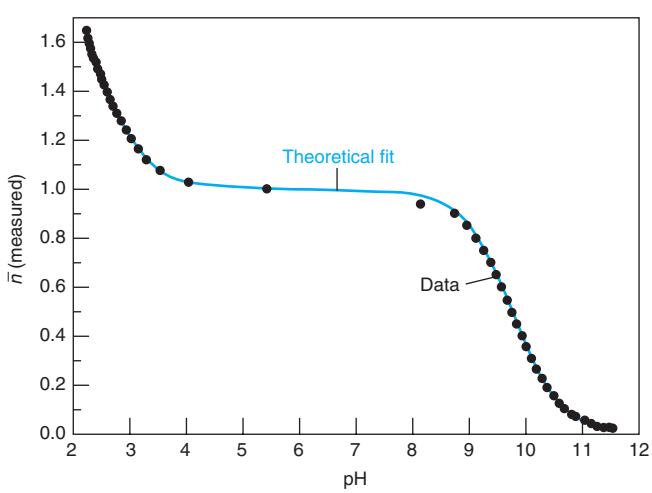


FIGURE 12-14 Bjerrum difference plot for the titration of glycine. Many experimental points are omitted from the figure for clarity.

Using Excel Solver to Optimize More Than One Parameter

We want values of pK_w', pK_1, and pK_2 that minimize the sum of squares of residuals in cell B12. Select Solver. In the Solver window, Set Target Cell B12 Equal To Min By Changing Cells B9, B10, B11. Then click Solve, and Solver finds the best values in cells B9, B10, and B11 to minimize the sum of squares of residuals in cell B12. Starting with 13.797, 2.35, and 9.78 in cells B9, B10, and B11 gives a sum of squares of residuals equal to 0.110 in cell B12.

After Solver is executed, cells B9, B10, and B11 become 13.807, 2.312, and 9.625. The sum in cell B12 is reduced to 0.004 8. When you use Solver to optimize several parameters at once, it is a good idea to try different starting values to see if the same solution is reached. Sometimes a local minimum can be reached that is not as low as another that might be reached elsewhere.

The theoretical curve $\bar{n}_H(\text{theoretical}) = 2\alpha_{H_2A} + \alpha_{HA^-}$ based on the results of Solver are contained in columns F, G, and H in Figure 12-13 and shown by the solid curve in Figure 12-14. The curve fits the experimental data well, a result suggesting that we have found reliable values of pK_1 and pK_2.

Strictly speaking, pK_1 and pK_2 should have primes to indicate that they apply in 0.10 M KCl. We left off the primes to avoid complicating the symbols. We did distinguish K_w, which applies at $\mu = 0$, from K'_w, which applies at $\mu = 0.10$ M.

It may seem inappropriate to allow pK'_w to vary, because we claimed to know pK'_w at the outset. The change of pK'_w from 13.797 to 13.807 significantly improved the fit. The value 13.797 gave values of $\bar{n}_H$(measured) that became level near 0.04 at the end of the titration in Figure 12-14. This behavior is qualitatively incorrect, because $\bar{n}_H$ must approach 0 at high pH. A small change in pK'_w markedly improves the fit as $\bar{n}_H$ approaches 0.

Terms to Understand

coupled equilibria

difference plot

Summary

Coupled equilibria are reversible reactions that have a species in common. Therefore, each reaction has an effect on the other.

The general treatment of acid-base systems begins with charge and mass balances and equilibrium expressions. There should be as many independent equations as chemical species. Substitute a fractional composition equation for each acid or base into the charge balance. After you enter known concentrations of species such as Na^+ and Cl^-, and substitute $K_w/[H^+]$ for $[OH^-]$, the remaining variable should be $[H^+]$. Use Excel Solver to find $[H^+]$ and then solve for all other concentrations from $[H^+]$. If there are equilibria in addition to acid-base reactions, such as ion pairing, then you need the full systematic treatment of equilibrium. Make maximum use of fractional composition equations to simplify the problem.

To use activity coefficients, first solve the equilibrium problem with all activity coefficients equal to unity. From the resulting concentrations, compute the ionic strength and use the Davies equation to find activity coefficients. With activity coefficients, calculate the effective equilibrium constant K' for each chemical reaction. K' is the equilibrium quotient of concentrations at a particular ionic strength. Solve the problem again with K' values and find a new ionic strength. Repeat the cycle until the concentrations reach constant values.

We considered solubility problems in which the cation and anion could each undergo one or more acid-base reactions and in which ion pairing could occur. Substitute fractional composition expressions for all acid-base species into the mass balance. In some systems, such as barium oxalate, the resulting equation contains the formal concentrations of anion and cation and $[H^+]$. The solubility product provides a relation between the formal concentrations of anion and cation, so you can eliminate one of them from the mass balance. By assuming a value for $[H^+]$, you can solve for the remaining formal concentration and, therefore, for all concentrations. By this means, find the composition as a function of pH. The pH of the unbuffered solution is the pH at which the charge balance is satisfied.

In the more difficult calcium fluoride solubility problem, ion pairing prevented us from reducing the equations to one unknown. Instead, $[H^+]$ and $[F^-]$ were both unknown. However, for a fixed value of $[H^+]$, we could use Solver to solve for $[F^-]$. The correct pH is the one at which the charge balance is satisfied.

To extract acid dissociation constants from an acid-base titration curve, we can construct a difference plot, or Bjerrum plot, which is a graph of the mean fraction of bound protons, $\bar{n}_H$, versus pH. This mean fraction can be measured from the quantities of reagents that were mixed and the measured pH. The theoretical shape of the difference plot is an expression in terms of fractional compositions. Use Excel Solver to vary equilibrium constants to obtain the best fit of the theoretical curve to the measured points. This process minimizes the sum of squares $[\bar{n}_H(\text{measured}) - \bar{n}_H(\text{theoretical})]^2$.

Exercises

Instructors: Most of these problems are quite long. Please be kind when you assign them.

12-A. Neglecting activity coefficients and ion pairing, find the pH and concentrations of species in 1.00 L of solution containing 0.010 mol hydroxybenzene (HA), 0.030 mol dimethylamine (B), and 0.015 mol HCl.

12-B. Repeat Exercise 12-A with activity coefficients from the Davies equation.

12-C. **(a)** Neglecting activity coefficients and ion pairing, find the pH and concentrations of species in 1.00 L of solution containing 0.040 mol 2-aminobenzoic acid (a neutral molecule, HA), 0.020 mol dimethylamine (B), and 0.015 mol HCl.

(b) What fraction of HA is in each of its three forms? What fraction of B is in each of its two forms? Compare your answers with what you would find if HCl reacted with B and then excess B reacted with HA. What pH do you predict from this simple estimate?

12-D. Include activity coefficients from the Davies equation to find the pH and concentrations of species in the mixture of sodium tartrate, pyridinium chloride, and KOH in Section 12-1. Consider only Reactions 12-1 through 12-4.

12-E. **(a)** Using the ion-pair equilibrium constant from Appendix J, with activity coefficients = 1, find the concentrations of species in 0.025 M $MgSO_4$. Hydrolysis of the cation and anion near neutral pH is negligible. Only consider ion-pair formation. You can solve this problem exactly with a quadratic equation. Alternatively, if you use Solver, set Precision to 1e-6 (not 1e-16) in the Solver Options. If Precision is much smaller, Solver does not find a satisfactory solution. The success of Solver in this problem depends on how close your initial guess is to the correct answer.

(b) Compute a new ionic strength and repeat part (**a**) with new activity coefficients from the Davies equation. Perform several iterations until the ionic strength is constant. The fraction of ion pairing that you find should be close to that in Box 7-1, which was derived with Debye-Hückel activity coefficients.

(c) We naively assigned the ionic strength of 0.025 M $MgSO_4$ to be 0.10 M. What is the actual ionic strength of this solution?

12-F. **(a)** Find the concentrations of species in saturated CaF_2 as a function of pH by using Reactions 12-32 through 12-36 and adding the following reaction:

$$HF(aq) + F^- \rightleftharpoons HF_2^- \qquad K_{HF_2^-} = 10^{0.58}$$

Do not include activity coefficients. Produce a graph similar to Figure 12-7.

(b) Find the pH and concentrations of species in saturated CaF_2.

12-G. Make a graph of $[Ag^+]$, $[AgOH(aq)]$, $[CN^-]$, and $[HCN]$ as a function of pH in a saturated solution of AgCN. Consider the following equilibria and do not consider activity coefficients. Find the pH if no buffer were added.

$$AgCN(s) \rightleftharpoons Ag^+ + CN^- \qquad pK_{sp} = 15.66$$

$$HCN(aq) \rightleftharpoons CN^- + H^+ \qquad pK_{HCN} = 9.21$$

$$Ag^+ + H_2O \rightleftharpoons AgOH(aq) + H^+ \qquad pK_{Ag} = 12.0$$

12-H. *Difference plot.* A solution containing 3.96 mmol acetic acid plus 0.484 mmol HCl in 200 mL of 0.10 M KCl was titrated with 0.490 5 M NaOH to measure K_a for acetic acid.

(a) Write expressions for the experimental mean fraction of protonation, $\bar{n}_H$(measured), and the theoretical mean fraction of protonation, $\bar{n}_H$(theoretical).

(b) From the following data, prepare a graph of $\bar{n}_H$(measured) versus pH. Find the best values of pK_a and pK'_w by minimizing the sum of the squares of the residuals, $\sum[\bar{n}_H(\text{measured}) - \bar{n}_H(\text{theoretical})]^2$.

V (mL)	pH	V (mL)	pH	V (mL)	pH	V (mL)	pH
0.00	2.79	2.70	4.25	5.40	4.92	8.10	5.76
0.30	2.89	3.00	4.35	5.70	4.98	8.40	5.97
0.60	3.06	3.30	4.42	6.00	5.05	8.70	6.28
0.90	3.26	3.60	4.50	6.30	5.12	9.00	7.23
1.20	3.48	3.90	4.58	6.60	5.21	9.30	10.14
1.50	3.72	4.20	4.67	6.90	5.29	9.60	10.85
1.80	3.87	4.50	4.72	7.20	5.38	9.90	11.20
2.10	4.01	4.80	4.78	7.50	5.49	10.20	11.39
2.40	4.15	5.10	4.85	7.80	5.61	10.50	11.54

Data from A. Kraft, J. Chem. Ed. ***2003****, 80, 554.*

Problems

Instructors: Most of these problems are quite long. Please be kind when you assign them.

12-1. Why does the solubility of a salt of a basic anion increase with decreasing pH? Write chemical reactions for the minerals galena (PbS) and cerussite ($PbCO_3$) to explain how acid rain mobilizes traces of metal from relatively inert forms into the environment, where the metals can be taken up by plants and animals.

12-2. **(a)** Considering just acid-base chemistry, not ion pairing and not activity coefficients, use the systematic treatment of equilibrium to find the pH of 1.00 L of solution containing 0.010 0 mol hydroxybenzene (HA) and 0.005 0 mol KOH.

(b) What pH would you have predicted from your knowledge of Chapter 8?

(c) Find the pH if [HA] and [KOH] were both reduced by a factor of 100.

12-3. Repeat part (**a**) of Problem 12-2 with Davies activity coefficients. Remember that $pH = -\log([H^+]\gamma_{H^+})$.

12-4. From pK_1 and pK_2 for glycine at $\mu = 0$ in Table 9-1, compute pK'_1 and pK'_2 that apply at $\mu = 0.1$ M. Use the Davies equation for activity coefficients. Compare your answer with experimental values in cells B10 and B11 of Figure 12-13.

12-5. Considering just acid-base chemistry, not ion pairing and not activity coefficients, use the systematic treatment of equilibrium to find the pH and concentrations of species in 1.00 L of solution containing 0.100 mol ethylenediamine and 0.035 mol HBr. Compare the pH to that found by the methods of Chapter 10.

12-6. Considering just acid-base chemistry, not ion pairing and not activity coefficients, find the pH and concentrations of species in 1.00 L of solution containing 0.040 mol benzene-1,2,3-tricarboxylic acid (H_3A), 0.030 mol imidazole (a neutral molecule, HB), and 0.035 mol NaOH.

12-7. Considering just acid-base chemistry, not ion pairing and not activity coefficients, find the pH and concentrations of species in 1.00 L of solution containing 0.020 mol arginine, 0.030 mol glutamic acid, and 0.005 mol KOH.

12-8. Solve Problem 12-7 by using Davies activity coefficients.

12-9. A solution containing 0.008 695 *m* KH_2PO_4 and 0.030 43 *m* Na_2HPO_4 is a primary standard buffer with a stated pH of 7.413 at 25°C. Calculate the pH of this solution by using the systematic treatment of equilibrium with activity coefficients from **(a)** the Davies equation and **(b)** the extended Debye-Hückel equation.

12-10. Considering just acid-base chemistry, not ion pairing and not activity coefficients, find the pH and composition of 1.00 L of solution containing 0.040 mol H_4EDTA (EDTA = ethylenedinitrilotetraacetic acid ≡ H_4A), 0.030 mol lysine (neutral molecule ≡ HL), and 0.050 mol NaOH.

12-11. The solution containing no added KNO_3 for Figure 7-1 contains 5.0 mM $Fe(NO_3)_3$, 5.0 μM NaSCN, and 15 mM HNO_3. We

will use Davies activity coefficients to find the concentrations of all species in the following reactions:

$$Fe^{3+} + SCN^- \rightleftharpoons Fe(SCN)^{2+} \qquad \log \beta_1 = 3.03\ (\mu = 0)$$
$$Fe^{3+} + 2SCN^- \rightleftharpoons Fe(SCN)_2^+ \qquad \log \beta_2 = 4.6\ (\mu = 0)$$
$$Fe^{3+} + H_2O \rightleftharpoons FeOH^{2+} + H^+ \qquad pK_a = 2.195\ (\mu = 0)$$

This problem is harder than you might think, so we will guide you through the steps.

(a) Write the four equilibrium expressions (including K_w). Express the effective equilibrium constants in terms of equilibrium constants and activity coefficients. For example, $K'_w = K_w/\gamma_{H^+}\gamma_{OH^-}$. Write expressions for $[Fe(SCN)^{2+}]$, $[Fe(SCN)_2^+]$, $[FeOH^{2+}]$, and $[OH^-]$ in terms of $[Fe^{3+}]$, $[SCN^-]$, and $[H^+]$.

(b) Write the charge balance.

(c) Write mass balances for iron, thiocyanate, Na^+, and NO_3^-.

(d) Substitute expressions from part (**a**) into the mass balance for thiocyanate to find an expression for $[Fe^{3+}]$ in terms of $[SCN^-]$.

(e) Substitute expressions from part (**a**) into the mass balance for iron to find an expression for $[H^+]$ in terms of $[Fe^{3+}]$ and $[SCN^-]$.

(f) In a spreadsheet, guess a value for $[SCN^-]$. From this value, compute $[Fe^{3+}]$ from part (**d**). From $[SCN^-]$ and $[Fe^{3+}]$, compute $[H^+]$ from part (**e**).

(g) Compute the concentrations of all other species from $[SCN^-]$, $[Fe^{3+}]$, and $[H^+]$.

(h) Compute the net charge. We want to vary $[SCN^-]$ to reduce the net charge to 0. When the net charge is 0, you have the correct concentrations. Solver did not work well for these equations. You have several recourses. One is to use Goal Seek, which is similar to Solver but only handles one unknown. Start with $\mu = 0$ and guess $[SCN^-]$ = 1e-6. In Excel 2007, click on the Microsoft Office button at the upper left of the spreadsheet. Click on Excel Options and select Formulas. In Calculation Options, set Maximum Change to 1e-16 and click OK. On the Data ribbon, click on What-If Analysis and then Goal Seek. In the Goal Seek dialog box, set Maximum Change to 1e-16. Set cell {net charge} To value 0 By changing cell {[SCN⁻]}. Click OK and Goal Seek finds a solution. Calculate the new ionic strength and activity coefficients from the Davies equation. Calculate effective equilibrium constants. Repeat the process until μ is constant to three significant digits. If Goal Seek fails to work at some stage, vary $[SCN^-]$ by hand to reduce the net charge to near 0. When you are close to a correct answer, Goal Seek can take you the rest of the way. When you have a solution, verify that mass balances are satisfied and compute $pH = -\log([H^+]\gamma_{H^+})$.

In earlier versions of Excel, go to the Tools menu, select Options and Calculation. Set Maximum Change to 1e-16. Then select Goal Seek from the Tools menu and continue as described above.

(i) Find the quotient $[Fe(SCN)^{2+}]/(\{[Fe^{3+}] + [FeOH^{2+}]\}[SCN^-])$. This is the point for $[KNO_3] = 0$ in Figure 7-1. Compare your answer with Figure 7-1. The ordinate of Figure 7-1 is labeled $[Fe(SCN)^{2+}]/([Fe^{3+}][SCN^-])$, but $[Fe^{3+}]$ really refers to the total concentration of iron not bound to thiocyanate.

(j) Find the quotient in part (**i**) when the solution also contains 0.20 M KNO_3. Compare your answer with Figure 7-1.

12-12. **(a)** Follow the steps of Problem 12-11 to solve this one. From the following equilibria, find the concentrations of species and the pH of 1.0 mM $La_2(SO_4)_3$. Use Davies activity coefficients. You may wish to use Goal Seek in place of Solver as described in Problem 12-11.

$$La^{3+} + SO_4^{2-} \rightleftharpoons La(SO_4)^+ \qquad \beta_1 = 10^{3.64}\ (\mu = 0)$$
$$La^{3+} + 2SO_4^{2-} \rightleftharpoons La(SO_4)_2^- \qquad \beta_2 = 10^{5.3}\ (\mu = 0)$$
$$La^{3+} + H_2O \rightleftharpoons LaOH^{2+} + H^+ \qquad K_a = 10^{-8.5}\ (\mu = 0)$$

(b) If $La_2(SO_4)_3$ were a strong electrolyte, what would be the ionic strength of 1.0 mM $La_2(SO_4)_3$? What is the actual ionic strength of this solution?

(c) What fraction of lanthanum is La^{3+}?

(d) Why did we not consider hydrolysis of SO_4^{2-} to give HSO_4^-?

(e) Will $La(OH)_3(s)$ precipitate in this solution?

12-13. Find the pH and composition of saturated $CaSO_4$ in water, considering Reactions 7-23 to 7-27 and using Davies activity coefficients. *Suggested procedure:* Use activity coefficients in all equilibrium expressions. Let the initial ionic strength be 0. (i) In the mass balance 7-29, express $[CaOH^+]$ in terms of $[Ca^{2+}]$ and $[H^+]$. Express $[HSO_4^-]$ in terms of $[SO_4^{2-}]$ and $[OH^-]$. (ii) From the K_{sp} equilibrium expression, express $[SO_4^{2-}]$ in terms of $[Ca^{2+}]$. From the K_w equilibrium, express $[OH^-]$ in terms of $[H^+]$. The mass balance now contains only $[Ca^{2+}]$, $[H^+]$, and equilibrium constants. (iii) Solve for $[Ca^{2+}]$ in terms of $[H^+]$. (iv) Set up a spreadsheet in which pH is the input. Guess an initial value pH = 7.00. Compute $[H^+] = 10^{-pH}/\gamma_{H^+}$. (v) From $[H^+]$, compute $[OH^-]$, $[Ca^{2+}]$, $[CaOH^+]$, $[SO_4^{2-}]$, and $[HSO_4^-]$. (vi) Compute the net charge of the solution from charge balance 7-28. (vii) Use Solver or Goal Seek to vary pH until the net charge is 0 ($<1 \times 10^{-18}$ M). (viii) Compute the ionic strength. (ix) With the new ionic strength, use Solver again to find the pH that reduces the net charge to $<1 \times 10^{-18}$ M. Perform several iterations until ionic strength no longer changes.

12-14. Find the composition of a saturated solution of AgCN containing 0.10 M KCN adjusted to pH 12.00 with NaOH. Consider the following equilibria and use Davies activity coefficients.

$$AgCN(s) \rightleftharpoons Ag^+ + CN^- \qquad pK_{sp} = 15.66$$
$$HCN(aq) \rightleftharpoons CN^- + H^+ \qquad pK_{HCN} = 9.21$$
$$Ag^+ + H_2O \rightleftharpoons AgOH(aq) + H^+ \qquad pK_{Ag} = 12.0$$
$$Ag^+ + CN^- + OH^- \rightleftharpoons Ag(OH)(CN)^- \qquad \log K_{AgOHCN} = 13.22$$
$$Ag^+ + 2CN^- \rightleftharpoons Ag(CN)_2^- \qquad \log \beta_2 = 20.48$$
$$Ag^+ + 3CN^- \rightleftharpoons Ag(CN)_3^{2-} \qquad \log \beta_3 = 21.7$$

Suggested procedure: Let $[CN^-]$ be the master variable. We know $[H^+]$ from the pH, and we can find $[Ag^+] = K'_{sp}/[CN^-]$. (i) Use equilibrium expressions to find $[OH^-]$, [HCN], [AgOH], $[Ag(OH)(CN)^-]$, $[Ag(CN)_2^-]$, and $[Ag(CN)_3^{2-}]$ in terms of $[CN^-]$, $[Ag^+]$, and $[H^+]$. (ii) Key mass balance: {total silver} + $[K^+]$ = {total cyanide}. (iii) Guess that ionic strength = 0.10 M and compute activity coefficients. (iv) Compute $[H^+] = 10^{-pH}/\gamma_{H^+}$. (v) Guess a value of $[CN^-]$ and compute the concentrations of all species in the mass balance. (vi) Use Solver to vary $[CN^-]$ to satisfy the mass balance. (vii) Compute $[Na^+]$ from the charge balance. (viii) Compute the ionic strength and perform several iterations of the entire process until the ionic strength no longer changes.

12-15. Consider the reactions of Fe^{2+} with the amino acid glycine:

$$Fe^{2+} + G^- \rightleftharpoons FeG^+ \qquad \log \beta_1 = 4.31$$
$$Fe^{2+} + 2G^- \rightleftharpoons FeG_2(aq) \qquad \log \beta_2 = 7.65$$
$$Fe^{2+} + 3G^- \rightleftharpoons FeG_3^- \qquad \log \beta_3 = 8.87$$
$$Fe^{2+} + H_2O \rightleftharpoons FeOH^+ + H^+ \qquad pK_a = 9.4$$
$$^+H_3NCH_2CO_2H \quad \text{glycine, } H_2G^+ \qquad pK_1 = 2.350,\ pK_2 = 9.778$$

Suppose that 0.050 mol of FeG_2 is dissolved in 1.00 L and enough HCl is added to adjust the pH to 8.50. Use Davies activity coefficients to find the composition of the solution. What fraction of iron is in each of its forms, and what fraction of glycine is in each of its forms? From the distribution of species, explain the principal chemistry that requires addition of HCl to obtain a pH of 8.50.

Suggested procedure: (i) Use equilibrium expressions to write all concentrations in terms of $[G^-]$, $[Fe^{2+}]$, and $[H^+]$. (ii) Write one mass balance for iron and one for glycine. (iii) Substitute expressions from step (i) into the mass balance for iron to find $[Fe^{2+}]$ in terms of $[G^-]$ and $[H^+]$. (iv) Guess an ionic strength of 0.01 M and compute activity coefficients. (v) Compute $[H^+] = 10^{-pH}/\gamma_{H^+}$. (vi) Guess a value of $[G^-]$ and compute all concentrations in the mass balance for glycine. (vii) Use Solver to vary $[G^-]$ to satisfy the mass balance for glycine. (viii) Compute $[Cl^-]$ from the charge balance. (ix) Compute the ionic strength and perform several iterations of the entire process until the ionic strength no longer changes.

12-16. Data for the glycine difference plot in Figure 12-14 are given below.

v (mL)	pH	v (mL)	pH	v (mL)	pH	v (mL)	pH
0.00	2.234	0.40	2.550	0.80	3.528	1.20	10.383
0.02	2.244	0.42	2.572	0.82	3.713	1.22	10.488
0.04	2.254	0.44	2.596	0.84	4.026	1.24	10.595
0.06	2.266	0.46	2.620	0.86	5.408	1.26	10.697
0.08	2.278	0.48	2.646	0.88	8.149	1.28	10.795
0.10	2.291	0.50	2.675	0.90	8.727	1.30	10.884
0.12	2.304	0.52	2.702	0.92	8.955	1.32	10.966
0.14	2.318	0.54	2.736	0.94	9.117	1.34	11.037
0.16	2.333	0.56	2.768	0.96	9.250	1.36	11.101
0.18	2.348	0.58	2.802	0.98	9.365	1.38	11.158
0.20	2.363	0.60	2.838	1.00	9.467	1.40	11.209
0.22	2.380	0.62	2.877	1.02	9.565	1.42	11.255
0.24	2.397	0.64	2.920	1.04	9.660	1.44	11.296
0.26	2.413	0.66	2.966	1.06	9.745	1.46	11.335
0.28	2.429	0.68	3.017	1.08	9.830	1.48	11.371
0.30	2.448	0.70	3.073	1.10	9.913	1.50	11.405
0.32	2.467	0.72	3.136	1.12	10.000	1.52	11.436
0.34	2.487	0.74	3.207	1.14	10.090	1.54	11.466
0.36	2.506	0.76	3.291	1.16	10.183	1.56	11.492
0.38	2.528	0.78	3.396	1.18	10.280	1.58	11.519
						1.60	11.541

Data from A. Kraft, J. Chem. Ed. ***2003****, 80, 554.*

(a) Reproduce the spreadsheet in Figure 12-13 and show that you get the same values of pK_1 and pK_2 in cells B10 and B11 after executing Solver. Start with different values of pK_1 and pK_2 and see if Solver finds the same solutions.

(b) Use Solver to find the best values of pK_1 and pK_2 while fixing pK'_w at its expected value of 13.797. Describe how $\bar{n}_H$(measured) behaves when pK'_w is fixed.

12-17. *Difference plot.* A solution containing 0.139 mmol of the triprotic acid tris(2-aminoethyl)amine · 3HCl plus 0.115 mmol HCl in 40 mL of 0.10 M KCl was titrated with 0.490 5 M NaOH to measure acid dissociation constants.

$$N(CH_2CH_2NH_3^+)_3 \cdot 3Cl^-$$

Tris(2-aminoethyl)amine · 3HCl

$H_3A^{3+} \cdot 3Cl^-$

(a) Write expressions for the experimental mean fraction of protonation, $\bar{n}_H$(measured), and the theoretical mean fraction of protonation, $\bar{n}_H$(theoretical).

(b) From the following data, prepare a graph of $\bar{n}_H$(measured) versus pH. Find the best values of pK_1, pK_2, pK_3, and pK'_w by minimizing the sum of the squares of the residuals, $\Sigma[\bar{n}_H(\text{measured}) - \bar{n}_H(\text{theoretical})]^2$.

v (mL)	pH	v (mL)	pH	v (mL)	pH	v (mL)	pH
0.00	2.709	0.36	8.283	0.72	9.687	1.08	10.826
0.02	2.743	0.38	8.393	0.74	9.748	1.10	10.892
0.04	2.781	0.40	8.497	0.76	9.806	1.12	10.955
0.06	2.826	0.42	8.592	0.78	9.864	1.14	11.019
0.08	2.877	0.44	8.681	0.80	9.926	1.16	11.075
0.10	2.937	0.46	8.768	0.82	9.984	1.18	11.128
0.12	3.007	0.48	8.851	0.84	10.042	1.20	11.179
0.14	3.097	0.50	8.932	0.86	10.106	1.22	11.224
0.16	3.211	0.52	9.011	0.88	10.167	1.24	11.268
0.18	3.366	0.54	9.087	0.90	10.230	1.26	11.306
0.20	3.608	0.56	9.158	0.92	10.293	1.28	11.344
0.22	4.146	0.58	9.231	0.94	10.358	1.30	11.378
0.24	5.807	0.60	9.299	0.96	10.414	1.32	11.410
0.26	6.953	0.62	9.367	0.98	10.476	1.34	11.439
0.28	7.523	0.64	9.436	1.00	10.545	1.36	11.468
0.30	7.809	0.66	9.502	1.02	10.615	1.38	11.496
0.32	8.003	0.68	9.564	1.04	10.686	1.40	11.521
0.34	8.158	0.70	9.626	1.06	10.756		

Data from A. Kraft, J. Chem. Ed. ***2003****, 80, 554.*

(c) Create a fractional composition graph showing the fractions of H_3A^{3+}, H_2A^{2+}, HA^+, and A as a function of pH.

12-18. **(a)** For the following reactions, prepare a diagram showing log(concentration) versus pH for all species in the pH range 2 to 12 for a solution made by dissolving 0.025 mol $CuSO_4$ in 1.00 L. Equilibrium constants apply at $\mu = 0.1$ M, which you should assume is constant. Do not use activity coefficients, because the equilibrium constants already apply at $\mu = 0.1$ M.

$Cu^{2+} + SO_4^{2-} \rightleftharpoons CuSO_4(aq)$	$\log K'_{ip} = 1.26$
$HSO_4^- \rightleftharpoons SO_4^{2-} + H^+$	$\log K'_a = -1.54$
$Cu^{2+} + OH^- \rightleftharpoons CuOH^+$	$\log \beta'_1 = 6.1$
$Cu^{2+} + 2OH^- \rightleftharpoons Cu(OH)_2(aq)$	$\log \beta'_2 = 11.2$*
$Cu^{2+} + 3OH^- \rightleftharpoons Cu(OH)_3^-$	$\log \beta'_3 = 14.5$*
$Cu^{2+} + 4OH^- \rightleftharpoons Cu(OH)_4^{2-}$	$\log \beta'_4 = 15.6$*
$2Cu^{2+} + OH^- \rightleftharpoons Cu_2(OH)^{3+}$	$\log \beta'_{12} = 8.2$*
$2Cu^{2+} + 2OH^- \rightleftharpoons Cu_2(OH)_2^{2+}$	$\log \beta'_{22} = 16.8$
$3Cu^{2+} + 4OH^- \rightleftharpoons Cu_3(OH)_4^{2+}$	$\log \beta'_{43} = 33.5$
$H_2O \rightleftharpoons H^+ + OH^-$	$\log K'_w = -13.79$

*Asterisk indicates that equilibrium constant was estimated for $\mu = 0.1$ M from data reported for a different ionic strength.

Remember that $pH = -\log([H^+]\gamma_{H^+})$ and $[OH^-] = K'_w/[H^+]$. Use $\gamma_{H^+} = 0.78$ for this problem.

Recommended procedure: From the mass balance for sulfate, find an expression for $[SO_4^{2-}]$ in terms of $[Cu^{2+}]$ and $[H^+]$. Set up a spreadsheet with pH values between 2 and 12 in column A. From pH,

compute $[H^+]$ and $[OH^-]$ in columns B and C. *Guess* a value for $[Cu^{2+}]$ in column D. From $[H^+]$ and $[Cu^{2+}]$, calculate $[SO_4^{2-}]$ from the equation derived from the mass balance for sulfate. From $[H^+]$, $[OH^-]$, $[Cu^{2+}]$, and $[SO_4^{2-}]$, calculate all other concentrations by using equilibrium expressions. Find the total concentration of Cu by adding the concentrations of all the species. Use Solver to vary $[Cu^{2+}]$ in column D so that the total concentration of copper is 0.025 M. You need to use Solver for each line in the spreadsheet with a different pH.

(b) Find the pH of 0.025 M $CuSO_4$ if nothing is added to adjust the pH. This is the pH at which the net charge is 0.

(c) At what pH does each of the following salts precipitate from 0.025 M $CuSO_4$?

$$Cu(OH)_{1.5}(SO_4)_{0.25}(s) \rightleftharpoons Cu^{2+} + 1.5OH^- + 0.25SO_4^{2-} \qquad \log K'_{sp}(\text{OH-SO}_4) = -16.68$$

$$Cu(OH)_2(s) \rightleftharpoons Cu^{2+} + 2OH^- \qquad \log K'_{sp}(\text{OH}) = -18.7^*$$

$$CuO(s) + H_2O \rightleftharpoons Cu^{2+} + 2OH^- \qquad \log K'_{sp}(\text{O}) = -19.7^*$$

*Asterisk indicates that equilibrium constant was estimated for $\mu = 0.1$ M from data reported for a different ionic strength.

12-19. *Ion-pairing in acid-base systems.* This problem incorporates ion-pair equilibria 12-12 and 12-13 into the acid-base chemistry of Section 12-1.

(a) From mass balance 12-15, derive Equation 12-16.

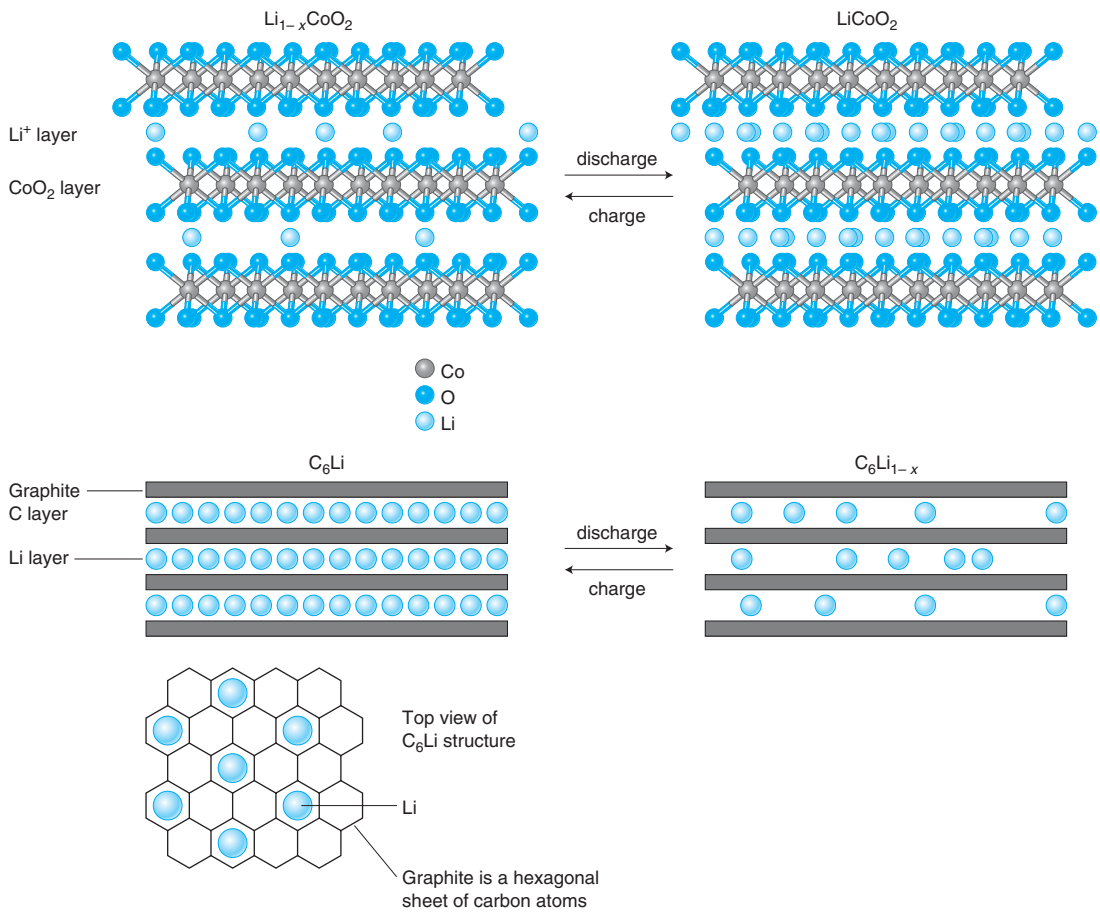
(b) Substitute equilibrium expressions into mass balance 12-17 to derive an expression for $[T^{2-}]$ in terms of $[H^+]$, $[Na^+]$, and various equilibrium constants.

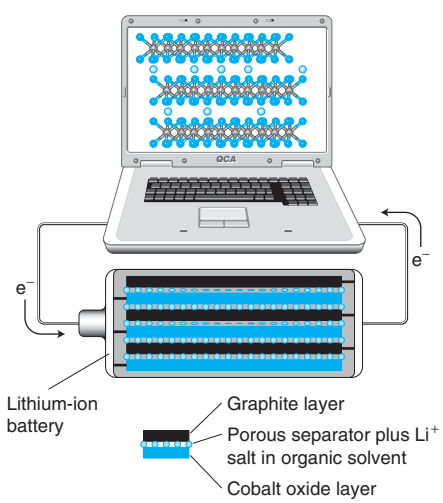
(c) With the same approach used in part **(b),** derive expressions for $[HT^-]$ and $[H_2T]$.

(d) Add the species $[NaT^-]$ and [NaHT] to the spreadsheet in Figure 12-1 and compute the composition and pH of the solution. Compute $[Na^+]$ with Equation 12-16. Compute $[H_2T]$, $[HT^-]$, and $[T^{2-}]$ from the expressions derived in parts **(b)** and **(c).** Excel will indicate a *circular reference* problem because, for example, the formula for $[Na^+]$ depends on $[T^{2-}]$ and the formula for $[T^{2-}]$ depends on $[Na^+]$. To handle this circular reference in Excel 2007, click the Microsoft Office button at the upper left of the spreadsheet. Click on Excel Options at the bottom of the window. Select Formulas. In Calculation Options, check Enable iterative calculation. Click OK and then use Solver to find the pH in cell H13 that reduces the net charge in cell E15 to (near) zero. In earlier versions of Excel, select the Tools menu and go to Options. Select the Calculations tab and choose Iteration. Click OK and then run Solver.

13 Fundamentals of Electrochemistry

LITHIUM-ION BATTERY





Direction of electron flow from lithium battery to laptop computer.

High-capacity, rechargeable lithium-ion batteries, such as those in cell phones and laptop computers, are a shining example of the fruits of materials chemistry research. The idealized chemistry is

$$C_6Li + Li_{1-x}CoO_2 \underset{\text{charge}}{\overset{\text{discharge}}{\rightleftharpoons}} C_6Li_{1-x} + LiCoO_2$$

In C_6Li, lithium atoms reside between layers of carbon in graphite. Atoms or molecules located between layers of a structure are said to be *intercalated*. During operation of the battery, lithium ions migrate from graphite to cobalt oxide. Lithium atoms leave electrons behind in the graphite, and the resulting Li^+ ions become intercalated between CoO_2 layers. To go from graphite to cobalt oxide, Li^+ passes through an electrolyte consisting of a lithium salt dissolved in a high-boiling organic solvent. A porous polymer separator between graphite and cobalt oxide is an electrical insulator that permits Li^+ ions to pass. Electrons travel through the external circuit to reach the cobalt oxide and maintain electroneutrality.

A single-cell lithium-ion battery produces ~3.7 volts. These batteries store twice as much energy per unit mass as the nickel-metal hydride batteries they replaced. Ongoing research is aimed at improved materials and high-area microstructures for the electrodes and the separator layer. Goals include higher energy density, longer life, and safer operation. Batteries are *galvanic cells*, which are the subject of this chapter. A galvanic cell uses a favorable chemical reaction to produce electricity.

Electrochemistry is a major branch of analytical chemistry that uses electrical measurements of chemical systems for analytical purposes.[1,2] For example, the opening of Chapter 1 showed an electrode being used to measure neurotransmitter molecules released by a nerve cell. Electrochemistry also refers to the use of electricity to drive a chemical reaction or to the use of a chemical reaction to produce electricity.

13-1 Basic Concepts

Oxidation: loss of electrons
Reduction: gain of electrons
Oxidizing agent: takes electrons
Reducing agent: gives electrons

A **redox reaction** involves transfer of electrons from one species to another. A species is said to be **oxidized** when it *loses electrons*. It is **reduced** when it *gains electrons*. An **oxidizing agent,** also called an **oxidant,** takes electrons from another substance and becomes reduced. A **reducing agent,** also called a **reductant,** gives electrons to another substance and is oxidized in the process. In the reaction

$$\underset{\text{Oxidizing agent}}{Fe^{3+}} + \underset{\text{Reducing agent}}{V^{2+}} \rightarrow Fe^{2+} + V^{3+} \qquad (13\text{-}1)$$

$$Fe^{3+} + e^- \rightarrow Fe^{2+}$$
$$V^{2+} \rightarrow V^{3+} + e^-$$

Fe^{3+} is the oxidizing agent because it takes an electron from V^{2+}. V^{2+} is the reducing agent because it gives an electron to Fe^{3+}. Fe^{3+} is reduced, and V^{2+} is oxidized as the reaction proceeds from left to right. Appendix D reviews oxidation numbers and balancing of redox equations.

Chemistry and Electricity

When electrons from a redox reaction flow through an electric circuit, we can learn something about the reaction by measuring current and voltage. Electric current is proportional to the rate of reaction, and the cell voltage is proportional to the free energy change for the electrochemical reaction. In techniques such as voltammetry, the voltage can be used to identify reactants.

Electric Charge

$$\text{Faraday constant } (F) = \frac{\text{coulombs}}{\text{mole of electrons}}$$

Electric charge (q) is measured in **coulombs** (C). The magnitude of the charge of a single electron is 1.602×10^{-19} C, so a mole of electrons has a charge of $(1.602 \times 10^{-19}\ \text{C})(6.022 \times 10^{23}\ \text{mol}^{-1}) = 9.649 \times 10^4$ C, which is called the **Faraday constant,** F.

Relation between charge and moles:

$$\underset{\text{Coulombs}}{q} = \underset{\text{mol e}^-}{n} \cdot \underset{\frac{\text{Coulombs}}{\text{mol e}^-}}{F} \qquad (13\text{-}2)$$

where n is the number moles of electrons transferred.

EXAMPLE **Relating Coulombs to Quantity of Reaction**

If 5.585 g of Fe^{3+} were reduced in Reaction 13-1, how many coulombs of charge must have been transferred from V^{2+} to Fe^{3+}?

Solution First, we find that 5.585 g of Fe^{3+} equal 0.100 0 mol of Fe^{3+}. Because each Fe^{3+} ion requires one electron in Reaction 13-1, 0.100 0 mol of electrons must have been transferred. Using the Faraday constant, we find that 0.100 0 mol of electrons corresponds to

$$q = nF = (0.100\,0\ \text{mol e}^-)\left(9.649 \times 10^4 \frac{\text{C}}{\text{mol e}^-}\right) = 9.649 \times 10^3\ \text{C}$$

Test Yourself How many moles of Sn^{4+} are reduced to Sn^{2+} by 1.00 C of electric charge? (***Answer:*** 5.18 μmol)

Electric Current

1 A = 1 C/s

The quantity of charge flowing each second through a circuit is called the **current.** The unit of current is the **ampere,** abbreviated A. A current of 1 ampere represents a charge of 1 coulomb per second flowing past a point in a circuit.

EXAMPLE **Relating Current to Rate of Reaction**

Suppose that electrons are forced into a platinum wire immersed in a solution containing Sn^{4+} (Figure 13-1), which is reduced to Sn^{2+} at a constant rate of 4.24 mmol/h. How much current passes through the solution?

Solution *Two* electrons are required to reduce *one* Sn^{4+} ion:

$$Sn^{4+} + 2e^- \rightarrow Sn^{2+}$$

Electrons flow at a rate of (2 mmol e^-/mmol Sn^{4+})(4.24 mmol Sn^{4+}/h) = 8.48 mmol e^-/h, which corresponds to

$$\frac{8.48 \text{ mmol } e^-/\text{h}}{3\,600 \text{ s/h}} = 2.356 \times 10^{-3} \frac{\text{mmol } e^-}{\text{s}} = 2.356 \times 10^{-6} \frac{\text{mol } e^-}{\text{s}}$$

To find the current, we convert moles of electrons per second into coulombs per second:

$$\text{Current} = \frac{\text{charge}}{\text{time}} = \frac{\text{coulombs}}{\text{second}} = \frac{\text{moles } e^-}{\text{second}} \cdot \frac{\text{coulombs}}{\text{mole}}$$
$$= \left(2.356 \times 10^{-6} \frac{\text{mol}}{\text{s}}\right)\left(9.649 \times 10^4 \frac{\text{C}}{\text{mol}}\right)$$
$$= 0.227 \text{ C/s} = 0.227 \text{ A}$$

Test Yourself What current reduces Sn^{4+} at a rate of 1.00 mmol/h? (***Answer:*** 53.6 mA)

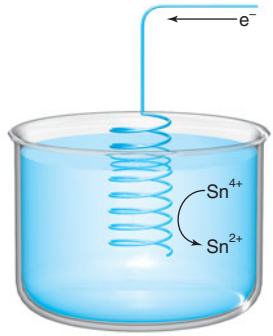


FIGURE 13-1 Electrons flowing into a coil of Pt wire at which Sn^{4+} ions in solution are reduced to Sn^{2+}. This process could not happen by itself, because there is no complete circuit. If Sn^{4+} is to be reduced at this Pt electrode, some other species must be oxidized at some other place.

In Figure 13-1, we encountered a Pt **electrode,** which conducts electrons into or out of a chemical species in the redox reaction. Platinum is a common *inert* electrode. It does not participate in the redox chemistry except as a conductor of electrons.

Voltage, Work, and Free Energy

It takes work to move like charges toward one another. Work can be done when opposite charges move toward one another.

The difference in **electric potential,** *E,* between two points is the work needed (or that can be done) when moving an electric charge from one point to the other. *Potential difference* is measured in **volts** (V). The greater the potential difference between two points, the stronger will be the "push" on a charged particle traveling between those points.

A good analogy for understanding current and potential is to think of water flowing through a garden hose (Figure 13-2). Current is the electric charge flowing past a point in a wire each second. Current is analogous to the volume of water flowing past a point in the hose each second. The difference in electric potential is a measure of the force pushing on the electrons. The greater the force, the more current flows. Potential difference is analogous to the pressure on the water in the hose. The greater the pressure, the faster the water flows.

When a charge, q, moves through a potential difference, E, the work done is

Relation between work and voltage:

$$\underbrace{\text{Work}}_{\text{Joules}} = \underbrace{E}_{\text{Volts}} \cdot \underbrace{q}_{\text{Coulombs}} \qquad (13\text{-}3)$$

Work has the dimensions of energy, whose units are **joules** (J). One *joule* of energy is gained or lost when 1 *coulomb* of charge moves between points whose potentials differ by 1 *volt*. Equation 13-3 tells us that the dimensions of volts are joules per coulomb (1 V = 1 J/C).

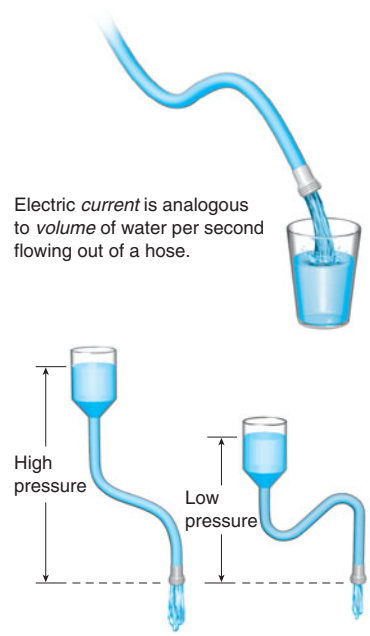


FIGURE 13-2 Analogy between the flow of water through a hose and the flow of electricity through a wire.

EXAMPLE **Electrical Work**

How much work can be done if 2.4 mmol of electrons fall through a potential difference of 0.27 V?

Solution To use Equation 13-3, we must convert moles of electrons into coulombs of charge. The relation is

$$q = nF = (2.4 \times 10^{-3} \text{ mol})(9.649 \times 10^4 \text{ C/mol}) = 2.3 \times 10^2 \text{ C}$$

The work that could be done is

$$\text{Work} = E \cdot q = (0.27 \text{ V})(2.3 \times 10^2 \text{ C}) = 62 \text{ J}$$

Test Yourself What must be the potential drop (V) for 1.00 μmol e^- to do 1.00 J of work? (***Answer:*** 10.4 V)

In the garden hose analogy, suppose that one end of a hose is raised 1 m above the other end and a volume of 1 L of water flows through the hose. The flowing water goes through a mechanical device to do a certain amount of work. If one end of the hose is raised 2 m above the other, the amount of work that can be done by the falling water is twice as great. The elevation difference between the ends of the hose is analogous to electric potential difference and the volume of water is analogous to electric charge. The greater the electric potential difference between two points in a circuit, the more work can be done by the charge flowing between those two points.

Section 6-2 gave a brief discussion of ΔG.

The free energy change, ΔG, for a chemical reaction conducted reversibly at constant temperature and pressure equals the maximum possible electrical work that can be done by the reaction on its surroundings:

$$\text{Work done on surroundings} = -\Delta G \tag{13-4}$$

The negative sign in Equation 13-4 indicates that the free energy of a system decreases when the work is done on the surroundings.

Combining Equations 13-2, 13-3, and 13-4 produces a relation of utmost importance:

$$\Delta G = -\text{work} = -E \cdot q$$

$q = nF$

Relation between free energy difference and electric potential difference:

$$\Delta G = -nFE \tag{13-5}$$

Equation 13-5 relates the free energy change of a chemical reaction to the electrical potential difference (that is, the voltage) that can be generated by the reaction.

Ohm's Law

Ohm's law states that current, I, is directly proportional to the potential difference (voltage) across a circuit and inversely proportional to the **resistance,** R, of the circuit.

The greater the voltage, the more current will flow. The greater the resistance, the less current will flow.

Box 13-1 shows measurements of the resistance of single molecules by measuring current and voltage and applying Ohm's law.

Ohm's law:

$$I = \frac{E}{R} \tag{13-6}$$

Units of resistance are **ohms,** assigned the Greek symbol Ω (omega). A current of 1 ampere flows through a circuit with a potential difference of 1 volt if the resistance is 1 ohm. From Equation 13-6, the unit ampere (A) is equivalent to V/Ω.

Power

Power, P, is the work done per unit time. The SI unit of power is J/s, better known as the **watt** (W).

$$P = \frac{\text{work}}{\text{s}} = \frac{E \cdot q}{\text{s}} = E \cdot \frac{q}{\text{s}} \tag{13-7}$$

Power (watts) = work per second

$P = E \cdot I = (IR) \cdot I = I^2R$

Because q/s is the current, I, we can write

$$P = E \cdot I \tag{13-8}$$

A cell capable of delivering 1 ampere at a potential difference of 1 volt has a power output of 1 watt.

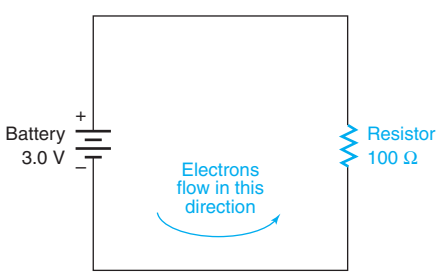


FIGURE 13-3 A circuit with a battery and a resistor. Benjamin Franklin investigated static electricity in the 1740s.[6] He thought electricity was a fluid that flows from a silk cloth to a glass rod when the rod is rubbed with the cloth. We now know that electrons flow from glass to silk. However, Franklin's convention for the direction of electric current has been retained, so we say that current flows from positive to negative—in the opposite direction of electron flow.

EXAMPLE Using Ohm's Law

In the circuit in Figure 13-3, the battery generates a potential difference of 3.0 V, and the resistor has a resistance of 100 Ω. We assume that the wire connecting the battery and the resistor has negligible resistance. Find the current and power delivered by the battery.

Solution The current is

$$I = \frac{E}{R} = \frac{3.0\ \text{V}}{100\ \Omega} = 0.030\ \text{A} = 30\ \text{mA}$$

The power produced by the battery is

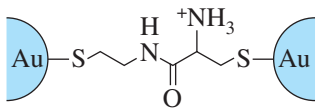
$$P = E \cdot I = (3.0\ \text{V})(0.030\ \text{A}) = 90\ \text{mW}$$

Test Yourself What voltage is required to produce 180 mW of power? (***Answer:*** 4.24 V)

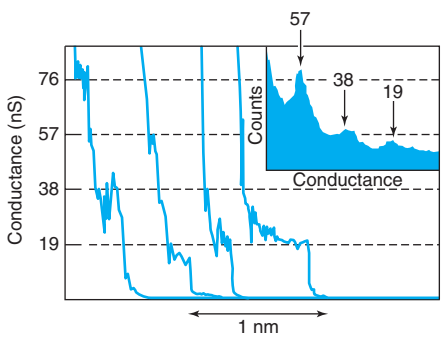
BOX 13-1 Ohm's Law, Conductance, and Molecular Wire[3]

The electrical conductance of a single molecule suspended between two gold electrodes is known from measurement of voltage and current by applying Ohm's law. Conductance is 1/resistance, so it has the units 1/ohm ≡ siemens (S).

To make molecular junctions, a gold scanning tunneling microscope tip was moved in and out of contact with a gold substrate in the presence of a solution containing a test molecule terminated by thiol (—SH) groups. Thiols spontaneously bind to gold, forming bridges such as that shown here. Nanoampere currents were observed with a potential difference of 0.1 V between the gold surfaces.

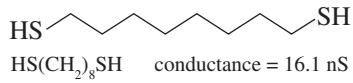


The graph shows four observations of conductance as the scanning tunneling microscope tip was pulled away from the Au substrate. Plateaus are observed at multiples of 19 nS. An interpretation is that a single molecule connecting two Au surfaces has a conductance of 19 nS (or a resistance of 50 MΩ). If two molecules form parallel bridges, conductance increases to 38 nS. Three molecules give a conductance of 57 nS. If there are three bridges and the electrodes are pulled apart, one of the bridges breaks and conductance drops to 38 nS. When the second bridge breaks, conductance drops to 19 nS. The exact conductance varies because the environment of each molecule on the Au surface is not identical. A histogram of >500 observations in the inset shows peaks at 19, 38, and 57 nS.

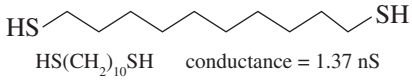


Change in conductance as Au scanning tunneling microscope tip immersed in dithiol solution is withdrawn from Au substrate. [From X. Xiao, B. Xu, and N. Tao, "Conductance Titration of Single-Peptide Molecules," *J. Am. Chem. Soc.* **2004**, *126*, 5370.]

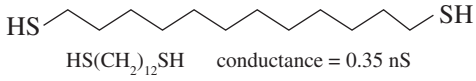
Alkane hydrocarbons can be thought of as prototypical electrical insulators. The conductance of alkane dithiols decreases exponentially as chain length increases:[4]



$HS(CH_2)_8SH$ conductance = 16.1 nS

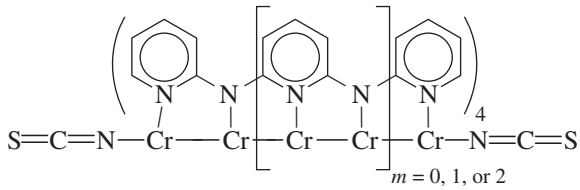


$HS(CH_2)_{10}SH$ conductance = 1.37 nS

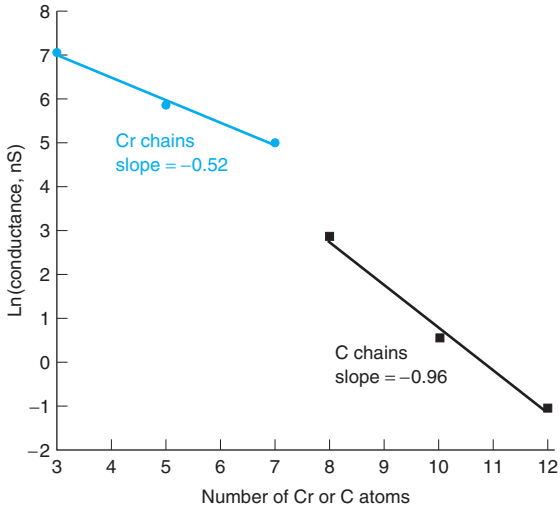


$HS(CH_2)_{12}SH$ conductance = 0.35 nS

The conductance of a chain of Cr atoms with pyridylamine ligands is greater than that of alkanes.[5] The chart shows that conductance decreases exponentially with chain length, but at a lower rate than for the alkanes.



Cr_3 chain (m = 0)	conductance = 1 100 nS
Cr_5 chain (m = 1)	conductance = 310 nS
Cr_7 chain (m = 2)	conductance = 140 nS



Dependence of conductivity on chain length.

What happens to the power generated by the circuit? *The energy appears as heat in the resistor*. The power (90 mW) equals the rate at which heat is produced in the resistor.

Here is a summary of symbols, units, and relations from the last few pages:

Relation between charge and moles:

$$\underset{\substack{\text{Charge}\\ \text{(coulombs, C)}}}{q} = \underset{\substack{\text{Moles}\\ \text{of } e^-}}{n} \cdot \underset{\text{C/mole}}{F}$$

Relation between work and voltage:

$$\underset{\substack{\text{Joules}\\ \text{(J)}}}{\text{Work}} = \underset{\substack{\text{Volts}\\ \text{(V)}}}{E} \cdot \underset{\substack{\text{Coulombs}\\ \text{(C)}}}{q}$$

Relation between free energy difference and electric potential difference:

$$\underset{\text{Joules}}{\Delta G} = -nFE$$

Ohm's law:

$$\underset{\substack{\text{Current}\\(\text{A})}}{I} = \underset{\substack{\text{Volts}\\(\text{V})}}{E} \,/\, \underset{\substack{\text{Resistance}\\(\text{ohms, }\Omega)}}{R}$$

Electric power:

$$\underset{\substack{\text{Power}\\(\text{watts, W})}}{P} = \underset{\text{J/s}}{\frac{\text{work}}{\text{s}}} = \underset{\text{Volts}}{E} \cdot \underset{\text{Amperes}}{I}$$

13-2 Galvanic Cells

A galvanic cell uses a spontaneous chemical reaction to generate electricity.

A **galvanic cell** (also called a *voltaic cell*) uses a *spontaneous* chemical reaction to generate electricity. To accomplish this, one reagent must be oxidized and another must be reduced. The two cannot be in contact, or electrons would flow directly from the reducing agent to the oxidizing agent. Instead, oxidizing and reducing agents are physically separated, and electrons are forced to flow through an external circuit to go from one reactant to the other. Batteries[7] and fuel cells[8] are galvanic cells that consume their reactants to generate electricity. A battery has a static compartment filled with reactants. In a fuel cell, fresh reactants flow past the electrodes and products are continuously flushed from the cell.

A Cell in Action

Figure 13-4 shows a galvanic cell with two electrodes suspended in a solution of $CdCl_2$. One electrode is cadmium; the other is metallic silver coated with solid AgCl. The reactions are

$$\text{Reduction:} \quad 2AgCl(s) + 2e^- \rightleftharpoons 2Ag(s) + 2Cl^-(aq)$$

$$\text{Oxidation:} \quad Cd(s) \rightleftharpoons Cd^{2+}(aq) + 2e^-$$

$$\text{Net reaction:} \quad Cd(s) + 2AgCl(s) \rightleftharpoons Cd^{2+}(aq) + 2Ag(s) + 2Cl^-(aq)$$

The net reaction is composed of a reduction and an oxidation, each of which is called a **half-reaction.** The two half-reactions are written with equal numbers of electrons so that their sum includes no free electrons.

Recall that ΔG is *negative* for a spontaneous reaction.

Oxidation of Cd metal to $Cd^{2+}(aq)$ provides electrons that flow through the circuit to the Ag electrode in Figure 13-4. At the Ag surface, Ag^+ (from AgCl) is reduced to $Ag(s)$. Chloride from AgCl goes into solution. The free energy change for the net reaction, −150 kJ per mole of Cd, provides the driving force that pushes electrons through the circuit.

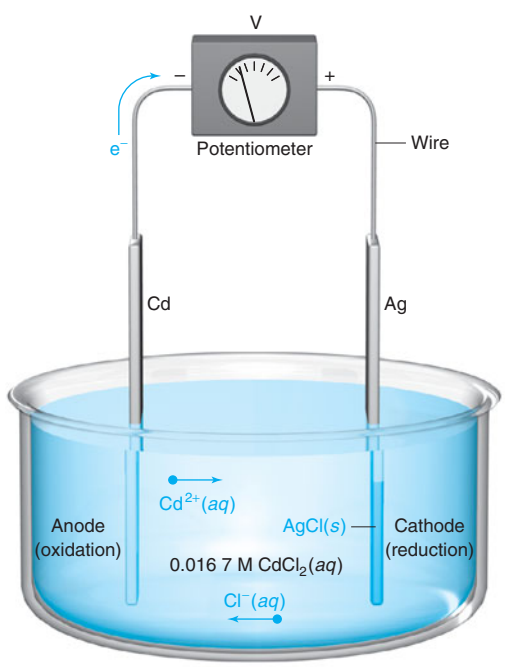


FIGURE 13-4 A simple galvanic cell. The **potentiometer** measures voltage. It has positive and negative terminals. When electrons flow into the negative terminal, as in this illustration, the voltage is positive.

EXAMPLE **Voltage Produced by a Chemical Reaction**

Calculate the voltage that would be measured by the potentiometer in Figure 13-4.

Solution Because $\Delta G = -150$ kJ per mol of Cd, we can use Equation 13-5 (where n is moles of electrons transferred in the balanced net reaction) to write

$$E = -\frac{\Delta G}{nF} = -\frac{-150 \times 10^3 \text{ J}}{(2 \text{ mol})\left(9.649 \times 10^4 \dfrac{\text{C}}{\text{mol}}\right)}$$
$$= +0.777 \text{ J/C} = +0.777 \text{ V}$$

Reminder: 1 J/C = 1 volt

A spontaneous chemical reaction (negative ΔG) produces a *positive voltage*.

Test Yourself Find E if $\Delta G = +150$ kJ and $n = 1$ mol. (***Answer:*** -1.55 V)

Chemists define the electrode at which *reduction* occurs as the **cathode.** The **anode** is the electrode at which *oxidation* occurs. In Figure 13-4, Ag is the cathode because reduction takes place at its surface ($2AgCl + 2e^- \rightarrow 2Ag + 2Cl^-$), and Cd is the anode because it is oxidized ($Cd \rightarrow Cd^{2+} + 2e^-$).

Cathode: where reduction occurs
Anode: where oxidation occurs

Salt Bridge

Consider the cell in Figure 13-5, in which the reactions are intended to be

$$\begin{array}{lr} \text{Cathode:} & 2Ag^+(aq) + \cancel{2e^-} \rightleftharpoons 2Ag(s) \\ \text{Anode:} & Cd(s) \rightleftharpoons Cd^{2+}(aq) + \cancel{2e^-} \\ \hline \text{Net reaction:} & Cd(s) + 2Ag^+(aq) \rightleftharpoons Cd^{2+}(aq) + 2Ag(s) \end{array} \qquad \textbf{(13-9)}$$

The net reaction is spontaneous, but little current flows through the circuit because Ag^+ is not forced to be reduced at the Ag electrode. Aqueous Ag^+ can react directly at the $Cd(s)$ surface, giving the same net reaction with no flow of electrons through the external circuit.

The cell in Figure 13-5 is *short-circuited.*

We can separate the reactants into two *half-cells*[11] if we connect the two halves with a **salt bridge,** as shown in Figure 13-6. The salt bridge is a U-shaped tube filled with a gel containing a high concentration of KNO_3 (or other electrolyte that does not affect the cell reaction). The ends of the bridge are porous glass disks that allow ions to diffuse but minimize mixing of solutions inside and outside the bridge. When the galvanic cell is operating, K^+ from the bridge migrates into the cathode compartment and a small amount of NO_3^- migrates from the cathode into the bridge. Ion migration offsets the charge buildup that would otherwise occur as electrons

A salt bridge maintains electroneutrality (no charge buildup) throughout the cell. See Demonstration 13-1.

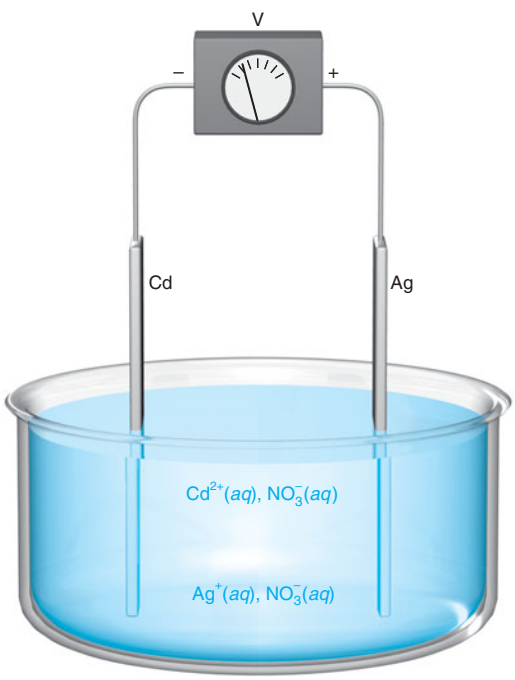


FIGURE 13-5 A cell that will not work. The solution contains $Cd(NO_3)_2$ and $AgNO_3$.

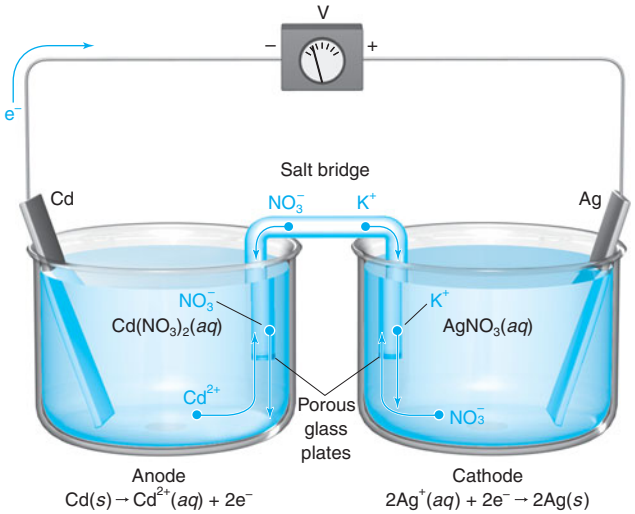


FIGURE 13-6 A cell that works—thanks to the salt bridge!

flow into the silver electrode. The migration of ions out of the bridge is greater than the migration of ions into the bridge because the salt concentration in the bridge is much higher than the salt concentration in the half-cells. At the left side of the salt bridge, NO_3^- migrates into the anode compartment and a little Cd^{2+} migrates into the bridge to prevent buildup of positive charge.

For reactions that do not involve Ag^+ or other species that react with Cl^-, the salt bridge usually contains KCl electrolyte. A typical salt bridge is prepared by heating 3 g of agar with 30 g of KCl in 100 mL of water until a clear solution is obtained. The solution is poured into the U-tube and allowed to gel. The bridge is stored in saturated aqueous KCl.

Line Notation

The salt bridge symbol || represents the two phase boundaries on either side of the bridge.

Electrochemical cells are described by a notation employing just two symbols:

| phase boundary || salt bridge

The cell in Figure 13-4 is represented by the *line diagram*

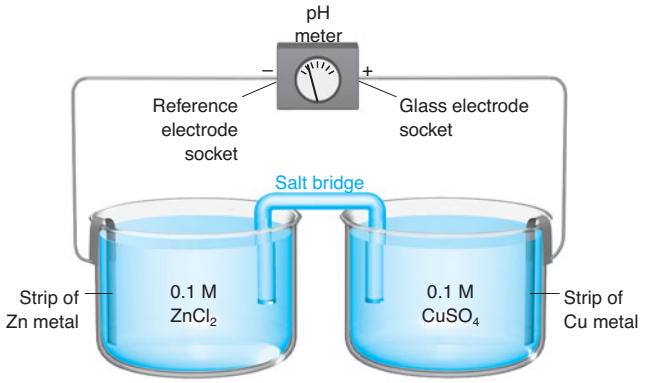
$$Cd(s)|CdCl_2(aq)|AgCl(s)|Ag(s)$$

Each phase boundary is indicated by a vertical line. The electrodes are shown at the extreme left- and right-hand sides of the line diagram. The cell in Figure 13-6 is

$$Cd(s)|Cd(NO_3)_2(aq)\ ||AgNO_3(aq)|Ag(s)$$

DEMONSTRATION 13-1 The Human Salt Bridge

A salt bridge is an ionic medium with a *semipermeable* barrier on each end. Small molecules and ions can cross a semipermeable barrier, but large molecules cannot. Demonstrate a "proper" salt bridge by filling a U-tube with agar and KCl as described in the text and construct the cell shown here.



The pH meter is a potentiometer whose negative terminal is the reference electrode socket.

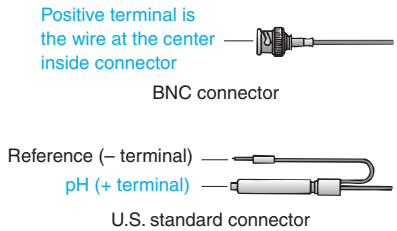
Write the half-reactions for this cell and use the Nernst equation to calculate the theoretical voltage. Measure the voltage with a conventional salt bridge. Then replace the salt bridge with filter paper soaked in NaCl solution and measure the voltage again. Finally, replace the filter-paper salt bridge with two fingers and measure the voltage again. A human is just a bag of salt housed in a semipermeable membrane. Small differences in voltage observed when the salt bridge is replaced can be attributed to the junction potential discussed in Section 14-3. To prove that it is hard to distinguish a chemistry instructor from a hot dog, use a hot dog as a salt bridge[9] and measure the voltage again.

Challenge One hundred eighty students at Virginia Tech made a salt bridge by holding hands.[10] Their resistance was lowered from $10^6\ \Omega$ per student to $10^4\ \Omega$ per student by wetting everyone's hands. Can your class beat this record?

13-3 Standard Potentials

The voltage measured in Figure 13-6 is the difference in electric potential between the Ag electrode on the right and the Cd electrode on the left. Voltage tells us how much work can be done by electrons flowing from one side to the other (Equation 13-3). The potentiometer (voltmeter) indicates a positive voltage when electrons flow into the negative terminal, as in Figure 13-6. If electrons flow the other way, the voltage is negative.

Sometimes the negative terminal of a voltmeter is labeled "common." It may be colored black and the positive terminal red. When a pH meter with a BNC socket is used as a potentiometer, the center wire is the positive input and the outer connection is the negative input. In older pH meters, the negative terminal is the narrow receptacle to which the reference electrode is connected.



To predict the voltage that will be observed when different half-cells are connected to each other, the **standard reduction potential,** $E°$, for each half-cell is measured by an experiment shown in an idealized form in Figure 13-7. The half-reaction of interest in this diagram is

$$Ag^+ + e^- \rightleftharpoons Ag(s) \qquad \textbf{(13-10)}$$

which occurs in the half-cell at the right connected to the *positive* terminal of the potentiometer. *Standard* means that activities of all species are unity. For Reaction 13-10 under standard conditions, $\mathcal{A}_{Ag^+} = 1$ and, by definition, the activity of Ag(s) also is unity.

The left half-cell, connected to the *negative* terminal of the potentiometer, is called the **standard hydrogen electrode** (S.H.E.). It consists of a catalytic Pt surface in contact with an acidic solution in which $\mathcal{A}_{H^+} = 1$. A stream of $H_2(g)$ bubbled through the electrode saturates the solution with $H_2(aq)$. The activity of $H_2(g)$ is unity if the pressure of $H_2(g)$ is 1 bar. The reaction that comes to equilibrium at the surface of the Pt electrode is

Question What is the pH of the standard hydrogen electrode?

$$\textit{S.H.E. half-reaction:} \quad H^+(aq, \mathcal{A} = 1) + e^- \rightleftharpoons \frac{1}{2}H_2(g, \mathcal{A} = 1) \qquad \textbf{(13-11)}$$

We will write all half-reactions as *reductions*. By convention, $E° = 0$ for S.H.E.

We *arbitrarily* assign a potential of 0 to the standard hydrogen electrode at 25°C. The voltage measured by the meter in Figure 13-7 can therefore be *assigned* to Reaction 13-10, which occurs in the right half-cell. The measured value $E° = +0.799$ V is the standard reduction potential for Reaction 13-10. The positive sign tells us that electrons flow from left to right through the meter.

We can arbitrarily *assign* a potential to Reaction 13-11 because it serves as a reference point from which we can measure other half-cell potentials. An analogy is the arbitrary assignment of 0°C to the freezing point of water. Relative to this freezing point, hexane boils at 69° and benzene boils at 80°. The difference between boiling points is 80° − 69° = 11°. If we were to assign the freezing point of water to be 200°C instead of 0°C, hexane would boil at 269° and benzene would boil at 280°. The difference is still 11°. Regardless of where we set zero on the scale, differences between points remain constant.

Walther Nernst appears to have been the first to assign the potential of the hydrogen electrode as 0 in 1897.[12]

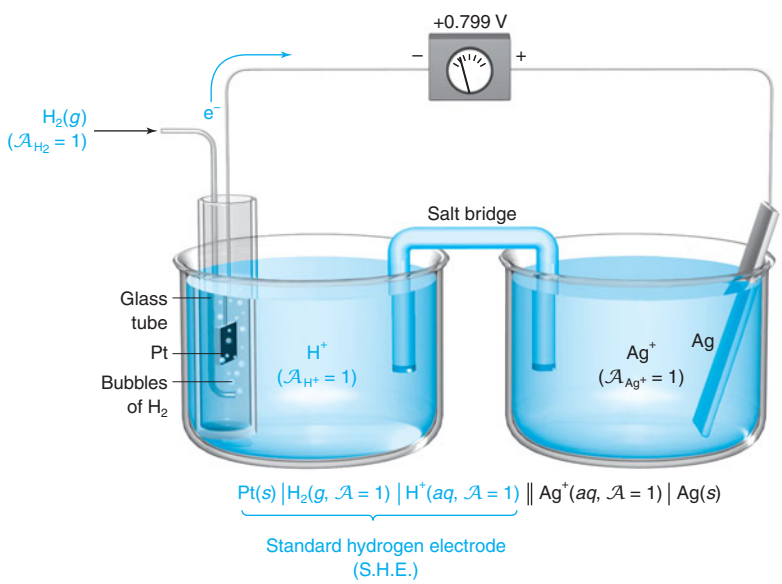


FIGURE 13-7 Cell used to measure the standard potential of the reaction $Ag^+ + e^- \rightleftharpoons Ag(s)$. This cell is hypothetical because it is usually not possible to adjust the activity of a species to 1.

TABLE 13-1 Ordered standard reduction potentials

Oxidizing agent	Reducing agent	$E°$(V)
$F_2(g) + 2e^-$	$\rightleftharpoons 2F^-$	2.890
$O_3(g) + 2H^+ + 2e^-$	$\rightleftharpoons O_2(g) + H_2O$	2.075
⋮	⋮	
$MnO_4^- + 8H^+ + 5e^-$	$\rightleftharpoons Mn^{2+} + 4H_2O$	1.507
⋮	⋮	
$Ag^+ + e^-$	$\rightleftharpoons Ag(s)$	0.799
⋮	⋮	
$Cu^{2+} + 2e^-$	$\rightleftharpoons Cu(s)$	0.339
⋮	⋮	
$2H^+ + 2e^-$	$\rightleftharpoons H_2(g)$	0.000
⋮	⋮	
$Cd^{2+} + 2e^-$	$\rightleftharpoons Cd(s)$	−0.402
⋮	⋮	
$K^+ + e^-$	$\rightleftharpoons K(s)$	−2.936
$Li^+ + e^-$	$\rightleftharpoons Li(s)$	−3.040

Oxidizing power increases ↑ (top to bottom); Reducing power increases ↓ (bottom to upward)

Question The potential for the reaction $K^+ + e^- \rightleftharpoons K(s)$ is −2.936 V. This means that K^+ is a very poor oxidizing agent. (It does not readily accept electrons.) Does this imply that K^+ is therefore a good reducing agent?

Answer: No! To be a good reducing agent, K^+ would have to give up electrons easily (forming K^{2+}), which it cannot do. (*But*, the large negative reduction potential does imply that K(*s*) is a good reducing agent.)

The line notation for the cell in Figure 13-7 is

$$Pt(s)|H_2(g, \mathcal{A} = 1)|H^+(aq, \mathcal{A} = 1)\,\|Ag^+(aq, \mathcal{A} = 1)|Ag(s)$$

or

$$S.H.E.\|Ag^+(aq, \mathcal{A} = 1)|Ag(s)$$

We always attach the left-hand electrode to the negative terminal of the potentiometer and the right-hand electrode to the positive terminal. The voltage on the meter is the difference:

voltage = right-hand electrode potential − left-hand electrode potential

By convention, the left-hand electrode (Pt) is attached to the negative (reference) terminal of the potentiometer and the right-hand electrode is attached to the positive terminal. A standard reduction potential is really a potential *difference* between the potential of the reaction of interest and the potential of S.H.E, which we have arbitrarily set to 0.

To measure the standard potential of the half-reaction

$$Cd^{2+} + 2e^- \rightleftharpoons Cd(s) \qquad \textbf{(13-12)}$$

we construct the cell

$$S.H.E.\|Cd^{2+}(aq, \mathcal{A} = 1)|Cd(s)$$

Challenge Draw a picture of the cell S.H.E || Cd^{2+} (*aq*, $\mathcal{A}$ = 1) | Cd(*s*) and show the direction of electron flow.

with the cadmium half-cell connected to the positive terminal of the potentiometer. In this case, we observe a *negative* voltage of −0.402 V. The negative sign means that electrons flow from Cd to Pt, a direction opposite that of the cell in Figure 13-7.

Appendix H contains standard reduction potentials arranged alphabetically by element. If the half-reactions were arranged according to descending value of $E°$ (as in Table 13-1), we would find the strongest oxidizing agents at the upper left and the strongest reducing agents at the lower right. If we connected the two half-cells represented by Reactions 13-10 and 13-12, Ag^+ would be reduced to Ag(*s*) as Cd(*s*) is oxidized to Cd^{2+}.

13-4 Nernst Equation

A reaction is spontaneous if ΔG is negative and E is positive. $\Delta G°$ and $E°$ refer to the free energy change and potential when the activities of reactants and products are unity. $\Delta G° = -nFE°$.

Le Châtelier's principle tells us that increasing reactant concentrations drives a reaction to the right and increasing the product concentrations drives a reaction to the left. The net driving force for a reaction is expressed by the **Nernst equation,** whose two terms include the driving force under standard conditions ($E°$, which applies when all activities are unity) and a term showing the dependence on reagent concentrations.

Nernst Equation for a Half-Reaction

For the half-reaction

$$aA + ne^- \rightleftharpoons bB$$

Challenge Show that Le Châtelier's principle requires a negative sign in front of the reaction quotient term in the Nernst equation. *Hint:* The more favorable a reaction, the more positive is *E*.

the Nernst equation giving the half-cell potential, *E*, is

Nernst equation:

$$E = E° - \frac{RT}{nF}\ln\frac{\mathcal{A}_B^b}{\mathcal{A}_A^a} \qquad \textbf{(13-13)}$$

where E° = standard reduction potential ($\mathcal{A}_A = \mathcal{A}_B = 1$)

R = gas constant (8.314 J/(K · mol) = 8.314(V · C)/(K · mol))

T = temperature (K)

n = number of electrons in the half-reaction

F = Faraday constant (9.649×10^4 C/mol)

$\mathcal{A}_i$ = activity of species i

The logarithmic term in the Nernst equation is the **reaction quotient,** Q.

$$Q = \mathcal{A}_B^b / \mathcal{A}_A^a \tag{13-14}$$

Q has the same form as the equilibrium constant, but the activities need not have their equilibrium values. Pure solids, pure liquids, and solvents are omitted from Q because their activities are unity (or close to unity). Concentrations of solutes are expressed as moles per liter and concentrations of gases are expressed as pressures in bars. When all activities are unity, $Q = 1$ and $\ln Q = 0$, thus giving $E = E^\circ$.

Converting the natural logarithm in Equation 13-13 into the base 10 logarithm and inserting $T = 298.15$ K (25.00°C) gives the most useful form of the Nernst equation:

Appendix A shows that $\log x = (\ln x)/(\ln 10) = (\ln x)/2.303$.

Nernst equation at 25°C:

$$E = E^\circ - \frac{0.059\,16\text{ V}}{n} \log \frac{\mathcal{A}_B^b}{\mathcal{A}_A^a} \tag{13-15}$$

The potential changes by $59.16/n$ mV for each factor-of-10 change in Q.

EXAMPLE Writing the Nernst Equation for a Half-Reaction

Let's write the Nernst equation for the reduction of white phosphorus to phosphine gas:

$$\frac{1}{4}P_4(s, \text{white}) + 3H^+ + 3e^- \rightleftharpoons \underset{\text{Phosphine}}{PH_3(g)} \qquad E^\circ = -0.046\text{ V}$$

Phosphine is a highly poisonous gas with the odor of decaying fish.

Solution We omit solids from the reaction quotient, and the concentration of a gas is expressed as the pressure of the gas. Therefore, the Nernst equation is

$$E = -0.046 - \frac{0.059\,16}{3} \log \frac{P_{PH_3}}{[H^+]^3}$$

Test Yourself With E° from Appendix H, write the Nernst equation for $ZnS(s) + 2e^- \rightleftharpoons Zn(s) + S^{2-}$. (***Answer:*** $E = -1.405 - \frac{0.059\,16}{2} \log[S^{2-}]$)

EXAMPLE Multiplying a Half-Reaction Does Not Change E°

If we multiply a half-reaction by any factor, E° does not change. However, the factor n before the log term and the form of the reaction quotient, Q, do change. Let's write the Nernst equation for the reaction in the preceding example, multiplied by 2:

$$\frac{1}{2}P_4(s, \text{white}) + 6H^+ + 6e^- \rightleftharpoons 2PH_3(g) \qquad E^\circ = -0.046\text{ V}$$

Solution

$$E = -0.046 - \frac{0.059\,16}{6} \log \frac{P_{PH_3}^2}{[H^+]^6}$$

Even though this Nernst equation does not look like the one in the preceding example, Box 13-2 shows that the numerical value of E is unchanged. The squared term in the reaction quotient cancels the doubled value of n in front of the log term.

Test Yourself Write the Nernst equation for $P_4 + 12H^+ + 12e^- \rightleftharpoons 4PH_3$. From Box 13-2, show that E is the same as if the reaction were written with $\frac{1}{2}P_4$ or $\frac{1}{4}P_4$.

BOX 13-2 $E°$ and the Cell Voltage Do Not Depend on How You Write the Cell Reaction

Multiplying a half-reaction by any number does not change the standard reduction potential, $E°$. The potential difference between two points is the work done *per coulomb of charge* carried through that potential difference (E = work/q). Work per coulomb is the same whether 0.1, 2.3, or 10^4 coulombs have been transferred. The total work is different in each case, but work per coulomb is constant. Therefore, we do not double $E°$ if we multiply a half-reaction by 2.

Multiplying a half-reaction by any number does not change the half-cell potential, E. Consider a half-cell reaction written with either one or two electrons:

$$Ag^+ + e^- \rightleftharpoons Ag(s) \qquad E = E° - 0.059\,16 \log \frac{1}{[Ag^+]}$$

$$2Ag^+ + 2e^- \rightleftharpoons 2Ag(s) \qquad E = E° - \frac{0.059\,16}{2} \log \frac{1}{[Ag^+]^2}$$

The two expressions are equal because $\log a^b = b \log a$:

$$\frac{0.059\,16}{2} \log \frac{1}{[Ag^+]^2} = \frac{\cancel{2} \times 0.059\,16}{\cancel{2}} \log \frac{1}{[Ag^+]}$$

$$= 0.059\,16 \log \frac{1}{[Ag^+]}$$

The exponent in the log term is canceled by the factor $1/n$ preceding the log term. Cell voltage is a measurable quantity that cannot depend on how you write the reaction.

Nernst Equation for a Complete Reaction

In Figure 13-6, the measured voltage is the difference between the potentials of the two electrodes:

Nernst equation for a complete cell: $$E = E_+ - E_- \qquad (13\text{-}16)$$

where E_+ is the potential of the electrode attached to the positive terminal of the potentiometer and E_- is the potential of the electrode attached to the negative terminal. The potential of each half-reaction (*written as a reduction*) is governed by a Nernst equation, and the voltage for the complete reaction is the difference between the two half-cell potentials.

Here is a procedure for writing a net cell reaction and finding its voltage:

Step 1 Write *reduction* half-reactions for both half-cells and find $E°$ for each in Appendix H. Multiply the half-reactions as necessary so that they both contain the same number of electrons. When you multiply a reaction, you *do not* multiply $E°$.

Step 2 Write a Nernst equation for the right half-cell, which is attached to the positive terminal of the potentiometer. This is E_+.

Step 3 Write a Nernst equation for the left half-cell, which is attached to the negative terminal of the potentiometer. This is E_-.

Step 4 Find the net cell voltage by subtraction: $E = E_+ - E_-$.

Step 5 Write the net cell reaction by subtracting the left half-reaction from the right half-reaction. (Subtraction is equivalent to reversing the left half-reaction and adding.)

$E > 0$: net cell reaction goes →
$E < 0$: net cell reaction goes ←

If the net cell voltage, E ($= E_+ - E_-$), is positive, then the net cell reaction is spontaneous in the forward direction. If the net cell voltage is negative, then the reaction is spontaneous in the reverse direction.

EXAMPLE Nernst Equation for a Complete Reaction

Find the voltage of the cell in Figure 13-6 if the right half-cell contains 0.50 M $AgNO_3(aq)$ and the left half-cell contains 0.010 M $Cd(NO_3)_2(aq)$. Write the net cell reaction and state whether it is spontaneous in the forward or reverse direction.

Solution

Step 1 Right electrode: $2Ag^+ + 2e^- \rightleftharpoons 2Ag(s)$ $\qquad E_+° = 0.799$ V

Left electrode: $Cd^{2+} + 2e^- \rightleftharpoons Cd(s)$ $\qquad E_-° = -0.402$ V

Step 2 Nernst equation for right electrode:

Pure solids, pure liquids, and solvents are omitted from Q.

$$E_+ = E_+° - \frac{0.059\,16}{2} \log \frac{1}{[Ag^+]^2} = 0.799 - \frac{0.059\,16}{2} \log \frac{1}{[0.50]^2} = 0.781 \text{ V}$$

Step 3 Nernst equation for left electrode:

$$E_- = E^\circ_- - \frac{0.059\,16}{2}\log\frac{1}{[Cd^{2+}]} = -0.402 - \frac{0.059\,16}{2}\log\frac{1}{[0.010]} = -0.461\text{ V}$$

Step 4 Cell voltage: $E = E_+ - E_- = 0.781 - (-0.461) = +1.242\text{ V}$

Step 5 Net cell reaction:

$$\begin{array}{rl} & 2Ag^+ + 2e^- \rightleftharpoons 2Ag(s) \\ - & Cd^{2+} + 2e^- \rightleftharpoons Cd(s) \\ \hline & Cd(s) + 2Ag^+ \rightleftharpoons Cd^{2+} + 2Ag(s) \end{array}$$

Subtracting a reaction is the same as reversing the reaction and adding.

The voltage is positive, so the reaction is spontaneous in the forward direction. Cd(s) is oxidized and Ag^+ is reduced. Electrons flow from the left-hand electrode to the right-hand electrode.

Test Yourself Is the reaction spontaneous if the cells contain 5.0 μM $AgNO_3$ and 1.0 M $Cd(NO_3)_2$? (***Answer:*** $E_+ = 0.485$ V, $E_- = -0.402$ V, $E = +0.887$ V, spontaneous)

What if you had written the Nernst equation for the right half-cell with just one electron instead of two?

$$Ag^+ + e^- \rightleftharpoons Ag(s)$$

Would the net cell voltage be different from what we calculated? It better not be, because the chemistry is still the same. Box 13-2 shows that *neither E° nor E depend on how we write the reaction*. Box 13-3 shows how to derive standard reduction potentials for half-reactions that are the sum of other half-reactions.

An Intuitive Way to Think About Cell Potentials[2]

In the preceding example, we found that E for the silver half-cell was 0.781 V and E for the cadmium half-cell was −0.461 V. Place these values on the number line in Figure 13-8 and note that e*lectrons always flow toward more positive potential.* Therefore, electrons in the circuit flow from cadmium to silver. The separation of the two half-cells is 1.242 V. This diagram works the same way even if both half-cell potentials are positive or both are negative. Electrons always flow toward more positive potential.

Electrons flow toward more positive potential.

Different Descriptions of the Same Reaction

In Figure 13-4, the right half-reaction can be written

$$AgCl(s) + e^- \rightleftharpoons Ag(s) + Cl^- \qquad E^\circ_+ = 0.222\text{ V} \tag{13-17}$$

$$E_+ = E^\circ_+ - 0.059\,16\log[Cl^-] = 0.222 - 0.059\,16\log(0.033\,4) = 0.309_3\text{ V} \tag{13-18}$$

The Cl^- in the silver half-reaction was derived from 0.016 7 M $CdCl_2(aq)$.

Suppose that a different, less handsome, author had written this book and had chosen to describe the half-reaction differently:

$$Ag^+ + e^- \rightleftharpoons Ag(s) \qquad E^\circ_+ = 0.799\text{ V} \tag{13-19}$$

This description is just as valid as the previous one. In both cases, Ag(I) is reduced to Ag(0).

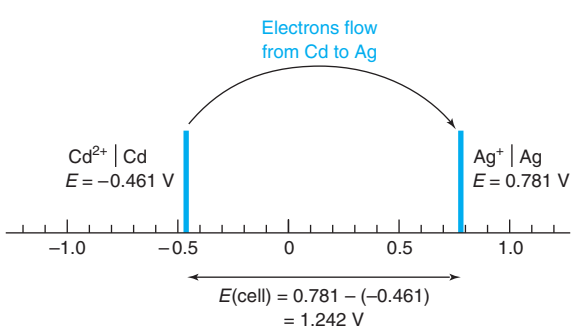
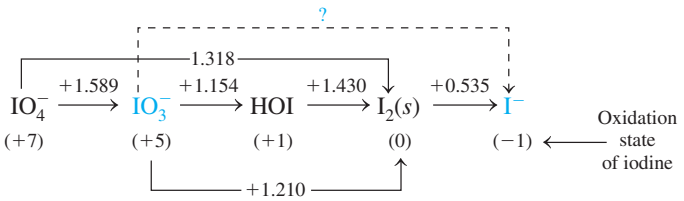


FIGURE 13-8 Electrons always flow from the more negative to the more positive electrode. That is, they always flow to the right in this diagram.[2]

BOX 13-3 Latimer Diagrams: How to Find $E°$ for a New Half-Reaction

A **Latimer diagram** displays standard reduction potentials, $E°$, connecting various oxidation states of an element.[13] For example, in acid solution, the following standard reduction potentials are observed:



The notation $IO_3^- \xrightarrow{+1.154} HOI$ stands for the balanced equation

$$IO_3^- + 5H^+ + 4e^- \rightleftharpoons HOI + 2H_2O \qquad E° = +1.154\ V$$

We can derive reduction potentials for arrows that are not shown in the diagram by using $\Delta G°$. For example, the reaction shown by the dashed line in the Latimer diagram is

$$IO_3^- + 6H^+ + 6e^- \rightleftharpoons I^- + 3H_2O$$

To find $E°$ for this reaction, express the reaction as a sum of reactions whose potentials are known.

The standard free energy change, $\Delta G°$, for a reaction is given by

$$\Delta G° = -nFE°$$

When two reactions are added, $\Delta G°$ is the sum of $\Delta G°$ values for each reaction.

To apply free energy to our problem, we write reactions whose sum is the desired reaction:

$$IO_3^- + 6H^+ + 5e^- \xrightarrow{E_1° = 1.210} \frac{1}{2}I_2(s) + 3H_2O \qquad \Delta G_1° = -5F(1.210)$$

$$\frac{1}{2}I_2(s) + e^- \xrightarrow{E_2° = 0.535} I^- \qquad \Delta G_2° = -1F(0.535)$$

$$IO_3^- + 6H^+ + 6e^- \xrightarrow{E_3° = ?} I^- + 3H_2O \qquad \Delta G_3° = -6FE_3°$$

But, because $\Delta G_1° + \Delta G_2° = \Delta G_3°$, we can solve for $E_3°$:

$$\Delta G_3° = \Delta G_1° + \Delta G_2°$$

$$-6FE_3° = -5F(1.210) - 1F(0.535)$$

$$E_3° = \frac{5(1.210) + 1(0.535)}{6} = 1.098\ V$$

If the two descriptions are equally valid, then they should predict the same voltage. The Nernst equation for Reaction 13-19 is

$$E_+ = 0.799 - 0.059\,16 \log \frac{1}{[Ag^+]}$$

To find the concentration of Ag^+, we use the solubility product for AgCl. Because the cell contains 0.033 4 M Cl^- and solid AgCl, we can say

$K_{sp} = [Ag^+][Cl^-]$

$$[Ag^+] = \frac{K_{sp}\,(\text{for AgCl})}{[Cl^-]} = \frac{1.8 \times 10^{-10}}{0.033\,4} = 5.4 \times 10^{-9}\ M$$

Putting this value into the Nernst equation gives

$$E_+ = 0.799 - 0.059\,16 \log \frac{1}{5.4 \times 10^{-9}} = 0.309_9\ V$$

which differs slightly from the value in Equation 13-18 because of the accuracy of K_{sp} and the neglect of activity coefficients. Reactions 13-17 and 13-19 give the same voltage in the Nernst equation because they describe the same cell.

The cell voltage cannot depend on how we write the reaction!

Advice for Finding Relevant Half-Reactions

How to figure out the half-cell reactions

When faced with a cell drawing or a line diagram, first write reduction reactions for each half-cell. To do this, *look in the cell for an element in two oxidation states*. For the cell

$$Pb(s)|PbF_2(s)|F^-(aq)\|Cu^{2+}(aq)|Cu(s)$$

we see Pb in two oxidation states, as Pb(s) and $PbF_2(s)$, and Cu in two oxidation states, as Cu^{2+} and Cu(s). Thus, the half-reactions are

Right half-cell: $$Cu^{2+} + 2e^- \rightleftharpoons Cu(s)$$

Left half-cell: $$PbF_2(s) + 2e^- \rightleftharpoons Pb(s) + 2F^- \qquad (13\text{-}20)$$

You might have chosen to write the Pb half-reaction as

Left half-cell: $$Pb^{2+} + 2e^- \rightleftharpoons Pb(s) \qquad (13\text{-}21)$$

because you know that if $PbF_2(s)$ is present, there must be some Pb^{2+} in the solution. Reactions 13-20 and 13-21 are equally valid and must predict the same cell voltage. Your choice of reactions depends on whether the F^- or Pb^{2+} concentration is easier to figure out.

We described the left half-cell in terms of a redox reaction involving Pb because Pb is the element that appears in two oxidation states. We would not write a reaction such as $F_2(g) + 2e^- \rightleftharpoons 2F^-$ because $F_2(g)$ is not shown in the line diagram of the cell.

Don't invent species not shown in the cell. Use what is shown in the line diagram to select the half-reactions.

The Nernst Equation Is Used in Measuring Standard Reduction Potentials

The standard reduction potential would be observed if the half-cell of interest (with unit activities) were connected to a standard hydrogen electrode, as it is in Figure 13-7. It is nearly impossible to construct such a cell, because we have no way to adjust concentrations and ionic strength to give unit activities. In reality, activities less than unity are used in each half-cell, and the Nernst equation is employed to extract the value of $E°$ from the cell voltage.[14] In the hydrogen electrode, standard buffers with known pH (Table 14-3) are used to obtain known activities of H^+.

Problem 13-20 gives an example of the use of the Nernst equation to find $E°$.

13-5 $E°$ and the Equilibrium Constant

A galvanic cell produces electricity because the cell reaction is not at equilibrium. The potentiometer allows negligible current (Box 13-4), so concentrations in the cell remain unchanged. If we replaced the potentiometer with a wire, there would be much more current and concentrations would change until the cell reached equilibrium. At that point, nothing would drive the reaction, and E would be 0. When a battery (which is a galvanic cell) runs down to 0 V, the chemicals inside have reached equilibrium and the battery is "dead."

At equilibrium, E (not $E°$) = 0.

Now let's relate E for a whole cell to the reaction quotient, Q, for the net cell reaction. For the two half-reactions

Right electrode:	$aA + ne^- \rightleftharpoons cC$	$E°_+$
Left electrode:	$dD + ne^- \rightleftharpoons bB$	$E°_-$

Net cell reaction:
$aA + bB \rightleftharpoons cC + dD$

the Nernst equation looks like this:

$$E = E_+ - E_- = E°_+ - \frac{0.059\,16}{n}\log\frac{\mathcal{A}_C^c}{\mathcal{A}_A^a} - \left(E°_- - \frac{0.059\,16}{n}\log\frac{\mathcal{A}_B^b}{\mathcal{A}_D^d}\right)$$

$$E = \underbrace{(E°_+ - E°_-)}_{E°} - \frac{0.059\,16}{n}\log\underbrace{\frac{\mathcal{A}_C^c\mathcal{A}_D^d}{\mathcal{A}_A^a\mathcal{A}_B^b}}_{Q} = E° - \frac{0.059\,16}{n}\log Q \qquad \textbf{(13-22)}$$

$\log a + \log b = \log ab$

Equation 13-22 is true at any time. In the special case when the cell is at equilibrium, $E = 0$ and $Q = K$, the equilibrium constant. Therefore, Equation 13-22 is transformed into these most important forms at equilibrium:

Finding $E°$ from K: $$E° = \frac{0.059\,16}{n}\log K \qquad \text{(at 25°C)} \qquad \textbf{(13-23)}$$

Finding K from $E°$: $$K = 10^{nE°/0.059\,16} \qquad \text{(at 25°C)} \qquad \textbf{(13-24)}$$

Equation 13-24 allows us to deduce the equilibrium constant from $E°$. Alternatively, we can find $E°$ from K with Equation 13-23.

To go from Equation 13-23 to 13-24:

$$\frac{0.059\,16}{n}\log K = E°$$
$$\log K = \frac{nE°}{0.059\,16}$$
$$10^{\log K} = 10^{nE°/0.059\,16}$$
$$K = 10^{nE°/0.059\,16}$$

BOX 13-4 Concentrations in the Operating Cell

Why doesn't operation of a cell change the concentrations in the cell? Cell voltage is measured under conditions of *negligible current flow*. The resistance of a high-quality pH meter is $10^{13}\ \Omega$. If a cell produces 1 V, the current through the circuit is

$$I = \frac{E}{R} = \frac{1\text{ V}}{10^{13}\ \Omega} = 10^{-13}\text{ A}$$

The electron flow is

$$\frac{10^{-13}\text{ C/s}}{9.649 \times 10^4\text{ C/mol}} = 10^{-18}\text{ mol e}^-\text{/s}$$

which produces negligible oxidation and reduction of reagents in the cell. *The meter measures the voltage of the cell without affecting concentrations in the cell.*

If a salt bridge were left in a real cell for very long, concentrations and ionic strength would change because of diffusion between each compartment and the salt bridge. Cells should be set up for such a short time that mixing is insignificant.

EXAMPLE Using $E°$ to Find the Equilibrium Constant

Find the equilibrium constant for the reaction

$$Cu(s) + 2Fe^{3+} \rightleftharpoons 2Fe^{2+} + Cu^{2+}$$

Solution Divide the reaction into two half-reactions found in Appendix H:

We associate $E°_-$ with the half-reaction that must be *reversed* to get the desired net reaction.

$$\begin{array}{rrcl} - & 2Fe^{3+} + 2e^- & \rightleftharpoons & 2Fe^{2+} \\ & Cu^{2+} + 2e^- & \rightleftharpoons & Cu(s) \\ \hline & Cu(s) + 2Fe^{3+} & \rightleftharpoons & 2Fe^{2+} + Cu^{2+} \end{array} \qquad \begin{array}{l} E°_+ = 0.771 \text{ V} \\ E°_- = 0.339 \text{ V} \end{array}$$

Then find $E°$ for the net reaction

$$E° = E°_+ - E°_- = 0.771 - 0.339 = 0.432 \text{ V}$$

and compute the equilibrium constant with Equation 13-24:

$$K = 10^{(2)(0.432)/(0.059\,16)} = 4 \times 10^{14}$$

Significant figures for logs and exponents were discussed in Section 3-2.

A modest value of $E°$ produces a large equilibrium constant. The value of K is correctly expressed with one significant figure, because $E°$ has three digits. Two are used for the exponent (14), and one is left for the multiplier (4).

Test Yourself Find K for the reaction $Cu(s) + 2Ag^+ \rightleftharpoons 2Ag(s) + Cu^{2+}$. (***Answer:*** $E° = 0.460$ V, $K = 4 \times 10^{15}$)

Finding K for Net Reactions That Are Not Redox Reactions

Consider the following half-reactions whose difference is the solubility reaction for iron(II) carbonate (which is not a redox reaction):

$$\begin{array}{rrcl} - & FeCO_3(s) + 2e^- & \rightleftharpoons & Fe(s) + CO_3^{2-} \\ & Fe^{2+} + 2e^- & \rightleftharpoons & Fe(s) \\ \hline & \underset{\text{Iron(II) carbonate}}{FeCO_3(s)} & \rightleftharpoons & Fe^{2+} + CO_3^{2-} \end{array} \qquad \begin{array}{l} E°_+ = -0.756 \text{ V} \\ E°_- = -0.44 \text{ V} \\ \hline E° = -0.756 - (-0.44) = -0.31_6 \text{ V} \end{array}$$

$E°$ for dissolution of iron(II) carbonate is negative, which means that the reaction is "not spontaneous." "Not spontaneous" simply means $K < 1$. The reaction proceeds until the concentrations of reactants and products satisfy the equilibrium condition.

$$K = K_{sp} = 10^{(2)(-0.31_6)/(0.059\,16)} = 10^{-11}$$

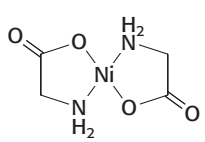
From $E°$ for the net reaction, we can compute K_{sp} for iron(II) carbonate. Potentiometric measurements allow us to find equilibrium constants that are too small or too large to measure by determining concentrations of reactants and products directly.

"Wait!" you protest. "How can there be a redox potential for a reaction that is not a redox reaction?" Box 13-3 shows that the redox potential is just another way of expressing the free energy change of the reaction. The more energetically favorable the reaction (the more negative $\Delta G°$), the more positive is $E°$.

The general form of a problem involving the relation between $E°$ values for half-reactions and K for a net reaction is

$$\begin{array}{rll} - & \text{Half-reaction:} & E°_+ \\ & \text{Half-reaction:} & E°_- \\ \hline & \text{Net reaction:} & E° = E°_+ - E°_- \end{array} \qquad K = 10^{nE°/0.059\,16}$$

If you know $E°_-$ and $E°_+$, you can find $E°$ and K for the net cell reaction. Alternatively, if you know $E°$ and either $E°_-$ or $E°_+$, you can find the missing standard potential. If you know K, you can calculate $E°$ and use it to find either $E°_-$ or $E°_+$, provided you know one of them.



Possible structure of $Ni(glycine)_2$

EXAMPLE Relating $E°$ and K

From the formation constant of $Ni(glycine)_2$ plus $E°$ for the $Ni^{2+} \mid Ni(s)$ couple,

$$\begin{array}{rcl} Ni^{2+} + 2\text{ glycine}^- & \rightleftharpoons & Ni(\text{glycine})_2 \\ Ni^{2+} + 2e^- & \rightleftharpoons & Ni(s) \end{array} \qquad \begin{array}{l} K \equiv \beta_2 = 1.2 \times 10^{11} \\ E° = -0.236 \text{ V} \end{array}$$

deduce the value of $E°$ for the reaction

$$\text{Ni(glycine)}_2 + 2e^- \rightleftharpoons \text{Ni}(s) + 2\ \text{glycine}^- \qquad \textbf{(13-25)}$$

Solution We need to see the relations among the three reactions:

$$\begin{array}{rll} & \text{Ni}^{2+} + 2e^- \rightleftharpoons \text{Ni}(s) & E°_+ = -0.236\ \text{V} \\ - & \text{Ni(glycine)}_2 + 2e^- \rightleftharpoons \text{Ni}(s) + 2\ \text{glycine}^- & E°_- = ? \\ \hline & \text{Ni}^{2+} + 2\ \text{glycine}^- \rightleftharpoons \text{Ni(glycine)}_2 & E° = ? \qquad K = 1.2 \times 10^{11} \end{array}$$

We know that $E°_+ - E°_-$ must equal $E°$, so we can deduce the value of $E°_-$ if we can find $E°$. But $E°$ can be determined from the equilibrium constant for the net reaction:

$$E° = \frac{0.059\ 16}{n} \log K = \frac{0.059\ 16}{2} \log(1.2 \times 10^{11}) = 0.328\ \text{V}$$

Hence, the standard reduction potential for half-reaction 13-25 is

$$E°_- = E°_+ - E° = -0.236 - 0.328 = -0.564\ \text{V}$$

The more negative potential of –0.564 V for reducing Ni(glycine)_2 compared to –0.236 V for reducing Ni^{2+} tells us that it is harder to reduce Ni(glycine)_2 than Ni^{2+}. Ni^{2+} is stabilized with respect to reduction by complexation with glycine.

Test Yourself Select half-reactions in Appendix H to find the formation constant β_2 for $Cu^+ + 2$ ethylenediamine $\rightleftharpoons$ $\text{Cu(ethylenediamine)}_2^+$. (***Answer:*** $E° = 0.637$ V, $\beta_2 = 6 \times 10^{10}$)

13-6 Cells as Chemical Probes[15]

It is essential to distinguish two classes of equilibria associated with galvanic cells:

1. Equilibrium *between* the two half-cells
2. Equilibrium *within* each half-cell

If a galvanic cell has a nonzero voltage, then the net cell reaction is not at equilibrium. We say that equilibrium *between* the two half-cells has not been established.

We allow half-cells to stand long enough to come to chemical equilibrium ***within*** *each half-cell*. For example, in the right-hand half-cell in Figure 13-9, the reaction

A chemical reaction that occurs *within one half-cell* will reach equilibrium and is assumed to remain at equilibrium. Such a reaction is not the net cell reaction.

$$\text{AgCl}(s) \rightleftharpoons \text{Ag}^+(aq) + \text{Cl}^-(aq)$$

is at equilibrium. It is not part of the net cell reaction. It simply occurs when AgCl(*s*) is in contact with water. In the left half-cell, the reaction

$$\text{CH}_3\text{CO}_2\text{H} \rightleftharpoons \text{CH}_3\text{CO}_2^- + \text{H}^+$$

has also come to equilibrium. Neither reaction is part of the net cell redox reaction.

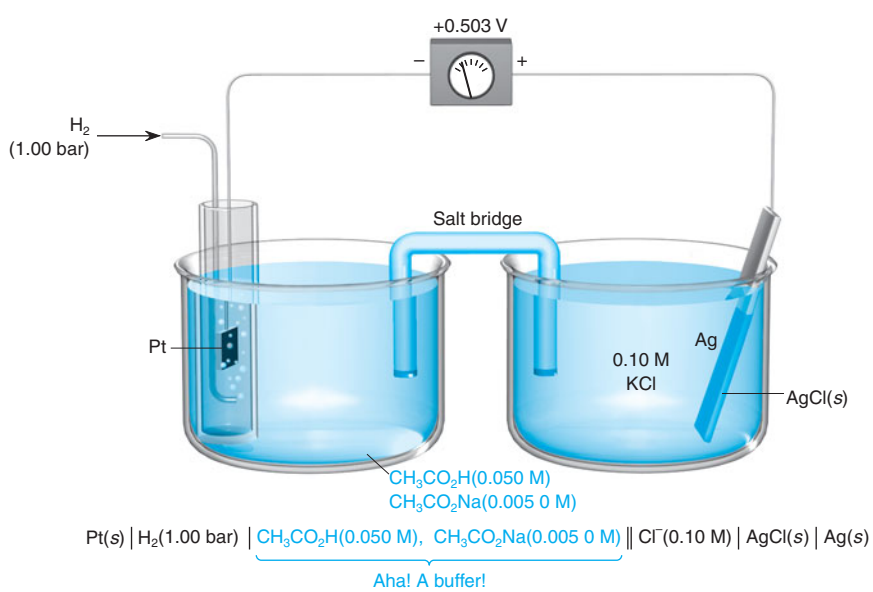


FIGURE 13-9 This galvanic cell can be used to measure the pH of the left half-cell.

The redox reaction for the right half-cell of Figure 13-9 is

$$AgCl(s) + e^- \rightleftharpoons Ag(s) + Cl^-(aq, 0.10\ M) \qquad E^\circ_+ = 0.222\ V$$

But what is the reaction in the left half-cell? The only element we find in two oxidation states is hydrogen. We see that $H_2(g)$ bubbles into the cell, and we also realize that every aqueous solution contains H^+. Therefore, hydrogen is present in two oxidation states, and the half-reaction can be written as

$$2H^+(aq, ?\ M) + 2e^- \rightleftharpoons H_2(g, 1.00\ bar) \qquad E^\circ_- = 0$$

The net cell reaction is not at equilibrium, because the measured voltage is 0.503 V, not 0 V.

The Nernst equation for the net cell reaction is

$$E = E_+ - E_- = (0.222 - 0.059\,16 \log[Cl^-]) - \left(0 - \frac{0.059\,16}{2} \log \frac{P_{H_2}}{[H^+]^2}\right)$$

After inserting the known quantities, we discover that the only unknown is $[H^+]$. *The measured voltage therefore allows us to find $[H^+]$ in the left half-cell*:

$$0.503 = (0.222 - 0.059\,16 \log[0.10]) - \left(0 - \frac{0.059\,16}{2} \log \frac{1.00}{[H^+]^2}\right)$$

$$\Rightarrow [H^+] = 1.8 \times 10^{-4}\ M$$

This, in turn, allows us to evaluate the equilibrium constant for the acid-base reaction that has come to equilibrium in the left half-cell:

$$K_a = \frac{[CH_3CO_2^-][H^+]}{[CH_3CO_2H]} = \frac{(0.005\,0)(1.8 \times 10^{-4})}{0.050} = 1.8 \times 10^{-5}$$

Question Why can we assume that the concentrations of acetic acid and acetate ion are equal to their initial (formal) concentrations?

The cell in Figure 13-9 acts as a *probe* to measure $[H^+]$ in the left half-cell. Using this type of cell, we could determine the equilibrium constant for acid dissociation or base hydrolysis in the left half-cell.

Survival Tips

Problems in this chapter include some brainbusters designed to bring together your knowledge of electrochemistry, chemical equilibrium, solubility, complex formation, and acid-base chemistry. They require you to find the equilibrium constant for a reaction that occurs in only one half-cell. The reaction of interest is not the net cell reaction and is not a redox reaction. Here is a good approach:

Half-reactions that you write *must* involve species that appear in two oxidation states in the cell.

Step 1 Write the two half-reactions and their standard potentials. If you choose a half-reaction for which you cannot find E°, then find another way to write the reaction.

Step 2 Write a Nernst equation for the net reaction and put in all the known quantities. If all is well, there will be only one unknown in the equation.

Step 3 Solve for the unknown concentration and use that concentration to solve the chemical equilibrium problem that was originally posed.

EXAMPLE Analyzing a Very Complicated Cell

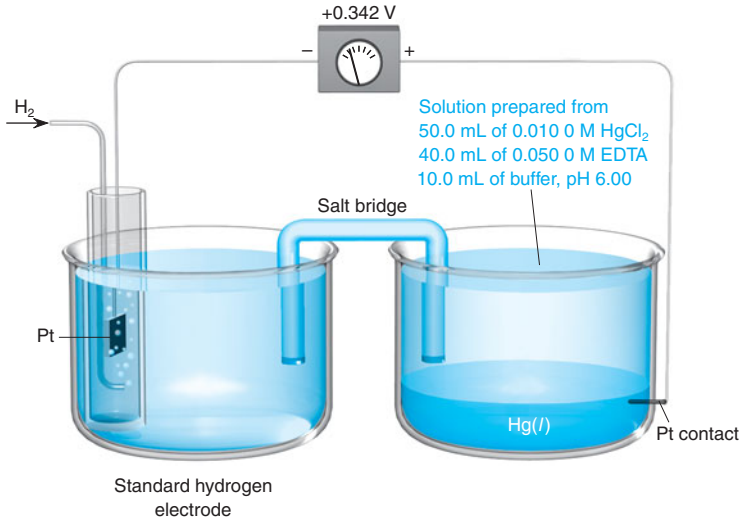
The cell in Figure 13-10 measures the formation constant (K_f) of $Hg(EDTA)^{2-}$. The right-hand compartment contains 0.500 mmol of Hg^{2+} and 2.00 mmol of EDTA in 0.100 L buffered to pH 6.00. The voltage is +0.342 V. Find the value of K_f for $Hg(EDTA)^{2-}$.

Solution

Step 1 The left half-cell is a standard hydrogen electrode for which we can say $E_- = 0$. In the right half-cell, mercury is in two oxidation states. So let's write the half-reaction

$$Hg^{2+} + 2e^- \rightleftharpoons Hg(l) \qquad E^\circ_+ = 0.852\ V$$

$$E_+ = 0.852 - \frac{0.059\,16}{2} \log\left(\frac{1}{[Hg^{2+}]}\right)$$



S.H.E. ‖ $Hg(EDTA)^{2-}$(*aq*, 0.005 00 M), EDTA(*aq*, 0.015 0 M) | Hg(*l*)

FIGURE 13-10 A galvanic cell that can be used to measure the formation constant for $Hg(EDTA)^{2-}$.

In the right half-cell, the reaction between Hg^{2+} and EDTA is

$$Hg^{2+} + Y^{4-} \overset{K_f}{\rightleftharpoons} HgY^{2-}$$

Because we expect K_f to be large, we assume that virtually all the Hg^{2+} has reacted to make HgY^{2-}. Therefore, the concentration of HgY^{2-} is 0.500 mmol/100 mL = 0.005 00 M. The remaining EDTA has a total concentration of (2.00 – 0.50) mmol/100 mL = 0.015 0 M. The right-hand compartment therefore contains 0.005 00 M HgY^{2-}, 0.015 0 M EDTA, and a small, unknown concentration of Hg^{2+}.

The formation constant for HgY^{2-} can be written

$$K_f = \frac{[HgY^{2-}]}{[Hg^{2+}][Y^{4-}]} = \frac{[HgY^{2-}]}{[Hg^{2+}]\alpha_{Y^{4-}}[EDTA]}$$

Recall that $[Y^{4-}] = \alpha_{Y^{4-}}[EDTA]$.

where [EDTA] is the formal concentration of EDTA not bound to metal. In this cell, [EDTA] = 0.015 0 M. The fraction of EDTA in the form Y^{4-} is $\alpha_{Y^{4-}}$ (Section 11-2). Because we know that $[HgY^{2-}]$ = 0.005 00 M, all we need to find is $[Hg^{2+}]$ in order to evaluate K_f.

Step 2 The Nernst equation for the net cell reaction is

$$E = 0.342 = E_+ - E_- = \left[0.852 - \frac{0.059\,16}{2}\log\left(\frac{1}{[Hg^{2+}]}\right)\right] - (0)$$

in which the only unknown is $[Hg^{2+}]$.

Step 3 Now we solve the Nernst equation to find $[Hg^{2+}] = 5.7 \times 10^{-18}$ M, and this value of $[Hg^{2+}]$ allows us to evaluate the formation constant for HgY^{2-}:

$$K_f = \frac{[HgY^{2-}]}{[Hg^{2+}]\alpha_{Y^{4-}}[EDTA]} = \frac{(0.005\,00)}{(5.7 \times 10^{-18})(1.8 \times 10^{-5})(0.015\,0)}$$
$$= 3 \times 10^{21}$$

$\alpha_{Y^{4-}}$ comes from Table 11-1.

The mixture of EDTA plus $Hg(EDTA)^{2-}$ in the cathode serves as a mercuric ion "buffer" that fixes the concentration of Hg^{2+}. This concentration, in turn, determines the cell voltage.

Test Yourself Find K_f if the cell voltage had been 0.300 V. (***Answer:*** 8×10^{22})

13-7 Biochemists Use $E^{\circ\prime}$

In respiration, molecules from food are oxidized by O_2 to yield energy or metabolic intermediates. The standard reduction potentials that we have been using so far apply to systems in which all activities of reactants and products are unity. If H^+ is involved in the reaction,

TABLE 13-2 Reduction potentials of biological interest

Reaction	$E°$ (V)	$E°'$ (V)
$O_2 + 4H^+ + 4e^- \rightleftharpoons 2H_2O$	+1.229	+0.815
$Fe^{3+} + e^- \rightleftharpoons Fe^{2+}$	+0.771	+0.771
$I_2 + 2e^- = 2I^-$	+0.535	+0.535
Cytochrome *a* (Fe^{3+}) + $e^- \rightleftharpoons$ cytochrome *a* (Fe^{2+})	+0.290	+0.290
$O_2(g) + 2H^+ + 2e^- \rightleftharpoons H_2O_2$	+0.695	+0.281
Cytochrome *c* (Fe^{3+}) + $e^- \rightleftharpoons$ cytochrome *c* (Fe^{2+})	—	+0.254
2,6-Dichlorophenolindophenol + $2H^+ + 2e^- \rightleftharpoons$ reduced 2,6-dichlorophenolindophenol	—	+0.22
Dehydroascorbate + $2H^+ + 2e^- \rightleftharpoons$ ascorbate + H_2O	+0.390	+0.058
Fumarate + $2H^+ + 2e^- \rightleftharpoons$ succinate	+0.433	+0.031
Methylene blue + $2H^+ + 2e^- \rightleftharpoons$ reduced product	+0.532	+0.011
Glyoxylate + $2H^+ + 2e^- \rightleftharpoons$ glycolate	—	−0.090
Oxaloacetate + $2H^+ + 2e^- \rightleftharpoons$ malate	+0.330	−0.102
Pyruvate + $2H^+ + 2e^- \rightleftharpoons$ lactate	+0.224	−0.190
Riboflavin + $2H^+ + 2e^- \rightleftharpoons$ reduced riboflavin	—	−0.208
FAD + $2H^+ + 2e^- \rightleftharpoons FADH_2$	—	−0.219
$(\text{Glutathione-S})_2 + 2H^+ + 2e^- \rightleftharpoons$ 2 glutathione-SH	—	−0.23
Safranine T + $2e^- \rightleftharpoons$ leucosafranine T	−0.235	−0.289
$(C_6H_5S)_2 + 2H^+ + 2e^- \rightleftharpoons 2C_6H_5SH$	—	−0.30
$NAD^+ + H^+ + 2e^- \rightleftharpoons NADH$	−0.105	−0.320
$NADP^+ + H^+ + 2e^- \rightleftharpoons NADPH$	—	−0.324
Cystine + $2H^+ + 2e^- \rightleftharpoons$ 2 cysteine	—	−0.340
Acetoacetate + $2H^+ + 2e^- \rightleftharpoons$ L-β-hydroxybutyrate	—	−0.346
Xanthine + $2H^+ + 2e^- \rightleftharpoons$ hypoxanthine + H_2O	—	−0.371
$2H^+ + 2e^- \rightleftharpoons H_2$	0.000	−0.414
Gluconate + $2H^+ + 2e^- \rightleftharpoons$ glucose + H_2O	—	−0.44
$SO_4^{2-} + 2e^- + 2H^+ \rightleftharpoons SO_3^{2-} + H_2O$	—	−0.454
$2SO_3^{2-} + 2e^- + 4H^+ \rightleftharpoons S_2O_4^{2-} + 2H_2O$	—	−0.527

$E°$ applies when pH = 0 ($\mathcal{A}_{H^+} = 1$). *Whenever H^+ appears in a redox reaction, or whenever reactants or products are acids or bases, reduction potentials are pH dependent.*

Because the pH inside a plant or animal cell is about 7, reduction potentials that apply at pH 0 are not particularly appropriate. For example, at pH 0, ascorbic acid (vitamin C) is a more powerful reducing agent than succinic acid. However, at pH 7, this order is reversed. It is the reducing strength at pH 7, not at pH 0, that is relevant to a living cell.

The formal potential at pH = 7 is called $E°'$.

The *standard potential* for a redox reaction is defined for a galvanic cell in which all activities are unity. The **formal potential** is the reduction potential that applies under a *specified* set of conditions (including pH, ionic strength, and concentration of complexing agents). Biochemists call the formal potential at pH 7 $\boldsymbol{E°'}$ (read "*E* zero prime"). Table 13-2 lists $E°'$ values for some biological redox couples.

Relation Between $E°$ and $E°'$

Consider the half-reaction

$$aA + ne^- \rightleftharpoons bB + mH^+ \qquad E°$$

in which A is an oxidized species and B is a reduced species. Both A and B might be acids or bases, as well. The Nernst equation for this half-reaction is

$$E = E° - \frac{0.059\,16}{n}\log\frac{[B]^b[H^+]^m}{[A]^a}$$

To find $E°'$, we rearrange the Nernst equation to a form in which the log term contains only the *formal concentrations* of A and B raised to the powers *a* and *b*, respectively.

Recipe for $E^{\circ\prime}$:

$$E = \underbrace{E^\circ + \text{other terms}}_{\substack{\text{All of this is called } E^{\circ\prime} \\ \text{when pH} = 7}} - \frac{0.059\,16}{n} \log \frac{F_B^b}{F_A^a} \qquad \textbf{(13-26)}$$

If we had included activity coefficients, they would appear in $E^{\circ\prime}$ also.

The entire collection of terms over the brace, evaluated at pH = 7, is called $E^{\circ\prime}$.

To convert [A] or [B] into F_A or F_B, we use fractional composition equations (Section 9-5), which relate the formal (that is, total) concentration of *all* forms of an acid or a base to its concentration in a *particular* form:

Monoprotic system:

$$[HA] = \alpha_{HA}F = \frac{[H^+]F}{[H^+] + K_a} \qquad \textbf{(13-27)}$$

$$[A^-] = \alpha_{A^-}F = \frac{K_aF}{[H^+] + K_a} \qquad \textbf{(13-28)}$$

For a monoprotic acid:

$F = [HA] + [A^-]$

For a diprotic acid:

$F = [H_2A] + [HA^-] + [A^{2-}]$

Diprotic system:

$$[H_2A] = \alpha_{H_2A}\,F = \frac{[H^+]^2F}{[H^+]^2 + [H^+]K_1 + K_1K_2} \qquad \textbf{(13-29)}$$

$$[HA^-] = \alpha_{HA^-}\,F = \frac{K_1[H^+]F}{[H^+]^2 + [H^+]K_1 + K_1K_2} \qquad \textbf{(13-30)}$$

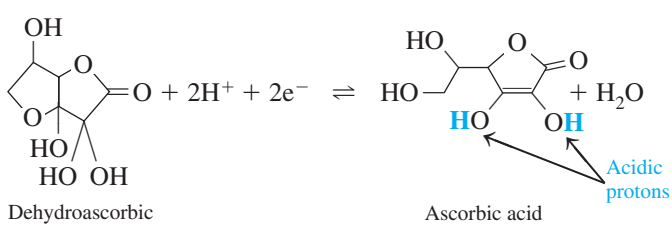
$$[A^{2-}] = \alpha_{A^{2-}}F = \frac{K_1K_2F}{[H^+]^2 + [H^+]K_1 + K_1K_2} \qquad \textbf{(13-31)}$$

where F is the formal concentration of HA or H_2A, K_a is the acid dissociation constant for HA, and K_1 and K_2 are the acid dissociation constants for H_2A.

One way to *measure* $E^{\circ\prime}$ is to establish a half-cell in which the formal concentrations of the oxidized and reduced species are equal and the pH is adjusted to 7. Then the log term in Equation 13-26 is zero and the measured potential (versus S.H.E.) is $E^{\circ\prime}$.

EXAMPLE Calculating the Formal Potential

Find $E^{\circ\prime}$ for the reaction



$E^\circ = 0.390$ V **(13-32)**

Dehydroascorbic acid (oxidized)

Ascorbic acid (vitamin C) (reduced)

$pK_1 = 4.10 \quad pK_2 = 11.79$

Solution Abbreviating dehydroascorbic acid[16] as D, and ascorbic acid as H_2A, we rewrite the reduction as

$$D + 2H^+ + 2e^- \rightleftharpoons H_2A + H_2O$$

for which the Nernst equation is

$$E = E^\circ - \frac{0.059\,16}{2} \log \frac{[H_2A]}{[D][H^+]^2} \qquad \textbf{(13-33)}$$

D is not an acid or a base, so its formal concentration equals its molar concentration: $F_D = [D]$. For the diprotic acid H_2A, we use Equation 13-29 to express $[H_2A]$ in terms of F_{H_2A}:

$$[H_2A] = \frac{[H^+]^2\,F_{H_2A}}{[H^+]^2 + [H^+]K_1 + K_1K_2}$$

Putting these values into Equation 13-33 gives

$$E = E^\circ - \frac{0.059\,16}{2}\log\left(\frac{[H^+]^2F_{H_2A}}{\dfrac{[H^+]^{2+}[H^+]K_1 + K_1K_2}{F_D[H^+]^2}}\right)$$

which can be rearranged to the form

$$E = \underbrace{E^\circ - \frac{0.059\,16}{2}\log\frac{1}{[H^+]^{2+}[H^+]K_1 + K_1K_2}}_{\substack{\text{Formal potential } (= E^{\circ\prime} \text{ if pH} = 7)\\ = +0.062\text{ V}}} - \frac{0.059\,16}{2}\log\frac{F_{H_2A}}{F_D} \qquad \textbf{(13-34)}$$

Putting the values of E°, K_1, and K_2 into Equation 13-34 and setting $[H^+] = 10^{-7.00}$, we find $E^{\circ\prime} = +0.062$ V.

Test Yourself Compute $E^{\circ\prime}$ for the reaction $O_2 + 4H^+ + 4e^- \rightleftharpoons 2H_2O$. (***Answer:*** 0.815 V)

Curve *a* in Figure 13-11 shows how the calculated formal potential for Reaction 13-32 depends on pH. The potential decreases as the pH increases, until pH $\approx$ pK_2. Above pK_2, A^{2-} is the dominant form of ascorbic acid, and no protons are involved in the net redox reaction. Therefore, the potential becomes independent of pH.

A biological example of $E^{\circ\prime}$ is the reduction of Fe(III) in the protein transferrin. This protein has two Fe(III)-binding sites, one in each half of the molecule designated C and N for the carboxyl and amino terminals of the peptide chain. Transferrin carries Fe(III) through the blood to cells that require iron. Membranes of these cells have a receptor that binds Fe(III)-transferrin and takes it into a compartment called an endosome into which H^+ is pumped to lower the pH to ~5.8. Iron is released from transferrin in the endosome and continues into the cell as Fe(II) attached to an intracellular metal-transport protein.

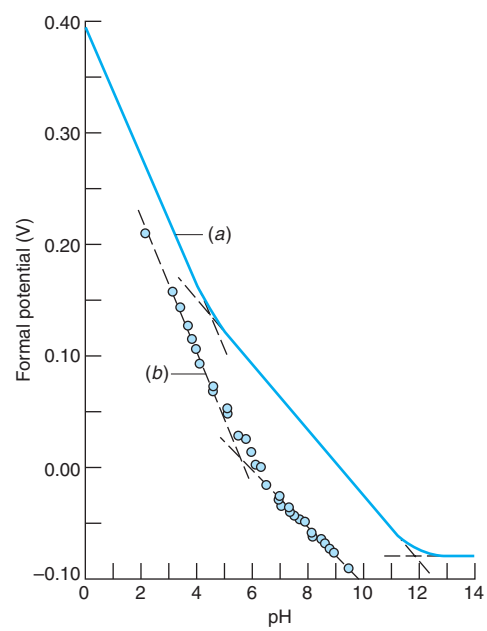


FIGURE 13-11 Reduction potential of ascorbic acid, showing its dependence on pH. (*a*) Graph of the function labeled formal potential in Equation 13-34. (*b*) Experimental polarographic half-wave reduction potential of ascorbic acid in a medium of ionic strength = 0.2 M. The half-wave potential (Chapter 16) is nearly the same as the formal potential. At high pH (>12), the half-wave potential does not level off to a slope of 0, as Equation 13-34 predicts. Instead, a hydrolysis reaction of ascorbic acid occurs and the chemistry is more complex than Reaction 13-32. [From J. J. Ruiz, A. Aldaz, and M. Dominguez, *Can. J. Chem.* **1977,** *55,* 2799; ibid. **1978,** *56,* 1533.]

The entire cycle of transferrin uptake, metal removal, and transferrin release back to the bloodstream takes 1–2 min. The time required for Fe(III) to dissociate from transferrin at pH 5.8 is ~6 min, which is too long to account for release in the endosome. The reduction potential of Fe(III)-transferrin at pH 5.8 is $E^{\circ\prime} = -0.52$ V, which is too low for physiologic reductants.

The mystery of how Fe(III) is released from transferrin in the endosome was solved by measuring $E^{\circ\prime}$ for the Fe(III)-transferrin-receptor complex at pH 5.8. To simplify the chemistry, transferrin was cleaved and only the C-terminal half of the protein (designated Trf_C) was used. Figure 13-12 shows measurements of $\log\{[Fe(III)Trf_C]/[Fe(II)Trf_C]\}$ for free protein and for the protein-receptor complex. In Equation 13-26, $E = E^{\circ\prime}$ when the log term is zero (that is, when $[Fe(III)Trf_C] = [Fe(II)Trf_C]$). Figure 13-12 shows that $E^{\circ\prime}$ for $Fe(III)Trf_C$ is near –0.50 V, but $E^{\circ\prime}$ for the $Fe(III)Trf_C$-receptor complex is –0.29 V. The reducing agents NADH and NADPH in Table 13-2 are strong enough to reduce $Fe(III)Trf_C$ bound to its receptor at pH 5.8, but not strong enough to reduce free Fe(III)-transferrin.

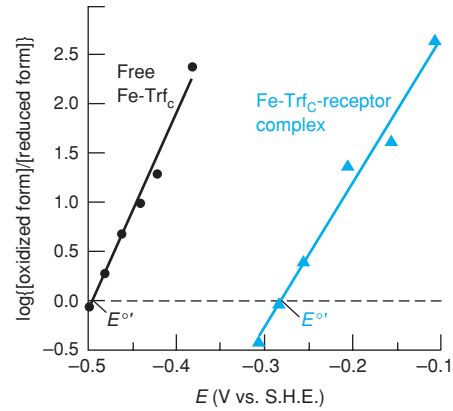


FIGURE 13-12 **Spectroscopic measurement of $\log\{[Fe(III)Trf_C]/[Fe(II)Trf_C]\}$ versus potential at pH 5.8.** [From S. Dhungana, C. H. Taboy, O. Zak, M. Larvie, A. L. Crumbliss, and P. Aisen, "Redox Properties of Human Transferrin Bound to Its Receptor," *Biochemistry* **2004,** *43,* 205.]

Terms to Understand

ampere
anode
cathode
coulomb
current
$E^{\circ\prime}$
electric potential
electrochemistry
electrode
Faraday constant
formal potential
galvanic cell
half-reaction
joule
Latimer diagram
Nernst equation
ohm
Ohm's law
oxidant
oxidation
oxidizing agent
potentiometer
power
reaction quotient
redox reaction
reducing agent
reductant
reduction
resistance
salt bridge
standard hydrogen electrode
standard reduction potential
volt
watt

Summary

Work done when a charge of q coulombs passes through a potential difference of E volts is work $= E \cdot q$. The maximum work that can be done on the surroundings by a spontaneous chemical reaction is related to the free energy change for the reaction: work $= -\Delta G$. If the chemical change produces a potential difference, E, the relation between free energy and the potential difference is $\Delta G = -nFE$. Ohm's law ($I = E/R$) describes the relation between current, voltage, and resistance in an electric circuit. It can be combined with the definitions of work and power (P = work per second) to give $P = E \cdot I = I^2R$.

A galvanic cell uses a spontaneous redox reaction to produce electricity. The electrode at which oxidation occurs is the anode, and the electrode at which reduction occurs is the cathode. Two half-cells are usually separated by a salt bridge that allows ions to migrate from one side to the other to maintain charge neutrality but prevents reactants in the two half-cells from mixing. The standard reduction potential of a half-reaction is measured by pairing that half-reaction with a standard hydrogen electrode. The term "standard" means that activities of reactants and products are unity. If several half-reactions are added to give another half-reaction, the standard potential of the net half-reaction can be found by equating the free energy of the net half-reaction to the sum of free energies of the component half-reactions.

The voltage for a complete reaction is the difference between the potentials of the two half-reactions: $E = E_+ - E_-$, where E_+ is the potential of the half-cell connected to the positive terminal of the potentiometer and E_- is the potential of the half-cell connected to the negative terminal. The potential of each half-reaction is given by the Nernst equation: $E = E^\circ - (0.059\ 16/n) \log Q$ (at 25°C), where each reaction is written as a reduction and Q is the reaction quotient. The reaction quotient has the same form as the equilibrium constant, but it is evaluated with concentrations existing at the time of interest. Electrons flow through the circuit from the electrode with the more negative potential to the electrode with the more positive potential.

Complex equilibria can be studied by making them part of an electrochemical cell. If we measure the voltage and know the concentrations (activities) of all but one of the reactants and products, the Nernst equation allows us to compute the concentration of the unknown species. The electrochemical cell serves as a probe for that species.

Biochemists use the formal potential of a half-reaction at pH 7 ($E^{\circ\prime}$) instead of the standard potential (E°), which applies at pH 0. $E^{\circ\prime}$ is found by writing the Nernst equation for the half-reaction and grouping together all terms except the logarithm containing the formal concentrations of reactant and product. The combination of terms, evaluated at pH 7, is $E^{\circ\prime}$.

Exercises

13-A. In olden days, mercury cells with the following chemistry were used to power heart pacemakers:

$$Zn(s) + HgO(s) \rightarrow ZnO(s) + Hg(l) \qquad E^\circ = 1.35\ V$$

What is the cell voltage? If the power required to operate the pacemaker is 0.010 0 W, how many kilograms of HgO (FM 216.59) will be consumed in 365 days? How many pounds of HgO is this? (1 pound = 453.6 g)

13-B. Calculate E° and K for each of the following reactions.

(a) $I_2(s) + 5Br_2(aq) + 6H_2O \rightleftharpoons 2IO_3^- + 10Br^- + 12H^+$

(b) $Cr^{2+} + Fe(s) \rightleftharpoons Fe^{2+} + Cr(s)$

(c) $Mg(s) + Cl_2(g) \rightleftharpoons Mg^{2+} + 2Cl^-$

(d) $5MnO_2(s) + 4H^+ \rightleftharpoons 3Mn^{2+} + 2MnO_4^- + 2H_2O$

(e) $Ag^+ + 2S_2O_3^{2-} \rightleftharpoons Ag(S_2O_3)_2^{3-}$

(f) $CuI(s) \rightleftharpoons Cu^+ + I^-$

13-C. Calculate the voltage of each of the following cells. With the reasoning in Figure 13-8, state the direction of electron flow.

(a) $Fe(s) \mid FeBr_2(0.010\ M) \parallel NaBr(0.050\ M) \mid Br_2(l) \mid Pt(s)$

(b) $Cu(s) \mid Cu(NO_3)_2(0.020\ M) \parallel Fe(NO_3)_2(0.050\ M) \mid Fe(s)$

(c) $Hg(l) \mid Hg_2Cl_2(s) \mid KCl(0.060\ M) \parallel KCl(0.040\ M) \mid Cl_2(g, 0.50\ bar) \mid Pt(s)$

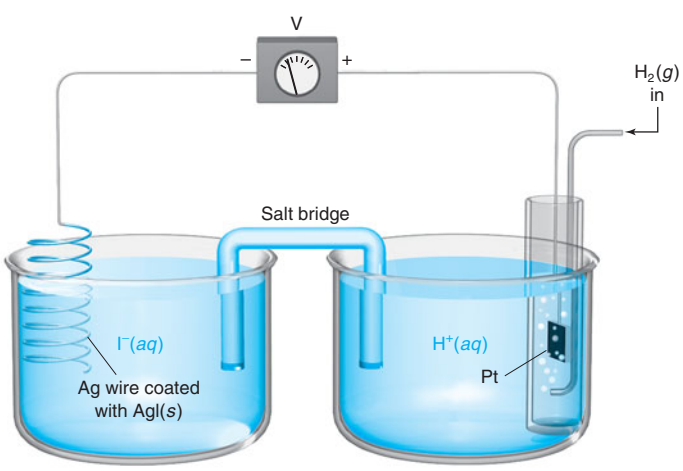
13-D. The left half-reaction of the cell drawn here can be written in *either* of two ways:

$$AgI(s) + e^- \rightleftharpoons Ag(s) + I^- \qquad (1)$$

$$Ag^+ + e^- \rightleftharpoons Ag(s) \qquad (2)$$

The right half-cell reaction is

$$H^+ + e^- \rightleftharpoons \frac{1}{2}H_2(g) \qquad (3)$$



$Ag(s) \mid AgI(s) \mid NaI\ (0.10\ M) \parallel HCl\ (0.10\ M) \mid H_2(g, 0.20\ bar) \mid Pt(s)$

(a) Using Reactions 2 and 3, calculate E° and write the Nernst equation for the cell.

(b) Use the value of K_{sp} for AgI to compute $[Ag^+]$ and find the cell voltage. By the reasoning in Figure 13-8, in which direction do electrons flow?

(c) Suppose, instead, that you wish to describe the cell with Reactions 1 and 3. We know that the cell voltage (E, not E°) must be the same, no matter which description we use. Write the Nernst equation for Reactions 1 and 3 and use it to find E° in Reaction 1. Compare your answer with the value in Appendix H.

13-E. Calculate the voltage of the cell

$$Cu(s) \mid Cu^{2+}(0.030\ M) \parallel K^+Ag(CN)_2^-(0.010\ M),\ HCN(0.10\ F),\ \text{buffer to pH } 8.21 \mid Ag(s)$$

by considering the following reactions:

$$Ag(CN)_2^- + e^- \rightleftharpoons Ag(s) + 2CN^- \qquad E^\circ = -0.310\ V$$

$$HCN \rightleftharpoons H^+ + CN^- \qquad pK_a = 9.21$$

By the reasoning in Figure 13-8, in which direction do electrons flow?

13-F. **(a)** Write a balanced equation for the reaction $PuO_2^+ \rightarrow Pu^{4+}$ and calculate E° for the reaction.

$$\begin{array}{ccccccc} PuO_2^{2+} & \xrightarrow{+0.966} & PuO_2^+ & \xrightarrow{?} & Pu^{4+} & \xrightarrow{+1.006} & Pu^{3+} \\ & & & \underset{1.021}{\longrightarrow} & & & \uparrow \end{array}$$

(b) Predict whether an equimolar mixture of PuO_2^{2+} and PuO_2^+ will oxidize H_2O to O_2 at a pH of 2.00 and $P_{O_2} = 0.20$ bar. Will O_2 be liberated at pH 7.00?

13-G. Calculate the voltage of the following cell, in which KHP is potassium hydrogen phthalate, the monopotassium salt of phthalic acid. By the reasoning in Figure 13-8, in which direction do electrons flow?

$$Hg(l) \mid Hg_2Cl_2(s) \mid KCl(0.10\ M) \parallel KHP(0.050\ M) \mid H_2(g, 1.00\ bar) \mid Pt(s)$$

13-H. The following cell has a voltage of 0.083 V:

$$Hg(l) \mid Hg(NO_3)_2(0.001\ 0\ M), KI(0.500\ M) \parallel S.H.E.$$

From this voltage, calculate the equilibrium constant for the reaction

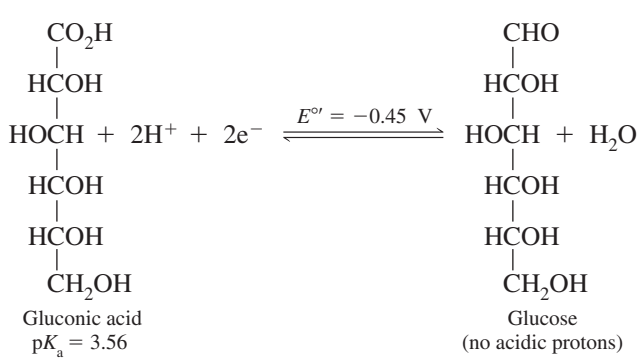
$$Hg^{2+} + 4I^- \rightleftharpoons HgI_4^{2-}$$

In 0.5 M KI, virtually all the mercury is present as HgI_4^{2-}.

13-I. The formation constant for $Cu(EDTA)^{2-}$ is 6.3×10^{18}, and E° is +0.339 V for the reaction $Cu^{2+} + 2e^- \rightleftharpoons Cu(s)$. From this information, find E° for the reaction

$$CuY^{2-} + 2e^- \rightleftharpoons Cu(s) + Y^{4-}$$

13-J. On the basis of the following reaction, state which compound, $H_2(g)$ or glucose, is the more powerful reducing agent at pH = 0.00.



13-K. Living cells convert energy derived from sunlight or combustion of food into energy-rich ATP (adenosine triphosphate)

molecules. For ATP synthesis, $\Delta G = +34.5$ kJ/mol. This energy is then made available to the cell when ATP is hydrolyzed to ADP (adenosine diphosphate). In animals, ATP is synthesized when protons pass through a complex enzyme in the mitochondrial membrane.[17] Two factors account for the movement of protons through this enzyme into the mitochondrion (see the figure): (1) $[H^+]$ is higher outside the mitochondrion than inside because protons are *pumped* out of the mitochondrion by enzymes that catalyze the oxidation of food. (2) The inside of the mitochondrion is negatively charged with respect to the outside.

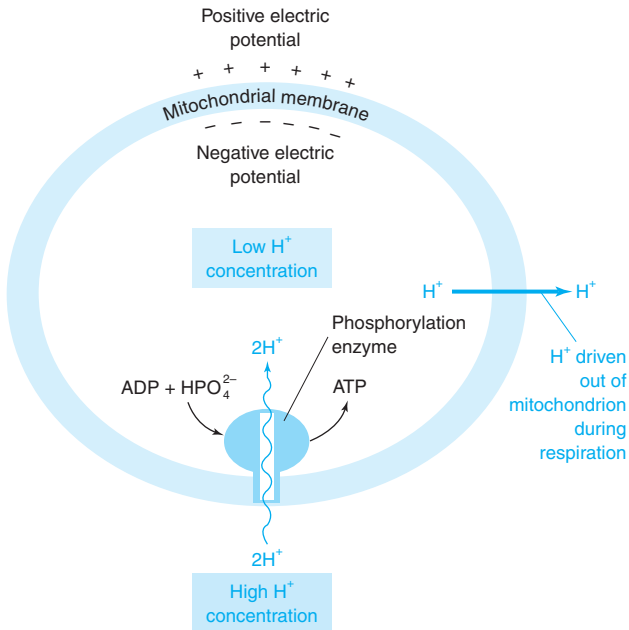
(a) The synthesis of one ATP molecule requires $2H^+$ to pass through the phosphorylation enzyme. The difference in free energy when a molecule travels from a region of high activity to a region of low activity is

$$\Delta G = -RT \ln \frac{\mathcal{A}_{\text{high}}}{\mathcal{A}_{\text{low}}}$$

How big must the pH difference be (at 298 K) if the passage of two protons is to provide enough energy to synthesize one ATP molecule?

(b) pH differences this large have not been observed in mitochondria. How great an electric potential difference between inside and outside is necessary for the movement of two protons to provide energy to synthesize ATP? In answering this question, neglect any contribution from the pH difference.

(c) The energy for ATP synthesis is thought to be provided by *both* the pH difference and the electric potential. If the pH difference is 1.00 pH unit, what is the magnitude of the potential difference?



Problems

Basic Concepts

13-1. Explain the difference between electric charge (q, coulombs), electric current (I, amperes), and electric potential (E, volts).

13-2. **(a)** How many electrons are in one coulomb?

(b) How many coulombs are in one mole of charge?

13-3. The basal rate of consumption of O_2 by a 70-kg human is about 16 mol of O_2 per day. This O_2 oxidizes food and is reduced to H_2O, providing energy for the organism:

$$O_2 + 4H^+ + 4e^- \rightleftharpoons 2H_2O$$

(a) To what current (in amperes = C/s) does this respiration rate correspond? (Current is defined by the flow of electrons from food to O_2.)

(b) Compare your answer in part (**a**) with the current drawn by a refrigerator using 5.00×10^2 W at 115 V. Remember that power (in watts) = work/s = $E \cdot I$.

(c) If the electrons flow from nicotinamide adenine dinucleotide (NADH) to O_2, they experience a potential drop of 1.1 V. What is the power output (in watts) of our human friend?

13-4. A 6.00-V battery is connected across a 2.00-kΩ resistor.

(a) How many electrons per second flow through the circuit?

(b) How many joules of heat are produced for each electron?

(c) If the circuit operates for 30.0 min, how many moles of electrons will have flowed through the resistor?

(d) What voltage would the battery need to deliver for the power to be 1.00×10^2 W?

13-5. Consider the redox reaction

$$I_2 + \underset{\text{Thiosulfate}}{2S_2O_3^{2-}} \rightleftharpoons 2I^- + \underset{\text{Tetrathionate}}{S_4O_6^{2-}}$$

(a) Identify the oxidizing agent on the left side of the reaction and write a balanced oxidation half-reaction.

(b) Identify the reducing agent of the left side of the reaction and write a balanced reduction half-reaction.

(c) How many coulombs of charge are passed from reductant to oxidant when 1.00 g of thiosulfate reacts?

(d) If the rate of reaction is 1.00 g of thiosulfate consumed per minute, what current (in amperes) flows from reductant to oxidant?

13-6. The space shuttle's expendable booster engines derive their power from solid reactants:

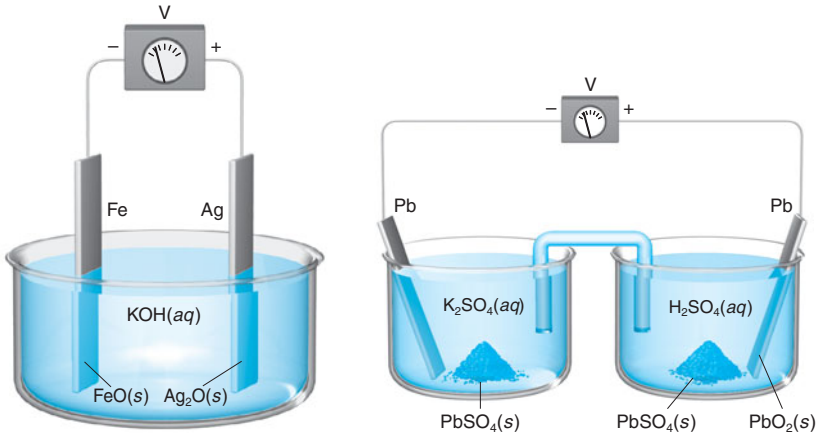
$$\underset{\text{FM 117.49}}{6NH_4^+ClO_4^-(s)} + 10Al(s) \rightarrow 3N_2(g) + 9H_2O(g) + 5Al_2O_3(s) + 6HCl(g)$$

(a) Find the oxidation numbers of the elements N, Cl, and Al in reactants and products. Which reactants act as reducing agents and which act as oxidants?

(b) The heat of reaction is –9 334 kJ for every 10 mol of Al consumed. Express this as heat released per gram of total reactants.

Galvanic Cells

13-7. Explain how a galvanic cell uses a spontaneous chemical reaction to generate electricity.



Galvanic cells for Problem 13.8

13-8. Write a line notation and two reduction half-reactions for each cell pictured above.

13-9. Draw a picture of the following cell and write reduction half-reactions for each electrode:
$Pt(s) \mid Fe^{3+}(aq), Fe^{2+}(aq) \parallel Cr_2O_7^{2-}(aq), Cr^{3+}(aq), HA(aq) \mid Pt(s)$

13-10. Consider the rechargeable battery:
$Zn(s) \mid ZnCl_2(aq) \parallel Cl^-(aq) \mid Cl_2(l) \mid C(s)$

(a) Write reduction half-reactions for each electrode. From which electrode will electrons flow from the battery into a circuit if the electrode potentials are not too different from $E°$ values?

(b) If the battery delivers a constant current of 1.00×10^3 A for 1.00 h, how many kilograms of Cl_2 will be consumed?

13-11. *Lithium-ion battery.*

(a) Ideal formulas for the electrodes of the Li^+-ion battery described in the chapter opener are C_6Li (FM 79.01) and $LiCoO_2$ (FM 97.87). When the battery operates, C_6Li is consumed and $LiCoO_2$ is formed. Write a half-reaction for each electrode, assuming that $x = 1$ in the reaction $C_6Li + Li_{1-x}CoO_2 \rightleftharpoons C_6Li_{1-x} + LiCoO_2$. (In fact, $x \neq 1$ in real cells.) Which is the anode and which is the cathode?

(b) Charge capacity of an electrode in a battery is expressed as mA·h/g, which is the number of milliamperes delivered by 1 g of material for 1 hour. How many coulombs are in 1 mA·h?

(c) Show that the theoretical capacity of the battery is 274 mA·h/g $LiCoO_2$.

(d) A Li^+-ion battery can deliver 140 mA·h/g $LiCoO_2$. What fraction of Li in the formula $LiCoO_2$ is available?

(e) Energy stored by a battery per unit mass of an electrode material is expressed as W·h/g. A Li^+-ion battery delivers 140 mA·h/g $LiCoO_2$ at 3.7 V. Express the energy storage as W·h/g $LiCoO_2$.

Standard Potentials

13-12. Which will be the strongest oxidizing agent under standard conditions (that is, all activities = 1): HNO_2, Se, UO_2^{2+}, Cl_2, H_2SO_3, or MnO_2?

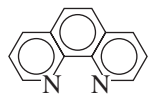
13-13. (a) Cyanide ion causes $E°$ for Fe(III) to decrease:

$$\underset{\text{Ferric}}{Fe^{3+}} + e^- \rightleftharpoons \underset{\text{Ferrous}}{Fe^{2+}} \qquad E° = 0.771 \text{ V}$$

$$\underset{\text{Ferricyanide}}{Fe(CN)_6^{3-}} + e^- \rightleftharpoons \underset{\text{Ferrocyanide}}{Fe(CN)_6^{4-}} \qquad E° = 0.356 \text{ V}$$

Which ion, Fe(III) or Fe(II), is stabilized more by complexing with CN^-?

(b) Using Appendix H, answer the same question when the ligand is phenanthroline instead of cyanide.



Phenanthroline

Nernst Equation

13-14. What is the difference between E and $E°$ for a redox reaction? Which one runs down to 0 when the complete cell comes to equilibrium?

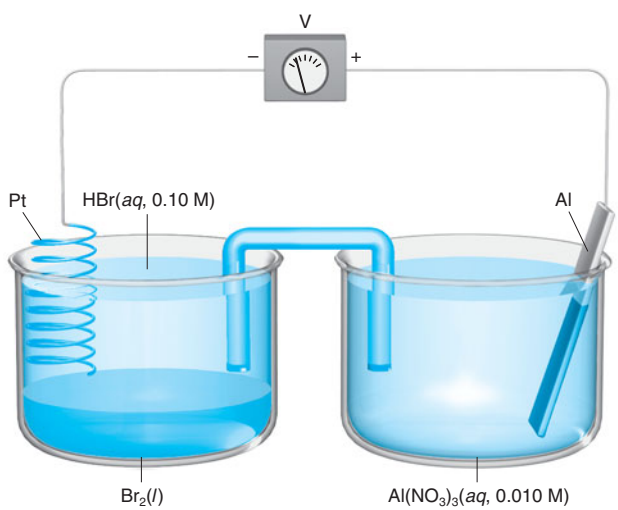
13-15. (a) Use the Nernst equation to write the spontaneous chemical reaction that occurs in the cell in Demonstration 13-1.

(b) If you use your fingers as a salt bridge in Demonstration 13-1, will your body take in Cu^{2+} or Zn^{2+}?

13-16. Write the Nernst equation for the following half-reaction and find E when pH = 3.00 and $P_{AsH_3} = 1.0$ mbar.

$$As(s) + 3H^+ + 3e^- \rightleftharpoons \underset{\text{Arsine}}{AsH_3(g)} \qquad E° = -0.238 \text{ V}$$

13-17. (a) Write the line notation for the following cell.



(b) Calculate the potential of each half-cell and the cell voltage, E. In which direction will electrons flow through the circuit? Write the spontaneous net cell reaction.

(c) The left half-cell was loaded with 14.3 mL of $Br_2(l)$ (density = 3.12 g/mL). The aluminum electrode contains 12.0 g of Al. Which element, Br_2 or Al, is the limiting reagent? (That is, which reagent will be used up first?)

(d) If the cell is somehow operated under conditions in which it produces a constant voltage of 1.50 V, how much electrical work will have been done when 0.231 mL of $Br_2(l)$ has been consumed?

(e) If the potentiometer is replaced by a 1.20-kΩ resistor and if the heat dissipated by the resistor is 1.00×10^{-4} J/s, at what rate (grams per second) is Al(*s*) dissolving? (In this question, the voltage is not 1.50 V.)

13-18. A nickel-metal hydride rechargeable battery formerly used in laptop computers is based on the following chemistry:

Cathode:

$$NiOOH(s) + H_2O + e^- \underset{\text{charge}}{\overset{\text{discharge}}{\rightleftharpoons}} Ni(OH)_2(s) + OH^-$$

Anode:

$$MH(s) + OH^- \underset{\text{charge}}{\overset{\text{discharge}}{\rightleftharpoons}} M(s) + H_2O + e^-$$

The anode material, MH, is a transition metal hydride or rare earth alloy hydride. Explain why the voltage remains nearly constant during the entire discharge cycle.

13-19. Suppose that the concentrations of NaF and KCl were each 0.10 M in the cell

$$Pb(s)|PbF_2(s)|F^-(aq)\|Cl^-(aq)|AgCl(s)|Ag(s)$$

(a) Using the half-reactions $2AgCl(s) + 2e^- \rightleftharpoons 2Ag(s) + 2Cl^-$ and $PbF_2(s) + 2e^- \rightleftharpoons Pb(s) + 2F^-$, calculate the cell voltage.

(b) By the reasoning in Figure 13-8, in which direction do electrons flow?

(c) Now calculate the cell voltage by using the reactions $2Ag^+ + 2e^- \rightleftharpoons 2Ag(s)$ and $Pb^{2+} + 2e^- \rightleftharpoons Pb(s)$. For this part, you will need the solubility products for PbF_2 and AgCl.

13-20. The following cell was set up to measure the standard reduction potential of the Ag^+ | Ag couple:

$$Pt(s)|HCl(0.010\,00\text{ M}), H_2(g)\|AgNO_3(0.010\,00\text{ M})|Ag(s)$$

The temperature was 25°C (the standard condition) and atmospheric pressure was 751.0 Torr. Because the vapor pressure of water is 23.8 Torr at 25°C, P_{H_2} in the cell was 751.0 – 23.8 = 727.2 Torr. The Nernst equation for the cell, including activity coefficients, is derived as follows:

Right electrode: $Ag^+ + e^- \rightleftharpoons Ag(s)$ $\qquad E^\circ_+ = E^\circ_{Ag^+|Ag}$

Left electrode: $H^+ + e^- \rightleftharpoons \frac{1}{2}H_2(g)$ $\qquad E^\circ_- = 0$ V

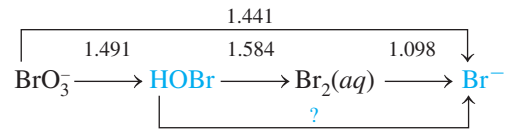
$$E_+ = E^\circ_{Ag^+|Ag} - 0.059\,16 \log\left(\frac{1}{[Ag^+]\gamma_{Ag^+}}\right)$$

$$E_- = 0 - 0.059\,16 \log\left(\frac{P^{1/2}_{H_2}}{[H^+]\gamma_{H^+}}\right)$$

$$E = E_+ - E_- = E^\circ_{Ag^+|Ag} - 0.059\,16 \log\left(\frac{[H^+]\gamma_{H^+}}{P^{1/2}_{H_2}[Ag^+]\gamma_{Ag^+}}\right)$$

Given a measured cell voltage of +0.798 3 V and using activity coefficients from Table 7-1, find $E^\circ_{Ag^+|Ag}$. Be sure to express P_{H_2} in bar in the reaction quotient.

13-21. Write a balanced chemical equation (in acidic solution) for the reaction represented by the question mark on the lower arrow.[18] Calculate E° for the reaction.



13-22. What must be the relation between E°_1 and E°_2 if the species X^+ is to diproportionate spontaneously under standard conditions to X^{3+} and X(*s*)? Write a balanced equation for the disproportionation.

$$X^{3+} \xrightarrow{E^\circ_1} X^+ \xrightarrow{E^\circ_2} X(s)$$

13-23. *Including activities,* calculate the voltage of the cell Ni(*s*) | $NiSO_4$(0.002 0 M) ‖ $CuCl_2$(0.003 0 M) | Cu(*s*). Assume that the salts are completely dissociated (that is, neglect ion-pair formation). By the reasoning in Figure 13-8, in which direction do electrons flow?

Relation of E° and the Equilibrium Constant

13-24. For the reaction $CO + \frac{1}{2}O_2 \rightleftharpoons CO_2$, $\Delta G^\circ = -257$ kJ per mole of CO at 298 K. Find E° and the equilibrium constant for the reaction.

13-25. Calculate E°, ΔG°, and K for the following reactions.

(a) $4Co^{3+} + 2H_2O \rightleftharpoons 4Co^{2+} + O_2(g) + 4H^+$

(b) $Ag(S_2O_3)^{3-}_2 + Fe(CN)^{4-}_6 \rightleftharpoons Ag(s) + 2S_2O^{2-}_3 + Fe(CN)^{3-}_6$

13-26. A solution contains 0.100 M Ce^{3+}, 1.00×10^{-4} M Ce^{4+}, 1.00×10^{-4} M Mn^{2+}, 0.100 M MnO^-_4, and 1.00 M $HClO_4$.

(a) Write a balanced net reaction that can occur between species in this solution.

(b) Calculate ΔG° and K for the reaction.

(c) Calculate E for the conditions given.

(d) Calculate ΔG for the conditions given.

(e) At what pH would the given concentrations of Ce^{4+}, Ce^{3+}, Mn^{2+}, and MnO^-_4 be in equilibrium at 298 K?

13-27. For the cell Pt(*s*) | VO^{2+}(0.116 M), V^{3+}(0.116 M), H^+(1.57 M) ‖ Sn^{2+}(0.031 8 M), Sn^{4+}(0.031 8 M) | Pt(*s*), E (not E°) = –0.289 V. Write the net cell reaction and calculate its equilibrium constant. Do not use E° values from Appendix H to answer this question.

13-28. Calculate E° for the half-reaction $Pd(OH)_2(s) + 2e^- \rightleftharpoons Pd(s) + 2OH^-$ given that K_{sp} for $Pd(OH)_2$ is 3×10^{-28} and E° = 0.915 V for the reaction $Pd^{2+} + 2e^- \rightleftharpoons Pd(s)$.

13-29. From the standard potentials for reduction of $Br_2(aq)$ and $Br_2(l)$ in Appendix H, calculate the solubility of Br_2 in water at 25°C. Express your answer as g/L.

13-30. Given the following information, calculate the standard potential for the reaction $FeY^- + e^- \rightleftharpoons FeY^{2-}$, where Y is EDTA.

$FeY^- + e^- \rightleftharpoons Fe^{2+} + Y^{4-}$ $\qquad E^\circ = -0.730$ V

FeY^{2-}: $\qquad K_f = 2.1 \times 10^{14}$

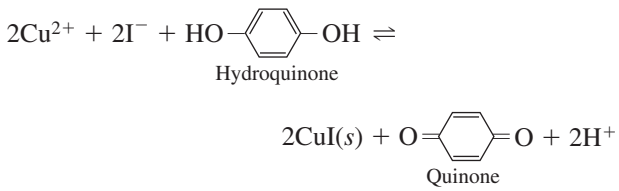
FeY^-: $\qquad K_f = 1.3 \times 10^{25}$

13-31. For modest temperature excursions away from 25°C, the change in $E°$ for a half-reaction can be written in the form

$$E°(T) = E° + \left(\frac{dE°}{dT}\right)\Delta T$$

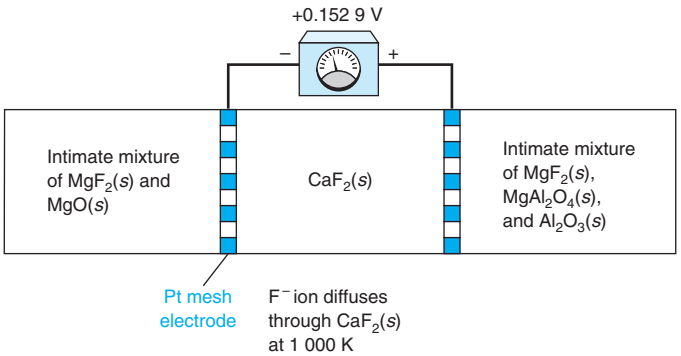
where $E°(T)$ is the standard reduction potential at temperature T (°C), and ΔT is $(T - 25)$. For the reaction $Al^{3+} + 3e^- \rightleftharpoons Al(s)$, $dE°/dT = 0.533$ mV/K near 25°C. Find $E°$ for this half-reaction at 50°C.

13-32. This problem is slightly tricky. Calculate $E°$, $\Delta G°$, and K for the reaction



which is the sum of *three* half-reactions listed in Appendix H. Use $\Delta G°$ $(= -nFE°)$ for each of the half-reactions to find $\Delta G°$ for the net reaction. Note that, if you reverse the direction of a reaction, you reverse the sign of $\Delta G°$.

13-33. *Thermodynamics of a solid-state reaction.* The following electrochemical cell is reversible at 1 000 K in an atmosphere of flowing $O_2(g)$:[19]



Left half-cell: $MgF_2(s) + \frac{1}{2}O_2(g) + 2e^- \rightleftharpoons MgO(s) + 2F^-$

Right half-cell: $MgF_2(s) + Al_2O_3(s) + \frac{1}{2}O_2(g) + 2e^- \rightleftharpoons MgAl_2O_4(s) + 2F^-$

(a) Write a Nernst equation for each half-cell. Write the net reaction and its Nernst equation. The activity of $O_2(g)$ is the same on both sides, and the activity of F^- is the same on both sides, governed by F^- ions diffusing through $CaF_2(s)$. Show that the observed voltage is $E°$ for the net reaction.

(b) From the relation $\Delta G° = -nFE°$, find $\Delta G°$ for the net reaction. Note that 1 V = 1 J/C.

(c) The cell voltage in the temperature range $T = 900$ to 1 250 K is $E(V) = 0.122\,3 + 3.06 \times 10^{-5}\,T$. Assuming that $\Delta H°$ and $\Delta S°$ are constant, find $\Delta H°$ and $\Delta S°$ from the relation $\Delta G° = \Delta H° - T\Delta S°$.

Using Cells as Chemical Probes

13-34. With Figure 13-10 as an example, explain what we mean when we say that there is equilibrium *within* each half-cell but not necessarily *between* the two half-cells.

13-35. The cell $Pt(s) \mid H_2(g, 1.00 \text{ bar}) \mid H^+(aq, pH = 3.60) \parallel Cl^-(aq, x \text{ M}) \mid AgCl(s) \mid Ag(s)$ can be used as a probe to find the concentration of Cl^- in the right compartment.

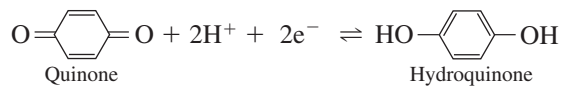
(a) Write reactions for each half-cell, a balanced net cell reaction, and the Nernst equation for the net cell reaction.

(b) Given a measured cell voltage of 0.485 V, find $[Cl^-]$ in the right compartment.

13-36. The quinhydrone electrode was introduced in 1921 as a means of measuring pH.[20]

$$Pt(s) \mid \text{1:1 mole ratio of quinone}(aq) \text{ and hydroquinone}(aq), \text{ unknown pH} \parallel Cl^-(aq, 0.50 \text{ M}) \mid Hg_2Cl_2(s) \mid Hg(l) \mid Pt(s)$$

The solution whose pH is to be measured is placed in the left half-cell, which also contains a 1:1 mole ratio of quinone and hydroquinone. The half-cell reaction is



(a) Write half-reactions and Nernst equations for each half-cell.

(b) Ignoring activities, rearrange the Nernst equation for the net reaction to the form $E(\text{cell}) = A + (B \cdot pH)$, where A and B are constants. Calculate A and B at 25°C.

(c) If the pH were 4.50, in which direction would electrons flow through the potentiometer?

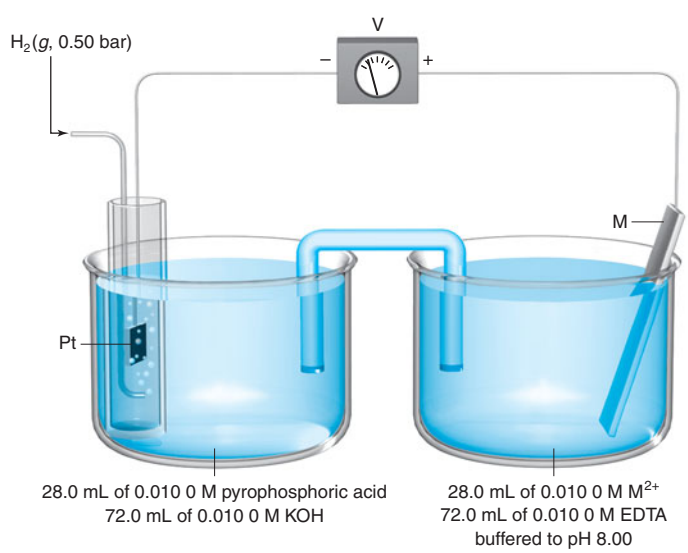
13-37. The voltage for the following cell is 0.490 V. Find K_b for the organic base RNH_2.

$$Pt(s) \mid H_2(1.00 \text{ bar}) \mid RNH_2(aq, 0.10 \text{ M}), RNH_3^+Cl^-(aq, 0.050 \text{ M}) \parallel \text{S.H.E.}$$

13-38. The voltage of the cell shown here is –0.246 V. The right half-cell contains the metal ion, M^{2+}, whose standard reduction potential is –0.266 V.

$$M^{2+} + 2e^- \rightleftharpoons M(s) \qquad E° = -0.266 \text{ V}$$

Calculate K_f for the metal-EDTA complex.



13-39. The following cell was constructed to find the difference in K_{sp} between two naturally occurring forms of $CaCO_3(s)$, called *calcite* and *aragonite*.[21]

$$Pb(s)|PbCO_3(s)|CaCO_3(s, \text{calcite})|\text{buffer(pH 7.00)}\|$$
$$\text{buffer(pH 7.00)}|CaCO_3(s, \text{aragonite})|PbCO_3(s)|Pb(s)$$

Each compartment of the cell contains a mixture of solid $PbCO_3$ ($K_{sp} = 7.4 \times 10^{-14}$) and either calcite or aragonite, both of which have $K_{sp} \approx 5 \times 10^{-9}$. Each solution was buffered to pH 7.00 with an inert buffer, and the cell was completely isolated from atmospheric CO_2. The measured cell voltage was –1.8 mV. Find the ratio of solubility products, K_{sp} (for calcite)/K_{sp} (for aragonite).

13-40. *Do not ignore activity coefficients in this problem.* If the voltage for the following cell is 0.512 V, find K_{sp} for $Cu(IO_3)_2$. Neglect any ion pairing.

$$Ni(s)|NiSO_4(0.002\,5\text{ M})\|KIO_3(0.10\text{ M})|Cu(IO_3)_2(s)|Cu(s)$$

Biochemists Use $E^{\circ\prime}$

13-41. Explain what $E^{\circ\prime}$ is and why it is preferred over E° in biochemistry.

13-42. We are going to find $E^{\circ\prime}$ for the reaction $C_2H_2(g) + 2H^+ + 2e^- \rightleftharpoons C_2H_4(g)$.

(a) Write the Nernst equation for the half-reaction, using E° from Appendix H.

(b) Rearrange the Nernst equation to the form

$$E = E^\circ + \text{other terms} - \frac{0.059\,16}{2}\log\left(\frac{P_{C_2H_4}}{P_{C_2H_2}}\right)$$

(c) The quantity (E° + other terms) is $E^{\circ\prime}$. Evaluate $E^{\circ\prime}$ for pH = 7.00.

13-43. Evaluate $E^{\circ\prime}$ for the half-reaction $(CN)_2(g) + 2H^+ + 2e^- \rightleftharpoons 2HCN(aq)$.

13-44. Calculate $E^{\circ\prime}$ for the reaction

$$\underset{\text{Oxalic acid}}{H_2C_2O_4} + 2H^+ + 2e^- \rightleftharpoons \underset{\text{Formic acid}}{2HCO_2H} \qquad E^\circ = 0.204\text{ V}$$

13-45. HOx is a monoprotic acid with $K_a = 1.4 \times 10^{-5}$ and H_2Red^- is a diprotic acid with $K_1 = 3.6 \times 10^{-4}$ and $K_2 = 8.1 \times 10^{-8}$. Find E° for the reaction

$$HOx + e^- \rightleftharpoons H_2Red^- \qquad E^{\circ\prime} = 0.062\text{ V}$$

13-46. Given the following information, find K_a for nitrous acid, HNO_2.

$$NO_3^- + 3H^+ + 2e^- \rightleftharpoons HNO_2 + H_2O \qquad E^\circ = 0.940\text{ V}$$
$$E^{\circ\prime} = 0.433\text{ V}$$

13-47. Using the reaction

$$HPO_4^{2-} + 2H^+ + 2e^- \rightleftharpoons HPO_3^{2-} + H_2O \qquad E^\circ = -0.234\text{ V}$$

and acid dissociation constants from Appendix G, calculate E° for the reaction

$$H_2PO_4^- + H^+ + 2e^- \rightleftharpoons HPO_3^{2-} + H_2O$$

13-48. This problem requires Beer's law from Chapter 17. The oxidized form (Ox) of a flavoprotein that functions as a one-electron reducing agent has a molar absorptivity (ε) of $1.12 \times 10^4\ M^{-1}cm^{-1}$ at 457 nm at pH 7.00. For the reduced form (Red), $\varepsilon = 3.82 \times 10^3\ M^{-1}cm^{-1}$ at 457 nm at pH 7.00.

$$Ox + e^- \rightleftharpoons Red \qquad E^{\circ\prime} = -0.128\text{ V}$$

The substrate (S) is the molecule reduced by the protein.

$$Red + S \rightleftharpoons Ox + S^-$$

Both S and S^- are colorless. A solution at pH 7.00 was prepared by mixing enough protein plus substrate (Red + S) to produce initial concentrations [Red] = [S] = 5.70×10^{-5} M. The absorbance at 457 mm was 0.500 in a 1.00-cm cell.

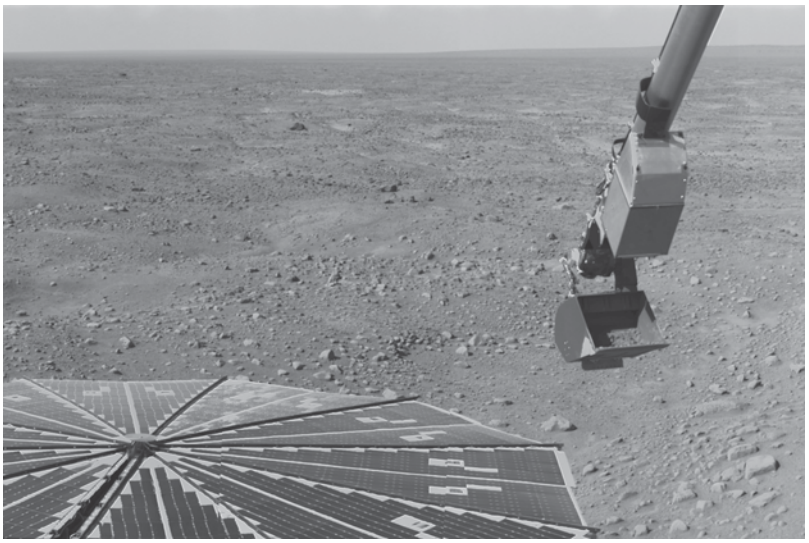
(a) Calculate the concentrations of Ox and Red from the absorbance data.

(b) Calculate the concentrations of S and S^-.

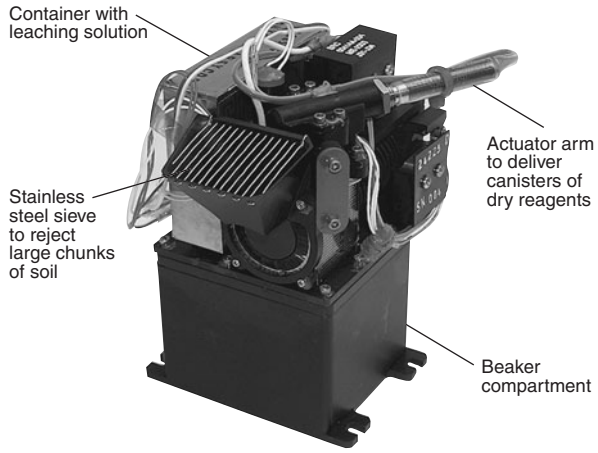
(c) Calculate the value of $E^{\circ\prime}$ for the reaction $S + e^- \rightleftharpoons S^-$.

14 Electrodes and Potentiometry

CHEM LAB ON MARS



Robotic arm of *Phoenix Mars Lander* scoops up soil for chemical analysis on Mars. [NASA photograph courtesy S. Kounaves, Tufts University.]



One of four Wet Chemistry Laboratory cells for soil analysis on *Phoenix*. [NASA photograph courtesy S. Kounaves, Tufts University.]

Sam Kounaves and his students at Tufts University had the thrill of a lifetime in 2008 when their Wet Chemistry Laboratory on the *Phoenix Mars Lander* began sending back data on soil scooped up near the north pole of Mars. The objective was to learn the chemical composition of salts that could be leached from the soil by stirring it with water. Measurements of dissolved salts were made by 23 electrochemical sensors, of which 15 were ion-selective electrodes similar to those discussed in this chapter. Sensors were embedded in the walls of four 40-mL epoxy plastic "beakers" used for the leaching experiments.[1]

The temperature on Mars is well below 0°C, so each operation began by using precious electric power for up to 90 min to melt an aqueous solution. A 25-mL solution containing 10^{-5} M ionic standards was added to the beaker and sensor responses were monitored for 15 min to obtain a first calibration point for each sensor. A crucible containing known masses of solid salts was then dropped into the beaker and the contents dissolved by stirring. Sensors were monitored for 30 min to obtain a second calibration point.

Earlier, the robotic arm scooped up soil and dumped it through a sieve to reject particles larger than 2 mm. Soil particles fell into a 1-mL drawer, which was later retracted to drop the soil into the leaching solution in the beaker. Each day, scientists on Earth wrote a series of commands to be carried out by the robotic arm. On the next day, photos transmitted by the Lander showed what the arm did and what the soil looked like. From the photos, scientists would plan commands for the following day.

Sensor response was monitored for 200 min while salts from the soil dissolved. The mixture was allowed to freeze during the Martian night and was thawed and measured the next day to observe changes induced by the freeze-thaw cycle. Then 4 mg of 2-nitrobenzoic acid were added to see what changes would be induced by weak acidification for 90 min. Finally, the solution was titrated by three additions of solid $BaCl_2$ to measure SO_4^{2-} by precipitating $BaSO_4$. Even on Mars in 2008, a precipitation titration has its place.

The sequence of operations measured Ca^{2+}, Mg^{2+}, K^+, NO_3^-, NH_4^+, SO_4^{2-}, Cl^-, Br^-, I^-, and pH with ion-selective electrodes. Other electrodes measured conductivity, reduction potential, redox couples, and reducible metals including Cu^{2+}, Cd^{2+}, Pb^{2+}, Fe^{2+}, Fe^{3+}, and Hg^{2+}. The biggest discovery was a completely unexpected, high concentration of ClO_4^- sensed by the nitrate electrode (Box 14-3). A second surprise was that sulfate was not observed.

Clever chemists have designed electrodes that respond selectively to specific analytes in solution or in the gas phase. Typical ion-selective electrodes are about the size of your pen. Really clever chemists created ion-sensing field effect transistors that are just hundreds of micrometers in size and can be inserted into a blood vessel. The use of electrodes to measure voltages that provide chemical information is called **potentiometry.**

In the simplest case, analyte is an *electroactive species* that is part of a galvanic cell. An **electroactive species** is one that can donate or accept electrons at an electrode. We turn the unknown solution into a half-cell by inserting an electrode, such as a Pt wire, that can transfer electrons to or from the analyte. Because this electrode responds to analyte, it is called the **indicator electrode.** We connect this half-cell to a second half-cell by a salt bridge. The second half-cell has a fixed composition, so it has a constant potential. Because of its constant potential, the second half-cell is called a **reference electrode.** The cell voltage is the difference between the variable potential of the analyte half-cell and the constant potential of the reference electrode.

Indicator electrode: responds to analyte activity

Reference electrode: maintains a fixed (reference) potential

14-1 Reference Electrodes

Suppose you want to measure the relative amounts of Fe^{2+} and Fe^{3+} in a solution. You can make this solution part of a galvanic cell by inserting a Pt wire and connecting the cell to a constant-potential half-cell by a salt bridge, as shown in Figure 14-1.

The two half-reactions (written as *reductions*) are

Right electrode: $Fe^{3+} + e^- \rightleftharpoons Fe^{2+}$ $\qquad E^\circ_+ = 0.771$ V

Left electrode: $AgCl(s) + e^- \rightleftharpoons Ag(s) + Cl^-$ $\qquad E^\circ_- = 0.222$ V

The electrode potentials are

$$E_+ = 0.771 - 0.059\,16 \log\left(\frac{[Fe^{2+}]}{[Fe^{3+}]}\right)$$

$$E_- = 0.222 - 0.059\,16 \log[Cl^-]$$

E_+ is the potential of the electrode attached to the positive input of the potentiometer. E_- is the potential of the electrode attached to the negative input of the potentiometer.

and the cell voltage is the difference $E_+ - E_-$:

$$E = \left\{0.771 - 0.059\,16 \log\left(\frac{[Fe^{2+}]}{[Fe^{3+}]}\right)\right\} - \{0.222 - 0.059\,16 \log[Cl^-]\}$$

But $[Cl^-]$ in the left half-cell is constant, fixed by the solubility of KCl, with which the solution is saturated. Therefore, the cell voltage changes only when the quotient $[Fe^{2+}]/[Fe^{3+}]$ changes.

The voltage really tells us the quotient of *activities*, $\mathcal{A}_{Fe^{2+}}/\mathcal{A}_{Fe^{3+}}$. We will neglect activity coefficients and write the Nernst equation with concentrations instead of activities.

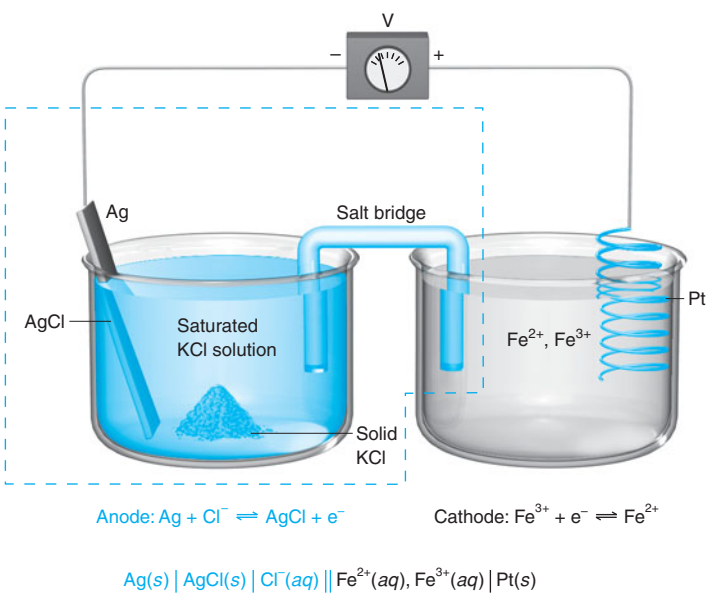


FIGURE 14-1 A galvanic cell that can be used to measure the quotient $[Fe^{2+}]/[Fe^{3+}]$ in the right half-cell. The Pt wire is the *indicator electrode*, and the entire left half-cell plus salt bridge (enclosed by the dashed line) can be considered a *reference electrode*.

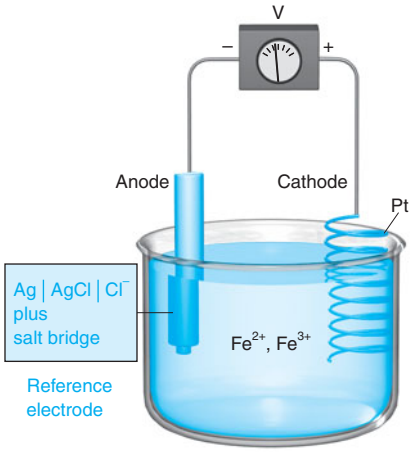


FIGURE 14-2 Another view of Figure 14-1. The contents of the dashed box in Figure 14-1 are now considered to be a reference electrode dipped into the analyte solution.

The half-cell on the left in Figure 14-1 acts as a *reference electrode*. We can picture the cell and salt bridge enclosed by the dashed line as a single unit dipped into the analyte solution, as shown in Figure 14-2. The Pt wire is the indicator electrode, whose potential responds to the quotient $[Fe^{2+}]/[Fe^{3+}]$. The reference electrode completes the redox reaction and provides a *constant potential* to the left side of the potentiometer. Changes in the cell voltage result from changes in the quotient $[Fe^{2+}]/[Fe^{3+}]$.

Silver-Silver Chloride Reference Electrode[2]

The half-cell enclosed by the dashed line in Figure 14-1 is called a **silver-silver chloride electrode.** Figure 14-3 shows how the electrode is reconstructed as a thin tube that can be dipped into analyte solution. Figure 14-4 shows a *double-junction electrode* that minimizes contact between analyte solution and KCl from the electrode. Silver-silver chloride and calomel reference electrodes (described next) are used because they are convenient. A standard hydrogen electrode (S.H.E.) is difficult to use because it requires H_2 gas and a freshly prepared catalytic Pt surface that is easily poisoned in many solutions.

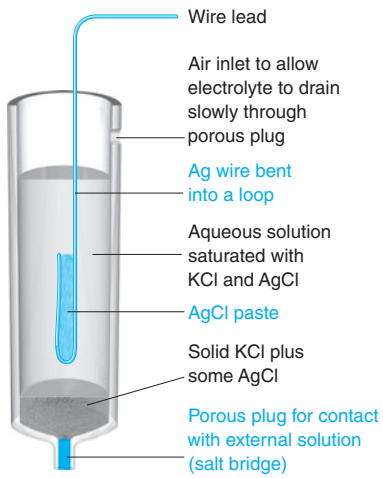


FIGURE 14-3 Silver-silver chloride reference electrode.

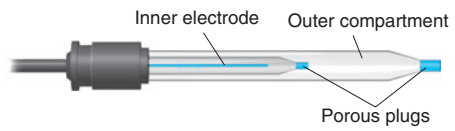


FIGURE 14-4 Double-junction reference electrode. The inner electrode is the same as the one in Figure 14-3. The solution in the outer compartment is compatible with analyte solution. For example, if you do not want Cl^- to contact the analyte, the outer electrode can be filled with KNO_3 solution. The inner and outer solutions slowly mix, so the outer compartment must be refilled periodically with fresh KNO_3 solution. [Courtesy Fisher Scientific, Pittsburgh, PA.]

The standard reduction potential for the AgCl | Ag couple is +0.222 V at 25°C. This would be the potential of a silver-silver chloride electrode if $\mathcal{A}_{Cl^-}$ were unity. But the activity of Cl^- in a saturated solution of KCl at 25°C is not unity, and the potential of the electrode in Figure 14-3 is +0.197 V with respect to S.H.E. at 25°C.

Ag | AgCl electrode: $\quad AgCl(s) + e^- \rightleftharpoons Ag(s) + Cl^-$ $\quad E^\circ = +0.222$ V

E(saturated KCl) = +0.197 V

A problem with reference electrodes is that porous plugs become clogged, thus causing sluggish, unstable electrical response. Some designs incorporate a free-flowing capillary in place of the porous plug. Other designs allow you to force fresh solution from the electrode through the electrode-analyte junction prior to a measurement.

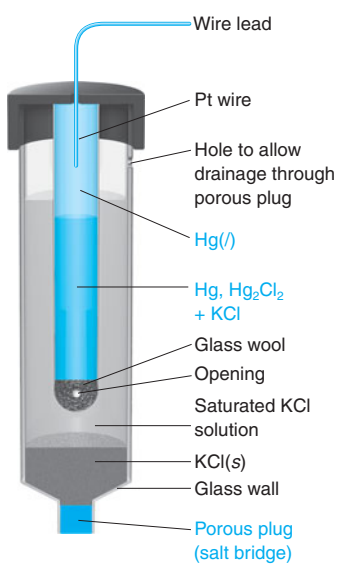


FIGURE 14-5 A saturated calomel electrode (S.C.E.).

Calomel Electrode

The **calomel electrode** in Figure 14-5 is based on the reaction

Calomel electrode: $\quad \frac{1}{2}Hg_2Cl_2(s) + e^- \rightleftharpoons Hg(l) + Cl^-$ $\quad E^\circ = +0.268$ V

Mercury(I) chloride (Calomel)

E(saturated KCl) = +0.241 V

The standard potential for this reaction is +0.268 V. If the cell is saturated with KCl at 25°C, the potential is +0.241 V. A calomel electrode saturated with KCl is called a **saturated calomel electrode,** abbreviated **S.C.E.** The advantage in using saturated KCl is that $[Cl^-]$ does not change if some liquid evaporates.

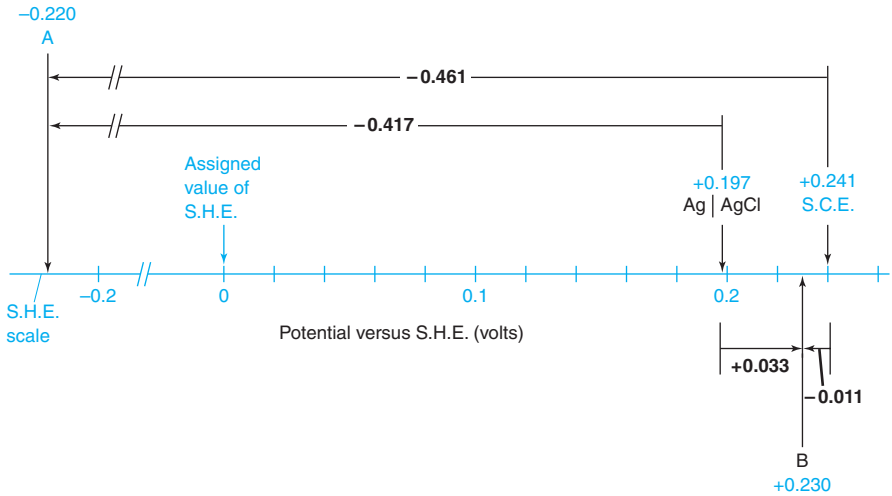


FIGURE 14-6 A diagram that helps us convert electrode potential between different reference scales.

Voltage Conversions Between Different Reference Scales

If an electrode has a potential of −0.461 V with respect to a calomel electrode, what is the potential with respect to a silver-silver chloride electrode? What would be the potential with respect to the standard hydrogen electrode?

To answer these questions, Figure 14-6 shows the positions of the calomel and silver-silver chloride electrodes with respect to the standard hydrogen electrode. We see that point A, which is −0.461 V from S.C.E., is −0.417 V from the silver-silver chloride electrode and −0.220 V with respect to S.H.E. Point B, whose potential is +0.033 V from silver-silver chloride, is −0.011 V from S.C.E. and +0.230 V from S.H.E. By keeping this diagram in mind, you can convert potentials from one scale into another.

14-2 Indicator Electrodes

We will study two broad classes of indicator electrodes. *Metal electrodes* described in this section develop an electric potential in response to a redox reaction at the metal surface. *Ion-selective electrodes* described later are not based on redox processes. Instead, selective binding of one type of ion to a membrane generates an electric potential.

The most common metal indicator electrode is platinum, which is relatively *inert*—it does not participate in many chemical reactions. Its purpose is simply to transmit electrons to or from species in solution. Gold electrodes are even more inert than Pt. Various types of carbon are used as indicator electrodes because the rates of many redox reactions on the carbon surface are fast. A metal electrode works best when its surface is large and clean. To clean the electrode, dip it in hot 8 M HNO_3 in a fume hood and rinse with distilled water.

Figure 14-7 shows how a silver electrode can be used with a reference electrode to measure Ag^+ concentration.[3] The reaction at the Ag indicator electrode is

$$Ag^+ + e^- \rightleftharpoons Ag(s) \qquad E^\circ_+ = 0.799 \text{ V}$$

The calomel reference half-cell reaction is

$$Hg_2Cl_2(s) + 2e^- \rightleftharpoons 2Hg(l) + 2Cl^- \qquad E_- = 0.241 \text{ V}$$

The reference potential (E_-, not E°_-) is fixed at 0.241 V because the reference cell is saturated with KCl. The Nernst equation for the entire cell is therefore

$$E = E_+ - E_- = \underbrace{\left\{0.799 - 0.059\,16 \log\left(\frac{1}{[Ag^+]}\right)\right\}}_{\text{Potential of Ag | Ag}^+\text{ indicator electrode}} - \underbrace{\{0.241\}}_{\text{Potential of S.C.E. reference electrode}}$$

$$E = 0.558 + 0.059\,16 \log[Ag^+] \qquad (14\text{-}1)$$

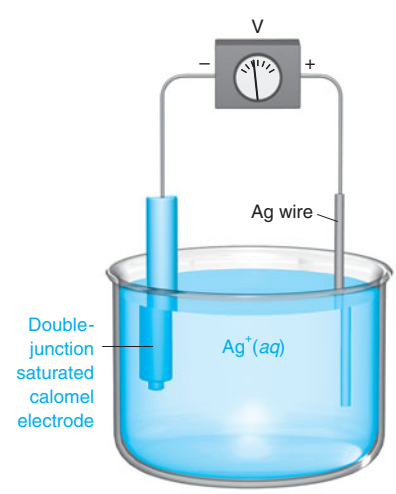


FIGURE 14-7 Use of Ag and calomel electrodes to measure $[Ag^+]$. The calomel electrode has a double junction, like that in Figure 14-4. The outer compartment of the electrode is filled with KNO_3, so there is no direct contact between Cl^- in the inner compartment and Ag^+ in the beaker.

That is, the voltage of the cell in Figure 14-7 provides a measure of $[Ag^+]$. Ideally, the voltage changes by 59.16 mV (at 25°C) for each factor-of-10 change in $[Ag^+]$.

EXAMPLE **Potentiometric Precipitation Titration**

A 100.0-mL solution containing 0.100 0 M NaCl was titrated with 0.100 0 M $AgNO_3$, and the voltage of the cell shown in Figure 14-7 was monitored. The equivalence volume is V_e = 100.0 mL. Calculate the voltage after the addition of **(a)** 65.0 and **(b)** 135.0 mL of $AgNO_3$.

Solution The titration reaction is

$$Ag^+ + Cl^- \rightarrow AgCl(s)$$

(a) At 65.0 mL, 65.0% of Cl^- has precipitated and 35.0% remains in solution:

$$[Cl^-] = \underbrace{(0.350)}_{\text{Fraction remaining}} \underbrace{(0.100\,0\text{ M})}_{\text{Original concentration of Cl}^-} \underbrace{\left(\frac{100.0}{165.0}\right)}_{\text{Dilution factor}} = 0.021\,2\text{ M}$$

Initial volume of Cl^-

Total volume of solution

To find the cell voltage in Equation 14-1, we need to know $[Ag^+]$:

$$[Ag^+][Cl^-] = K_{sp} \Rightarrow [Ag^+] = \frac{K_{sp}}{[Cl^-]} = \frac{1.8 \times 10^{-10}}{0.021\,2\text{ M}} = 8.5 \times 10^{-9}\text{ M}$$

The cell voltage is therefore

$$E = 0.558 + 0.059\,16 \log(8.5 \times 10^{-9}) = 0.081\text{ V}$$

(b) At 135.0 mL, there is an excess of 35.0 mL of $AgNO_3$ = 3.50 mmol Ag^+ in a total volume of 235.0 mL. Therefore, $[Ag^+]$ = (3.50 mmol)/(235.0 mL) = 0.014 9 M. The cell voltage is

$$E = 0.558 + 0.059\,16 \log(0.014\,9) = 0.450\text{ V}$$

Test Yourself Find the voltage after addition of 99.0 mL of $AgNO_3$. (***Answer:*** 0.177 V)

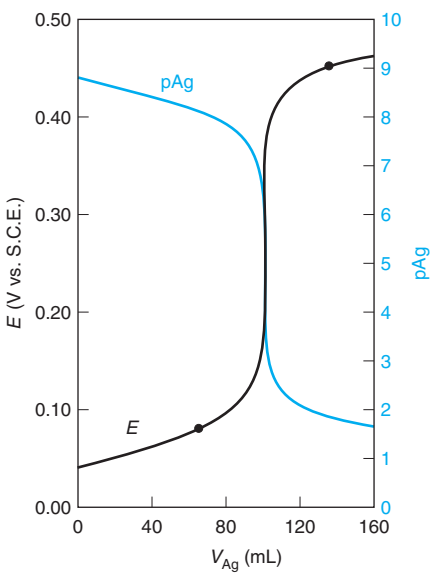


FIGURE 14-8 Titration curve computed for the addition of 0.100 0 M Ag^+ to 100.0 mL of 0.100 0 M Cl^- with the electrodes in Figure 14-7. Points computed at 65.0 and 135.0 mL are shown. Colored line is pAg = $-\log[Ag^+]$.

Figure 14-8 shows the titration curve for the preceding example. There is a strong analogy to acid-base titrations, with Ag^+ replacing H^+ and Cl^- acting as a base being titrated. As the acid-base titration proceeds, $[H^+]$ increases and pH decreases. As the Ag^+/Cl^- titration proceeds, $[Ag^+]$ increases and pAg ($\equiv -\log[Ag^+]$) decreases. The silver electrode measures pAg, which you can see by substituting pAg = $-\log[Ag^+]$ into Equation 14-1:

$$E = 0.558 - 0.059\,16\text{ pAg} \qquad \textbf{(14-2)}$$

The cell responds to a change in $[Cl^-]$, which necessarily changes $[Ag^+]$ because $[Ag^+][Cl^-] = K_{sp}$.

A silver electrode is also a halide electrode, if solid silver halide is present.[4] If the solution contains AgCl(*s*), we substitute $[Ag^+] = K_{sp}/[Cl^-]$ into Equation 14-1 to find an expression relating the cell voltage to $[Cl^-]$:

$$E = 0.558 + 0.059\,16 \log\left(\frac{K_{sp}}{[Cl^-]}\right) \qquad \textbf{(14-3)}$$

Demonstration 14-1 is a great example of indicator and reference electrodes.

Metals including Ag, Cu, Zn, Cd, and Hg can be used as indicator electrodes for their aqueous ions. Most metals, however, are unsuitable for this purpose because the equilibrium $M^{n+} + ne^- \rightleftharpoons M$ is not readily established at the metal surface.

DEMONSTRATION 14-1 Potentiometry with an Oscillating Reaction[5]

The Belousov-Zhabotinskii reaction is a cerium-catalyzed oxidation of malonic acid by bromate, in which the quotient $[Ce^{3+}]/[Ce^{4+}]$ oscillates by a factor of 10 to 100.[6]

$$\underset{\text{Malonic acid}}{3CH_2(CO_2H)_2} + \underset{\text{Bromate}}{2BrO_3^-} + 2H^+ \rightarrow \underset{\text{Bromomalonic acid}}{2BrCH(CO_2H)_2} + 3CO_2 + 4H_2O$$

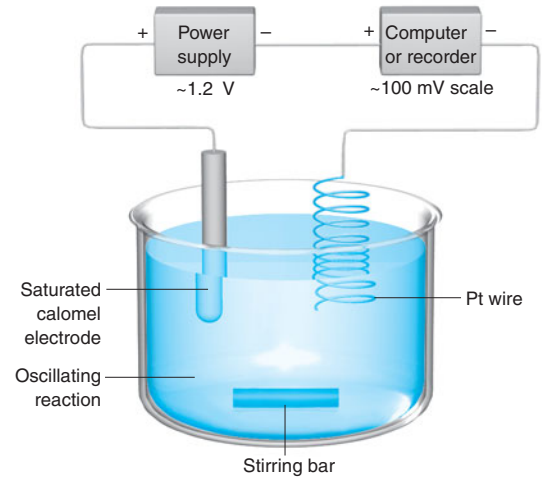
When the Ce^{4+} concentration is high, the solution is yellow. When Ce^{3+} predominates, the solution is colorless. With redox indicators (Section 15-2), this reaction oscillates through a sequence of colors.[7]

Oscillation between yellow and colorless is set up in a 300-mL beaker with the following solutions:

160 mL of 1.5 M H_2SO_4
40 mL of 2 M malonic acid
30 mL of 0.5 M $NaBrO_3$ (or saturated $KBrO_3$)
4 mL of saturated ceric ammonium sulfate, $(Ce(SO_4)_2 \cdot 2(NH_4)_2SO_4 \cdot 2H_2O)$

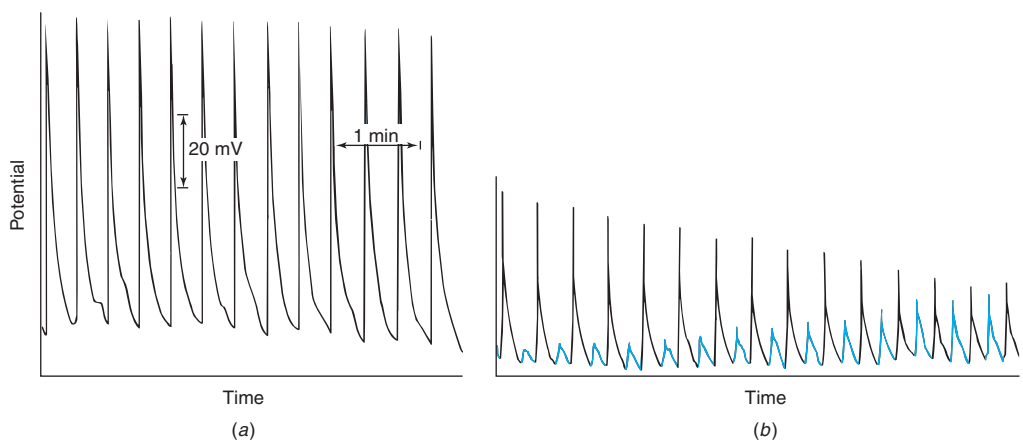
After an induction period of 5 to 10 min with magnetic stirring, oscillations can be initiated by adding 1 mL of ceric ammonium sulfate solution. The reaction may need more Ce^{4+} over a 5-min period to initiate oscillations.

A galvanic cell is built around the reaction as shown in the figure. The quotient $[Ce^{3+}]/[Ce^{4+}]$ is monitored by Pt and calomel electrodes. You should be able to write the cell reactions and a Nernst equation for this experiment.



Apparatus used to monitor the quotient $[Ce^{3+}]/[Ce^{4+}]$ for an oscillating reaction. [The idea for this demonstration came from George Rossman, California Institute of Technology.]

In place of a potentiometer (a pH meter), use a computer or recorder to show the oscillations. Because the potential oscillates over a range of ~100 mV but is centered near ~1.2 V, the cell voltage is offset by ~1.2 V with any available power supply.[8] Trace *a* shows what is usually observed. The potential changes rapidly during the abrupt colorless-to-yellow change and gradually during the gentle yellow-to-colorless change. Trace *b* shows two different cycles superimposed in the same solution. This unusual event occurred in a reaction that had been oscillating normally for about 30 min.[9]



14-3 What Is a Junction Potential?

Whenever dissimilar electrolyte solutions are in contact, a voltage difference called the **junction potential** develops at their interface. This small voltage (usually a few millivolts) is found at each end of a salt bridge connecting two half-cells. *The junction potential puts a fundamental limitation on the accuracy of direct potentiometric measurements*, because we usually do not know the contribution of the junction to the measured voltage.

$$E_{observed} = E_{cell} + E_{junction}$$

Because the junction potential is usually unknown, E_{cell} is uncertain.

TABLE 14-1 Mobilities of ions in water at 25°C

Ion	Mobility $[m^2/(s \cdot V)]^a$
H^+	36.30×10^{-8}
Rb^+	7.92×10^{-8}
K^+	7.62×10^{-8}
NH_4^+	7.61×10^{-8}
La^{3+}	7.21×10^{-8}
Ba^{2+}	6.59×10^{-8}
Ag^+	6.42×10^{-8}
Ca^{2+}	6.12×10^{-8}
Cu^{2+}	5.56×10^{-8}
Na^+	5.19×10^{-8}
Li^+	4.01×10^{-8}
OH^-	20.50×10^{-8}
$Fe(CN)_6^{4-}$	11.45×10^{-8}
$Fe(CN)_6^{3-}$	10.47×10^{-8}
SO_4^{2-}	8.27×10^{-8}
Br^-	8.13×10^{-8}
I^-	7.96×10^{-8}
Cl^-	7.91×10^{-8}
NO_3^-	7.40×10^{-8}
ClO_4^-	7.05×10^{-8}
F^-	5.70×10^{-8}
HCO_3^-	4.61×10^{-8}
$CH_3CO_2^-$	4.24×10^{-8}

a. The mobility of an ion is the terminal velocity that the particle achieves in an electric field of 1 V/m. Mobility = velocity/field. The units of mobility are therefore (m/s)/(V/m) = $m^2/(s \cdot V)$.

TABLE 14-2 Liquid junction potentials at 25°C

Junction	Potential (mV)
0.1 M NaCl | 0.1 M KCl	−6.4
0.1 M NaCl | 3.5 M KCl	−0.2
1 M NaCl | 3.5 M KCl	−1.9
0.1 M HCl | 0.1 M KCl	+27
0.1 M HCl | 3.5 M KCl	+3.1

NOTE: A positive sign means that the right side of the junction becomes positive with respect to the left side.

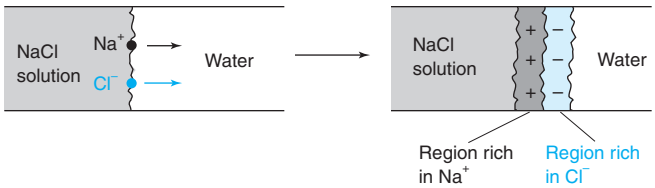


FIGURE 14-9 Development of the junction potential caused by unequal mobilities of Na^+ and Cl^-.

To see why the junction potential occurs, consider a solution of NaCl in contact with distilled water (Figure 14-9). Na^+ and Cl^- ions begin to diffuse from the NaCl solution into the water. However, Cl^- ion has a greater **mobility** than Na^+. That is, Cl^- diffuses faster than Na^+. As a result, a region rich in Cl^-, with excess negative charge, develops at the front. Behind it is a positively charged region depleted of Cl^-. The result is an electric potential difference at the junction of the NaCl and H_2O phases. The junction potential opposes the movement of Cl^- and accelerates the movement of Na^+. The steady-state junction potential represents a balance between the unequal mobilities that create a charge imbalance and the tendency of the resulting charge imbalance to retard the movement of Cl^-.

Table 14-1 shows mobilities of several ions and Table 14-2 lists some liquid junction potentials. Saturated KCl is used in a salt bridge because K^+ and Cl^- have similar mobilities. Junction potentials at the two interfaces of a KCl salt bridge are slight.

Nonetheless, the junction potential of 0.1 M HCl | 3.5 M KCl is 3.1 mV. A pH electrode has a response of 59 mV per pH unit. A pH electrode dipped into 0.1 M HCl will have a junction potential of ~3 mV, or an error of 0.05 pH units (12% error in $[H^+]$).

EXAMPLE Junction Potential

A 0.1 M NaCl solution was placed in contact with a 0.1 M $NaNO_3$ solution. Which side of the junction is positive?

Solution Because $[Na^+]$ is equal on both sides, there is no net diffusion of Na^+ across the junction. However, Cl^- diffuses into $NaNO_3$, and NO_3^- diffuses into NaCl. The mobility of Cl^- is greater than that of NO_3^-, so the NaCl region will be depleted of Cl^- faster than the $NaNO_3$ region will be depleted of NO_3^-. The $NaNO_3$ side will become negative, and the NaCl side will become positive.

Test Yourself Which side of the 0.05 M NaCl | 0.05 M LiCl junction will be positive? (***Answer:*** LiCl)

14-4 How Ion-Selective Electrodes Work[10]

Ion-selective electrodes discussed in the remainder of this chapter respond selectively to one ion. These electrodes are fundamentally different from metal electrodes in that ion-selective electrodes do not involve redox processes. The key feature of an ideal ion-selective electrode is a thin membrane capable of binding only the intended ion.

Hydrophobic: "water hating" (does not mix with water)

Consider the *liquid-based ion-selective electrode* in Figure 14-10a. The electrode is said to be "liquid based" because the ion-selective membrane is a *hydrophobic* organic polymer impregnated with a viscous organic solution containing an ion exchanger and, sometimes, a ligand that selectively binds the analyte cation, C^+. The inside of the electrode contains filling solution with the ions $C^+(aq)$ and $B^-(aq)$. The outside of the electrode is immersed in analyte solution containing $C^+(aq)$, $A^-(aq)$, and, perhaps, other ions. Ideally, it does not matter what A^- and B^- and the other ions are. The electric potential difference (the voltage) across the ion-selective membrane is measured by two reference electrodes, which might be Ag | AgCl. If the concentration (really, the activity) of C^+ in the analyte solution changes, the voltage measured between the two reference electrodes also changes. By using a calibration curve, the voltage tells us the activity of C^+ in the analyte solution.

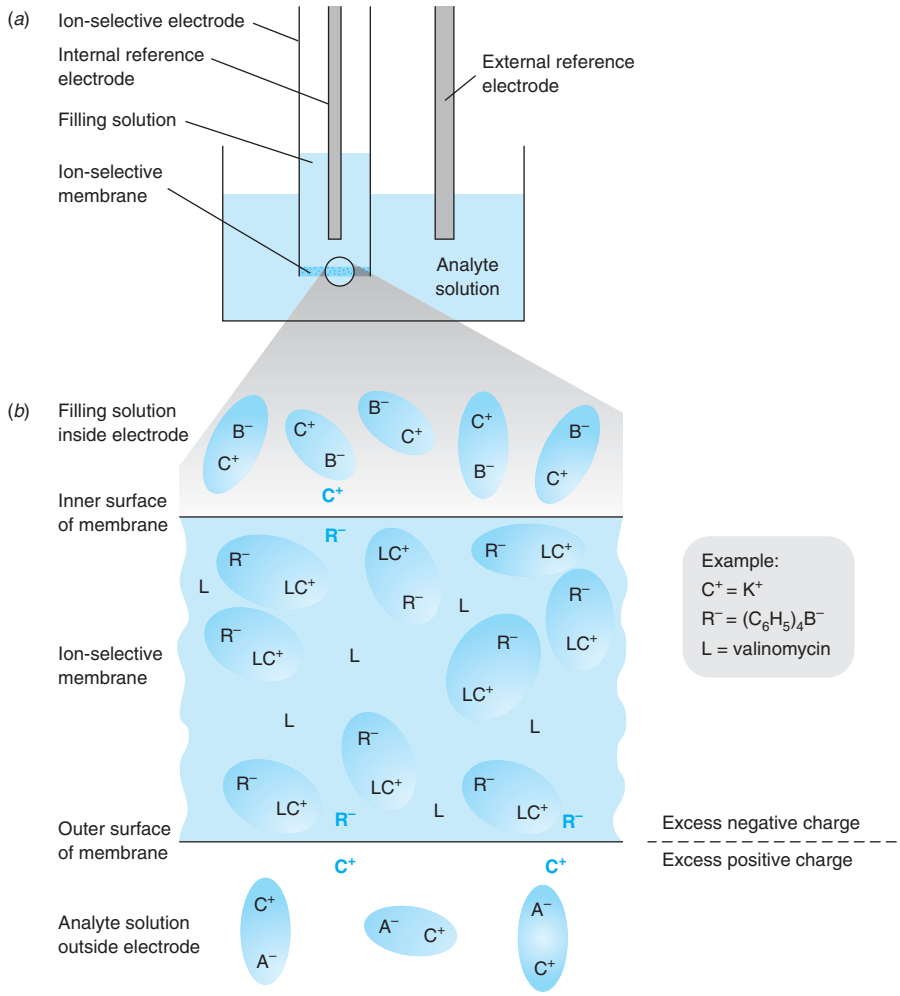
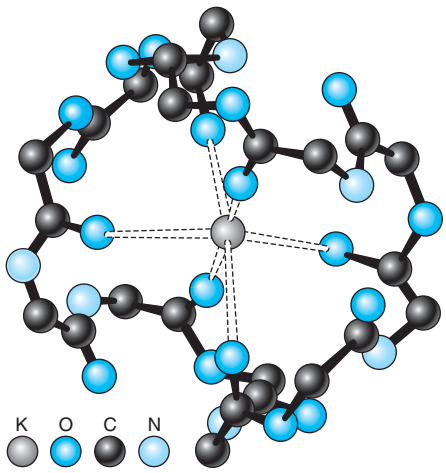


FIGURE 14-10 (*a*) Ion-selective electrode immersed in aqueous solution containing analyte cation, C^+. Typically, the membrane is made of poly(vinyl chloride) impregnated with the *plasticizer* dioctyl sebacate, a nonpolar liquid that softens the membrane and dissolves the ion-selective ionophore (L), the complex (LC^+), and a hydrophobic anion (R^-). (*b*) Close-up of membrane. Ellipses encircling pairs of ions are a guide for the eye to count the charge in each phase. Bold colored ions represent excess charge in each phase. The electric potential difference across each surface of the membrane depends on the activity of analyte ion in the aqueous solution contacting the membrane.



Valinomycin-K^+ complex has six carbonyl oxygen atoms in octahedral coordination around K^+. [From L. Stryer, *Biochemistry*, 4th ed. (New York: W. H. Freeman and Company, 1995), p. 273.]

Figure 14-10b shows how the electrode works. The key in this example is the ligand, L (called an *ionophore*), which is soluble inside the membrane and selectively binds analyte ion. In a potassium ion-selective electrode, for example, L could be valinomycin, a natural antibiotic secreted by certain microorganisms to carry K^+ ion across cell membranes. *The ligand, L, is chosen to have a high affinity for analyte cation, C^+, and low affinity for other ions.* In an ideal electrode, L binds only C^+. Real electrodes always have some affinity for other cations, so these cations interfere to some degree with the measurement of C^+. For charge neutrality, the membrane also contains a hydrophobic anion, R^-, such as tetraphenylborate, $(C_6H_5)_4B^-$, that is soluble in the membrane and poorly soluble in water.

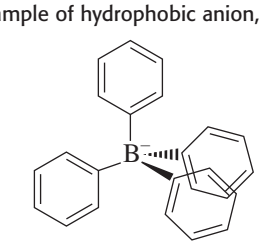
L has some ability to bind other ions besides C^+, so those other ions interfere to some extent with the measurement of C^+. An ion-selective electrode uses a ligand with a strong preference to bind the desired ion.

Almost all analyte ion inside the membrane in Figure 14-10b is bound in the complex LC^+, which is in equilibrium with a small amount of free C^+ in the membrane. The membrane also contains excess free L. C^+ can diffuse across the interface. In an ideal electrode, R^- cannot leave the membrane, because it is not soluble in water, and the aqueous anion A^- cannot enter the membrane, because it is not soluble in the organic phase. As soon as a few C^+ ions diffuse from the membrane into the aqueous phase, there is excess positive charge in the aqueous phase. This imbalance creates an electric potential difference that opposes diffusion of more C^+ into the aqueous phase. The region of charge imbalance extends just a few nanometers into the membrane and into the neighboring solution.

When C^+ diffuses from a region of activity $\mathcal{A}_m$ in the membrane to a region of activity $\mathcal{A}_o$ in the outer solution, the free energy change is

$$\Delta G = \underbrace{\Delta G_{\text{solvation}}}_{\substack{\Delta G \text{ due to change} \\ \text{in solvent}}} - \underbrace{RT \ln\left(\frac{\mathcal{A}_m}{\mathcal{A}_o}\right)}_{\substack{\Delta G \text{ due to} \\ \text{change in activity} \\ \text{(concentration)}}}$$

Example of hydrophobic anion, R^-:



Tetraphenylborate, $(C_6H_5)_4B^-$

where R is the gas constant and T is temperature (K). $\Delta G_{\text{solvation}}$ is the change in solvation energy when the environment around C^+ changes from the organic liquid in the membrane to the aqueous solution outside the membrane. The term $-RT\ln(\mathcal{A}_m/\mathcal{A}_o)$ gives the free energy change when a species diffuses between regions of different activities (concentrations). In the absence of a phase boundary, ΔG would always be negative when a species diffuses from a region of high activity to one of lower activity.

The driving force for diffusion of C^+ from the membrane to the aqueous solution is the favorable solvation of the ion by water. As C^+ diffuses from the membrane into the water, there is a buildup of positive charge in the water immediately adjacent to the membrane. The charge separation creates an electric potential difference (E_{outer}) across the membrane. The free energy difference for C^+ in the two phases is $\Delta G = -nFE_{\text{outer}}$, where F is the Faraday constant and n is the charge of the ion. At equilibrium, the net change in free energy for diffusion of C^+ across the membrane boundary must be 0:

$$\underbrace{\Delta G_{\text{solvation}} - RT\ln\left(\frac{\mathcal{A}_m}{\mathcal{A}_o}\right)}_{\substack{\Delta G \text{ due to transfer between phases} \\ \text{and activity difference}}} + \underbrace{(-nFE_{\text{outer}})}_{\substack{\Delta G \text{ due to} \\ \text{charge imbalance}}} = 0$$

Solving for E_{outer}, we find that the electric potential difference across the boundary between the membrane and the outer aqueous solution in Figure 14-10b is

Electric potential difference across phase boundary between membrane and analyte:

$$E_{\text{outer}} = \frac{\Delta G_{\text{solvation}}}{nF} - \left(\frac{RT}{nF}\right)\ln\left(\frac{\mathcal{A}_m}{\mathcal{A}_o}\right) \tag{14-4}$$

There is also a potential difference E_{inner} at the boundary between the inner filling solution and the membrane, with terms analogous to those in Equation 14-4.

The potential difference between the outer analyte solution and the inner filling solution is the difference $E = E_{\text{outer}} - E_{\text{inner}}$. In Equation 14-4, E_{outer} depends on the activities of C^+ in the analyte solution and in the membrane near its outer surface. E_{inner} is constant because the activity of C^+ in the filling solution is constant.

But the activity of C^+ in the membrane ($\mathcal{A}_m$) is very nearly constant for the following reason: The high concentration of LC^+ in the membrane is in equilibrium with free L and a small concentration of free C^+ in the membrane. The hydrophobic anion R^- is poorly soluble in water and therefore cannot leave the membrane. *Very little* C^+ can diffuse out of the membrane because each C^+ that enters the aqueous phase leaves behind one R^- in the membrane. (This separation of charge is the source of the potential difference at the phase boundary.) As soon as a tiny fraction of C^+ diffuses from the membrane into solution, further diffusion is prevented by excess positive charge in the solution near the membrane.

So the potential difference between the outer and the inner solutions is

$$E = E_{\text{outer}} - E_{\text{inner}} = \frac{\Delta G_{\text{solvation}}}{nF} - \left(\frac{RT}{nF}\right)\ln\left(\frac{\mathcal{A}_m}{\mathcal{A}_o}\right) - E_{\text{inner}}$$

$\ln\frac{x}{y} = \ln x - \ln y$

$$E = \underbrace{\frac{\Delta G_{\text{solvation}}}{nF}}_{\text{Constant}} + \left(\frac{RT}{nF}\right)\ln\mathcal{A}_o - \underbrace{\left(\frac{RT}{nF}\right)\ln\mathcal{A}_m}_{\text{Constant}} - \underbrace{E_{\text{inner}}}_{\text{Constant}}$$

Combining the constant terms, we find that the potential difference across the membrane depends only on the activity of analyte in the outer solution:

$$E = \text{constant} + \left(\frac{RT}{nF}\right)\ln\mathcal{A}_o$$

From Appendix A, $\ln x = (\ln 10)(\log x) = 2.303\log x$

Converting ln into log and inserting values of R, T, and F gives a useful expression for the potential difference across the membrane:

The number 0.059 16 V is $\frac{RT\ln 10}{F}$ at 25°C.

Electric potential difference for ion-selective electrode:

$$E = \text{constant} + \frac{0.059\,16}{n}\log\mathcal{A}_o \text{ (volts at 25°C)} \tag{14-5}$$

where n is the charge of the analyte ion and $\mathcal{A}_o$ is its activity in the outer (unknown) solution. Equation 14-5 applies to any ion-selective electrode, including a glass pH electrode. If the analyte is an anion, the sign of n is negative. Later, we will modify the equation to account for interfering ions.

A difference of 59.16 mV (at 25°C) builds up across a glass pH electrode for every factor-of-10 change in activity of H^+ in the analyte solution. Because a factor-of-10 difference in activity of H^+ is 1 pH unit, a difference of, say, 4.00 pH units would lead to a potential difference of $4.00 \times 59.16 = 237$ mV. The charge of a calcium ion is $n = 2$, so a potential difference of $59.16/2 = 29.58$ mV is expected for every factor-of-10 change in activity of Ca^{2+} in the analyte measured with a calcium ion-selective electrode.

14-5 pH Measurement with a Glass Electrode

The **glass electrode** used to measure pH is the most common *ion-selective electrode*. A typical pH **combination electrode,** incorporating both glass and reference electrodes in one body, is shown in Figure 14-11. A line diagram of this cell can be written as follows:

M. Cremer at the Institute of Physiology at Munich discovered in 1906 that a potential difference of 0.2 V developed across a glass membrane with acid on one side and neutral saline solution on the other. The student Klemensiewicz, working with F. Haber in Karlsruhe in 1908, improved the glass electrode and carried out the first acid-base titration to be monitored with a glass electrode.[11]

Glass membrane selectively binds H^+

$$\underbrace{Ag(s) \mid AgCl(s) \mid Cl^-(aq)}_{\text{Outer reference electrode}} \parallel \underbrace{H^+(aq, \text{outside})}_{\substack{H^+ \text{ outside} \\ \text{glass electrode} \\ \text{(analyte solution)}}} \vdots \underbrace{H^+(aq, \text{inside})}_{\substack{H^+ \text{ inside} \\ \text{glass} \\ \text{electrode}}}, \underbrace{Cl^-(aq) \mid AgCl(s) \mid Ag(s)}_{\text{Inner reference electrode}}$$

The pH-sensitive part of the electrode is the thin glass bulb or cone at the bottom of the electrodes in Figures 14-11 and 14-12. The reference electrode at the left of the preceding

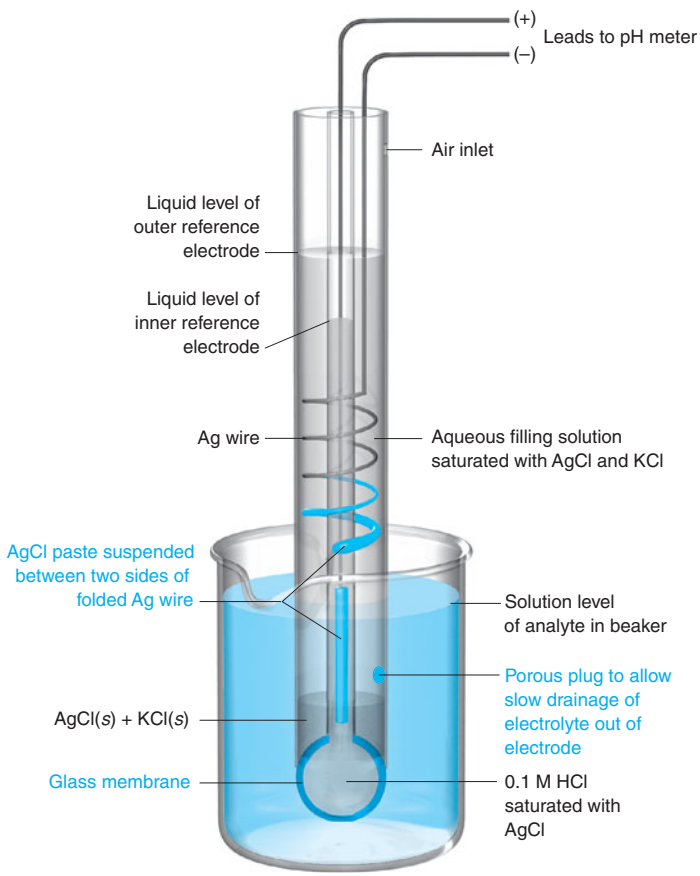


FIGURE 14-11 Diagram of a glass combination electrode with a silver-silver chloride reference electrode. The glass electrode is immersed in a solution of unknown pH so that the porous plug on the lower right is below the surface of the liquid. The two Ag | AgCl electrodes measure the voltage across the glass membrane.

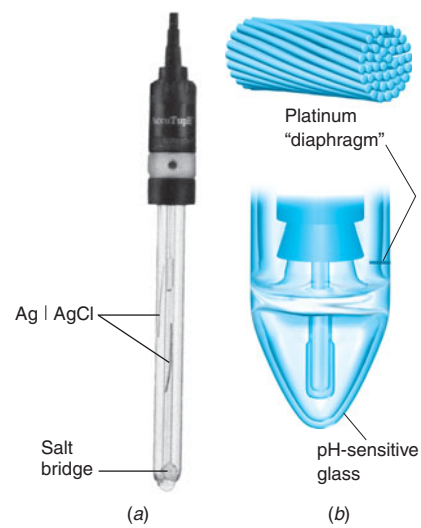


FIGURE 14-12 (*a*) Glass-body combination electrode with pH-sensitive glass bulb at the bottom. The porous ceramic plug (the salt bridge) connects analyte solution to the reference electrode. Two silver wires coated with AgCl are visible inside the electrode. [Courtesy Fisher Scientific, Pittsburgh PA.] (*b*) A pH electrode with a platinum diaphragm (a bundle of Pt wires), which is said to be less prone to clogging than a ceramic plug. [From W. Knappek, *Am. Lab. News Ed.,* July 2003, p. 14.]

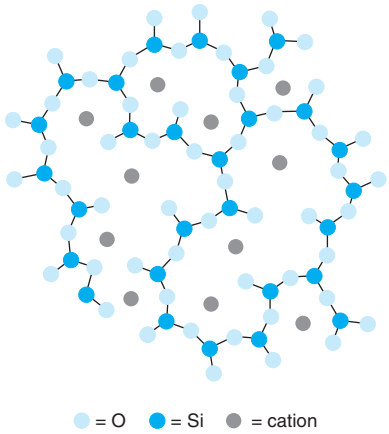


FIGURE 14-13 Schematic structure of glass, which consists of an irregular network of SiO_4 tetrahedra connected through oxygen atoms. Cations such as Li^+, Na^+, K^+, and Ca^{2+} are coordinated to the oxygen atoms. The silicate network is not planar. This diagram is a projection of each tetrahedron onto the plane of the page. [Adapted from G. A. Perley, "Glasses for Measurement of pH," *Anal. Chem.* **1949**, *21*, 394.]

So little current flows across a glass electrode that it was not practical when discovered in 1906. One of the first people to use a vacuum tube amplifier to measure pH with a glass electrode was an undergraduate, W. H. Wright at the University of Illinois in 1928, who knew about electronics from amateur radio. Arnold Beckman at Caltech invented a portable, rugged, vacuum tube pH meter in 1935, a device that revolutionized chemical instrumentation.[12]

Beckman's pH meter

line diagram is the coiled Ag | AgCl electrode in the combination electrode in Figure 14-11. The reference electrode at the right side of the line diagram is the straight Ag | AgCl electrode at the center of the electrode in Figure 14-11. The two reference electrodes measure the electric potential difference across the glass membrane. The salt bridge in the line diagram is the porous plug at the bottom right side of the combination electrode in Figure 14-11.

Figure 14-13 shows the irregular structure of the silicate lattice in glass. Negatively charged oxygen atoms in glass can bind to cations of suitable size. Monovalent cations, particularly Na^+, can move sluggishly through the silicate lattice. A schematic cross section of the glass membrane of a pH electrode is shown in Figure 14-14. The two surfaces swell as they absorb water. Metal ions in these *hydrated gel* regions of the membrane diffuse out of the glass and into solution. H^+ can diffuse into the membrane to replace the metal ions. The reaction in which H^+ replaces cations in the glass is an **ion-exchange equilibrium** (Figure 14-15). A pH electrode responds selectively to H^+ because H^+ is the only ion that binds significantly to the hydrated gel layer.

To perform an electrical measurement, at least some tiny current must flow through the entire circuit—even across the glass pH electrode membrane. Studies with tritium (radioactive ^3H) show that H^+ does not cross the glass membrane. However, Na^+ sluggishly crosses the membrane. The H^+-sensitive membrane may be thought of as two surfaces electrically connected by Na^+ transport. The membrane's resistance is typically $10^8\ \Omega$, so little current actually flows across it.

The potential difference between the inner and outer silver-silver chloride electrodes in Figure 14-11 depends on the chloride concentration in each electrode compartment and on the potential difference across the glass membrane. Because $[Cl^-]$ is fixed in each compartment and because $[H^+]$ is fixed on the inside of the glass membrane, the only variable is the pH of analyte solution outside the glass membrane. Equation 14-5 states that *the voltage of the ideal pH electrode changes by 59.16 mV for every pH-unit change of analyte activity at 25°C.*

The response of real glass electrodes is described by the Nernst-like equation

The number 0.059 16 V is (*RT/F*) ln 10, where *R* is the gas constant, *T* is temperature, and *F* is the Faraday constant.

Response of glass electrode:

$$E = \text{constant} + \beta(0.059\ 16)\log \mathcal{A}_{H^+}(\text{outside})$$

$$E = \text{constant} - \beta(0.059\ 16)\ \text{pH(outside)} \quad (\text{at } 25°\text{C}) \qquad \textbf{(14-6)}$$

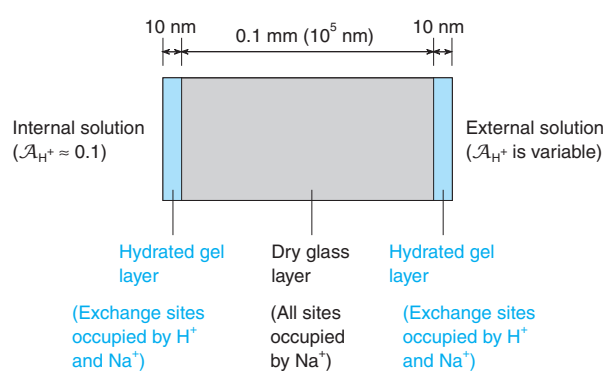


FIGURE 14-14 Schematic cross section of the glass membrane of a pH electrode.

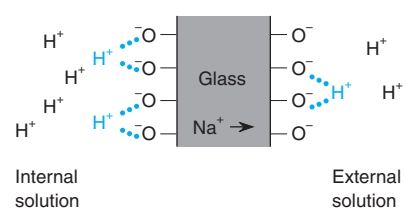


FIGURE 14-15 Ion-exchange equilibria on surfaces of a glass membrane: H^+ replaces metal ions bound to the negatively charged oxygen atoms. The pH of the internal solution is fixed. As the pH of the external solution (the sample) changes, the electric potential difference across the glass membrane changes.

The value of β, the *electromotive efficiency*, is close to 1.00 (typically >0.98). We measure the constant and β when we calibrate the electrode in solutions of known pH.

Calibrating a Glass Electrode

A pH electrode should be calibrated with two (or more) standard buffers selected so that the pH of the unknown lies within the range of the standards. Standards in Table 14-3 are accurate to ±0.01 pH unit.[13]

A pH electrode **must** be calibrated before it can be used. It should be calibrated every 2 h during sustained use.

When you calibrate an electrode with standard buffers, you measure a voltage with the electrode in each buffer (Figure 14-16). The pH of buffer S1 is pH_{S1} and the measured electrode potential in this buffer is E_{S1}. The pH of buffer S2 is pH_{S2} and the measured electrode potential is E_{S2}. The equation of the line through the two standard points is

$$\frac{E - E_{S1}}{pH - pH_{S1}} = \frac{E_{S2} - E_{S1}}{pH_{S2} - pH_{S1}} \tag{14-7}$$

The slope of the line is $\Delta E/\Delta pH = (E_{S2} - E_{S1})/(pH_{S2} - pH_{S1})$, which is 59.16 mV/pH unit at 25°C for an ideal electrode and β(59.16) mV/pH unit for a real electrode, where β is the correction factor in Equation 14-6.

To measure the pH of an unknown, measure the potential of the unknown with the calibrated electrode and find pH by substitution in Equation 14-7:

$$\frac{E_{unknown} - E_{S1}}{pH_{unknown} - pH_{S1}} = \frac{E_{S2} - E_{S1}}{pH_{S2} - pH_{S1}} \tag{14-8}$$

Alas, modern pH meters are "black boxes" that do these calculations for us by applying Equations 14-7 and 14-8 and automatically displaying pH.

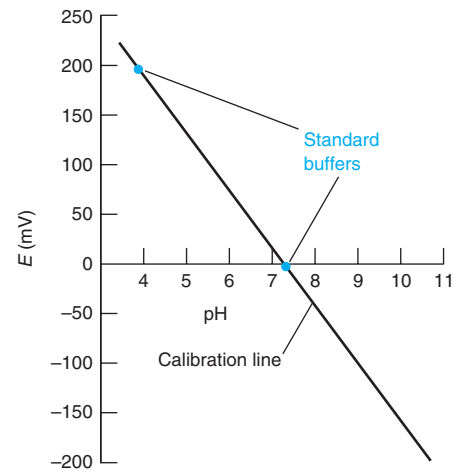


FIGURE 14-16 Two-point calibration of a pH electrode.

Before using a pH electrode, be sure that the air inlet near the upper end of the electrode in Figure 14-11 is not capped. (This hole is capped during storage to prevent evaporation of the reference electrode filling solution.) Wash the electrode with distilled water and gently *blot* it dry with a tissue. Do not *wipe* it, because this action might produce a static charge on the glass.

To calibrate the electrode, dip it in a standard buffer whose pH is near 7 and allow the electrode to equilibrate with stirring for at least a minute. Following the manufacturer's instructions, press a key that might say "Calibrate" or "Read" on a microprocessor-controlled meter or adjust the reading of an analog meter to indicate the pH of the standard buffer. Then wash the electrode with water, blot it dry, and immerse it in a second standard whose pH is further from 7 than the pH of the first standard. Enter the second buffer on the meter. Finally, dip the electrode in the unknown, stir the liquid, allow the reading to stabilize, and read the pH.

Store a glass electrode in aqueous solution to prevent dehydration of the glass. Ideally, the solution should be similar to that inside the reference compartment of the electrode. If the electrode has dried, recondition it in dilute acid for several hours. If the electrode is to be used above pH 9, soak it in a high-pH buffer. (The field effect transistor pH electrode in Section 14-8 is stored dry. Prior to use, scrub it gently with a soft brush and soak it in pH 7 buffer for 10 min.)

Do not leave a glass electrode out of water (or in a nonaqueous solvent) any longer than necessary.

If electrode response becomes sluggish or if an electrode cannot be calibrated properly, try soaking it in 6 M HCl, followed by water. As a last resort, soak the electrode in 20 wt% aqueous ammonium bifluoride, NH_4HF_2, for 1 min in a plastic beaker. This reagent dissolves glass and exposes fresh surface. Wash the electrode with water and try calibrating it again. Avoid contact with ammonium bifluoride, which produces a painful HF burn.

Errors in pH Measurement

1. *Standards*. A pH measurement cannot be more accurate than our standards, which are typically ±0.01 pH unit.
2. *Junction potential*. A *junction potential* exists at the porous plug near the bottom of the electrode in Figure 14-11. If the ionic composition of the analyte solution is different from that of the standard buffer, the junction potential will change *even if the pH of the two solutions is the same* (Box 14-1, page 322). This effect gives an uncertainty of at least ~0.01 pH unit.

The apparent pH will change if the ionic composition of the analyte changes, even when the actual pH is constant.

3. *Junction potential drift*. Most combination electrodes have a Ag | AgCl reference electrode containing saturated KCl solution. More than 350 mg Ag per liter dissolve in the KCl, mainly as $AgCl_4^{3-}$ and $AgCl_3^{2-}$. In the porous plug, KCl is diluted and AgCl can precipitate. If analyte solution contains a reducing agent, Ag(*s*) also can precipitate

TABLE 14-3 pH values of National Institute of Standards and Technology buffers

Temperature (°C)	0.05 *m* potassium tetroxalate (1)	Saturated (25°C) potassium hydrogen tartrate (2)	0.05 *m* potassium dihydrogen citrate (3)	0.05 *m* potassium hydrogen phthalate (4)	0.08 *m* MOPSO 0.08 *m* NaMOPSO 0.08 *m* NaCl (5)
0	1.667	—	3.863	4.003	7.268
5	1.666	—	3.840	3.999	7.182
10	1.665	—	3.820	3.998	7.098
15	1.669	—	3.802	3.999	7.018
20	1.672	—	3.788	4.002	6.940
25	1.677	3.557	3.776	4.008	6.865
30	1.681	3.552	3.766	4.015	6.792
35	1.688	3.549	3.759	4.024	6.722
37	—	3.548	3.756	4.028	6.695
40	1.694	3.547	3.753	4.035	6.654
45	1.699	3.547	3.750	4.047	6.588
50	1.706	3.549	3.749	4.060	6.524
55	1.713	3.554	—	4.075	—
60	1.722	3.560	—	4.091	—
70	—	3.580	—	4.126	—
80	—	3.609	—	4.164	—
90	—	3.650	—	4.205	—
95	—	3.674	—	4.227	—

NOTE: The designation m stands for molality. Masses in the buffer recipes below are apparent masses measured in air.

In the buffer solution preparations, it is essential to use high-purity materials and freshly distilled or deionized water of resistivity greater than 2 000 ohm · m. Solutions having pH 6 or above should be stored in plastic containers, preferably ones with an NaOH trap to prevent ingress of atmospheric carbon dioxide. They can normally be kept for 2–3 weeks, or slightly longer in a refrigerator. Buffer materials in this table are available as Standard Reference Materials from the National Institute of Standards and Technology. http://ts.nist.gov/srm. pH standards for D_2O and aqueous-organic solutions can be found in P. R. Mussini, T Mussini, and S. Rondinini, Pure Appl. Chem. ***1997,*** *69, 1007.*

1. 0.05 m potassium tetroxalate, $KHC_2O_4 \cdot H_2C_2O_4$. Dissolve 12.71 g of potassium tetroxalate dehydrate (Standard Reference Material used without drying) in 1 kg of water. pH values from P. M. Juusola, J. I. Partanen, K. P. Vahteristo, P. O. Minkkinen, and A. K. Covington, J. Chem. Eng. Data ***2007****, 52, 973.*

2. Saturated (25°C) potassium hydrogen tartrate, $KHC_4H_4O_6$. An excess of the salt is shaken with water, and it can be stored in this way. Before use, it should be filtered or decanted at a temperature between 22° and 28°C.

3. 0.05 m potassium dihydrogen citrate, $KH_2C_6H_5O_7$. Dissolve 11.41 g of the salt in 1 L of solution at 25°C.

4. 0.05 m potassium hydrogen phthalate. Although this is not usually essential, the crystals may be dried at 100°C for 1 h, then cooled in a desiccator. At 25°C, 10.12 g $C_6H_4(CO_2H)(CO_2K)$ are dissolved in water, and the solution made up to 1 L.

5. 0.08 m MOPSO ((3-N-morpholino)-2-hydroxypropanesulfonic acid, Table 8-2), 0.08 m sodium salt of MOPSO, 0.08 m NaCl. Buffers 5 and 7 are recommended for 2-point standardization of electrodes for pH measurements of physiologic fluids. MOPSO is crystallized twice from 70 wt% ethanol and dried in vacuum at 50°C for 24 h. NaCl is dried at 110°C for 4 h. Na^+MOPSO^- may be prepared by neutralization of MOPSO with standard NaOH. The sodium salt is also available as a Standard Reference Material. Dissolve 18.00 g MOPSO, 19.76 g Na^+MOPSO^-, and 4.674 g NaCl in 1.000 kg H_2O.

Challenge Use Equation 14-6 to show that the potential of the glass electrode changes by 1.3 mV when $\mathcal{A}_{H^+}$ changes by 5.0%. Show that 1.3 mV = 0.02 pH unit.

Moral: A small uncertainty in voltage (1.3 mV) or pH (0.02 unit) corresponds to a large uncertainty (5%) in analyte concentration. Similar uncertainties arise in other potentiometric measurements.

in the plug. Both effects change the junction potential, causing a slow drift of the pH reading (solid colored circles in Figure 14-17). You can compensate for this error by recalibrating the electrode every 2 h.

4. *Sodium error*. When $[H^+]$ is very low and $[Na^+]$ is high, the electrode responds to Na^+ and the apparent pH is lower than the true pH. This is called the **sodium error** or *alkaline error* (Figure 14-18).

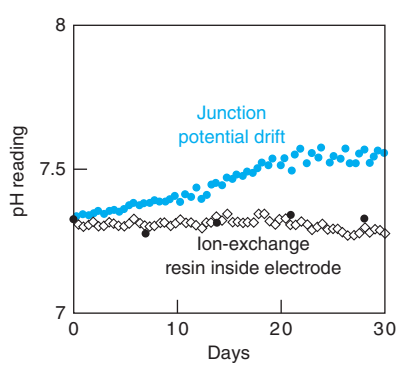


FIGURE 14-17 Solid colored circles show the drift in apparent pH of a low-conductivity industrial water supply measured continuously by a single electrode. Individual measurements with a freshly calibrated electrode (black circles) demonstrate that the pH is not drifting. Drift is attributed to slow clogging of the electrode's porous plug with AgCl(*s*). When a cation-exchange resin was placed inside the reference electrode near the porous plug, Ag(I) was bound by the resin and did not precipitate. This electrode gave the drift-free, continuous reading shown by open diamonds. [From S. Ito, H. Hachiya, K. Baba, Y. Asano, and H. Wada, "Improvement of the Ag | AgCl Reference Electrode and Its Application to pH Measurement," *Talanta* **1995**, *42,* 1685.]

TABLE 14-3 (*continued*) pH values of National Institute of Standards and Technology buffers

0.025 *m* potassium dihydrogen phosphate 0.025 *m* disodium hydrogen phosphate (6)	0.08 *m* HEPES 0.08 *m* NaHEPES 0.08 *m* NaCl (7)	0.008 695 *m* potassium dihydrogen phosphate 0.030 43 *m* disodium hydrogen phosphate (8)	0.01 *m* borax (9)	0.025 *m* sodium bicarbonate 0.025 *m* sodium carbonate (10)
6.984	7.853	7.534	9.464	10.317
6.951	7.782	7.500	9.395	10.245
6.923	7.713	7.472	9.332	10.179
6.900	7.645	7.448	9.276	10.118
6.881	7.580	7.429	9.225	10.062
6.865	7.516	7.413	9.180	10.012
6.853	7.454	7.400	9.139	9.966
6.844	7.393	7.389	9.102	9.925
6.840	7.370	7.385	9.088	9.910
6.838	7.335	7.380	9.068	9.889
6.834	7.278	7.373	9.038	9.856
6.833	7.223	7.367	9.011	9.828
6.834	—	—	8.985	—
6.836	—	—	8.962	—
6.845	—	—	8.921	—
6.859	—	—	8.885	—
6.877	—	—	8.850	—
6.886	—	—	8.833	—

6. 0.025 m disodium hydrogen phosphate, 0.025 m potassium dihydrogen phosphate. The anhydrous salts are best; each should be dried for 2 h at 120°C and cooled in a desiccator, because they are slightly hygroscopic. Higher drying temperatures should be avoided to prevent formation of condensed phosphates. Dissolve 3.53 g Na_2HPO_4 and 3.39 g KH_2PO_4 in water to give 1 L of solution at 25°C.

7. 0.08 m HEPES (N-2-hydroxyethylpiperazine-N′-2-ethanesulfonic acid, Table 8-2), 0.08 m sodium salt of HEPES, 0.08 m NaCl. Buffers 5 and 7 are recommended for 2-point standardization of electrodes for pH measurements of physiologic fluids. HEPES is crystallized twice from 80 wt% ethanol and dried in vacuum at 50°C for 24 h. NaCl is dried at 110°C for 4 h. Na^+HEPES^- may be prepared by neutralization of HEPES with standard NaOH. The sodium salt is also available as a Standard Reference Material. Dissolve 19.04 g HEPES, 20.80 g Na^+HEPES^-, and 4.674 g NaCl in 1.000 kg H_2O.

8. 0.008 695 m potassium dihydrogen phosphate, 0.030 43 m disodium hydrogen phosphate. Prepare like Buffer 6; dissolve 1.179 g KH_2PO_4 and 4.30 g Na_2HPO_4 in water to give 1 L of solution at 25°C.

9. 0.01 m sodium tetraborate decahydrate. Dissolve 3.80 g $Na_2B_4O_7 \cdot 10H_2O$ in water to give 1 L of solution. This borax solution is particularly susceptible to pH change from carbon dioxide absorption, and it should be correspondingly protected.

10. 0.025 m sodium bicarbonate, 0.025 m sodium carbonate. Primary standard grade Na_2CO_3 is dried at 250°C for 90 min and stored over $CaCl_2$ and Drierite. Reagent-grade $NaHCO_3$ is dried over molecular sieves and Drierite for 2 days at room temperature. Do not heat $NaHCO_3$, or it may decompose to Na_2CO_3. Dissolve 2.092 g of $NaHCO_3$ and 2.640 g of Na_2CO_3 in 1 L of solution at 25°C.

SOURCES: R. G. Bates, J. Res. Natl. Bureau Stds. ***1962,*** *66A, 179; B. R. Staples and R. G. Bates, J. Res. Natl. Bureau Stds.* ***1969,*** *73A, 37. Data on HEPES and MOPSO are from Y. C Wu, P. A. Berezansky, D. Feng, and W. F. Koch, Anal. Chem.* ***1993,*** *65, 1084, and D. Feng, W. F Koch, and Y. C Wu, Anal. Chem.* ***1989,*** *61, 1400. Instructions for preparing some of these solutions are from G. Mattock in C. N. Reilley, ed., Advances in Analytical Chemistry and Instrumentation (New York: Wiley, 1963), Vol. 2, p. 45. See also R. G. Bates, Determination of pH: Theory and Practice, 2nd ed. (New York: Wiley, 1973), Chap. 4.*

5. *Acid error*. In strong acid, the measured pH is higher than the actual pH (Figure 14-18), perhaps because the glass is saturated with H^+ and cannot be further protonated.
6. *Equilibration time*. It takes time for an electrode to equilibrate with a solution. A well-buffered solution requires ~30 s with adequate stirring. A poorly buffered solution (such as one near the equivalence point of a titration) needs many minutes.
7. *Hydration of glass*. A dry electrode requires several hours of soaking before it responds to H^+ correctly.
8. *Temperature*. A pH meter should be calibrated at the same temperature at which the measurement will be made.
9. *Cleaning*. If an electrode has been exposed to a hydrophobic liquid, such as oil, it should be cleaned with a solvent that will dissolve the liquid and then conditioned well in aqueous solution. The reading of an improperly cleaned electrode can drift for hours while the electrode re-equilibrates with aqueous solution.

Errors 1 and 2 limit the accuracy of pH measurement with the glass electrode to ±0.02 pH unit, at best. Measurement of pH *differences* between solutions can be accurate to about ±0.002 pH unit, but knowledge of the true pH will still be at least an order of magnitude more uncertain. An uncertainty of ±0.02 pH unit corresponds to an uncertainty of ±5% in $\mathcal{A}_{H^+}$.

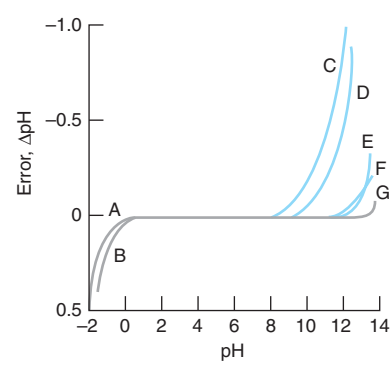
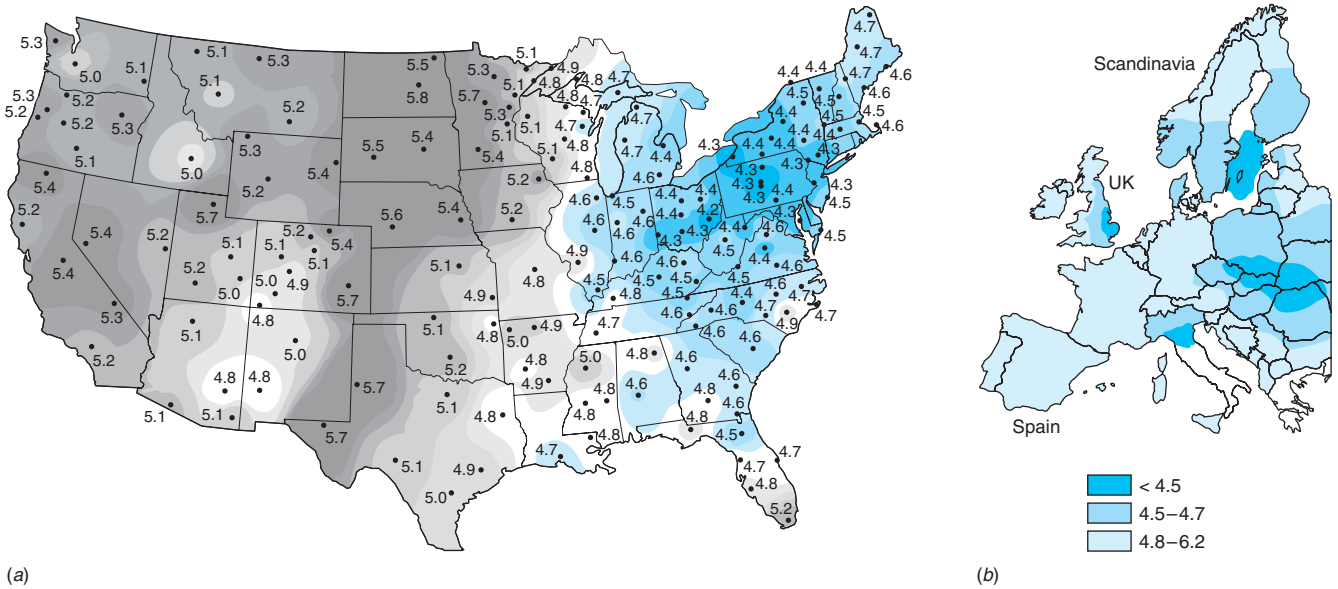


FIGURE 14-18 Acid and alkaline errors of some glass electrodes. A: Corning 015, H_2SO_4. B: Corning 015, HCl. C: Corning 015, 1 M Na^+. D: Beckman-GP, 1 M Na^+. E: L & N Black Dot, 1 M Na^+. F: Beckman Type E, 1 M Na^+. G: Ross electrode.[19] [From R. G. Bates, *Determination of pH: Theory and Practice,* 2nd ed. (New York: Wiley, 1973). Ross electrode data is from Orion *Ross pH Electrode Instruction Manual.*]

BOX 14-1 Systematic Error in Rainwater pH Measurement: The Effect of Junction Potential



(*a*) pH of precipitation in the United States in 2001. The lower the pH, the more acidic the water. [From National Atmospheric Deposition Program (NRSP-3)/National Trends Network (2002). Illinois State Water Survey, 2204 Griffith Dr., Champaign, IL 61820. See also http://nadp.sws.uiuc.edu and www.epa.gov/acidrain]

(*b*) pH of rain in Europe. No values are reported for Italy and Greece. [From H. Rodhe, F. Dentener, and M. Schulz, *Environ. Sci. Technol.* **2002,** *36,* 4382.]

Combustion products from automobiles and factories include nitrogen oxides and sulfur dioxide, which react with water in the atmosphere to produce acids.[14]

$$SO_2 + H_2O \rightarrow \underset{\text{Sulfurous acid}}{H_2SO_3} \xrightarrow{\text{oxidation}} \underset{\text{Sulfuric acid}}{H_2SO_4}$$

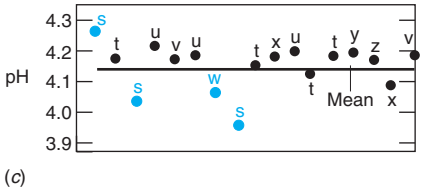
Acid rain in North America is most severe in the East, downwind of many coal-fired power plants. In the three-year period 1995–1997, after SO_2 emissions were limited by a new law, concentrations of SO_4^{2-} and H^+ in precipitation decreased by 10–25% in the eastern United States.[15]

Acid rain threatens lakes and forests throughout the world. Monitoring the pH of rainwater is a critical component of programs to measure and reduce the production of acid rain.

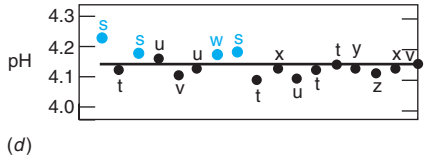
To identify systematic errors in the measurement of pH of rainwater, a careful study was conducted with 17 laboratories.[16] Eight samples were provided to each laboratory, along with instructions on how to conduct the measurements. Each laboratory used two buffers to standardize pH meters. Sixteen laboratories successfully measured the pH of Unknown A (within ±0.02 pH unit), which was 4.008 at 25°C. One lab whose measurement was 0.04 pH unit low had a faulty commercial standard buffer.

Panel (*c*) shows typical results for the pH of rainwater. The average of the 17 measurements is given by the horizontal line at pH 4.14, and the letters s, t, u, v, w, x, y, and z identify types of pH electrodes. Types s and w had relatively large systematic errors. The type s electrode was a combination electrode (Figure 14-11) containing a reference electrode liquid junction with an exceptionally large area. Electrode type w had a reference electrode filled with a gel.

A hypothesis was that variations in the liquid junction potential (Section 14-3) led to variations among the pH measurements. Standard buffers have ionic strengths of 0.05 to 0.1 M, whereas rainwater samples have ionic strengths two or more orders of magnitude lower. To see whether junction potential caused systematic errors, 2×10^{-4} M HCl was used as a pH standard in place of high ionic strength buffers. Panel (*d*) shows good results from all but the first lab. The standard deviation of 17 measurements was reduced from 0.077 pH unit (with standard buffer) to 0.029 pH unit (with HCl standard). It was concluded that junction potential caused most of the variability between labs and that a low ionic strength standard is appropriate for rainwater pH measurements.[17,18]



(*c*) pH of rainwater from identical samples measured at 17 different labs using standard buffers for calibration. Letters designate different types of pH electrodes.



(*d*) Rainwater pH measured by using low ionic strength HCl for calibration.

Not All pH Electrodes Are Glass

Glass electrodes are the most common, but not the only means, for measuring pH. Solid-state pH electrodes based on the field effect transistor are described at the end of this chapter. Liquid-based ion-selective electrodes for H^+ are described in Section 14-6.

An anhydrous IrO_2 layer formed by oxidation of iridium wire responds to pH by a half-reaction that might be[20]

$$IrO_2(s) + H^+ + e^- \rightleftharpoons IrOOH(s)$$

$$E = E^\circ - 0.059\,16 \log\left(\frac{1}{[H^+]}\right) = E^\circ - 0.059\,16\ \text{pH}$$

Other metal oxide electrodes have been used under extreme conditions. For example, a ZrO_2 electrode can measure pH up to 300°C.[21]

The *Phoenix Mars Lander* described at the opening of this chapter had two liquid-based ion-selective electrodes in each Wet Chemistry Lab to measure the pH of Martian soil suspended in water. It was not certain that these electrodes would survive the temperatures and pressures encountered during the mission, so a rugged IrO_2 pH electrode was added. The IrO_2 electrode remains accurate at pH > 9, a condition at which ion-selective electrodes were nonresponsive.

TABLE 14-4 Critical care profile

Function	Analyte
Conduction	K^+, Ca^{2+}
Contraction	Ca^{2+}, Mg^{2+}
Energy level	Glucose, P_{O_2}, lactate, hematocrit
Ventilation	P_{O_2}, P_{CO_2}
Perfusion	Lactate, SO_2%, hematocrit
Acid-base	pH, P_{CO_2}, HCO_3^-
Osmolality	Na^+, glucose
Electrolyte balance	Na^+, K^+, Ca^{2+}, Mg^{2+}
Renal function	Blood urea nitrogen, creatinine

SOURCE: *C. C. Young, "Evolution of Blood Chemistry Analyzers Based on Ion Selective Electrodes," J. Chem. Ed.* ***1997,*** *74, 177.*

14-6 Ion-Selective Electrodes[22, 23]

A critically ill patient is wheeled into the emergency room, and the doctor needs blood chemistry information quickly to help her make a diagnosis. Analytes in Table 14-4 are part of the critical care profile of blood chemistry. Every analyte in the table can be measured by electrochemical means. Ion-selective electrodes are the method of choice for Na^+, K^+, Cl^-, pH, and P_{CO_2}. The "Chem 7" test constitutes up to 70% of tests performed in the hospital lab. It measures Na^+, K^+, Cl^-, total CO_2, glucose, urea, and creatinine, four of which are analyzed with ion-selective electrodes.

The United States conducts more than 200 million clinical assays of K^+ each year with ion-selective electrodes.

Most ion-selective electrodes fall into one of the following classes:

1. *Glass membranes* for H^+ and certain monovalent cations
2. *Solid-state electrodes* based on inorganic crystals or, recently, conductive polymers
3. *Liquid-based electrodes* using a hydrophobic polymer membrane saturated with a hydrophobic liquid ion exchanger
4. *Compound electrodes* with an analyte-selective electrode enclosed by a membrane that separates analyte from other species or that generates analyte in a chemical reaction.

Reminder: How Ion-Selective Electrodes Work

In Figure 14-10, analyte ions equilibrate with ion-exchange sites at the outer surface of the ion-selective membrane. Diffusion of analyte ions out of the membrane creates a slight charge imbalance (an electric potential difference) across the interface between the membrane and the analyte solution. Changes in analyte ion concentration in the solution change the potential difference across the outer boundary of the ion-selective membrane. A calibration curve relates the potential difference to analyte concentration.

Analyte ions establish an ion-exchange equilibrium at the surface of the ion-selective membrane. Other ions that bind to the same sites interfere.

An ion-selective electrode responds to the activity of *free analyte*, not complexed analyte. For example, when Pb^{2+} in tap water at pH 8 was measured with an ion-selective electrode, the result was $[Pb^{2+}] = 2 \times 10^{-10}$ M.[24] When lead in the same tap water was measured by inductively coupled plasma–mass spectrometry (Section 20-6), the result was more than 10 times greater: 3×10^{-9} M. The discrepancy arose because the inductively coupled plasma measures *all* lead and the ion-selective electrode measures *free* Pb^{2+}. In tap water at pH 8, much of the lead is complexed by CO_3^{2-}, OH^-, and other anions. When the pH of tap water was adjusted to 4, Pb^{2+} dissociated from its complexes and the concentration indicated by the ion-selective electrode was 3×10^{-9} M—the same value found by inductively coupled plasma.

The ion-selective electrode responds to Pb^{2+} with little response to $Pb(OH)^+$ or $Pb(CO_3)(aq)$.

Selectivity Coefficient

No electrode responds exclusively to one kind of ion, but the glass pH electrode is among the most selective. Sodium ion is the principal interfering species. Its effect on the pH reading is only significant when $[H^+] \lesssim 10^{-12}$ M and $[Na^+] \gtrsim 10^{-2}$ M (Figure 14-18).

An electrode intended to measure ion A also responds to ion X. The **selectivity coefficient** gives the relative response to different species with the same charge:

Selectivity coefficient:

$$K^{\text{Pot}}_{\text{A,X}} = \frac{\text{response to X}}{\text{response to A}} \tag{14-9}$$

The superscript "Pot" for "potentiometric" is customary in the chemical literature. The smaller the selectivity coefficient, the less the interference by X. A K^+ ion-selective electrode that uses the chelator valinomycin as the liquid ion exchanger has selectivity coefficients $K^{\text{Pot}}_{\text{K}^+,\text{Na}^+} = 1 \times 10^{-5}$, $K^{\text{Pot}}_{\text{K}^+,\text{Cs}^+} = 0.44$, and $K^{\text{Pot}}_{\text{K}^+,\text{Rb}^+} = 2.8$. These coefficients tell us that Na^+ hardly interferes with the measurement of K^+, but Cs^+ and Rb^+ interfere strongly. In fact, the electrode responds more to Rb^+ than to K^+.

If the response to each ion is Nernstian, then the response of an ion-selective electrode to its primary ion (A) and to interfering ions of the *same charge* (X) is[10,25]

Response of ion-selective electrode:

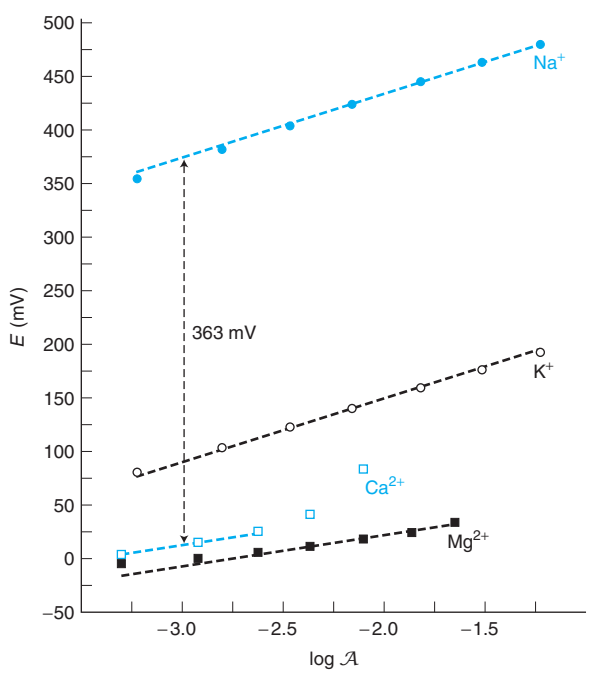
$$E = \text{constant} \pm \frac{0.059\,16}{z_{\text{A}}} \log\left[\mathcal{A}_{\text{A}} + \sum_{\text{X}} K^{\text{Pot}}_{\text{A,X}}\,\mathcal{A}_{\text{X}}\right] \tag{14-10}$$

where z_{A} is the magnitude of the charge of A, $\mathcal{A}_{\text{A}}$ and $\mathcal{A}_{\text{X}}$ are activities, and $K^{\text{Pot}}_{\text{A,X}}$ is the selectivity coefficient for each interfering ion. If the ion-selective electrode is connected to the positive terminal of the potentiometer, the sign of the log term is positive if A is a cation and negative if A is an anion. Box 14-2 describes how selectivity coefficients are measured.

BOX 14-2 Measuring Selectivity Coefficients for an Ion-Selective Electrode

When measuring selectivity coefficients, you must *demonstrate* that the response of the electrode to each interfering ion follows the Nernst equation.[26,27,28] This is not as simple as it sounds. An ion-selective membrane that has equilibrated with its primary ion may become kinetically insensitive to weakly bound interfering ions.

The graph shows the *separate solution method* for measuring selectivity coefficients. In this method, a calibration curve is constructed for each ion by itself. Other common procedures are the *fixed interference method* and the *matched potential method*.[26]



Measurement of selectivity coefficients of Na^+ ion-selective electrode. Activities on the abscissa were calculated from concentrations and activity coefficients. [Adapted from E. Bakker, "Determination of Unbiased Selectivity Coefficients of Neutral Carrier-Based Cation-Selective Electrodes," *Anal. Chem.* **1997**, *69*, 1061.]

The graph shows the response of a sodium ion-selective electrode to the interfering ions K^+, Ca^{2+}, and Mg^{2+}. To obtain a Nernstian response to interfering ions, the electrode was prepared in the absence of Na^+. The electrode was filled with 0.01 M KCl and soaked in 0.01 M KCl overnight to condition the ion-selective membrane prior to measurements. After measuring K^+, Ca^{2+}, and Mg^{2+}, Na^+ was measured. For subsequent use to measure Na^+, the inner filling solution is replaced by 0.01 M NaCl.

The data demonstrate a near-Nernstian response for each ion. At the laboratory temperature of 21.5°C, Nernstian response would be $(RT \ln 10)/zF = 58.5/z$ mV per decade (factor of 10) of ion activity, where z is the charge of the ion. Measured slopes are 61.3 ± 1.5 mV for Na^+, 56.3 ± 0.6 mV for K^+, 26.0 ± 1.0 mV for Mg^{2+}, and 31.2 ± 0.7 mV for Ca^{2+}. The deviation of Ca^{2+} from a straight line above an activity of $10^{-2.5}$ is attributed to Na^+ impurity in high-purity $CaCl_2$. Electrode response to Na^+ is much greater than to Ca^{2+}, so a little Na^+ has a large effect.

To find the selectivity coefficient, we measure the difference between the Na^+ calibration line and the line for an interfering ion at any chosen activity and apply the formula

$$\log K^{\text{Pot}}_{\text{A,X}} = \frac{z_{\text{A}}F(E_{\text{X}} - E_{\text{A}})}{RT \ln 10} + \log\left(\frac{\mathcal{A}_{\text{A}}}{(\mathcal{A}_{\text{X}})^{z_{\text{A}}/z_{\text{X}}}}\right) \tag{14-11}$$

where A = Na^+ with charge $z_{\text{A}} = 1$ and X is an interfering ion of charge z_{X}. At an activity of 10^{-3}, the dashed line shows a difference of $E_{\text{Ca}^{2+}} - E_{\text{Na}^+} = -363$ mV. The selectivity coefficient is

$$\log K^{\text{Pot}}_{\text{Na}^+,\text{Ca}^{2+}} = \frac{(+1)F(-0.363\text{ V})}{RT \ln 10} + \log\left(\frac{10^{-3}}{(10^{-3})^{1/2}}\right) = -7.0$$

We could choose a different activity to measure $E_{\text{Ca}^{2+}} - E_{\text{Na}^+}$ and should find the same $K^{\text{Pot}}_{\text{Na}^+,\text{Ca}^{2+}}$. The other lines in the graph give $\log K^{\text{Pot}}_{\text{Na}^+,\text{Mg}^{2+}} = -8.0$ and $\log K^{\text{Pot}}_{\text{Na}^+,\text{K}^+} = -4.9$.

Problem 14-43 provides a formula for estimating the error in measuring primary ion A caused by interfering ion X, which need not have the same charge as A.

EXAMPLE **Using the Selectivity Coefficient**

A fluoride ion-selective electrode has a selectivity coefficient $K^{\text{Pot}}_{\text{F}^-,\text{OH}^-} = 0.1$. What will be the change in electrode potential when 1.0×10^{-4} M F^- at pH 5.5 is raised to pH 10.5?

Solution From Equation 14-10, we find the potential with negligible OH^- at pH 5.5:

$$E = \text{constant} - 0.059\,16 \log[1.0 \times 10^{-4}] = \text{constant} + 236.6 \text{ mV}$$

At pH 10.50, $[OH^-] = 3.2 \times 10^{-4}$ M, so the electrode potential is

$$E = \text{constant} - 0.059\,16 \log[1.0 \times 10^{-4} + (0.1)(3.2 \times 10^{-4})]$$
$$= \text{constant} + 229.5 \text{ mV}$$

The change is $229.5 - 236.6 = -7.1$ mV, which is quite significant. If you didn't know about the pH change, you would think that the concentration of F^- had increased by 32%.

Test Yourself Find the change in potential when 1.0×10^{-4} M F^- at pH 5.5 is raised to pH 9.5. (***Answer:*** -0.8 mV)

Solid-State Electrodes

A **solid-state ion-selective electrode** based on an inorganic crystal is shown in Figure 14-19. A common electrode of this type is the fluoride electrode, employing a crystal of LaF_3 doped with Eu^{2+}. *Doping* means adding a small amount of Eu^{2+} in place of La^{3+}. The filling solution contains 0.1 M NaF and 0.1 M NaCl. Fluoride electrodes are used to monitor the fluoridation of municipal water supplies.

To conduct a tiny electric current, F^- migrates across the LaF_3 crystal, as shown in Figure 14-20. Anion vacancies are created within the crystal when we dope LaF_3 with EuF_2. An adjacent fluoride ion can jump into the vacancy, leaving a new vacancy behind. In this manner, F^- diffuses from one side to the other.

By analogy with the pH electrode, the response of the F^- electrode is

Response of F^- electrode: $$E = \text{constant} - \beta(0.059\,16) \log \mathcal{A}_{\text{F}^-}(\text{outside}) \qquad \textbf{(14-12)}$$

where β is close to 1.00. Equation 14-12 has a negative sign before the log term because fluoride is an anion. The F^- electrode has a nearly Nernstian response over a F^- concentration range from about 10^{-6} M to 1 M (Figure 14-21). The electrode is more responsive to F^- than to most other ions by >1 000. The only interfering species is OH^-, for which the selectivity coefficient is $K^{\text{Pot}}_{\text{F}^-,\text{OH}^-} = 0.1$. At low pH, F^- is converted to HF ($pK_a = 3.17$), to which the electrode is insensitive.

A routine procedure for measuring F^- is to dilute the unknown in a high ionic strength buffer containing acetic acid, sodium citrate, NaCl, and NaOH to adjust the pH to 5.5. The

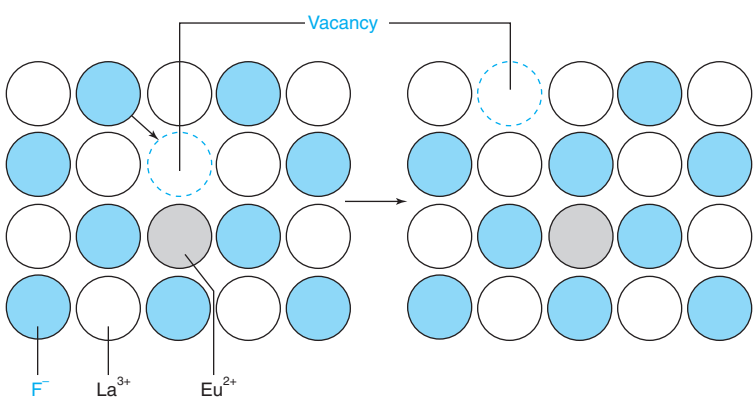


FIGURE 14-20 Migration of F^- through LaF_3 doped with EuF_2. Because Eu^{2+} has less charge than La^{3+}, an anion vacancy occurs for every Eu^{2+}. A neighboring F^- can jump into the vacancy, thereby moving the vacancy to another site. Repetition of this process moves F^- through the lattice.

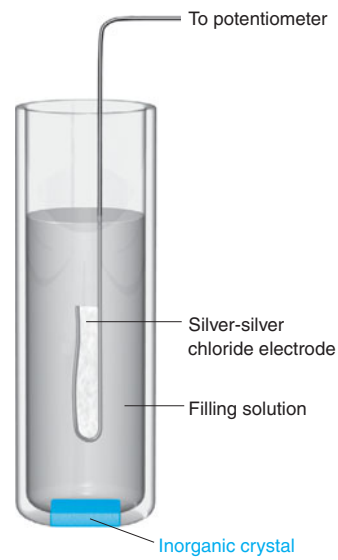


FIGURE 14-19 Diagram of an ion-selective electrode employing an inorganic salt crystal as the ion-selective membrane.

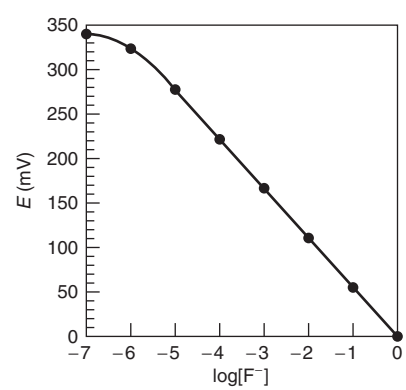


FIGURE 14-21 Calibration curve for fluoride ion-selective electrode. [Data from M. S. Frant and J. W. Ross, Jr., "Electrode for Sensing Fluoride Ion Activity in Solution," *Science* **1966**, *154*, 1553.]

buffer keeps all standards and unknowns at a constant ionic strength, so the fluoride activity coefficient is constant in all solutions (and can therefore be ignored).

$$E = \text{constant} - \beta(0.059\,16)\log[F^-]\gamma_{F^-}$$
$$= \underbrace{\text{constant} - \beta(0.059\,16)\log\gamma_{F^-}}_{\substack{\text{This expression is constant because} \\ \gamma_{F^-}\text{ is constant at constant ionic strength}}} - \beta(0.059\,16)\log[F^-]$$

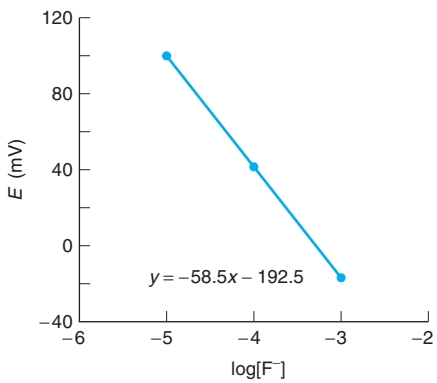
At pH 5.5, there is no interference by OH^- and little conversion of F^- to HF. Citrate complexes Fe^{3+} and Al^{3+}, which would otherwise bind F^- and interfere with the analysis.

EXAMPLE **Response of an Ion-Selective Electrode**

When a fluoride electrode was immersed in standard solutions (maintained at a constant ionic strength of 0.1 M with $NaNO_3$), the following potentials (versus S.C.E.) were observed:

$[F^-]$ (M)	E (mV)
1.00×10^{-5}	100.0
1.00×10^{-4}	41.5
1.00×10^{-3}	−17.0

Because the ionic strength is constant, the response should depend on the logarithm of the F^- *concentration*. Find $[F^-]$ in an unknown that gave a potential of 0.0 mV.



Solution We fit the calibration data with Equation 14-12:

$$\underset{y}{E} = m\,\underbrace{\log[F^-]}_{x} + b$$

Plotting E versus $\log[F^-]$ gives a straight line with a slope $m = -58.5$ mV and a y-intercept $b = -192.5$ mV. Setting $E = 0.0$ mV, we solve for $[F^-]$:

$$0.0\text{ mV} = (-58.5\text{ mV})\log[F^-] - 192.5\text{ mV} \Rightarrow [F^-] = 5.1 \times 10^{-4}\text{ M}$$

Test Yourself Find $[F^-]$ if $E = 81.2$ mV. Is the calibration curve valid for $E = 110.7$ mV? (***Answer:*** 2.1×10^{-4} M; no, because calibration points do not go above 100 mV)

Another common inorganic crystal electrode uses Ag_2S for the membrane. This electrode responds to Ag^+ and to S^{2-}. If we dope the electrode with CuS, CdS, or PbS, we can prepare electrodes sensitive to Cu^{2+}, Cd^{2+}, or Pb^{2+}, respectively (Table 14-5).

Figure 14-22 illustrates the mechanism by which a CdS crystal responds selectively to certain ions. The crystal can be cleaved to expose planes of Cd atoms or S atoms. The Cd plane in Figure 14-22a selectively adsorbs HS^- ions, whereas an S plane does not interact strongly with HS^-. Figure 14-22b shows strong response of the exposed Cd face to HS^-, but only weak response when the S face is exposed. The opposite behavior is observed in response to Cd^{2+} ions. The partial response of the S face to HS^- in the upper curve is attributed to about 10% of the exposed atoms actually being Cd instead of S.

TABLE 14-5 **Properties of solid-state ion-selective electrodes**

Ion	Concentration range (M)	Membrane material	pH range	Interfering species
F^-	10^{-6}–1	LaF_3	5–8	OH^-(0.1 M)
Cl^-	10^{-4}–1	AgCl	2–11	CN^-, S^{2-}, I^-, $S_2O_3^{2-}$, Br^-
Br^-	10^{-5}–1	AgBr	2–12	CN^-, S^{2-}, I^-
I^-	10^{-6}–1	AgI	3–12	S^{2-}
SCN^-	10^{-5}–1	AgSCN	2–12	S^{2-}, I^-, CN^-, Br^-, $S_2O_3^{2-}$
CN^-	10^{-6}–10^{-2}	AgI	11–13	S^{2-}, I^-
S^{2-}	10^{-5}–1	Ag_2S	13−14	

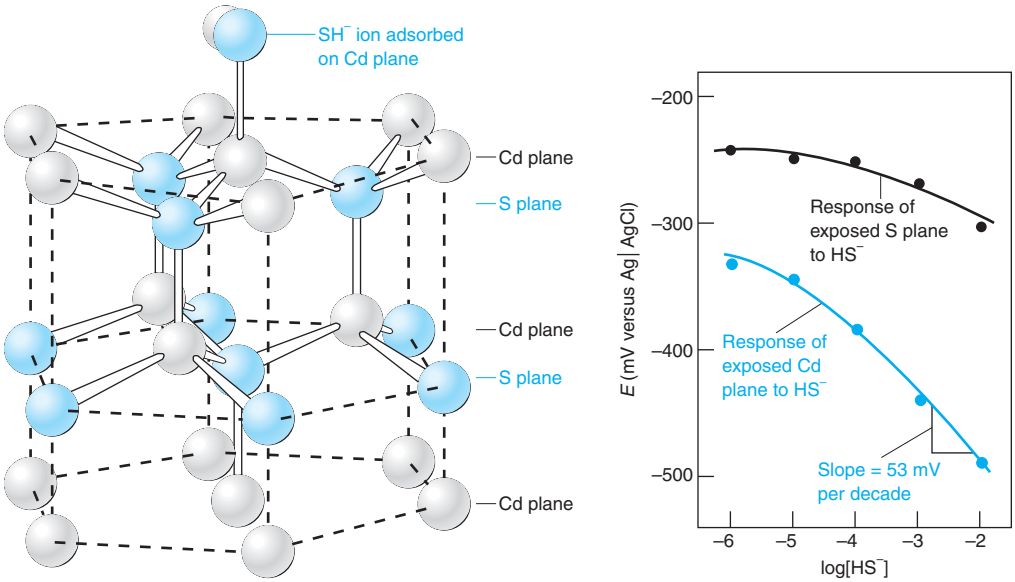


FIGURE 14-22 (*a*) Crystal structure of hexagonal CdS, showing alternating planes of Cd and S along the vertical axis (the crystal *c*-axis). HS^- is shown adsorbed to the uppermost Cd plane. (*b*) Potentiometric response of exposed crystal faces to HS^-. [From K. Uosaki, Y. Shigematsu, H. Kita, Y. Umezawa, and R. Souda, "Crystal-Face-Specific Response of a Single-Crystal Cadmium Sulfide Based Ion-Selective Electrode," *Anal. Chem.* **1989**, *61*, 1980.]

Liquid-Based Ion-Selective Electrodes

A **liquid-based ion-selective electrode** is similar to the solid-state electrode in Figure 14-19, except that the liquid-based electrode has a hydrophobic membrane impregnated with a hydrophobic ion exchanger (called an *ionophore*) that is selective for analyte ion (Figure 14-23). The response of a Ca^{2+} ion-selective electrode is given by

$$\textit{Response of } Ca^{2+} \textit{ electrode:} \quad E = \text{constant} + \beta\left(\frac{0.059\,16}{2}\right)\log \mathcal{A}_{Ca^{2+}}(\text{outside}) \qquad \textbf{(14-13)}$$

where β is close to 1.00. Equations 14-13 and 14-12 have different signs before the log term because one involves an anion and the other a cation. Note also that the charge of Ca^{2+} requires a factor of 2 in the denominator before the logarithm.

The membrane at the bottom of the electrode in Figure 14-23 is made from poly(vinyl chloride) impregnated with ion exchanger. One particular Ca^{2+} liquid ion exchanger consists

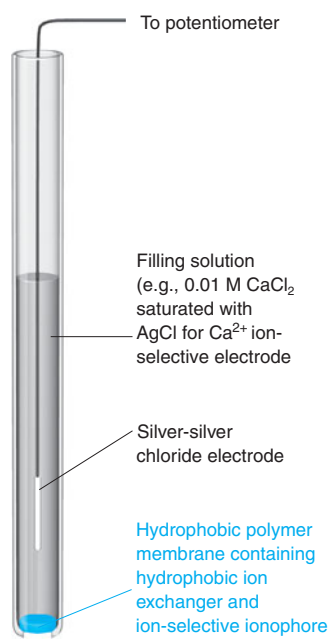


FIGURE 14-23 Calcium ion-selective electrode with a liquid ion exchanger.

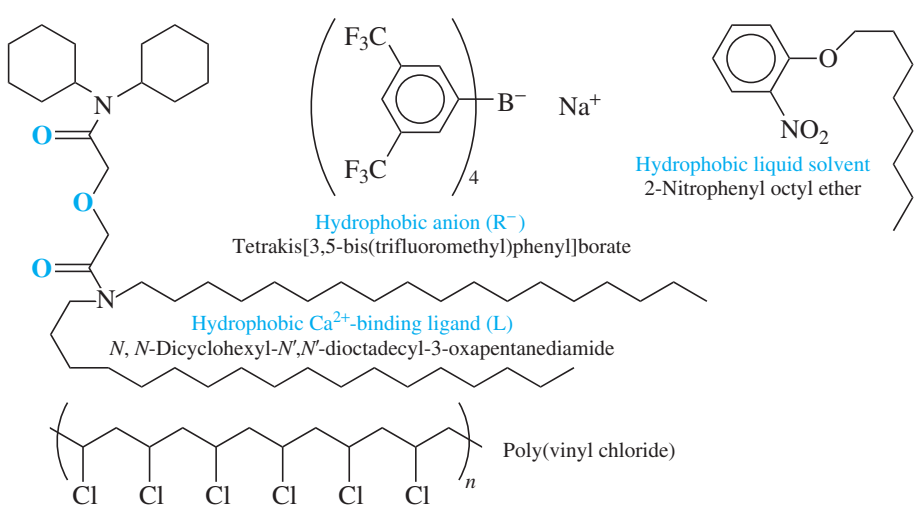


FIGURE 14-24 Membrane components of a Ca^{2+} ion-selective electrode. Ligand L is an ionophore that selectively binds Ca^{2+}.

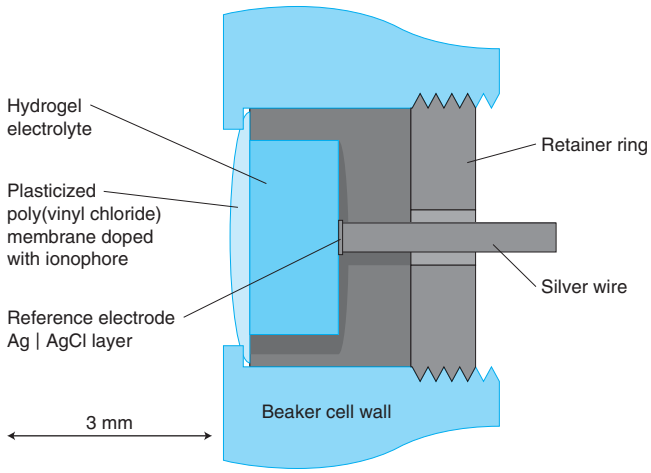


FIGURE 14-25 Liquid-based ion-selective electrodes built into walls of Wet Chemistry Lab beakers of *Phoenix Mars Lander*. Hydrogel electrolyte is a poly(2-hydroxyethyl methacrylate) gel that retains aqueous phase containing 1 mM M^+Cl^-, where M^+ is the cation being measured. [From S. P. Kounaves et al., "The 2007 Mars Scout Lander MECA Wet Chemistry Laboratory," *J. Geophys. Res.* **2009,** *113,* E00A19.]

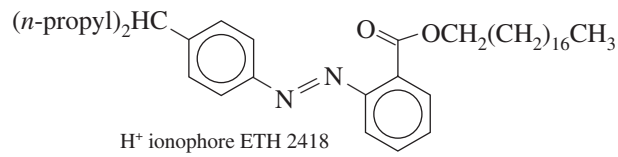


FIGURE 14-26 Ionophore ETH 2418 for liquid-based H^+ ion-selective electrodes. ETH stands for the Swiss Federal Institute of Technology (Eidgenössische Technische Hochschule Zürich) where many ionophores were synthesized.

of the neutral hydrophobic ligand (L), called an *ionophore*, and a salt of the hydrophobic anion (Na^+R^-) dissolved in a hydrophobic liquid (Figure 14-24) in the poly(vinyl chloride) membrane. The most serious interference comes from Sr^{2+}. The selectivity coefficient in Equation 14-9 is $K^{Pot}_{Ca^{2+},Sr^{2+}} = 0.13$, which means that the response to Sr^{2+} is 13% as great as the response to an equal concentration of Ca^{2+}. For most cations, $K^{Pot}_{Ca^{2+},X} < 10^{-3}$.

The *Phoenix Mars Lander* at the opening of this chapter had 11 liquid-based ion-selective electrodes (Figure 14-25) and 4 solid-state electrodes built into the walls of each Wet Chemistry Laboratory beaker. The liquid-based ion-selective electrodes for H^+ used an ionophore called ETH 2418 (Figure 14-26). This ionophore responds over the pH range 1 to 9 and has selectivity coefficients $K^{Pot}_{H^+,Na^+} = 10^{-8.6}$, $K^{Pot}_{H^+,K^+} = 10^{-9.7}$, and $K^{Pot}_{H^+,Ca^{2+}} = 10^{-7.8}$. Box 14-3 tells how electrode interference led to the discovery of perchlorate on Mars.[29]

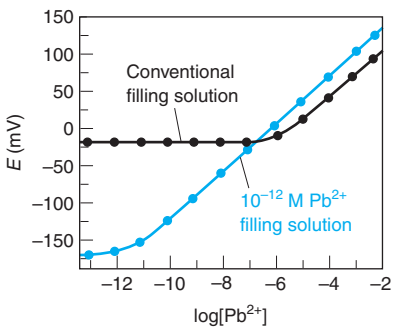


FIGURE 14-27 Response of Pb^{2+} liquid-based ion-selective electrode with (*black curve*) conventional filling solution containing 0.5 mM Pb^{2+} or (*colored curve*) metal ion buffer filling solution in which $[Pb^{2+}] = 10^{-12}$ M. [From T. Sokalski, A. Ceresa, T. Zwickl, and E. Pretsch, "Large Improvement of the Lower Detection Limit of Ion-Selective Polymer Membrane Electrodes," *J. Am. Chem. Soc.* **1997,** *119,* 11347.]

Breakthrough in Ion-Selective Electrode Detection Limits[24]

The black curve in Figure 14-27 is typical of many liquid-based ion-selective electrodes. The electrode detects changes in Pb^{2+} concentration above 10^{-6} M but is unresponsive for $[Pb^{2+}] < 10^{-6}$ M. The solution in the internal electrode compartment contains 0.5 mM $PbCl_2$.

The colored curve in Figure 14-27 was obtained with the same electrode, but the internal filling solution was replaced by a *metal ion buffer* (Section 14-7) that fixes $[Pb^{2+}]$ at 10^{-12} M. Now the electrode responds to changes in $[Pb^{2+}]$ down to ~10^{-11} M.

The sensitivity of liquid-based ion-selective electrodes has been limited by leakage of the primary ion (Pb^{2+}, in this case) from the internal filling solution through the ion-exchange membrane. Leakage provides a substantial concentration of primary ion at the external surface of the membrane. If analyte concentration is below 10^{-6} M, leakage from the electrode maintains an effective concentration near 10^{-6} M at the outer surface of the electrode. If we can lower the concentration of primary ion inside the electrode, the concentration of leaking

BOX 14-3 How Was Perchlorate Discovered on Mars?[29]

Nobody expected perchlorate (ClO_4^-) to be abundant on Mars, so the *Phoenix Mars Lander* Wet Chemistry Laboratory was not designed to look for ClO_4^-. However, the nitrate ion-selective electrode sent to Mars was 1 000 times *more sensitive* to ClO_4^- than to NO_3^-. That is, $K^{Pot}_{NO_3^-,ClO_4^-} = 10^3$. Liquid used to leach ions from the soil had a constant NO_3^- background near 1 mM. Nitrate would only be detected if it were present at concentrations above 1 mM.

When salts were leached from soil in the Wet Chemistry Laboratory, the NO_3^- electrode potential changed by 200 mV, corresponding to an apparent NO_3^- concentration above 1 M, which would have required more NO_3^- than the mass of soil that was analyzed. However, 4–6 mg of ClO_4^- in 1 g of soil would have produced the observed response. Heating the soil released a product at 400°–600°C with a molecular mass of 32 (likely O_2), consistent with thermal decomposition of ClO_4^-. Perchlorate occurs at similar levels on Earth in arid regions including the Atacama Desert. On Earth, ClO_4^- is thought to arise from photochemical reactions of ozone (O_3) with chlorine species in the atmosphere.

TABLE 14-6 Detection limits and selectivity coefficients for liquid-based ion-selective electrodes operating without leakage of primary ion

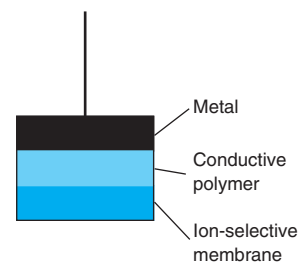
Primary ion (A)	Detection limit for A (nM)	Selectivity coefficient for some interfering ions (X) $\log K^{Pot}_{A,X}$ (Equation 14-9)
Na^+	30	H^+, −4.8; K^+, −2.7; Ca^{2+}, −6.0
K^+	5	Na^+, −4.2; Mg^{2+}, −7.6; Ca^{2+}, −6.9
NH_3	20	
Cs^+	8	Na^+, −4.7; Mg^{2+}, −8.7; Ca^{2+}, −8.5
Ca^{2+}	0.1	H^+, −4.9; Na^+, −4.8; Mg^{2+}, −5.3
Ag^+	0.03	H^+, −10.2; Na^+, −10.3; Ca^{2+}, −11.3
Pb^{2+}	0.06	H^+, −5.6; Na^+, −5.6; Mg^{2+}, −13.8
Cd^{2+}	0.1	H^+, −6.7; Na^+, −8.4; Mg^{2+}, −13.4
Cu^{2+}	2	H^+, −0.7; Na^+, <−5.7; Mg^{2+}, <−6.9
ClO_4^-	20	OH^-, −5.0; Cl^-, −4.9; NO_3^-, −3.1
I^-	2	OH^-, −1.7

SOURCE: *E. Bakker and E. Pretsch, "Modern Potentiometry," Angew. Chem. Int. Ed.* **2007,** *46, 5660.*

ion outside the membrane is reduced by orders of magnitude and the detection limit is correspondingly reduced. The sensitivity of a solid-state electrode cannot be lowered by changing the filling solution, because analyte concentration is governed by the solubility of the inorganic salt crystal forming the ion-sensitive membrane.

The response of the electrode with 10^{-12} M Pb^{2+} in the filling solution is limited by interference from Na^+ in the internal solution, which contains 0.05 M Na_2EDTA from the metal ion buffer. When the filling solution is buffered to 10^{-12} M Pb^{2+}, the apparent selectivity coefficient is decreased by one to five orders of magnitude for most interfering cations. Not only is the detection limit for Pb^{2+} improved by 10^5, but the selectivity for Pb^{2+} over other cations increases by several orders of magnitude. Table 14-6 gives detection limits and selectivity coefficients for ion-selective electrodes in which precautions are taken to prevent leakage of the primary ion.

A new direction in ion-selective electrodes is to eliminate the internal filling solution entirely. Ionophore is coated onto or dissolved in an electrically conducting polymer that serves as an ion-to-electron transducer.[30] A nitrate-selective all-solid-state electrode based on the conductive polymer polypyrrole can be made in a student experiment.[31]



Compound Electrodes

Compound electrodes contain a conventional electrode surrounded by a membrane that isolates (or generates) the analyte to which the electrode responds. The CO_2 gas-sensing electrode in Figure 14-28 consists of an ordinary glass pH electrode surrounded by a thin layer of electrolyte solution enclosed in a semipermeable membrane made of rubber, Teflon,

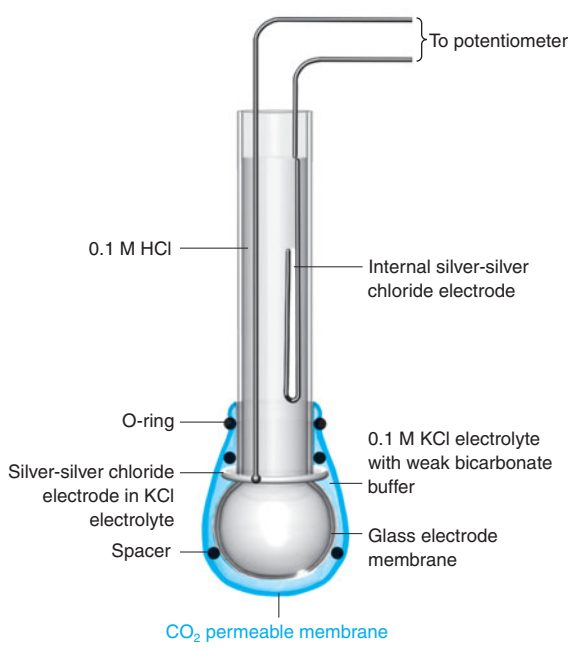


FIGURE 14-28 CO_2 gas-sensing electrode. The membrane is stretched taut, and there is a thin layer of electrolyte between the membrane and the glass bulb.

or polyethylene.[32] A Ag | AgCl reference electrode is immersed in the electrolyte solution. When CO_2 diffuses through the semipermeable membrane, it lowers the pH in the electrolyte. The response of the glass electrode to the change in pH is a measure of the CO_2 concentration outside the electrode. Other acidic or basic gases, including NH_3, SO_2, H_2S, NO_x (nitrogen oxides), and HN_3 (hydrazoic acid) can be detected in the same manner. These electrodes can be used to measure gases in solution or *in the gas phase*.

It is not necessary to use the compound electrode for CO_2 and NH_3 in aqueous solution. Ionophores are available to measure CO_3^{2-} and NH_4^+ with conventional liquid-based ion-selective electrodes.[33]

Numerous ingenious compound electrodes use *enzymes*.[34] These devices contain a conventional electrode coated with an enzyme that catalyzes a reaction of the analyte. The product of the reaction is detected by the electrode.

Advantages of ion-selective electrodes:

- linear response to log $\mathcal{A}$ over a wide range
- nondestructive
- noncontaminating
- short response time
- unaffected by color or turbidity

A 1-mV error in potential corresponds to a 4% error in monovalent ion activity. A 5-mV error corresponds to a 22% error. The relative error *doubles* for divalent ions and *triples* for trivalent ions.

14-7 Using Ion-Selective Electrodes

Ion-selective electrodes respond linearly to the logarithm of analyte activity over four to six orders of magnitude. Electrodes do not consume unknowns, and they introduce negligible contamination. Response time is seconds or minutes, so electrodes are used to monitor flow streams in industrial applications. Color and turbidity do not hinder electrodes. Microelectrodes can be used inside living cells.

Precision is rarely better than 1% and is usually worse. Electrodes can be fouled by proteins or other organic solutes and the fouling leads to sluggish, drifting response. Certain ions interfere with or poison particular electrodes. Some electrodes are fragile and have limited shelf life.

Electrodes respond to the *activity* of *uncomplexed* analyte ion. Therefore, ligands must be absent or masked. Because we usually wish to know concentrations, not activities, an inert salt is often used to bring all standards and samples to a high, constant ionic strength. If activity coefficients are constant, the electrode potential gives concentrations directly.

Human blood plasma has eight major calcium-containing species that can be separated by capillary electrophoresis and measured by inductively coupled plasma atomic emission spectrometry (Figure 14-29) You will learn about these techniques later in this book. Of the eight species, one with a concentration of 1.05 mM was identified as free Ca^{2+}. In the other seven species, with a total concentration of 1.21 mM, Ca^{2+} is bound to proteins or other ligands. When Ca^{2+} in blood was measured with an ion-selective electrode, only free Ca^{2+} was observed.[35] Calcium bound to ligands is invisible to an ion-selective electrode.

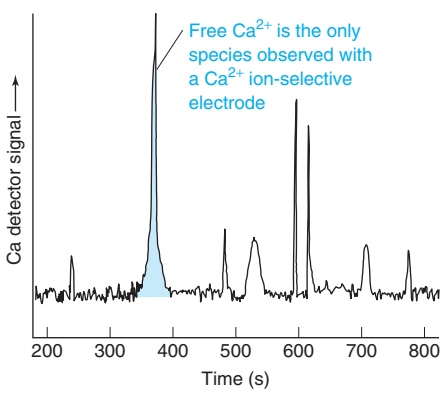


FIGURE 14-29 Separation of calcium-containing species in human blood plasma. The largest peak is free Ca^{2+}. Other peaks are proteins or small molecules to which Ca^{2+} is bound. The detector measures calcium.
[From B. Deng, P. Zhu, Y. Wang, J. Feng, X. Li, X. Xu, H. Lu, and Q. Xu, "Determination of Free Calcium and Calcium-Containing Species in Human Plasma by Capillary Electrophoresis-Inductively Coupled Plasma Optical Emission Spectrometry," *Anal. Chem.* **2008,** *80,* 5721.]

Standard Addition with Ion-Selective Electrodes

When ion-selective electrodes are used, it is important that the composition of the standard solution closely approximates the composition of the unknown. The medium in which the analyte exists is called the **matrix.** For complex or unknown matrixes, the **standard addition** method (Section 5-3) can be used. In this technique, the electrode is immersed in unknown and the potential is recorded. Then a small volume of standard solution is added, so as not to perturb the ionic strength of the unknown. The change in potential tells how the electrode responds to analyte and, therefore, how much analyte was in the unknown. It is best to add several successive aliquots and use a graphical procedure to extrapolate back to the concentration of unknown. Standard addition is best if the additions increase analyte to 1.5 to 3 times its original concentration.

The graphical procedure is based on the equation for the response of the ion-selective electrode, which we will write in the form

$$E = k + \beta\left(\frac{RT \ln 10}{nF}\right)\log[X] \qquad \textbf{(14-14)}$$

R = gas constant
T = temperature (K)
n = charge of the ion being detected
F = Faraday constant

where E is the meter reading in volts and [X] is the concentration of analyte. This reading is the difference in potential of the ion-selective electrode and the reference electrode. The constants k and β depend on the particular ion-selective electrode. The factor (RT/F) ln 10 is 0.059 16 V at 298.15 K. If $\beta = 1$, then the response is Nernstian. We abbreviate the term $(\beta RT/nF)$ ln 10 as S.

Let the initial volume of unknown be V_0 and the initial concentration of analyte be c_X. Let the volume of added standard be V_S and the concentration of standard be c_S. Then the total concentration of analyte after standard is added is $(V_0c_X + V_Sc_S)/(V_0 + V_S)$. Substituting this expression for [X] in Equation 14-14 and doing some rearrangement gives

Standard addition plot for ion-selective electrode:

$$\underbrace{(V_0 + V_S)\,10^{E/S}}_{y} = \underbrace{10^{k/S}\,V_0 c_X}_{b} + \underbrace{10^{k/S}\,c_S}_{m}\underbrace{V_S}_{x} \qquad \textbf{(14-15)}$$

A graph of $(V_0 + V_S)10^{E/S}$ on the y-axis versus V_S on the x-axis has a slope $m = 10^{k/S}\,c_S$ and a y-intercept of $10^{k/S}\,V_0 c_X$ (Figure 14-30). The x-intercept is found by setting $y = 0$:

$$x\text{-intercept} = -\frac{b}{m} = -\frac{10^{k/S}\,V_0 c_X}{10^{k/S}\,c_S} = -\frac{V_0 c_X}{c_S} \qquad \textbf{(14-16)}$$

Equation 14-16 gives us the concentration of unknown, c_X, from V_0, c_S, and the x-intercept.

A weakness of standard addition with ion-selective electrodes is that we cannot measure β in Equation 14-14 in the unknown matrix. We could measure β in a series of standard solutions (not containing unknown) and use this value to compute S in the function $(V_0 + V_S)10^{E/S}$ in Equation 14-15. Another procedure is to add a concentrated, known matrix to the unknown and to all standards so that the matrix is essentially the same in all solutions.

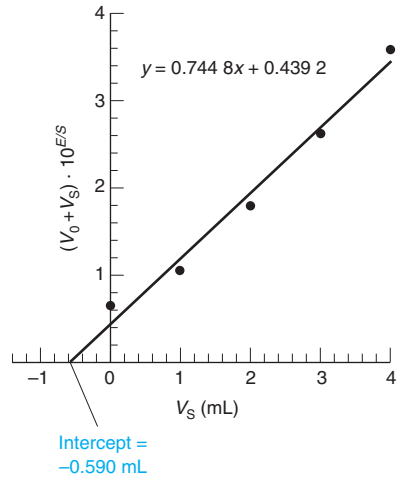


FIGURE 14-30 Standard addition graph for ion-selective electrode based on Equation 14-15. See Exercise 14-F. [Data from G. Li, B. J. Polk, L. A. Meazell, and D. W. Hatchett, "ISE Analysis of Hydrogen Sulfide in Cigarette Smoke," *J. Chem. Ed.* **2000**, *77*, 1049.]

Metal Ion Buffers

It is pointless to dilute $CaCl_2$ to 10^{-6} M for standardizing an ion-selective electrode. At this low concentration, Ca^{2+} might be lost by adsorption on glass or reaction with impurities.

Plastic bottles are better than glass for very dilute solutions of metal salts because ions are adsorbed by glass.

An alternative is to prepare a **metal ion buffer** from the metal and a suitable ligand. For example, consider the reaction of Ca^{2+} with EDTA at pH 6.00 at which the fraction of EDTA in the form Y^{4-} is $\alpha_{Y^{4-}} = 1.8 \times 10^{-5}$ (Table 11-1):

$$Ca^{2+} + Y^{4-} \rightleftharpoons CaY^{2-}$$

$$K_f = 10^{10.65} = \frac{[CaY^{2-}]}{[Ca^{2+}]\alpha_{Y^{4-}}[EDTA]} \qquad \textbf{(14-17)}$$

[EDTA] = total concentration of all forms of EDTA not bound to metal ion.

$\alpha_{Y^{4-}}$ = fraction of unbound EDTA in the form Y^{4-}.

If equal concentrations of CaY^{2-} and EDTA are present in a solution,

$$[Ca^{2+}] = \frac{[CaY^{2-}]}{K_f\alpha_{Y^{4-}}[EDTA]} = \frac{\cancel{[CaY^{2-}]}}{(10^{10.65})(1.8 \times 10^{-5})\cancel{[EDTA]}} = 1.2 \times 10^{-6}\ \text{M}$$

EXAMPLE Preparing a Metal Ion Buffer

What concentration of EDTA should be added to 0.010 M CaY^{2-} at pH 6.00 to give $[Ca^{2+}] = 1.0 \times 10^{-6}$ M?

Solution From Equation 14-17, we write

$$[EDTA] = \frac{[CaY^{2-}]}{K_f\alpha_{Y^{4-}}[Ca^{2+}]} = \frac{0.010}{(10^{10.65})(1.8 \times 10^{-5})(1.00 \times 10^{-6})} = 0.012_4\ \text{M}$$

These are practical concentrations of CaY^{2-} and of EDTA.

Test Yourself What concentration of EDTA should be added to 0.010 M CaY^{2-} at pH 6.00 to give $[Ca^{2+}] = 1.0 \times 10^{-7}$ M? (***Answer:*** 0.12_4 M)

A metal ion buffer is the only way to obtain $[Pb^{2+}] = 10^{-12}$ M for the electrode filling solution in Figure 14-27.

14-8 Solid-State Chemical Sensors[36]

Solid-state chemical sensors are fabricated by the same technology used for microelectronic chips. The field effect transistor (FET) is the heart of many sensors such as the pH electrode in Figure 14-31.

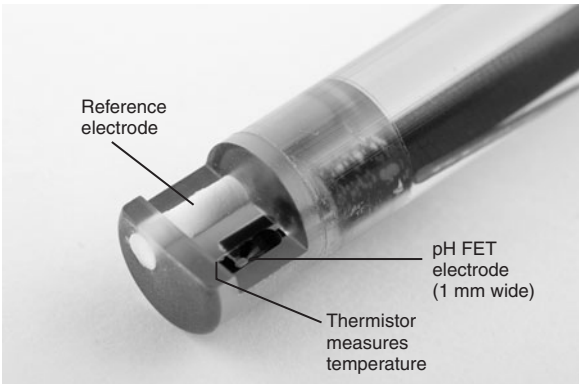


FIGURE 14-31 Combination pH electrode based on field effect transistor. The thermistor senses temperature and is used for automatic temperature compensation. [Courtesy SENTRON, Europe BV.]

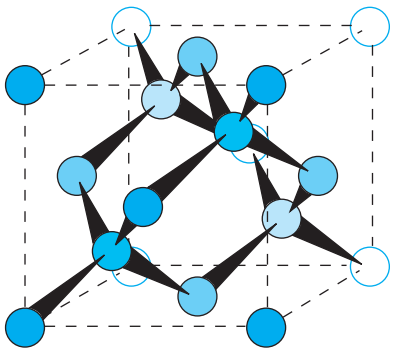


FIGURE 14-32 Diamondlike structure of silicon. Each atom is tetrahedrally bonded to four neighbors, with a Si—Si distance of 235 pm. All atoms in this diagram are Si. The darkest color is for atoms on the front face of the cube. Atoms with successively lighter shades are on planes that are successively further from the front face.

Semiconductors and Diodes

Semiconductors such as Si (Figure 14-32), Ge, and GaAs are materials whose electrical *resistivity*[37] lies between those of conductors and insulators. The four valence electrons of the pure materials are all involved in bonds between atoms (Figure 14-33a). A phosphorus impurity, with five valence electrons, provides one extra **conduction electron** that is free to move through the crystal (Figure 14-33b). An aluminum impurity has one less bonding electron than necessary, creating a vacancy called a **hole,** which behaves as a positive charge carrier. When a neighboring electron fills the hole, a new hole appears at an adjacent position (Figure 14-33c). A semiconductor with excess conduction electrons is called *n-type*, and one with excess holes is called *p-type*.

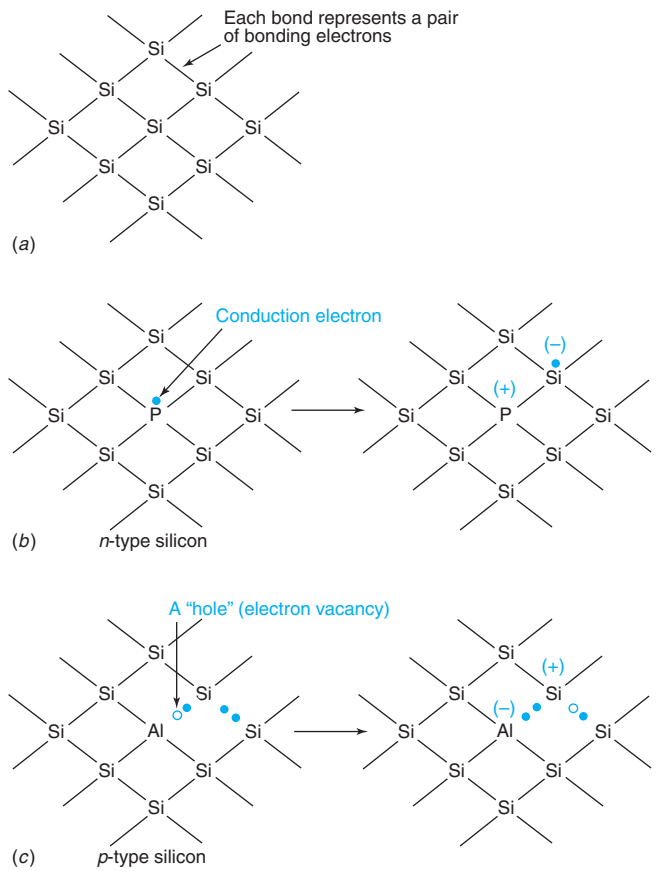


FIGURE 14-33 (*a*) The electrons of pure silicon are all involved in the sigma-bonding framework. (*b*) An impurity atom such as phosphorus adds one extra electron (•), which is relatively free to move through the crystal. (*c*) An aluminum impurity atom lacks one electron needed for the sigma-bonding framework. The hole (○) introduced by the Al atom can be occupied by an electron from a neighboring bond, effectively moving the hole to the neighboring bond.

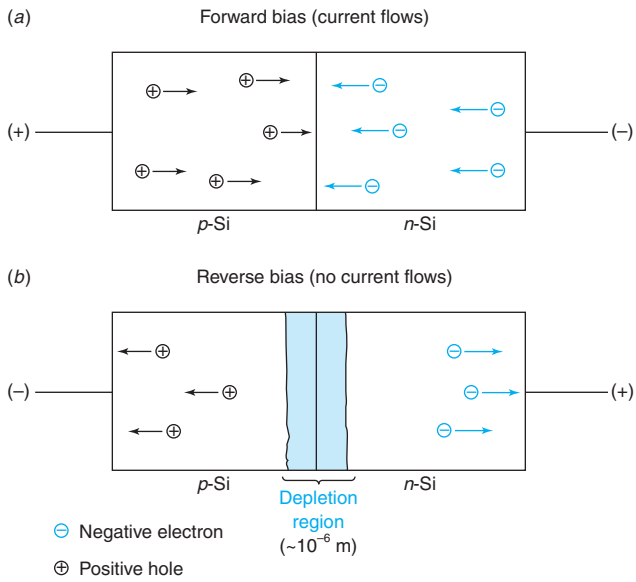


FIGURE 14-34 Behavior of a *pn* junction, showing that current (*a*) can flow under forward bias conditions, but (*b*) is prevented from flowing under reverse bias.

An *activation energy* is needed to get the charge carriers to move across the diode. For Si, ~0.6 V of forward bias is required before current will flow. For Ge, the requirement is ~0.2 V.

For moderate reverse bias voltages, no current flows. If the voltage is sufficiently negative, *breakdown* occurs and current flows in the reverse direction.

A **diode** is a *pn* junction (Figure 14-34a). If *n*-Si is made negative with respect to *p*-Si, electrons flow from the external circuit into the *n*-Si. At the *pn* junction, electrons and holes combine. As electrons move from the *p*-Si into the circuit, a fresh supply of holes is created in the *p*-Si. The net result is that current flows when *n*-Si is negative with respect to *p*-Si. The diode is said to be *forward biased*.

If the polarity is reversed (Figure 14-34b), electrons are drawn out of *n*-Si and holes are drawn out of *p*-Si, leaving a thin *depletion region* devoid of charge carriers near the *pn* junction. The diode is *reverse biased* and does not conduct current in the reverse direction.

Chemical-Sensing Field Effect Transistor

The *base* of the **field effect transistor** in Figure 14-35 is constructed of *p*-Si with two *n*-type regions called *source* and *drain*. An insulating surface layer of SiO_2 is overcoated by a conductive metal *gate* between source and drain. The source and the base are held at the same electric potential. When a voltage is applied between source and drain (Figure 14-35a), little current flows because the drain-base interface is a *pn* junction in reverse bias.

If the gate is made positive, electrons from the base are attracted toward the gate and form a conductive channel between source and drain (Figure 14-35b). Current increases as the gate is made more positive. *The gate potential regulates the current between source and drain.*

The more positive the gate, the more current can flow between source and drain.

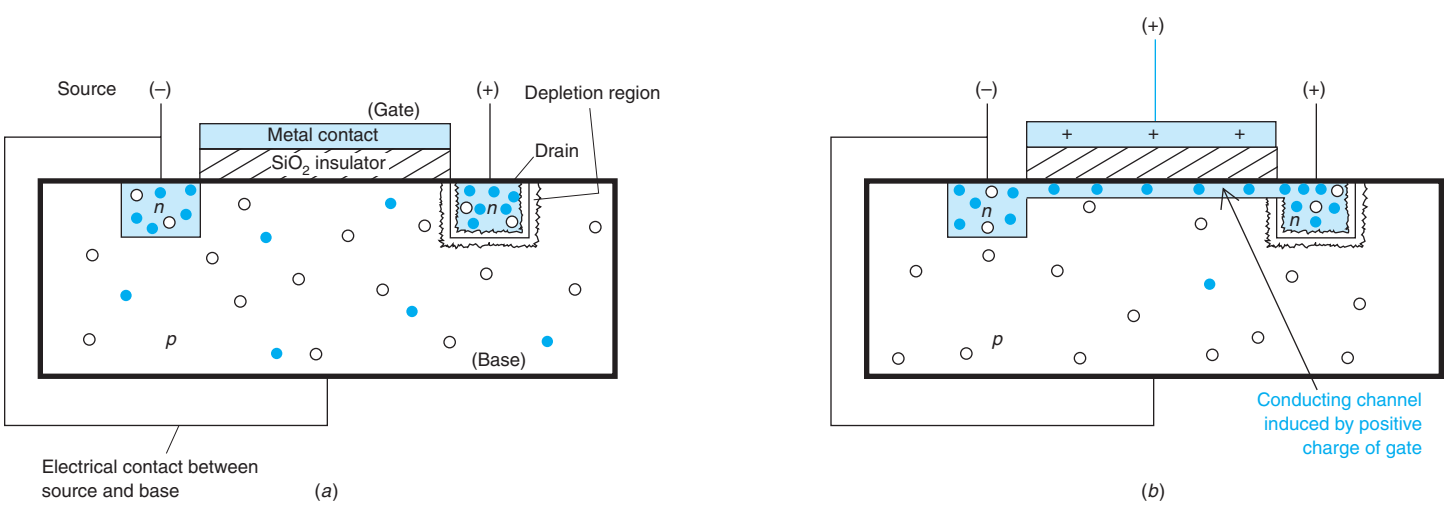


FIGURE 14-35 Operation of a field effect transistor. (*a*) Nearly random distribution of holes and electrons in the base in the absence of gate potential. (*b*) Positive gate potential attracts electrons that form a conductive channel beneath the gate. Current can flow through this channel between source and drain.

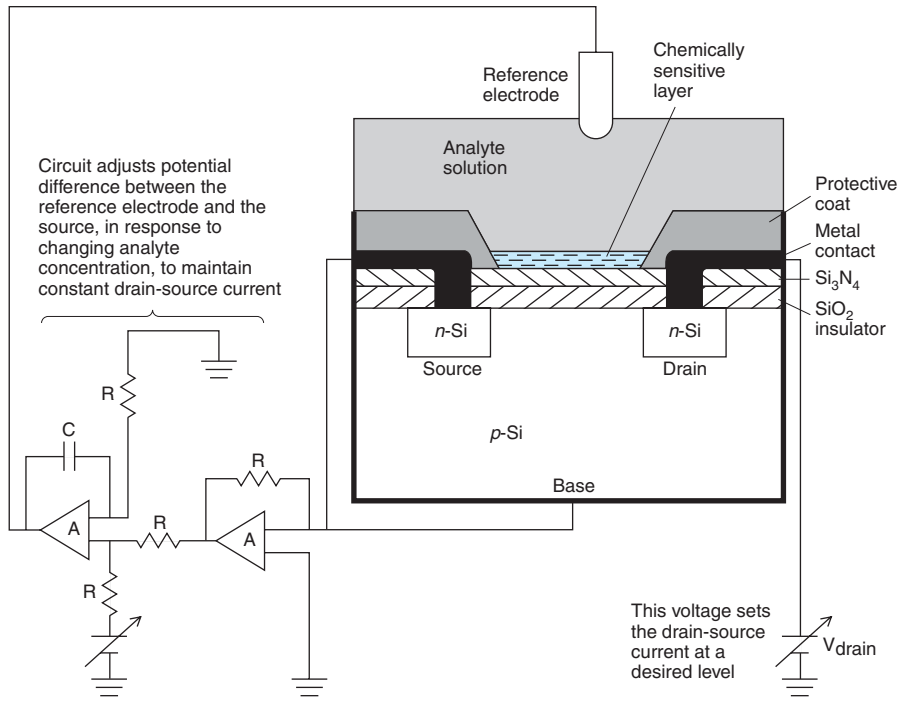


FIGURE 14-36 Operation of a chemical-sensing field effect transistor. The transistor is coated with an insulating SiO_2 layer and a second layer of Si_3N_4 (silicon nitride), which is impervious to ions and improves electrical stability. The circuit at the lower left adjusts the potential difference between the reference electrode and the source in response to changes in the analyte solution, such that a constant drain-source current is maintained.

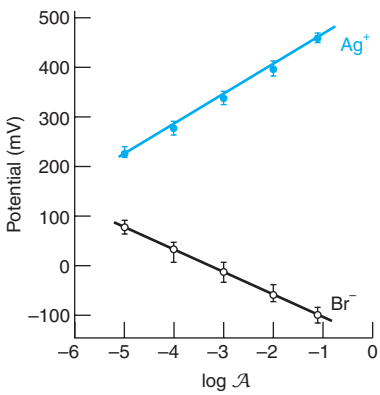


FIGURE 14-37 Response of a silver bromide-coated field effect transistor. Error bars are 95% confidence intervals for data obtained from 195 sensors prepared from different chips. [From R. P. Buck and D. E. Hackleman, "Field Effect Potentiometric Sensors," *Anal. Chem.* **1977,** *49,* 2315.]

The essential feature of the chemical-sensing field effect transistor in Figure 14-36 is the chemically sensitive layer over the gate. An example is a layer of AgBr. When exposed to silver nitrate solution, Ag^+ is adsorbed on the AgBr (Figure 26-2), thereby giving it a positive charge and increasing current between source and drain. *The voltage that must be applied by an external circuit to bring the current back to its initial value is the response to* Ag^+. Figure 14-37 shows that Ag^+ makes the gate more positive and Br^- makes the gate more negative. The response is close to 59 mV for a 10-fold concentration change. The transistor is smaller (Figure 14-31) and more rugged than ion-selective electrodes. The sensing surface is typically only 1 mm^2. Chemical-sensing field effect transistors have been designed for species such as H^+,[38] NH_4^+, Ca^{2+}, NO_3^-,[39] CO_2,[40] pesticides (detection limit = 10^{-12} M),[41,42] adrenaline,[43] and specific sequences of DNA.[44]

Terms to Understand

calomel electrode
combination electrode
compound electrode
conduction electron
diode
electroactive species
field effect transistor
glass electrode
hole
indicator electrode
ion-exchange equilibrium
ion-selective electrode
junction potential
liquid-based ion-selective electrode
matrix
metal ion buffer
mobility
potentiometry
reference electrode
saturated calomel electrode (S.C.E.)
selectivity coefficient
semiconductor
silver-silver chloride electrode
sodium error
solid-state ion-selective electrode
standard addition

Summary

In potentiometric measurements, the indicator electrode responds to changes in the activity of analyte, and the reference electrode is a self-contained half-cell with a constant potential. The most common reference electrodes are calomel and silver-silver chloride. Common indicator electrodes include (1) the inert Pt electrode, (2) a silver electrode responsive to Ag^+, halides, and other ions that react with Ag^+, and (3) ion-selective electrodes. Unknown junction potentials at liquid-liquid interfaces limit the accuracy of most potentiometric measurements.

Ion-selective electrodes, including the glass pH electrode, respond mainly to one ion that is selectively bound to the ion-exchange membrane of the electrode. The potential difference across the membrane, E, depends on the activity ($\mathcal{A}_o$) of the target ion in the external analyte solution. At 25°C, the ideal relation is $E(\text{V}) = \text{constant} + (0.059\,16/n)\ln \mathcal{A}_o$, where n is the charge of the target ion. For interfering ions (X) with the same charge as the primary ion (A), the response of ion-selective electrodes is $E = \text{constant} \pm (0.059\,16/n)\log[\mathcal{A}_A + \Sigma K^{Pot}_{A,X}\mathcal{A}_X]$, where $K^{Pot}_{A,X}$

is the selectivity coefficient for each species. Common ion-selective electrodes can be classified as solid state, liquid based, and compound. Quantitation with ion-selective electrodes is usually done with a calibration curve or by the method of standard addition. Metal ion buffers are appropriate for establishing and maintaining low concentrations of ions. A chemical-sensing field effect transistor is a solid-state device that uses a chemically sensitive coating to alter the electrical properties of a semiconductor in response to changes in the chemical environment.

Exercises

14-A. The apparatus in Figure 14-7 was used to monitor the titration of 50.0 mL of 0.100 M $AgNO_3$ with 0.200 M NaBr. Calculate the cell voltage at each volume of NaBr, and sketch the titration curve: 1.0, 12.5, 24.0, 24.9, 25.1, 26.0, and 35.0 mL.

14-B. The apparatus in the figure can follow the course of an EDTA titration and was used to generate the curves in Figure 11-10. The heart of the cell is a pool of liquid Hg in contact with the solution and with a Pt wire. A small amount of HgY^{2-} added to the analyte equilibrates with a very tiny amount of Hg^{2+}:

$$Hg^{2+} + Y^{4-} \rightleftharpoons HgY^{2-}$$

$$K_f = \frac{[HgY^{2-}]}{[Hg^{2+}][Y^{4-}]} = 10^{21.5} \qquad \textbf{(A)}$$

The redox equilibrium $Hg^{2+} + 2e^- \rightleftharpoons Hg(l)$ is established rapidly at the surface of the Hg electrode, so the Nernst equation for the cell can be written in the form

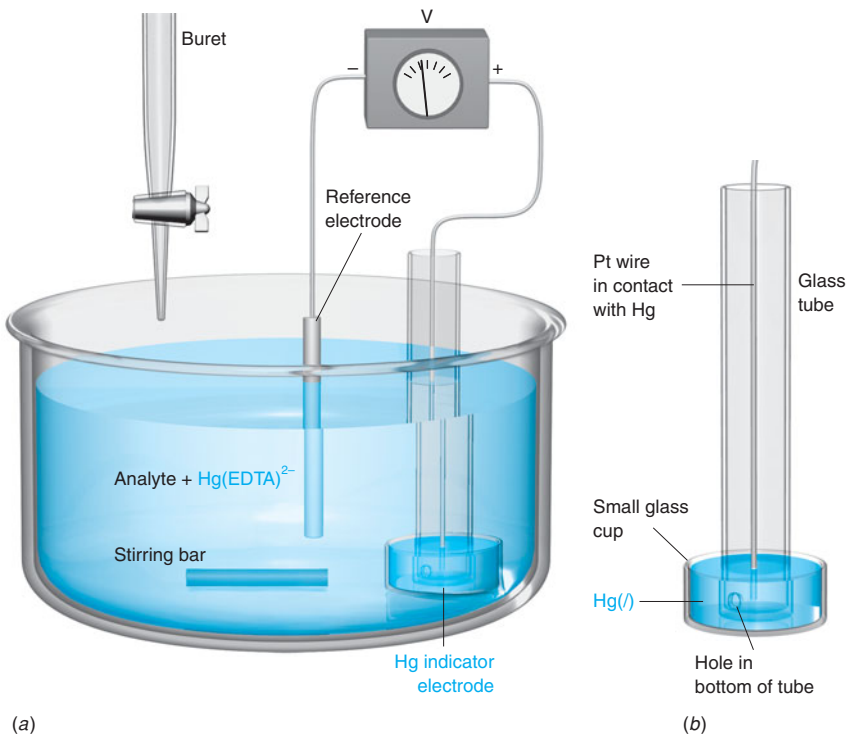
$$E = E_+ - E_- = \left(0.852 - \frac{0.059\,16}{2}\log\left(\frac{1}{[Hg^{2+}]}\right)\right) - E_- \qquad \textbf{(B)}$$

where E_- is the constant potential of the reference electrode. From Equation A, $[Hg^{2+}] = [HgY^{2-}] / K_f[Y^{4-}]$, and this can be substituted into Equation B to give

$$E = 0.852 - \frac{0.059\,16}{2}\log\left(\frac{[Y^{4-}]K_f}{[HgY^{2-}]}\right) - E_-$$

$$= 0.852 - E_- - \frac{0.059\,16}{2}\log\left(\frac{K_f}{[HgY^{2-}]}\right) - \frac{0.059\,16}{2}\log[Y^{4-}] \qquad \textbf{(C)}$$

where K_f is the formation constant for HgY^{2-}. This apparatus thus responds to the changing EDTA concentration during an EDTA titration.



(*a*) Apparatus for Exercise 14-B. (*b*) Enlarged view of mercury electrode.

Suppose that you titrate 50.0 mL of 0.010 0 M $MgSO_4$ with 0.020 0 M EDTA at pH 10.0, using the apparatus in the figure with an S.C.E. reference electrode. Analyte contains 1.0×10^{-4} M $Hg(EDTA)^{2-}$ added at the beginning of the titration. Calculate the cell voltage at the following volumes of added EDTA, and draw a graph of millivolts versus milliliters: 0, 10.0, 20.0, 24.9, 25.0, and 26.0 mL.

14-C. A solid-state fluoride ion-selective electrode responds to F^- but not to HF. It also responds to hydroxide ion at high concentration when $[OH^-] \approx [F^-]/10$. Suppose that such an electrode gave a potential of +100 mV (versus S.C.E.) in 10^{-5} M NaF and +41 mV in 10^{-4} M NaF. Sketch qualitatively how the potential would vary if the electrode were immersed in 10^{-5} M NaF and the pH ranged from 1 to 13.

14-D. One glass-membrane sodium ion-selective electrode has a selectivity coefficient $K^{\text{Pot}}_{\text{Na}^+,\text{H}^+} = 36$. When this electrode was immersed in 1.00 mM NaCl at pH 8.00, a potential of −38 mV (versus S.C.E.) was recorded.

(a) Neglecting activity coefficients, calculate the potential with Equation 14-10 if the electrode were immersed in 5.00 mM NaCl at pH 8.00.

(b) What would the potential be for 1.00 mM NaCl at pH 3.87? You can see that pH is a critical variable for the sodium electrode.

14-E. An ammonia gas-sensing electrode gave the following calibration points when all solutions contained 1 M NaOH.

NH_3 (M)	E (mV)	NH_3 (M)	E (mV)
1.00×10^{-5}	268.0	5.00×10^{-4}	368.0
5.00×10^{-5}	310.0	1.00×10^{-3}	386.4
1.00×10^{-4}	326.8	5.00×10^{-3}	427.6

A dry food sample weighing 312.4 mg was digested by the Kjeldahl procedure (Section 10-8) to convert all nitrogen into NH_4^+. The digestion solution was diluted to 1.00 L, and 20.0 mL were transferred to a 100-mL volumetric flask. The 20.0-mL aliquot was treated with 10.0 mL of 10.0 M NaOH plus enough NaI to complex the Hg catalyst from the digestion and diluted to 100.0 mL. When measured with the ammonia electrode, this solution gave a reading of 339.3 mV. Calculate the wt% nitrogen in the food sample.

14-F. H_2S from cigarette smoke was collected by bubbling smoke through aqueous NaOH and measured with a sulfide ion-selective electrode. Standard additions of volume V_S containing Na_2S at concentration $c_S = 1.78$ mM were then made to $V_0 = 25.0$ mL of unknown and the electrode response, E, was measured.

V_S (mL)	E (V)	V_S (mL)	E (V)
0	0.046 5	3.00	0.030 0
1.00	0.040 7	4.00	0.026 5
2.00	0.034 4		

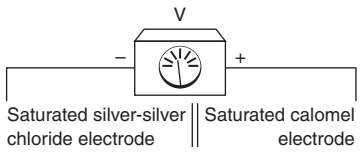
From a separate calibration curve, it was found that $\beta = 0.985$ in Equation 14-14. Using $T = 298.15$ K and $n = -2$ (the charge of S^{2-}), prepare a standard addition graph with Equation 14-15 and find the concentration of sulfide in the unknown.

Problems

Reference Electrodes

14-1. (a) Write the half-reactions for the silver-silver chloride and calomel reference electrodes.

(b) Predict the voltage for the following cell.



14-2. Convert the following potentials. The Ag | AgCl and calomel reference electrodes are saturated with KCl.

(a) 0.523 V versus S.H.E. = ? versus Ag | AgCl

(b) −0.111 V versus Ag | AgCl = ? versus S.H.E.

(c) −0.222 V versus S.C.E. = ? versus S.H.E.

(d) 0.023 V versus Ag | AgCl = ? versus S.C.E.

(e) −0.023 V versus S.C.E. = ? versus Ag | AgCl

14-3. Suppose that the silver-silver chloride electrode in Figure 14-2 is replaced by a saturated calomel electrode. Calculate the cell voltage if $[Fe^{2+}] / [Fe^{3+}] = 2.5 \times 10^{-3}$.

14-4. From the following potentials, calculate the *activity* of Cl^- in 1 M KCl.

$$E^\circ(\text{calomel electrode}) = 0.268 \text{ V}$$

$$E(\text{calomel electrode, 1 M KCl}) = 0.280 \text{ V}$$

14-5. For a silver-silver chloride electrode, the following potentials are observed:

$$E^\circ = 0.222 \text{ V} \qquad E(\text{saturated KCl}) = 0.197 \text{ V}$$

From these potentials, find the activity of Cl^- in saturated KCl. Calculate E for a calomel electrode saturated with KCl, given that E° for the calomel electrode is 0.268 V. (Your answer will not be exactly the value 0.241 used in this book.)

Indicator Electrodes

14-6. A cell was prepared by dipping a Cu wire and a saturated calomel electrode into 0.10 M $CuSO_4$ solution. The Cu wire was attached to the positive terminal of a potentiometer and the calomel electrode was attached to the negative terminal.

(a) Write a half-reaction for the Cu electrode.

(b) Write the Nernst equation for the Cu electrode.

(c) Calculate the cell voltage.

14-7. Explain why a silver electrode can be an indicator electrode for Ag^+ and for halides.

14-8. A 10.0-mL solution of 0.050 0 M $AgNO_3$ was titrated with 0.025 0 M NaBr in the cell

$$\text{S.C.E.} \parallel \text{titration solution} \mid \text{Ag}(s)$$

Find the cell voltage for 0.1 and 30.0 mL of titrant.

14-9. A solution containing 50.0 mL of 0.100 M EDTA buffered to pH 10.00 was titrated with 50.0 mL of 0.020 0 M $Hg(ClO_4)_2$ in the cell shown in Exercise 14-B:

$$\text{S.C.E.} \parallel \text{titration solution} \mid \text{Hg}(l)$$

From the cell voltage $E = -0.027$ V, find the formation constant of $Hg(EDTA)^{2-}$.

14-10. Consider the cell S.C.E. ‖ cell solution | Pt(s), whose voltage is −0.126 V. The cell solution contains 2.00 mmol of $Fe(NH_4)_2(SO_4)_2$, 1.00 mmol of $FeCl_3$, 4.00 mmol of Na_2EDTA, and lots of buffer, pH 6.78, in a volume of 1.00 L.

(a) Write a reaction for the right half-cell.

(b) Find the quotient $[Fe^{2+}]/[Fe^{3+}]$ in the cell solution. (This expression gives the ratio of *uncomplexed* ions.)

(c) Find the quotient of formation constants: (K_f for $FeEDTA^-$)/(K_f for $FeEDTA^{2-}$).

14-11. *An equilibrium challenge:* Here's a cell you'll really like:

$$Ag(s) \mid AgCl(s) \mid KCl(aq, \text{saturated}) \parallel \text{cell solution} \mid Cu(s)$$

The cell solution was made by mixing

25.0 mL of 4.00 mM KCN
25.0 mL of 4.00 mM $KCu(CN)_2$
25.0 mL of 0.400 M acid, HA, with $pK_a = 9.50$
25.0 mL of KOH solution

The measured voltage was −0.440 V. *Calculate the molarity of the* KOH *solution*. Assume that essentially all copper(I) is $Cu(CN)_2^-$. A little HCN comes from the reaction of KCN with HA. Neglect the small amount of HA consumed by reaction with HCN. For the right half-cell, the reaction is $Cu(CN)_2^- + e^- \rightleftharpoons Cu(s) + 2CN^-$. *Suggested procedure:* From E, find $[CN^-]$. From $[CN^-]$, find pH. From pH, figure out how much OH^- had been added.

Junction Potential

14-12. What causes a junction potential? How does this potential limit the accuracy of potentiometric analyses? Identify a cell in the illustrations in Section 13-2 that has no junction potential.

14-13. Why is the 0.1 M HCl | 0.1 M KCl junction potential of opposite sign and greater magnitude than the 0.1 M NaCl | 0.1 M KCl potential in Table 14-2?

14-14. Which side of the liquid junction 0.1 M KNO_3 | 0.1 M NaCl will be negative?

14-15. Refer to the footnote in Table 14-1. How many seconds will it take for **(a)** H^+ and **(b)** NO_3^- to migrate a distance of 12.0 cm in a field of 7.80×10^3 V/m?

14-16. Suppose that an ideal hypothetical cell such as that in Figure 13-7 were set up to measure $E°$ for the half-reaction $Ag^+ + e^- \rightleftharpoons Ag(s)$.

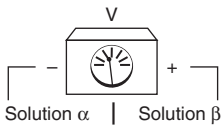
(a) Calculate the equilibrium constant for the net cell reaction.

(b) If there were a junction potential of +2 mV (increasing E from 0.799 to 0.801 V), by what percentage would the calculated equilibrium constant increase?

(c) Answer parts **(a)** and **(b)**, using 0.100 V instead of 0.799 V for the value of $E°$ for the silver reaction.

14-17. Explain how the cell Ag(*s*) | AgCl(*s*) | 0.1 M HCl | 0.1 M KCl | AgCl(*s*) | Ag(*s*) can be used to measure the 0.1 M HCl | 0.1 M KCl junction potential.

14-18. *Henderson equation*. The junction potential, E_j, between solutions α and β can be estimated with the Henderson equation:



$$E_j \approx \frac{\sum_i \frac{|z_i|u_i}{z_i}[C_i(\beta) - C_i(\alpha)]}{\sum_i |z_i|u_i[C_i(\beta) - C_i(\alpha)]} \frac{RT}{F} \ln \frac{\sum_i |z_i|u_i\, C_i(\alpha)}{\sum_i |z_i|u_i\, C_i(\beta)}$$

where z_i is the charge of species i, u_i is the *mobility* of species i (Table 14-1), $C_i(\alpha)$ is the concentration of species i in phase α, and $C_i(\beta)$ is the concentration in phase β. (Activity coefficients are neglected in this equation.)

(a) Using your calculator, show that the junction potential of 0.1 M HCl | 0.1 M KCl is 26.9 mV at 25°C. (Note that $(RT/F) \ln x = 0.059\,16 \log x$.)

(b) Set up a spreadsheet to reproduce the result in part **(a)**. Then use your spreadsheet to compute and plot the junction potential for 0.1 M HCl | x M KCl, where x varies from 1 mM to 4 M.

(c) Use your spreadsheet to explore the behavior of the junction potential for y M HCl | x M KCl, where $y = 10^{-4}$, 10^{-3}, 10^{-2}, and 10^{-1} M and x = 1 mM or 4 M.

pH Measurement with a Glass Electrode

14-19. Describe how you would calibrate a pH electrode and measure the pH of blood (~7.5) *at 37°C*. Use the standard buffers in Table 14-3.

14-20. List the sources of error associated with pH measurement with the glass electrode.

14-21. If electrode C in Figure 14-18 were placed in a solution of pH 11.0, what would the pH reading be?

14-22. Which National Institute of Standards and Technology buffer(s) would you use to calibrate an electrode for pH measurements in the range 3–4?

14-23. Why do glass pH electrodes tend to indicate a pH lower than the actual pH in strongly basic solution?

14-24. Suppose that the Ag | AgCl outer electrode in Figure 14-11 is filled with 0.1 M NaCl instead of saturated KCl. Suppose that the electrode is calibrated in a dilute buffer containing 0.1 M KCl at pH 6.54 at 25°C. The electrode is then dipped in a second buffer *at the same pH* and same temperature, but containing 3.5 M KCl. Use Table 14-2 to estimate how much the indicated pH will change.

14-25. (a) When the difference in pH across the membrane of a glass electrode at 25°C is 4.63 pH units, how much voltage is generated by the pH gradient?

(b) What would the voltage be for the same pH difference at 37°C?

14-26. When calibrating a glass electrode, 0.025 *m* potassium dihydrogen phosphate/0.025 *m* disodium hydrogen phosphate buffer (Table 14-3) gave a reading of −18.3 mV at 20°C and 0.05 *m* potassium hydrogen phthalate buffer gave a reading of +146.3 mV. What is the pH of an unknown giving a reading of +50.0 mV? What is the slope of the calibration curve (mV/pH unit) and what is the theoretical slope at 20°C? Find the value of β in Equation 14-6.

14-27. *Activity problem*. The 0.025 0 *m* KH_2PO_4/0.025 0 *m* Na_2HPO_4 buffer (6) in Table 14-3 has a pH of 6.865 at 25°C.

(a) Show that the ionic strength of the buffer is $\mu = 0.100$ *m*.

(b) From the pH and K_2 for phosphoric acid, find the quotient of activity coefficients, $\gamma_{HPO_4^{2-}}/\gamma_{H_2PO_4^-}$, at $\mu = 0.100$ *m*.

(c) You have the urgent need to prepare a pH 7.000 buffer to be used as a calibration standard.[45] You can use the activity coefficient ratio from part **(b)** to accurately prepare such a buffer if the ionic strength is kept at 0.100 *m*. What molalities of KH_2PO_4 and Na_2HPO_4 should be mixed to obtain a pH of 7.000 and $\mu = 0.100$ *m*?

Ion-Selective Electrodes

14-28. Explain the principle of operation of ion-selective electrodes. How does a compound electrode differ from a simple ion-selective electrode?

14-29. What does the selectivity coefficient tell us? Is it better to have a large or a small selectivity coefficient?

14-30. What makes a liquid-based ion-selective electrode specific for one analyte?

14-31. Why is it preferable to use a metal ion buffer to achieve pM = 8 rather than just dissolving enough M to give a 10^{-8} M solution?

14-32. To determine the *concentration* of a dilute analyte with an ion-selective electrode, why do we use standards with a constant, high concentration of an inert salt?

14-33. A cyanide ion-selective electrode obeys the equation

$$E = \text{constant} - 0.059\,16 \log[CN^-]$$

The potential was −0.230 V when the electrode was immersed in 1.00 mM NaCN.

(a) Evaluate the constant in the equation.

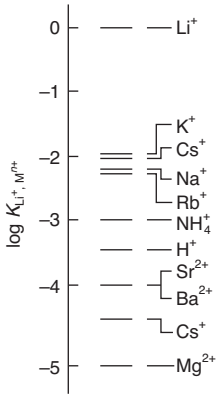
(b) Using the result from part **(a)**, find $[CN^-]$ if $E = -0.300$ V.

(c) Without using the constant from part **(a)**, find $[CN^-]$ if $E = -0.300$ V.

14-34. By how many volts will the potential of an ideal Mg^{2+} ion-selective electrode change if the electrode is removed from 1.00×10^{-4} M $MgCl_2$ and placed in 1.00×10^{-3} M $MgCl_2$ at 25°C?

14-35. When measured with a F^- ion-selective electrode with a Nernstian response at 25°C, the potential due to F^- in unfluoridated groundwater in Foxboro, Massachusetts, was 40.0 mV more positive than the potential of tap water in Providence, Rhode Island. Providence maintains its fluoridated water at the recommended level of 1.00 ± 0.05 mg F^-/L. What is the concentration of F^- in mg/L in groundwater in Foxboro? (Disregard the uncertainty.)

14-36. The selectivities of a Li^+ ion-selective electrode are indicated on the following diagram. Which alkali metal (Group 1) ion causes the most interference? Which alkaline earth (Group 2) ion causes the most interference? How much greater must be $[K^+]$ than $[Li^+]$ for the two ions to give equal response?



14-37. A metal ion buffer was prepared from 0.030 M ML and 0.020 M L, where ML is a metal-ligand complex and L is free ligand.

$$M + L \rightleftharpoons ML \qquad K_f = 4.0 \times 10^8$$

Calculate the concentration of free metal ion, M, in this buffer.

14-38. *Calibration curve and propagation of uncertainty for exponents*. The following data were obtained when a Ca^{2+} ion-selective electrode was immersed in standard solutions whose ionic strength was constant at 2.0 M.

Ca^{2+} (M)	E (mV)
3.38×10^{-5}	−74.8
3.38×10^{-4}	−46.4
3.38×10^{-3}	−18.7
3.38×10^{-2}	+10.0
3.38×10^{-1}	+37.7

(a) Prepare a calibration curve and find the least-squares slope and intercept and their standard deviations.

(b) Calculate the value of β in Equation 14-13.

(c) For a measured potential, the calibration curve gives us $\log[Ca^{2+}]$. We can compute $[Ca^{2+}] = 10^{\log[Ca^{2+}]}$. Using rules for propagation of uncertainty in Table 3-1, calculate $[Ca^{2+}]$ and its associated uncertainty of a sample that gave a reading of −22.5 (±0.3) mV in four replicate measurements.

14-39. The selectivity coefficient, $K^{Pot}_{Li^+,H^+}$, for a Li^+ ion-selective electrode is 4×10^{-4}. When this electrode is placed in 3.44×10^{-4} M Li^+ solution at pH 7.2, the potential is −0.333 V versus S.C.E. What would be the potential if the pH were lowered to 1.1 and the ionic strength were kept constant?

14-40. *Standard addition*. A particular CO_2 compound electrode like the one in Figure 14-28 obeys the equation E = constant − $[\beta RT(\ln 10)/2F] \log[CO_2]$, where R is the gas constant, T is temperature (303.15 K), F is the Faraday constant, and β = 0.933 (measured from a calibration curve). $[CO_2]$ represents all forms of dissolved carbon dioxide at the pH of the experiment, which was 5.0. Standard additions of volume V_S containing a standard concentration c_S = 0.020 0 M $NaHCO_3$ were made to an unknown solution whose initial volume was V_0 = 55.0 mL.

V_S (mL)	E (V)	V_S (mL)	E (V)
0	0.079 0	0.300	0.058 8
0.100	0.072 4	0.800	0.050 9
0.200	0.065 3		

Prepare a graph with Equation 14-15 and find $[CO_2]$ in the unknown.

14-41. *Standard addition with confidence interval*. Ammonia in seawater was measured with an ammonia-selective electrode. A 100.0 mL aliquot of seawater was treated with 1.00 mL of 10 M NaOH to convert NH_4^+ to NH_3. Therefore, V_0 = 101.0 mL. A reading was then taken with the electrode. Then a series of 10.00 mL aliquots of standard $NH_4^+Cl^-$ were added with results in the table.

V_S (mL)	E (V)	V_S (mL)	E (V)
0	−0.084 4	30.00	−0.039 4
10.00	−0.058 1	40.00	−0.034 7
20.00	−0.046 9		

SOURCE: *Data derived from H. Van Ryswyk, E. W. Hall, S. J. Petesch, and A. E. Wiedeman, "Extending the Marine Microcosm Laboratory," J. Chem. Ed.* ***2007****, 84, 306.*

The standard contains 100.0 ppm (mg/L) of nitrogen in the form of $NH_4^+Cl^-$. A separate experiment determined that the electrode slope $\beta RT(\ln 10)/F$ is 0.056 6 V.

(a) Prepare a standard addition graph. Find the concentration and 95% confidence interval for ammonia nitrogen (ppm) in the 100.0 mL of seawater.

(b) Standard addition is best if the additions increase analyte to 1.5 to 3 times its original concentration. Does this experiment fall in that range? A criticism of this experiment is that too much added standard creates error because the standards contribute too much to the computed result and the reading from the initial solution is not weighted heavily enough.

14-42. Data below come from the graph in Box 14-2, for which the separate solutions method was used to measure selectivity coefficients for a sodium ion-selective electrode at 21.5°C. Use Equation 14-11 to calculate log K^{Pot} for each line below.

$(E_{Mg^{2+}} - E_{Na^+})$ at $\mathcal{A} = 10^{-3} = -0.385$ V $\Rightarrow \log K^{Pot}_{Na^+,Mg^{2+}} = ?$

$(E_{Mg^{2+}} - E_{Na^+})$ at $\mathcal{A} = 10^{-2} = -0.418$ V $\Rightarrow \log K^{Pot}_{Na^+,Mg^{2+}} = ?$

$(E_{K^+} - E_{Na^+})$ at $\mathcal{A} = 10^{-3} = -0.285$ V $\Rightarrow \log K^{Pot}_{Na^+,K^+} = ?$

$(E_{K^+} - E_{Na^+})$ at $\mathcal{A} = 10^{-1.5} = -0.285$ V $\Rightarrow \log K^{Pot}_{Na^+,K^+} = ?$

14-43. The H^+ ion-selective electrode on the *Phoenix Mars Lander* has selectivity coefficients $K^{Pot}_{H^+,Na^+} = 10^{-8.6}$ and $K^{Pot}_{H^+,Ca^{2+}} = 10^{-7.8}$. Let A be the primary ion sensed by the electrode and let its charge be z_A. Let X be an interfering ion with charge z_X. The relative error in primary ion activity due to an interfering ion is[46]

$$\text{Error in } \mathcal{A}_A\,(\%) = \frac{(K^{Pot}_{A,X})^{z_X/z_A}\,\mathcal{A}_X}{\mathcal{A}_A^{z_X/z_A}} \times 100$$

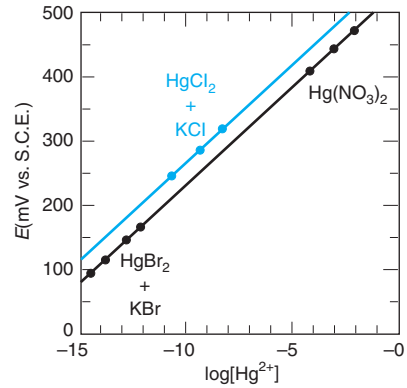
This expression applies for errors less than ~10%. If the pH is 8.0 ($\mathcal{A}_{H^+} = 10^{-8.0}$) and $\mathcal{A}_{Na^+} = 10^{-2.0}$, what is the relative error in measuring $\mathcal{A}_{H^+}$? If the pH is 8.0 and $\mathcal{A}_{Ca^{2+}} = 10^{-2.0}$, what is the relative error in measuring $\mathcal{A}_{H^+}$?

14-44. A Ca^{2+} ion-selective electrode was calibrated in metal ion buffers with ionic strength fixed at 0.50 M. Using the following electrode readings, write an equation for the response of the electrode to Ca^{2+} and Mg^{2+}.

$[Ca^{2+}]$ (M)	$[Mg^{2+}]$ (M)	mV
1.00×10^{-6}	0	−52.6
2.43×10^{-4}	0	+16.1
1.00×10^{-6}	3.68×10^{-3}	−38.0

14-45. The Pb^{2+} ion buffer used inside the electrode for the colored curve in Figure 14-27 was prepared by mixing 1.0 mL of 0.10 M $Pb(NO_3)_2$ with 100.0 mL of 0.050 M Na_2EDTA. At the measured pH of 4.34, $\alpha_{Y^{4-}} = 1.46 \times 10^{-8}$ (Equation 11-4). Show that $[Pb^{2+}] = 1.4 \times 10^{-12}$ M.

14-46. Solutions with a wide range of Hg^{2+} concentrations were prepared to calibrate an experimental Hg^{2+} ion-selective electrode. For the range $10^{-5} < [Hg^{2+}] < 10^{-1}$ M, $Hg(NO_3)_2$ was used directly. The range $10^{-11} < [Hg^{2+}] < 10^{-6}$ M could be covered by the buffer system $HgCl_2(s) + KCl(aq)$ (based on pK_{sp} for $HgCl_2 = 13.16$). The range $10^{-15} < [Hg^{2+}] < 10^{-11}$ M was obtained with $HgBr_2(s) + KBr(aq)$ (based on pK_{sp} for $HgBr_2 = 17.43$). The resulting calibration curve is shown in the figure. Calibration points for the $HgCl_2$ / KCl buffer are not in line with the other data. Suggest a possible explanation.



Hg^{2+} ion-selective electrode calibration curve from J. A. Shatkin, H. S. Brown, and S. Licht, "Composite Graphite Ion Selective Electrode Array Potentiometry for the Detection of Mercury and Other Relevant Ions in Aquatic Systems," *Anal. Chem.* **1995**, *67*, 1147. It was not stated in the paper, but we presume that all solutions had the same ionic strength.

14-47. *Activity problem.* Citric acid is a triprotic acid (H_3A) whose anion (A^{3-}) forms stable complexes with many metal ions.

$$Ca^{2+} + A^{3-} \overset{K_f}{\rightleftharpoons} CaA^-$$

When a Ca^{2+} ion-selective electrode with a slope of 29.58 mV was immersed in a solution having $\mathcal{A}_{Ca^{2+}} = 1.00 \times 10^{-3}$, the reading was +2.06 mV. Calcium citrate solution was prepared by mixing equal volumes of solutions 1 and 2.

Solution 1:
$[Ca^{2+}] = 1.00 \times 10^{-3}$ M, pH = 8.00, $\mu = 0.10$ M

Solution 2:
$[\text{Citrate}]_{total} = 1.00 \times 10^{-3}$ M, pH = 8.00, $\mu = 0.10$ M

The calcium citrate solution gave an electrode reading of −25.90 mV.

(a) Refer to the discussion with Figure B-2 in Appendix B. Calculate the activity of Ca^{2+} in the calcium citrate solution.

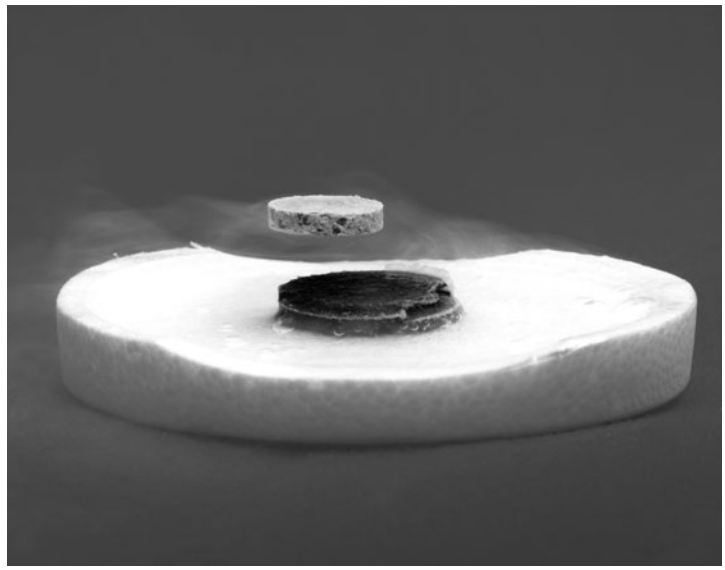
(b) Calculate the formation constant, K_f, for CaA^-. Assume that the size of CaA^- is 500 pm. At pH 8.00 and $\mu = 0.10$ M, the fraction of free citrate in the form A^{3-} is 0.998.

Solid-State Chemical Sensors

14-48. What does analyte do to a chemical-sensing field effect transistor to produce a signal related to the activity of analyte?

15 Redox Titrations

CHEMICAL ANALYSIS OF HIGH-TEMPERATURE SUPERCONDUCTORS



Permanent magnet levitates above superconducting disk cooled in a pool of liquid nitrogen. Redox titrations are crucial in measuring the chemical composition of a superconductor. [Photo courtesy D. Cornelius, Michelson Laboratory, with materials from T. Vanderah.]

Superconductors are materials that lose all electrical resistance when cooled below a critical temperature. Prior to 1987, all known superconductors required cooling to temperatures near that of liquid helium (4 K), a process that is costly and impractical for all but a few applications. In 1987, a giant step was taken when "high-temperature" superconductors that retain their superconductivity above the boiling point of liquid nitrogen (77 K) were discovered. The most startling characteristic of a superconductor is magnetic levitation, shown above. When a magnetic field is applied to a superconductor, current flows in the outer skin of the material such that the applied magnetic field is exactly canceled by the induced magnetic field, and the net field inside the specimen is zero. Expulsion of a magnetic field from a superconductor is called the *Meissner effect*.

A prototypical high-temperature superconductor is yttrium barium copper oxide, $YBa_2Cu_3O_7$, in which two-thirds of the copper is in the +2 oxidation state and one-third is in the unusual +3 state. Another example is $Bi_2Sr_2(Ca_{0.8}Y_{0.2})Cu_2O_{8.295}$, in which the average oxidation state of copper is +2.105 and the average oxidation state of bismuth is +3.090 (which is formally a mixture of Bi^{3+} and Bi^{5+}). The most reliable means to unravel these complex formulas is through "wet" oxidation-reduction titrations described in this chapter.

Iron and its compounds are environmentally acceptable redox agents that are finding increased use in remediating toxic waste in groundwaters:[1]

$$\underset{\substack{\text{Dissolved}\\\text{chromate}\\\text{(carcinogen)}}}{CrO_4^{2-}} + \underset{\substack{\text{Iron}\\\text{particles}\\\text{(reductant)}}}{Fe(0)} + 4H_2O \rightarrow \underbrace{Cr(OH)_3(s) + Fe(OH)_3(s)}_{\substack{\text{Mixed hydroxide precipitate}\\\text{(relatively safe)}}} + 2OH^-$$

$$\underset{\text{Pollutant}}{3H_2S} + \underset{\substack{\text{Ferrate(VI)}\\\text{(oxidant)}}}{8HFeO_4^-} + 6H_2O \rightarrow \underbrace{8Fe(OH)_3(s) + 3SO_4^{2-}}_{\text{(safe products)}} + 2OH^-$$

A **redox titration** is based on an oxidation-reduction reaction between analyte and titrant. In addition to the many common analytes in chemistry, biology, and environmental and materials science that can be measured by redox titrations, exotic oxidation states of elements in uncommon materials such as superconductors and laser materials are measured by redox titrations. For example, chromium added to laser crystals to increase their efficiency is found in the common oxidation states +3 and +6, and the unusual +4 state. A redox titration is a good way to unravel the nature of this complex mixture of chromium ions.

This chapter introduces the theory of redox titrations and discusses some common reagents. A few of the oxidants and reductants in Table 15-1 can be used as titrants.[2] Most reductants used as titrants react with O_2 and, therefore, require protection from air.

15-1 The Shape of a Redox Titration Curve

Consider the titration of iron(II) with standard cerium(IV), monitored potentiometrically with Pt and calomel electrodes as shown in Figure 15-1. The titration reaction is

Titration reaction: $$\underset{\text{Ceric titrant}}{Ce^{4+}} + \underset{\text{Ferrous analyte}}{Fe^{2+}} \rightarrow \underset{\text{Cerous}}{Ce^{3+}} + \underset{\text{Ferric}}{Fe^{3+}} \qquad (15\text{-}1)$$

The titration reaction goes to completion after each addition of titrant. The equilibrium constant is $K = 10^{nE^\circ/0.059\ 16}$ at 25°C.

for which $K \approx 10^{16}$ in 1 M $HClO_4$. Each mole of ceric ion oxidizes 1 mol of ferrous ion rapidly and quantitatively. The titration reaction creates a mixture of Ce^{4+}, Ce^{3+}, Fe^{2+}, and Fe^{3+} in the beaker in Figure 15-1. Box 15-1 describes the likely mechanism of Reaction 15-1.

At the Pt indicator electrode, *two* reactions come to equilibrium:

Indicator half-reaction: $$Fe^{3+} + e^- \rightleftharpoons Fe^{2+} \qquad E^\circ = 0.767\ \text{V} \qquad (15\text{-}2)$$

Indicator half-reaction: $$Ce^{4+} + e^- \rightleftharpoons Ce^{3+} \qquad E^\circ = 1.70\ \text{V} \qquad (15\text{-}3)$$

Equilibria 15-2 and 15-3 are both established at the Pt electrode.

The potentials are the formal potentials that apply in 1 M $HClO_4$. The Pt indicator electrode responds to the relative concentrations (really, activities) of Ce^{4+} and Ce^{3+} or Fe^{3+} and Fe^{2+}.

We now set out to calculate how the cell voltage changes as Fe^{2+} is titrated with Ce^{4+}. The titration curve has three regions.

Region 1: Before the Equivalence Point

As each aliquot of Ce^{4+} is added, titration reaction 15-1 consumes Ce^{4+} and creates an equal number of moles of Ce^{3+} and Fe^{3+}. Prior to the equivalence point, excess unreacted Fe^{2+} remains in solution. Therefore, we can find the concentrations of Fe^{2+} and Fe^{3+} without difficulty. On the other hand, we cannot find the concentration of Ce^{4+} without solving a fancy little equilibrium problem. Because the amounts of Fe^{2+} and Fe^{3+} are both

We can use either Reaction 15-2 or Reaction 15-3 to describe the cell voltage at any time. However, because we know $[Fe^{2+}]$ and $[Fe^{3+}]$, it is more convenient for now to use Reaction 15-2.

TABLE 15-1 Oxidizing and reducing agents

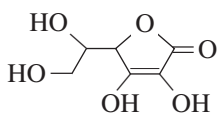
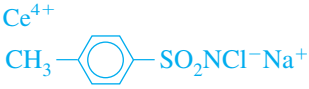
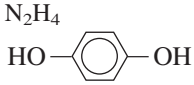
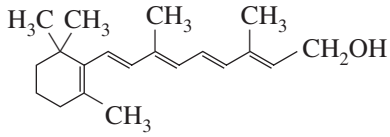
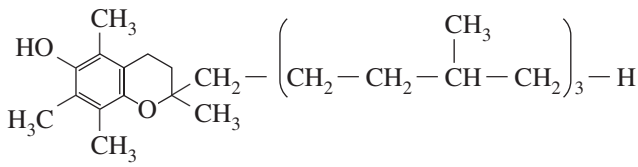
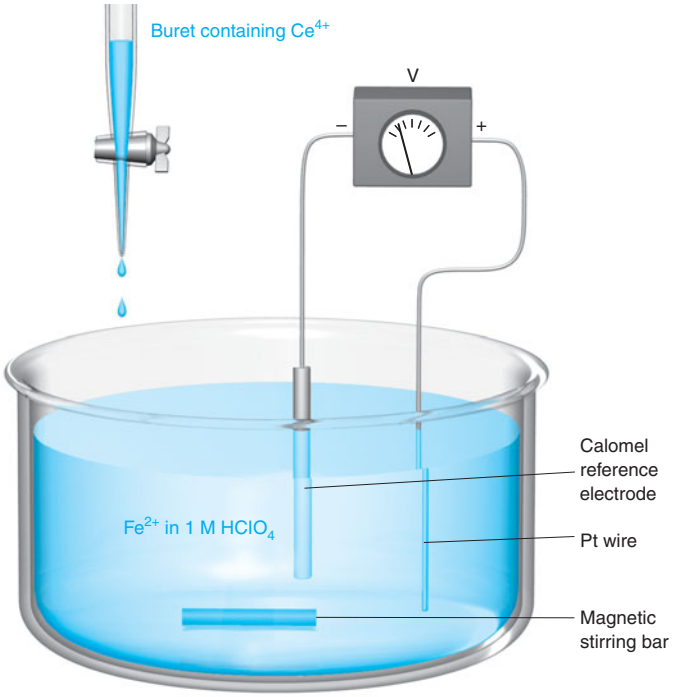
Oxidants		Reductants	
BiO_3^-	Bismuthate		Ascorbic acid (vitamin C)
BrO_3^-	Bromate	BH_4^-	Borohydride
Br_2	Bromine	Cr^{2+}	Chromous
Ce^{4+}	Ceric	$S_2O_4^{2-}$	Dithionite
	Chloramine T	Fe^{2+}	Ferrous
Cl_2	Chlorine	N_2H_4	Hydrazine
ClO_2	Chlorine dioxide		Hydroquinone
$Cr_2O_7^{2-}$	Dichromate	NH_2OH	Hydroxylamine
FeO_4^{2-}	Ferrate(VI)	H_3PO_2	Hypophosphorous acid
H_2O_2	Hydrogen peroxide		Retinol (vitamin A)
$Fe^{2+} + H_2O_2$	Fenton reagent[3]	Sn^{2+}	Stannous
OCl^-	Hypochlorite	SO_3^{2-}	Sulfite
IO_3^-	Iodate	SO_2	Sulfur dioxide
I_2	Iodine	$S_2O_3^{2-}$	Thiosulfate
$Pb(acetate)_4$	Lead(IV) acetate		α-Tocopherol (vitamin E)[4]
HNO_3	Nitric acid		
O	Atomic oxygen		
O_2	Dioxygen (oxygen)		
O_3	Ozone		
$HClO_4$	Perchloric acid		
IO_4^-	Periodate		
MnO_4^-	Permanganate		
$S_2O_8^{2-}$	Peroxydisulfate		

FIGURE 15-1 Apparatus for potentiometric titration of Fe^{2+} with Ce^{4+}.



known, it is *convenient* to calculate the cell voltage by using Reaction 15-2 instead of Reaction 15-3.

E_+ is the potential of the Pt electrode connected to the positive terminal of the potentiometer in Figure 15-1. E_- is the potential of the calomel electrode connected to the negative terminal.

$$E = E_+ - E_- \tag{15-4}$$

$$E = \left[\underset{\substack{\uparrow \\ \text{Formal potential for } Fe^{3+} \\ \text{reduction in} \\ \text{1 M } HClO_4}}{0.767} - 0.059\,16 \log\left(\frac{[Fe^{2+}]}{[Fe^{3+}]}\right)\right] - \underset{\substack{\uparrow \\ \text{Potential of} \\ \text{saturated calomel} \\ \text{electrode}}}{0.241} \tag{15-5}$$

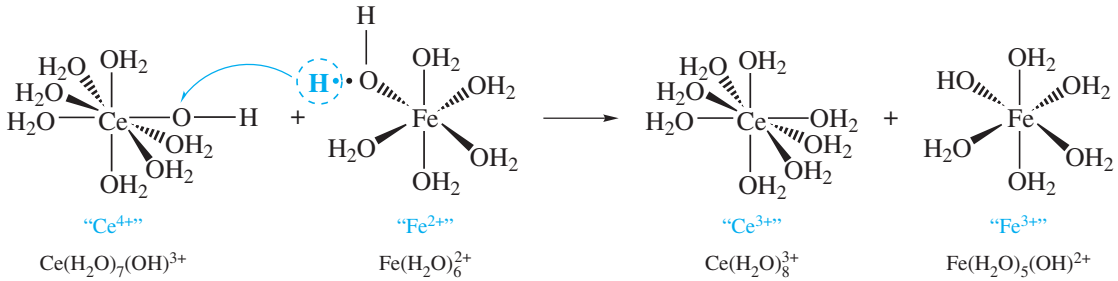
$$E = 0.526 - 0.059\,16 \log\left(\frac{[Fe^{2+}]}{[Fe^{3+}]}\right) \tag{15-6}$$

For Reaction 15-2, $E_+ = E°(Fe^{3+} \mid Fe^{2+})$ when $V = \frac{1}{2}V_e$.

One special point is reached before the equivalence point. When the volume of titrant is one-half of the amount required to reach the equivalence point ($V = \frac{1}{2}V_e$), $[Fe^{3+}] =$

BOX 15-1 Many Redox Reactions Are Atom-Transfer Reactions

Reaction 15-1 appears as if an electron moves from Fe^{2+} to Ce^{4+} to give Fe^{3+} and Ce^{3+}. In fact, this reaction and many others are thought to proceed through atom transfer, not electron transfer.[5] In this case, a hydrogen atom (a proton plus an electron) could be transferred from aqueous Fe^{2+} to aqueous Ce^{4+} species:



Other common redox reactions between metallic species could proceed via transfer of oxygen atoms or halogen atoms to effect net electron transfer from one metal to another.

$[Fe^{2+}]$. In this case, the log term is 0, and $E_+ = E°$ for the $Fe^{3+} \mid Fe^{2+}$ couple. *The point at which $V = \frac{1}{2}V_e$ is analogous to the point at which $pH = pK_a$ when $V = \frac{1}{2}V_e$ in an acid-base titration.*

The voltage at zero titrant volume cannot be calculated, because we do not know how much Fe^{3+} is present. If $[Fe^{3+}] = 0$, the voltage calculated with Equation 15-6 would be $-\infty$. In fact, there must be some Fe^{3+} in each reagent, either as an impurity or from oxidation of Fe^{2+} by atmospheric oxygen. In any case, the voltage could never be lower than that needed to reduce the solvent ($H_2O + e^- \rightarrow \frac{1}{2}H_2 + OH^-$).

Region 2: At the Equivalence Point

Exactly enough Ce^{4+} has been added to react with all the Fe^{2+}. Virtually all cerium is in the form Ce^{3+}, and virtually all iron is in the form Fe^{3+}. Tiny amounts of Ce^{4+} and Fe^{2+} are present at equilibrium. From the stoichiometry of Reaction 15-1, we can say that

$$[Ce^{3+}] = [Fe^{3+}] \tag{15-7}$$

$$[Ce^{4+}] = [Fe^{2+}] \tag{15-8}$$

To understand why Equations 15-7 and 15-8 are true, imagine that *all* the cerium and the iron have been converted into Ce^{3+} and Fe^{3+}. Because we are at the equivalence point, $[Ce^{3+}] = [Fe^{3+}]$. Now let Reaction 15-1 come to equilibrium:

$$Fe^{3+} + Ce^{3+} \rightleftharpoons Fe^{2+} + Ce^{4+} \qquad \text{(reverse of Reaction 15-1)}$$

If a little bit of Fe^{3+} goes back to Fe^{2+}, an equal number of moles of Ce^{4+} must be made. So $[Ce^{4+}] = [Fe^{2+}]$.

At any time, Reactions 15-2 and 15-3 are *both* in equilibrium at the Pt electrode. At the equivalence point, it is *convenient* to use both reactions to describe the cell voltage. The Nernst equations for these reactions are

$$E_+ = 0.767 - 0.059\,16 \log\left(\frac{[Fe^{2+}]}{[Fe^{3+}]}\right) \tag{15-9}$$

$$E_+ = 1.70 - 0.059\,16 \log\left(\frac{[Ce^{3+}]}{[Ce^{4+}]}\right) \tag{15-10}$$

At the equivalence point, we use both Reactions 15-2 and 15-3 to calculate the cell voltage. This is strictly a matter of algebraic convenience.

Here is where we stand: Equations 15-9 and 15-10 are each a statement of algebraic truth. But neither one alone allows us to find E_+, because we do not know exactly what tiny concentrations of Fe^{2+} and Ce^{4+} are present. It is possible to solve the four simultaneous equations 15-7 through 15-10 by first *adding* Equations 15-9 and 15-10:

$$2E_+ = 0.767 + 1.70 - 0.059\,16 \log\left(\frac{[Fe^{2+}]}{[Fe^{3+}]}\right) - 0.059\,16 \log\left(\frac{[Ce^{3+}]}{[Ce^{4+}]}\right)$$

$$2E_+ = 2.46_7 - 0.059\,16 \log\left(\frac{[Fe^{2+}][Ce^{3+}]}{[Fe^{3+}][Ce^{4+}]}\right)$$

$\log a + \log b = \log ab$
$-\log a - \log b = -\log ab$

But, because $[Ce^{3+}] = [Fe^{3+}]$ and $[Ce^{4+}] = [Fe^{2+}]$ at the equivalence point, the ratio of concentrations in the log term is unity. Therefore, the logarithm is 0 and

$$2E_+ = 2.46_7 \text{ V} \Rightarrow E_+ = 1.23 \text{ V}$$

The cell voltage is

$$E = E_+ - E(\text{calomel}) = 1.23 - 0.241 = 0.99 \text{ V} \tag{15-11}$$

In this particular titration, the equivalence-point voltage is independent of the concentrations and volumes of the reactants.

Region 3: After the Equivalence Point

Now virtually all iron atoms are Fe^{3+}. The moles of Ce^{3+} equal the moles of Fe^{3+}, and there is a known excess of unreacted Ce^{4+}. Because we know both $[Ce^{3+}]$ and $[Ce^{4+}]$, it is *convenient* to use Reaction 15-3 to describe the chemistry at the Pt electrode:

$$E = E_+ - E(\text{calomel}) = \left[1.70 - 0.059\,16 \log\left(\frac{[Ce^{3+}]}{[Ce^{4+}]}\right)\right] - 0.241 \tag{15-12}$$

After the equivalence point, we use Reaction 15-3 because we can easily calculate $[Ce^{3+}]$ and $[Ce^{4+}]$. It is not convenient to use Reaction 15-2, because we do not know the concentration of Fe^{2+}, which has been "used up."

At the special point when $V = 2V_e$, $[Ce^{3+}] = [Ce^{4+}]$ and $E_+ = E°(Ce^{4+} \mid Ce^{3+}) = 1.70$ V.

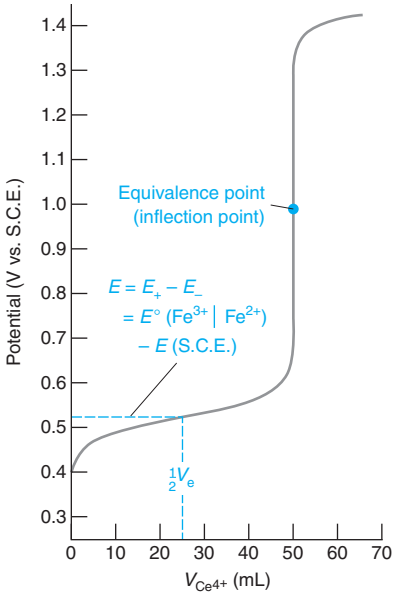


FIGURE 15-2 Theoretical curve for titration of 100.0 mL of 0.050 0 M Fe^{2+} with 0.100 M Ce^{4+} in 1 M $HClO_4$. You cannot calculate the potential for zero titrant, but you can start at a small volume such as $V_{Ce^{4+}} = 0.1$ mL.

Anyone with a serious need to calculate redox titration curves should use a spreadsheet with a more general set of equations than we use in this section.[7] The supplement at www.whfreeman.com/qca explains how to use spreadsheets to compute redox titration curves.

The curve in Figure 15-2 is essentially independent of the concentrations of analyte and titrant. The curve is symmetric near V_e because the stoichiometry is 1:1.

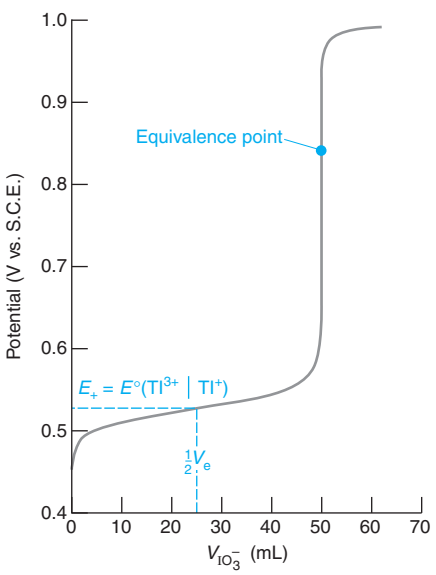


FIGURE 15-3 Theoretical curve for titration of 100.0 mL of 0.010 0 M Tl^+ with 0.010 0 M IO_3^- in 1.00 M HCl. The equivalence point at 0.842 V is not at the center of the steep part of the curve because the stoichiometry of the reaction is not 1:1.

Before V_e, the indicator electrode potential is fairly steady near $E^\circ(Fe^{3+} | Fe^{2+}) = 0.77$ V.[6] After V_e, the indicator electrode potential levels off near $E^\circ(Ce^{4+} | Ce^{3+}) = 1.70$ V. At V_e, there is a rapid rise in voltage.

EXAMPLE **Potentiometric Redox Titration**

Suppose that we titrate 100.0 mL of 0.050 0 M Fe^{2+} with 0.100 M Ce^{4+}, using the cell in Figure 15-1. The equivalence point occurs when $V_{Ce^{4+}} = 50.0$ mL. Calculate the cell voltage at 36.0, 50.0, and 63.0 mL.

Solution *At 36.0 mL:* This is 36.0/50.0 of the way to the equivalence point. Therefore, 36.0/50.0 of the iron is in the form Fe^{3+} and 14.0/50.0 is in the form Fe^{2+}. Putting $[Fe^{2+}]/[Fe^{3+}] = 14.0/36.0$ into Equation 15-6 gives $E = 0.550$ V.

At 50.0 mL: Equation 15-11 tells us that the cell voltage at the equivalence point is 0.99 V, regardless of the concentrations of reagents for this particular titration.

At 63.0 mL: The first 50.0 mL of cerium were converted into Ce^{3+}. There is an excess of 13.0 mL of Ce^{4+}, so $[Ce^{3+}]/[Ce^{4+}] = 50.0/13.0$ in Equation 15-12, and $E = 1.424$ V.

Test Yourself Find E at $V_{Ce^{4+}} = 20.0$ and 51.0 mL (***Answer:*** 0.516, 1.358 V)

Shapes of Redox Titration Curves

The calculations above allow us to plot the titration curve in Figure 15-2, which shows potential as a function of the volume of added titrant. The equivalence point is marked by a steep rise in voltage. The value of E_+ at $\frac{1}{2}V_e$ is the formal potential of the $Fe^{3+} | Fe^{2+}$ couple, because the quotient $[Fe^{2+}]/[Fe^{3+}]$ is unity at this point. The voltage at any point in this titration depends only on the *ratio* of reactants; their *concentrations* do not figure in any calculations in this example. We expect, therefore, that the curve in Figure 15-2 will be independent of dilution. We should observe the same curve if both reactants were diluted by a factor of 10.

For Reaction 15-1, the titration curve in Figure 15-2 is symmetric near the equivalence point because the reaction stoichiometry is 1:1. Figure 15-3 shows the curve calculated for the titration of Tl^+ by IO_3^- in 1.00 M HCl.

$$IO_3^- + 2Tl^+ + 2Cl^- + 6H^+ \rightarrow ICl_2^- + 2Tl^{3+} + 3H_2O \qquad \textbf{(15-13)}$$

The curve is *not symmetric about the equivalence point* because the stoichiometry of reactants is 2:1, not 1:1. Still, the curve is so steep near the equivalence point that negligible error is introduced if the center of the steep part is taken as the end point. Demonstration 15-1 provides an example of an asymmetric titration curve whose shape also depends on the pH of the reaction medium.

The voltage change near the equivalence point increases as the difference between E° of the two redox couples in the titration increases. The larger the difference in E°, the greater the equilibrium constant for the titration reaction. For Figure 15-2, half-reactions 15-2 and 15-3 differ by 0.93 V, and there is a large break at the equivalence point in the titration curve. For Figure 15-3, the half-reactions differ by 0.47 V, so there is a smaller break at the equivalence point.

$$IO_3^- + 2Cl^- + 6H^+ + 4e^- \rightleftharpoons ICl_2^- + 3H_2O \qquad E^\circ = 1.24 \text{ V}$$

$$Tl^{3+} + 2e^- \rightleftharpoons Tl^+ \qquad E^\circ = 0.77 \text{ V}$$

Clearest results are achieved with the strongest oxidizing and reducing agents. The same rule applies to acid-base titrations, where strong-acid or strong-base titrants give the sharpest break at the equivalence point.

15-2 Finding the End Point

As in acid-base titrations, indicators and electrodes are commonly used to find the end point of a redox titration.

DEMONSTRATION 15-1 Potentiometric Titration of Fe^{2+} With MnO_4^-

This reaction illustrates many principles of potentiometric titrations:

$$\underset{\text{Titrant}}{MnO_4^-} + \underset{\text{Analyte}}{5Fe^{2+}} + 8H^+ \rightarrow Mn^{2+} + 5Fe^{3+} + 4H_2O \qquad \textbf{(A)}$$

Dissolve 0.60 g of $Fe(NH_4)_2(SO_4)_2 \cdot 6H_2O$ (FM 392.13; 1.5 mmol) in 400 mL of 1 M H_2SO_4. Titrate the well-stirred solution with 0.02 M $KMnO_4$ ($V_e \approx 15$ mL), using Pt and calomel electrodes with a pH meter as a potentiometer. Before use, zero the meter by connecting the two inputs directly to each other and setting the millivolt scale to 0.

Calculate some points on the theoretical titration curve before performing the experiment. Then compare the theoretical and experimental results. Also note the coincidence of the potentiometric and visual end points.

Question Potassium permanganate is purple, and all the other species in this titration are colorless (or very faintly colored). What color change is expected at the equivalence point?

To calculate the theoretical curve, we use the following half-reactions:

$$Fe^{3+} + e^- \rightleftharpoons Fe^{2+} \qquad E^\circ = 0.68 \text{ V in 1 M } H_2SO_4 \qquad \textbf{(B)}$$

$$MnO_4^- + 8H^+ + 5e^- \rightarrow Mn^{2+} + 4H_2O \qquad E^\circ = 1.507 \text{ V} \qquad \textbf{(C)}$$

Prior to V_e, calculations are similar to those in Section 15-1 for the titration of Fe^{2+} by Ce^{4+}, but with $E^\circ = 0.68$ V. After V_e, you can find the potential by using Reaction C. For example, suppose that you titrate 0.400 L of 3.75 mM Fe^{2+} with 0.020 0 M $KMnO_4$. From the stoichiometry of Reaction A, $V_e = 15.0$ mL. When you have added 17.0 mL of $KMnO_4$, the concentrations of species in Reaction C are $[Mn^{2+}] = 0.719$ mM, $[MnO_4^-] = 0.095\,9$ mM, and $[H^+] = 0.959$ M (neglecting the small quantity of H^+ consumed in the titration). The voltage should be

$$E = E_+ - E(\text{calomel})$$

$$= \left[1.507 - \frac{0.059\,16}{5}\log\left(\frac{[Mn^{2+}]}{[MnO_4^-][H^+]^8}\right)\right] - 0.241$$

$$= \left[1.507 - \frac{0.059\,16}{5}\log\left(\frac{7.19 \times 10^{-4}}{(9.59 \times 10^{-5})(0.959)^8}\right)\right] - 0.241$$

$$= 1.254 \text{ V}$$

To calculate the voltage at V_e, we add the Nernst equations for Reactions B and C, as we did for the cerium and iron reactions in Section 15-1. Before doing so, however, multiply the permanganate equation by 5 so that we can add the log terms:

$$E_+ = 0.68 - 0.059\,16 \log\left(\frac{[Fe^{2+}]}{[Fe^{3+}]}\right)$$

$$5E_+ = 5\left[1.507 - \frac{0.059\,16}{5}\log\left(\frac{[Mn^{2+}]}{[MnO_4^-][H^+]^8}\right)\right]$$

Now add the two equations to get

$$6E_+ = 8.215 - 0.059\,16 \log\left(\frac{[Mn^{2+}][Fe^{2+}]}{[MnO_4^-][Fe^{3+}][H^+]^8}\right) \qquad \textbf{(D)}$$

The stoichiometry of the titration reaction A tells us that, at V_e, $[Fe^{3+}] = 5[Mn^{2+}]$ and $[Fe^{2+}] = 5[MnO_4^-]$. Substituting these values into Equation D gives

$$6E_+ = 8.215 - 0.059\,16 \log\left(\frac{\cancel{[Mn^{2+}]}(\cancel{5}\cancel{[MnO_4^-]})}{\cancel{[MnO_4^-]}(\cancel{5}\cancel{[Mn^{2+}]})[H^+]^8}\right)$$

$$= 8.215 - 0.059\,16 \log\left(\frac{1}{[H^+]^8}\right) \qquad \textbf{(E)}$$

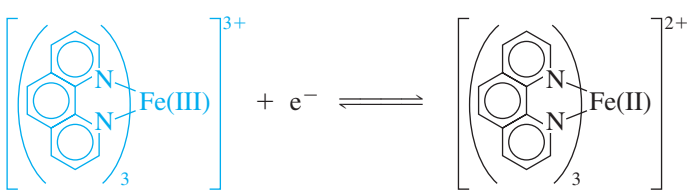
Inserting the concentration of $[H^+]$, which is (400/415)(1.00 M) = 0.964 M, we find

$$6E_+ = 8.215 - 0.059\,16 \log\left(\frac{1}{(0.964)^8}\right) \quad \Rightarrow \quad E_+ = 1.368 \text{ V}$$

The predicted cell voltage at V_e is $E = E_+ - E(\text{calomel}) = 1.368 - 0.241 = 1.127$ V.

Redox Indicators

A **redox indicator** is a compound that changes color when it goes from its oxidized to its reduced state. The indicator ferroin changes from pale blue (almost colorless) to red.



Oxidized ferroin (pale blue) In(oxidized) — Reduced ferroin (red) In(reduced)

To predict the potential range over which the indicator color will change, we first write a Nernst equation for the indicator.

$$\text{In(oxidized)} + ne^- \rightleftharpoons \text{In(reduced)}$$

$$E = E^\circ - \frac{0.059\,16}{n}\log\left(\frac{[\text{In(reduced)}]}{[\text{In(oxidized)}]}\right) \qquad \textbf{(15-14)}$$

As with acid-base indicators, the color of In(reduced) will be observed when

$$\frac{[\text{In(reduced)}]}{[\text{In(oxidized)}]} \gtrsim \frac{10}{1}$$

and the color of In(oxidized) will be observed when

$$\frac{[\text{In(reduced)}]}{[\text{In(oxidized)}]} \lesssim \frac{1}{10}$$

Putting these quotients into Equation 15-14 tells us that the color change will occur over the range

A redox indicator changes color over a range of $\pm(59/n)$ mV, centered at $E°$ for the indicator. n is the number of electrons in the indicator half-reaction.

$$E = \left(E° \pm \frac{0.059\ 16}{n}\right) \text{volts}$$

For ferroin, with $E° = 1.147$ V (Table 15-2), we expect the color change to occur in the approximate range 1.088 V to 1.206 V with respect to the standard hydrogen electrode. With a saturated calomel reference electrode, the indicator transition range will be

Figure 14-6 should help you understand Equation 15-15.

The indicator transition range should overlap the steep part of the titration curve.

$$\begin{pmatrix}\text{Indicator transition}\\ \text{range versus calomel}\\ \text{electrode (S.C.E.)}\end{pmatrix} = \begin{pmatrix}\text{Transition range}\\ \text{versus standard hydrogen}\\ \text{electrode (S.H.E.)}\end{pmatrix} - E(\text{calomel}) \qquad \textbf{(15-15)}$$

$$= (1.088 \text{ to } 1.206) - (0.241)$$

$$= 0.847 \text{ to } 0.965 \text{ V (versus S.C.E.)}$$

Ferroin would therefore be a useful indicator for the titrations in Figures 15-2 and 15-3.

The larger the difference in standard potential between titrant and analyte, the greater the break in the titration curve at the equivalence point. A redox titration is usually feasible if the difference between analyte and titrant is $\gtrsim 0.2$ V. However, the end point of such a titration is not very sharp and is best detected potentiometrically. If the difference in formal potentials is $\gtrsim 0.4$ V, then a redox indicator usually gives a satisfactory end point.

Gran Plot

With the apparatus in Figure 15-1, we measure electrode potential, E, versus volume of titrant, V, during a redox titration. The end point is the maximum of the first derivative, $\Delta E/\Delta V$, or the zero crossing of the second derivative, $\Delta(\Delta E/\Delta V)/\Delta V$ (Figure 10-5).

A more accurate way to use potentiometric data is to prepare a Gran plot[8,9] as we did for acid-base titrations in Section 10-5. The Gran plot uses data from well before the equivalence point (V_e) to locate V_e. Potentiometric data taken close to V_e are the least accurate because electrodes are slow to equilibrate with species in solution when one member of a redox couple is nearly used up.

TABLE 15-2 Redox indicators

Indicator	Color: Oxidized	Color: Reduced	$E°$
Phenosafranine	Red	Colorless	0.28
Indigo tetrasulfonate	Blue	Colorless	0.36
Methylene blue	Blue	Colorless	0.53
Diphenylamine	Violet	Colorless	0.75
4′-Ethoxy-2,4-diaminoazobenzene	Yellow	Red	0.76
Diphenylamine sulfonic acid	Red-violet	Colorless	0.85
Diphenylbenzidine sulfonic acid	Violet	Colorless	0.87
Tris(2,2′-bipyridine)iron	Pale blue	Red	1.120
Tris(1,10-phenanthroline)iron (ferroin)	Pale blue	Red	1.147
Tris(5-nitro-1,10-phenanthroline)iron	Pale blue	Red-violet	1.25
Tris(2,2′-bipyridine)ruthenium	Pale blue	Yellow	1.29

For the oxidation of Fe^{2+} to Fe^{3+}, the potential prior to V_e is

$$E = \left[E^{\circ\prime} - 0.059\,16 \log\left(\frac{[Fe^{2+}]}{[Fe^{3+}]}\right)\right] - E_{ref} \qquad \textbf{(15-16)}$$

where $E^{\circ\prime}$ is the formal potential for $Fe^{3+} \mid Fe^{2+}$ and E_{ref} is the potential of the reference electrode (which we have also been calling E_{-}). If the volume of titrant is V and if the reaction goes "to completion" with each addition of titrant, then $[Fe^{2+}]/[Fe^{3+}] = (V_e - V)/V$. Substituting this expression into Equation 15-16 and rearranging, we eventually stumble onto a linear equation:

$$\underbrace{V \cdot 10^{-nE/0.059\,16}}_{y} = \underbrace{V_e \cdot 10^{-n(E_{ref} - E^{\circ\prime})/0.059\,16}}_{b} - \underset{\uparrow\, x}{V} \cdot \underbrace{10^{-n(E_{ref} - E^{\circ\prime})/0.059\,16}}_{m} \qquad \textbf{(15-17)}$$

where n is the number of electrons in the half-reaction at the indicator electrode.

A graph of $V \cdot 10^{-nE/0.059\,16}$ versus V should be a straight line with x-intercept $= V_e$ (Figure 15-4). If the ionic strength of the reaction is constant, the activity coefficients are constant, and Equation 15-17 gives a straight line over a wide volume range. If ionic strength varies as titrant is added, we just use the last 10–20% of the data prior to V_e.

The constant 0.059 16 V is $(RT \ln 10)/nF$, where R is the gas constant, T is 298.15 K, F is the Faraday constant, and n is the number of electrons in the $Fe^{3+} \mid Fe^{2+}$ redox half-reaction ($n = 1$). For $T \neq 298.15$ K or $n \neq 1$, the number 0.059 16 will change.

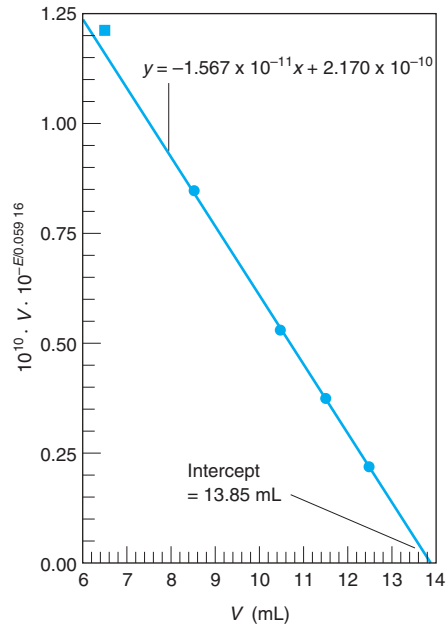


FIGURE 15-4 Gran plot for titration of Fe^{2+} by Ce^{4+} in Exercise 15-D.[8] The line was fit to the four points shown by circles. In the function on the ordinate, the value of n is 1. Numerical values were multiplied by 10^{10} for ease of display. Multiplication does not change the x-intercept.

The Starch-Iodine Complex

Numerous analytical procedures are based on redox titrations involving iodine. Starch[10] is the indicator of choice for these procedures because it forms an intense blue complex with iodine. Starch is not a redox indicator; it responds specifically to the presence of I_2, not to a change in redox potential.

The active fraction of starch is amylose, a polymer of the sugar α-D-glucose, with the repeating unit shown in Figure 15-5. Small molecules can fit into the center of the coiled, helical polymer. In the presence of starch, iodine forms I_6 chains inside the amylose helix and the color turns dark blue.

I··I··I··I··I··I

Starch is readily biodegraded, so it should be freshly dissolved or the solution should contain a preservative, such as HgI_2 (~1 mg/100 mL) or thymol. A hydrolysis product of starch is glucose, which is a reducing agent. Therefore, partially hydrolyzed starch solution can be a source of error in a redox titration.

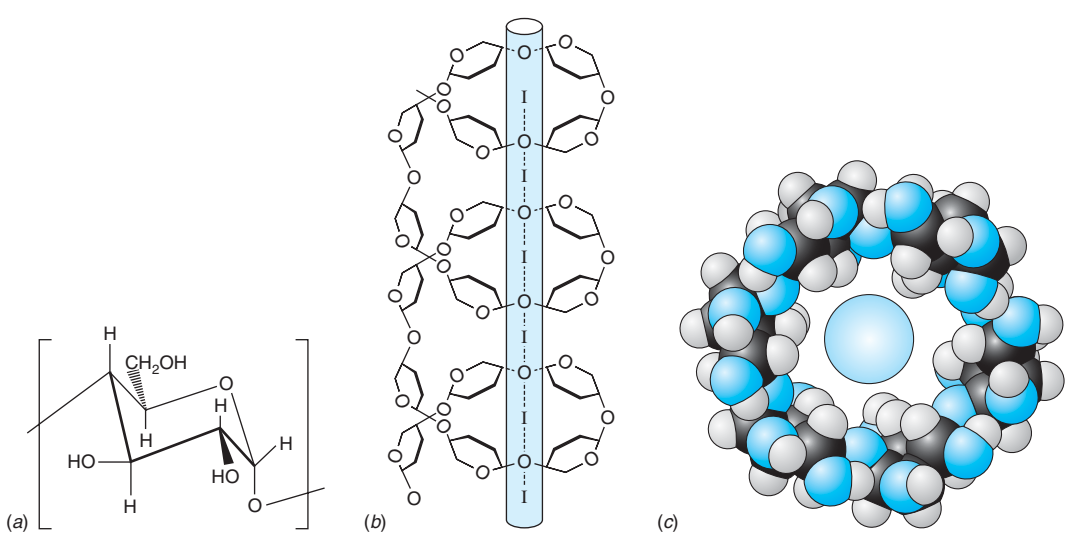


FIGURE 15-5 (*a*) Structure of the repeating unit of amylose. (*b*) Schematic structure of the starch-iodine complex. The amylose chain forms a helix around I_6 units. [Adapted from A. T. Calabrese and A. Khan, "Amylose-Iodine Complex Formation with KI: Evidence for Absence of Iodide Ions within the Complex," *J. Polymer Sci.* 1999, *A37,* 2711.] (*c*) View down the starch helix, showing iodine inside the helix.[10] [Figure kindly provided by R. D. Hancock, Power Engineering, Salt Lake City.]

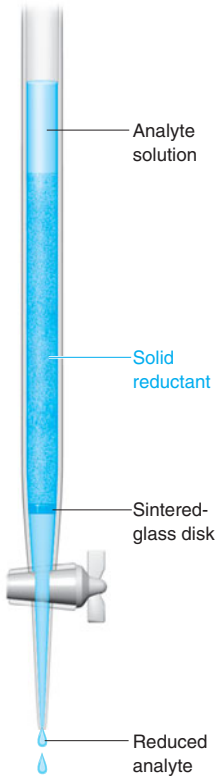


FIGURE 15-6 A column filled with a solid reagent used for prereduction of analyte is called a *reductor*.

In *disproportionation*, a reactant is converted into products in higher and lower oxidation states. The compound oxidizes and reduces *itself*.

Challenge Write a half-reaction in which H_2O_2 behaves as an oxidant and a half-reaction in which it behaves as a reductant.

15-3 Adjustment of Analyte Oxidation State

Sometimes we need to adjust the oxidation state of analyte before it can be titrated. For example, Mn^{2+} can be **preoxidized** to MnO_4^- and then titrated with standard Fe^{2+}. Preadjustment must be quantitative, and you must eliminate excess preadjustment reagent so that it will not interfere in the subsequent titration.

Preoxidation

Several powerful oxidants can be easily removed after preoxidation. *Peroxydisulfate* ($S_2O_8^{2-}$, also called *persulfate*) is a strong oxidant that requires Ag^+ as a catalyst.

$$S_2O_8^{2-} + Ag^+ \rightarrow SO_4^{2-} + \underbrace{SO_4^- + Ag^{2+}}_{\text{Two powerful oxidants}}$$

Excess reagent is destroyed by boiling the solution after oxidation of analyte is complete.

$$2S_2O_8^{2-} + 2H_2O \xrightarrow{\text{boiling}} 4SO_4^{2-} + O_2 + 4H^+$$

The $S_2O_8^{2-}$ and Ag^+ mixture oxidizes Mn^{2+} to MnO_4^-, Ce^{3+} to Ce^{4+}, Cr^{3+} to $Cr_2O_7^{2-}$, and VO^{2+} to VO_2^+.

Silver(II) oxide (AgO) dissolves in concentrated mineral acids to give Ag^{2+}, with oxidizing power similar to $S_2O_8^{2-}$ plus Ag^+. Excess Ag^{2+} can be removed by boiling:

$$4Ag^{2+} + 2H_2O \xrightarrow{\text{boiling}} 4Ag^+ + O_2 + 4H^+$$

Solid *sodium bismuthate* ($NaBiO_3$) has an oxidizing strength similar to that of Ag^{2+} and $S_2O_8^{2-}$. Excess solid oxidant is removed by filtration.

Hydrogen peroxide is a good oxidant in basic solution. It can transform Co^{2+} into Co^{3+}, Fe^{2+} into Fe^{3+}, and Mn^{2+} into MnO_2. In acidic solution, it can *reduce* $Cr_2O_7^{2-}$ to Cr^{3+} and MnO_4^- to Mn^{2+}. Excess H_2O_2 spontaneously **disproportionates** in boiling water.

$$2H_2O_2 \xrightarrow{\text{boiling}} O_2 + 2H_2O$$

Prereduction

Stannous chloride ($SnCl_2$) will reduce Fe^{3+} to Fe^{2+} in hot HCl. Excess reductant is destroyed by adding excess $HgCl_2$:

$$Sn^{2+} + 2HgCl_2 \rightarrow Sn^{4+} + Hg_2Cl_2 + 2Cl^-$$

The Fe^{2+} is then titrated with an oxidant.

Chromous chloride is a powerful reductant sometimes used to **prereduce** analyte to a lower oxidation state. Excess Cr^{2+} is oxidized by atmospheric O_2. *Sulfur dioxide* and *hydrogen sulfide* are mild reducing agents that can be expelled by boiling an acidic solution after the reduction is complete.

An important prereduction technique uses a column packed with a solid reducing agent. Figure 15-6 shows the *Jones reductor*, which contains zinc coated with zinc *amalgam*. An **amalgam** is a solution of anything in mercury. The amalgam is prepared by mixing granular zinc with 2 wt% aqueous $HgCl_2$ for 10 min and then washing with water. You can reduce Fe^{3+} to Fe^{2+} by passage through a Jones reductor, using 1 M H_2SO_4 as solvent. Wash the column well with water and titrate the combined washings with standard MnO_4^-, Ce^{4+}, or $Cr_2O_7^{2-}$. Pass a solution containing only the matrix through the reductor in the same manner as the unknown for a blank determination.

Most reduced analytes are reoxidized by atmospheric oxygen. To prevent oxidation, the reduced analyte can be collected in an acidic solution of Fe^{3+}. Ferric ion is reduced to Fe^{2+}, which is stable in acid. The Fe^{2+} is then titrated with an oxidant. By this means, elements such as Cr, Ti, V, and Mo can be indirectly analyzed.

Zinc is a powerful reducing agent, with $E^\circ = -0.764$ for the reaction $Zn^{2+} + 2e^- \rightleftharpoons Zn(s)$, so the Jones reductor is not very selective. The *Walden reductor*, filled with solid Ag and 1 M HCl, is more selective. The reduction potential for Ag | AgCl (0.222 V) is high enough that species such as Cr^{3+} and TiO^{2+} are not reduced and therefore do not interfere in the analysis of a metal such as Fe^{3+}. Another selective reductor uses granular Cd

metal. To determine levels of nitrogen oxides for air-pollution monitoring,[11] the gases are first converted into NO_3^-, which is not easy to analyze. Passing nitrate through a Cd-filled column reduces NO_3^- to NO_2^-, for which a convenient spectrophotometric analysis is available.

15-4 Oxidation with Potassium Permanganate

Potassium permanganate ($KMnO_4$) is a strong oxidant with an intense violet color. In strongly acidic solutions (pH $\lesssim 1$), it is reduced to colorless Mn^{2+}.

$$\underset{\text{Permanganate}}{MnO_4^-} + 8H^+ + 5e^- \rightleftharpoons \underset{\text{Manganous}}{Mn^{2+}} + 4H_2O \qquad E^\circ = 1.507\ \text{V}$$

In neutral or alkaline solution, the product is the brown solid, MnO_2.

$$MnO_4^- + 4H^+ + 3e^- \rightleftharpoons \underset{\text{Manganese dioxide}}{MnO_2(s)} + 2H_2O \qquad E^\circ = 1.692\ \text{V}$$

In strongly alkaline solution (2 M NaOH), green manganate ion is produced.

$$MnO_4^- + e^- \rightleftharpoons \underset{\text{Manganate}}{MnO_4^{2-}} \qquad E^\circ = 0.56\ \text{V}$$

Representative permanganate titrations are listed in Table 15-3. For titrations in strongly acidic solution, $KMnO_4$ serves as its own indicator because the product, Mn^{2+},

$KMnO_4$ serves as its own indicator in acidic solution.

TABLE 15-3 Analytical applications of permanganate titrations

Species analyzed	Oxidation reaction	Notes
Fe^{2+}	$Fe^{2+} \rightleftharpoons Fe^{3+} + e^-$	Fe^{3+} is reduced to Fe^{2+} with Sn^{2+} or a Jones reductor. Titration is carried out in 1 M H_2SO_4 or 1 M HCl containing Mn^{2+}, H_3PO_4, and H_2SO_4. Mn^{2+} inhibits oxidation of Cl^- by MnO_4. H_3PO_4 complexes Fe^{3+} to prevent formation of yellow Fe^{3+}-chloride complexes.
$H_2C_2O_4$	$H_2C_2O_4 \rightleftharpoons 2CO_2 + 2H^+ + 2e^-$	Add 95% of titrant at 25°C, then complete titration at 55°–60°C.
Br^-	$Br^- \rightleftharpoons \frac{1}{2}Br_2(g) + e^-$	Titrate in boiling 2 M H_2SO_4 to remove $Br_2(g)$.
H_2O_2	$H_2O_2 \rightleftharpoons O_2(g) + 2H^+ + 2e^-$	Titrate in 1 M H_2SO_4.
HNO_2	$HNO_2 + H_2O \rightleftharpoons NO_3^- + 3H^+ + 2e^-$	Add excess standard $KMnO_4$ and back-titrate after 15 min at 40°C with Fe^{2+}.
As^{3+}	$H_3AsO_3 + H_2O \rightleftharpoons H_3AsO_4 + 2H^+ + 2e^-$	Titrate in 1 M HCl with KI or ICl catalyst.
Sb^{3+}	$H_3SbO_3 + H_2O \rightleftharpoons H_3SbO_4 + 2H^+ + 2e^-$	Titrate in 2 M HCl.
Mo^{3+}	$Mo^{3+} + 2H_2O \rightleftharpoons MoO_2^{2+} + 4H^+ + 3e^-$	Reduce Mo in a Jones reductor, and run the Mo^{3+} into excess Fe^{3+} in 1 M H_2SO_4. Titrate the Fe^{2+} formed.
W^{3+}	$W^{3+} + 2H_2O \rightleftharpoons WO_2^{2+} + 4H^+ + 3e^-$	Reduce W with Pb(Hg) at 50°C and titrate in 1 M HCl.
U^{4+}	$U^{4+} + 2H_2O \rightleftharpoons UO_2^{2+} + 4H^+ + 2e^-$	Reduce U to U^{3+} with a Jones reductor. Expose to air to produce U^{4+}, which is titrated in 1 M H_2SO_4.
Ti^{3+}	$Ti^{3+} + H_2O \rightleftharpoons TiO^{2+} + 2H^+ + e^-$	Reduce Ti to Ti^{3+} with a Jones reductor, and run the Ti^{3+}into excess Fe^{3+} in 1 M H_2SO_4. Titrate the Fe^{2+} that is formed.
Mg^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+}, Zn^{2+}, Co^{2+}, La^{3+}, Th^{4+}, Pb^{2+}, Ce^{3+}, BiO^+, Ag^+	$H_2C_2O_4 \rightleftharpoons 2CO_2 + 2H^+ + 2e^-$	Precipitate the metal oxalate. Dissolve in acid and titrate the $H_2C_2O_4$.
$S_2O_8^{2-}$	$S_2O_8^{2-} + 2Fe^{2+} + 2H^+ \rightleftharpoons 2Fe^{3+} + 2HSO_4^-$	Peroxydisulfate is added to excess standard Fe^{2+} containing H_3PO_4. Unreacted Fe^{2+} is titrated with MnO_4^-.
PO_4^{3-}	$Mo^{3+} + 2H_2O \rightleftharpoons MoO_2^{2+} + 4H^+ + 3e^-$	$(NH_4)_3PO_4 \cdot 12MoO_3$ is precipitated and dissolved in H_2SO_4. The Mo(VI) is reduced (as above) and titrated.

is colorless (Color Plate 7). The end point is taken as the first persistent appearance of pale pink MnO_4^-. If the titrant is too dilute to be seen, an indicator such as ferroin can be used.

Preparation and Standardization

$KMnO_4$ is not a primary standard.

Potassium permanganate is not a primary standard because traces of MnO_2 are invariably present. In addition, distilled water usually contains enough organic impurities to reduce some freshly dissolved MnO_4^- to MnO_2. To prepare a 0.02 M stock solution, dissolve $KMnO_4$ in distilled water, boil it for an hour to hasten the reaction between MnO_4^- and organic impurities, and filter the resulting mixture through a clean, sintered-glass filter to remove precipitated MnO_2. Do not use filter paper (organic matter!) for the filtration. Store the reagent in a dark glass bottle. Aqueous $KMnO_4$ is unstable by virtue of the reaction

$$4MnO_4^- + 2H_2O \rightarrow 4MnO_2(s) + 3O_2 + 4OH^-$$

which is slow in the absence of MnO_2, Mn^{2+}, heat, light, acids, and bases. Permanganate should be standardized often for the most accurate work. Prepare and standardize fresh dilute solutions from 0.02 M stock solution, using water distilled from alkaline $KMnO_4$.

Potassium permanganate can be standardized by titration of sodium oxalate ($Na_2C_2O_4$) by Reaction 1-7 or pure electrolytic iron wire. Dissolve dry (105°C, 2 h) sodium oxalate (available as a 99.9–99.95% pure primary standard) in 1 M H_2SO_4 and treat it with 90–95% of the required $KMnO_4$ solution at room temperature. Then warm the solution to 55–60°C and complete the titration by slow addition of $KMnO_4$. Subtract a blank value to account for the quantity of titrant (usually one drop) needed to impart a pink color to the solution.

If pure Fe wire is used as a standard, dissolve it in warm 1.5 M H_2SO_4 under N_2. The product is Fe^{2+}, and the cooled solution can be used to standardize $KMnO_4$ (or other oxidants) with no special precautions. Adding 5 mL of 86 wt% H_3PO_4 per 100 mL of solution masks the yellow color of Fe^{3+} and makes the end point easier to see. Ferrous ammonium sulfate, $Fe(NH_4)_2(SO_4)_2 \cdot 6H_2O$, and ferrous ethylenediammonium sulfate, $Fe(H_3NCH_2CH_2NH_3)(SO_4)_2 \cdot 2H_2O$, are sufficiently pure to be standards for most purposes.

15-5 Oxidation with Ce^{4+}

Reduction of Ce^{4+} to Ce^{3+} proceeds cleanly in acidic solutions. The aquo ion, $Ce(H_2O)_n^{4+}$, probably does not exist in any of these solutions, because Ce(IV) binds anions (ClO_4^-, SO_4^{2-}, NO_3^-, Cl^-). Variation of the $Ce^{4+} \mid Ce^{3+}$ formal potential with the medium is indicative of these interactions:

Different formal potentials imply that different cerium species are present in each solution.

$$Ce^{4+} + e^- \rightleftharpoons Ce^{3+} \qquad \text{Formal potential} \begin{cases} 1.70 \text{ V in 1 F } HClO_4 \\ 1.61 \text{ V in 1 F } HNO_3 \\ 1.47 \text{ V in 1 F } HCl \\ 1.44 \text{ V in 1 F } H_2SO_4 \end{cases}$$

Ce^{4+} is yellow and Ce^{3+} is colorless, but the color change is not distinct enough for cerium to be its own indicator. Ferroin and other substituted phenanthroline redox indicators (Table 15-2) are well suited to titrations with Ce^{4+}.

Ce^{4+} can be used in place of $KMnO_4$ in most procedures. In the oscillating reaction in Demonstration 14-1, Ce^{4+} oxidizes malonic acid to CO_2 and formic acid:

$$\underset{\text{Malonic acid}}{CH_2(CO_2H)_2} + 2H_2O + 6Ce^{4+} \rightarrow 2CO_2 + \underset{\text{Formic acid}}{HCO_2H} + 6Ce^{3+} + 6H^+$$

This reaction can be used for quantitative analysis of malonic acid by heating a sample in 4 M $HClO_4$ with excess standard Ce^{4+} and back-titrating unreacted Ce^{4+} with Fe^{2+}. Analogous procedures are available for many alcohols, aldehydes, ketones, and carboxylic acids.

Preparation and Standardization

Primary-standard-grade ammonium hexanitratocerate(IV), $(NH_4)_2Ce(NO_3)_6$, can be dissolved in 1 M H_2SO_4 and used directly. Although the oxidizing strength of Ce^{4+} is greater in $HClO_4$ or HNO_3, these solutions undergo slow photochemical decomposition with concomitant oxidation of water. Ce^{4+} in H_2SO_4 is stable indefinitely, despite the fact that the reduction potential of 1.44 V is great enough to oxidize H_2O to O_2. Reaction with water is slow, even though it is thermodynamically favorable. Solutions in HCl are unstable because Cl^- is oxidized to Cl_2—rapidly, when the solution is hot. Sulfuric acid solutions of Ce^{4+} can be used for titrations of unknowns in HCl because the reaction with analyte is fast, whereas reaction with Cl^- is slow. Less expensive salts, including $Ce(HSO_4)_4$, $(NH_4)_4Ce(SO_4)_4 \cdot 2H_2O$, and $CeO_2 \cdot xH_2O$ (also called $Ce(OH)_4$), are adequate for preparing titrants that are subsequently standardized with $Na_2C_2O_4$ or Fe as described for MnO_4^-.

15-6 Oxidation with Potassium Dichromate

In acidic solution, orange dichromate ion is a powerful oxidant that is reduced to chromic ion:

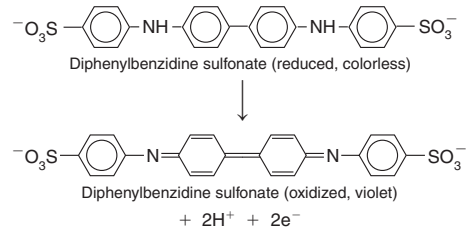
Cr(VI) waste is carcinogenic and should not be poured down the drain. See page 31 for disposal method.

$$\underset{\text{Dichromate}}{Cr_2O_7^{2-}} + 14H^+ + 6e^- \rightleftharpoons \underset{\text{Chromic}}{2Cr^{3+}} + 7H_2O \qquad E^\circ = 1.36\ V$$

In 1 M HCl, the formal potential is just 1.00 V and, in 2 M H_2SO_4, it is 1.11 V; so dichromate is a less powerful oxidizing agent than MnO_4^- or Ce^{4+}. In basic solution, $Cr_2O_7^{2-}$ is converted into yellow chromate ion (CrO_4^{2-}), whose oxidizing power is nil:

$$CrO_4^{2-} + 4H_2O + 3e^- \rightleftharpoons Cr(OH)_3(s, \text{hydrated}) + 5OH^- \qquad E^\circ = -0.12\ V$$

Potassium dichromate, $K_2Cr_2O_7$, is a primary standard. Its solutions are stable, and it is cheap. Dichromate is orange and Cr^{3+} complexes range from green to violet, so indicators with distinctive color changes, such as diphenylamine sulfonic acid or diphenylbenzidine sulfonic acid, are used to find a dichromate end point. Alternatively, reactions can be monitored with Pt and calomel electrodes.



$K_2Cr_2O_7$ is not as strong an oxidant as $KMnO_4$ or Ce^{4+}. It is employed chiefly for the determination of Fe^{2+} and, indirectly, for species that will oxidize Fe^{2+} to Fe^{3+}. For indirect analyses, the unknown is treated with a measured excess of Fe^{2+}. Then unreacted Fe^{2+} is titrated with $K_2Cr_2O_7$. For example, ClO_3^-, NO_3^-, MnO_4^-, and organic peroxides can be analyzed this way. Box 15-2 describes the use of dichromate in water pollution analysis.

15-7 Methods Involving Iodine

When a reducing analyte is titrated with iodine (to produce I^-), the method is called *iodimetry*. In *iodometry*, an oxidizing analyte is added to excess I^- to produce iodine, which is then titrated with standard thiosulfate solution.

Iodimetry: titration *with* iodine

Iodometry: titration *of* iodine produced by a chemical reaction

Molecular iodine is only slightly soluble in water (1.3×10^{-3} M at 20°C), but its solubility is enhanced by complexation with iodide.

$$\underset{\text{Iodine}}{I_2(aq)} + \underset{\text{Iodide}}{I^-} \rightleftharpoons \underset{\text{Triiodide}}{I_3^-} \qquad K = 7 \times 10^2$$

A solution made from 1.5 mM I_2 + 1.5 mM KI in water contains[20]

0.9 mM I_2	5 μM I_5^-
0.9 mM I^-	40 nM I_6^{2-}
0.6 mM I_3^-	0.3 μM HOI

A typical 0.05 M solution of I_3^- for titrations is prepared by dissolving 0.12 mol of KI plus 0.05 mol of I_2 in 1 L of water. When we speak of using iodine as a titrant, we almost always mean that we are using a solution of I_2 plus excess I^-.

Use of Starch Indicator

As described in Section 15-2, starch is used as an indicator for iodine. In a solution with no other colored species, it is possible to see the color of ~5 μM I_3^-. With starch, the limit of detection is extended by about a factor of 10.

In iodimetry (titration *with* I_3^-), starch can be added at the beginning of the titration. The first drop of excess I_3^- after the equivalence point causes the solution to turn dark blue.

BOX 15-2 Environmental Carbon Analysis and Oxygen Demand

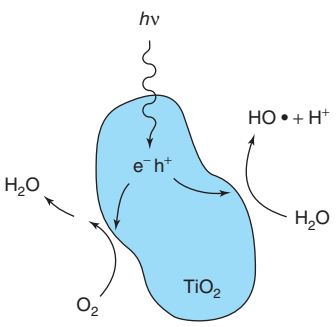
Drinking water and industrial waste streams are partially characterized and regulated on the basis of their carbon content and oxygen demand.[12] *Inorganic carbon* (IC) is the $CO_2(g)$ liberated when water is acidified to pH < 2 with H_3PO_4 and purged with Ar or N_2. IC corresponds to CO_3^{2-} and HCO_3^- in the sample. After inorganic carbon is removed, *total organic carbon* (TOC) is the CO_2 produced by oxidizing the remaining organic matter:

$$\textit{TOC analysis:} \quad \text{Organic carbon} \xrightarrow[\text{metal catalyst}]{O_2/\sim 700°C} CO_2$$

Total carbon (TC) is defined as the sum TC = TOC + IC.

Different oxidation techniques produce different values for TOC, because not all organic matter is oxidized by each technique. The state of the art is such that TOC is defined by the result obtained with a particular instrument.

Commercial instruments that measure TOC by thermal oxidation have detection limits of 4–50 ppb (4–50 μg C/L). A typical 20-μL water sample is analyzed in 3 min with infrared absorption used to measure CO_2. Other instruments oxidize organic matter by irradiating a suspension of solid TiO_2 catalyst (0.2 g/L) in water at pH 3.5 with ultraviolet light.[13] Light creates electron-hole pairs (Section 14-8) in the TiO_2. Holes oxidize H_2O to hydroxyl radical (HO•), a powerful oxidant that converts organic carbon into CO_2, which is measured by the electrical conductivity of carbonic acid.[14] Color Plate 8 shows an instrument in which $K_2S_2O_8$ in acid is exposed to ultraviolet radiation to generate sulfate radical ($\cdot SO_4^-$), which oxidizes organic matter to CO_2. (Pure TiO_2 hardly absorbs visible light, so it cannot use sunlight efficiently. By doping TiO_2 with ~1 wt% carbon, the efficiency of using visible light is markedly increased.[15])



Ultraviolet radiation absorbed by TiO_2 creates an electron-hole pair. The hole oxidizes H_2O to the powerful oxidant HO•. The electron reduces O_2 to H_2O by a chain of reactions. TiO_2 is a catalyst and O_2 is consumed in the net reaction: organic C + O_2 → CO_2.

TOC is widely used to determine compliance with discharge laws. Municipal and industrial wastewater typically has TOC > 1 mg C/mL. Tap water TOC is 50–500 ng C/mL. High-purity water for the electronics industry has TOC < 1 ng C/mL.

Total oxygen demand (TOD) tells us how much O_2 is required for complete combustion of pollutants in a waste stream. A volume of N_2 containing a known quantity of O_2 is mixed with the sample and complete combustion is carried out. The remaining O_2 is measured by a potentiometric sensor. Different species in the waste stream consume different amounts of O_2. For example, urea consumes five times as much O_2 as formic acid does. Species such as NH_3 and H_2S also contribute to TOD.

Pollutants can be oxidized by refluxing with dichromate ($Cr_2O_7^{2-}$). *Chemical oxygen demand* (COD) is defined as the O_2 that is chemically equivalent to the $Cr_2O_7^{2-}$ consumed in this process. Each $Cr_2O_7^{2-}$ consumes $6e^-$ (to make $2Cr^{3+}$) and each O_2 consumes $4e^-$ (to make H_2O). Therefore, 1 mol of $Cr_2O_7^{2-}$ is chemically equivalent to 1.5 mol of O_2 for this computation. COD analysis is carried out by refluxing polluted water for 2 h with excess standard $Cr_2O_7^{2-}$ in H_2SO_4 solution containing Ag^+ catalyst. Unreacted $Cr_2O_7^{2-}$ is measured by titration with standard Fe^{2+} or by spectrophotometry. Permits for industry may include COD limits for waste streams. "Oxidizability," which is used in Europe, is analogous to COD. Oxidizability is measured by refluxing with permanganate in acid solution at 100°C for 10 min. Each MnO_4^- consumes five electrons and is chemically equivalent to 1.25 O_2. Electrochemical methods based on photooxidation with TiO_2 could replace cumbersome refluxing with $Cr_2O_7^{2-}$ or MnO_4^-. Problem 16-21 describes one proven method.

Biological oxygen demand (BOD) is the O_2 required for biological degradation of organic matter by microorganisms. The procedure calls for incubating a sealed container of wastewater with no extra air space for 5 days at 20°C in the dark while microbes metabolize organic compounds in the waste. Dissolved O_2 is measured before and after incubation. The difference is BOD.[17] BOD also measures species such as HS^- and Fe^{2+} that may be in the water. Inhibitors are added to prevent oxidation of nitrogen species such as NH_3. There is interest in developing a rapid analysis to provide information equivalent to BOD. This goal could be achieved by substituting ferricyanide ($Fe(CN)_6^{3-}$) for O_2 as the electron sink for bacterial degradation of organic matter. Ferricyanide requires just 3 h, and results are similar to that of the 5-day standard procedure.[18]

Bound nitrogen includes all nitrogen-containing compounds, except N_2, dissolved in water. Kjeldahl nitrogen analysis described in Section 10-8 is excellent for amines and amides but fails to respond to many other forms of nitrogen. Combustion can convert most forms of nitrogen in aqueous samples into NO, which can be measured by chemiluminescence after reaction with ozone:[19]

$$\textit{Bound nitrogen analysis:} \quad \text{Nitrogen compounds} \xrightarrow[\text{catalyst}]{O_2/\sim 1\,000°C} NO$$

$$\underset{\text{Nitrous oxide}}{NO} + \underset{\text{Ozone}}{O_3} \rightarrow \underset{\text{Nitric oxide, Excited electronic state}}{NO_2^*}$$

$$NO_2^* \rightarrow NO_2 + \underset{\text{Characteristic light emission}}{h\nu}$$

Azide (N_3^-) and hydrazines ($RNHNH_2$) are not quantitatively converted into NO by combustion. Bound nitrogen measurements are required for compliance with wastewater discharge regulations.

TiO_2-blended PVC before irradiation

After irradiation for 20 days

Here is a "green" idea: TiO_2 can be blended into poly(vinyl chloride) (PVC) plastic so that the plastic is degraded by sunlight.[16] Ordinary PVC lasts many years in municipal landfills after it is discarded. TiO_2-blended PVC would decompose in a short time. [Courtesy H. Hidaka and S. Horikoshi, Meisei University, Tokyo.]

In iodometry (titration *of* I_3^-), I_3^- is present throughout the reaction up to the equivalence point. *Starch should not be added until immediately before the equivalence point* (as detected visually, by fading of the I_3^-; Color Plate 9). Otherwise some iodine tends to remain bound to starch particles after the equivalence point is reached.

Starch-iodine complexation is temperature dependent. At 50°C, the color is only one-tenth as intense as at 25°C. If maximum sensitivity is required, cooling in ice water is recommended.[22] Organic solvents decrease the affinity of iodine for starch and markedly reduce the utility of the indicator.

An alternative to using starch is to add a few milliliters of *p*-xylene to the vigorously stirred titration vessel. After each addition of reagent near the end point, stop stirring long enough to examine the color of the organic phase. I_2 is 400 times more soluble in *p*-xylene than in water, and its color is readily detected in the organic phase.[21]

Preparation and Standardization of I_3^- Solutions

Triiodide (I_3^-) is prepared by dissolving solid I_2 in excess KI. Sublimed I_2 is pure enough to be a primary standard, but it is seldom used as a standard because it evaporates while it is being weighed. Instead, the approximate amount is rapidly weighed, and the solution of I_3^- is standardized with a pure sample of analyte or $Na_2S_2O_3$.

There is a significant vapor pressure of toxic I_2 above solid I_2 and aqueous I_3^-. Vessels containing I_2 or I_3^- should be capped and kept in a fume hood. Waste solutions of I_3^- should not be dumped into a sink in the open lab.

Acidic solutions of I_3^- are unstable because the excess I^- is slowly oxidized by air:

$$6I^- + O_2 + 4H^+ \rightarrow 2I_3^- + 2H_2O$$

In neutral solutions, oxidation is insignificant in the absence of heat, light, and metal ions. At pH $\gtrsim$ 11, triiodide disproportionates to hypoiodous acid, iodate, and iodide.

HOI hypoiodous acid
IO_3^- iodate

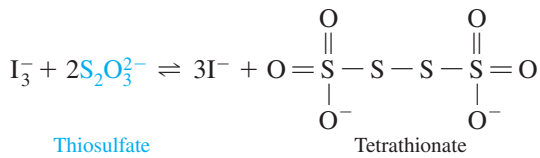
An excellent way to prepare standard I_3^- is to add a weighed quantity of the primary standard potassium iodate (KIO_3) to a small excess of KI.[23] Then add excess strong acid (giving pH $\approx$ 1) to produce I_3^- by quantitative reverse disproportionation:

$$IO_3^- + 8I^- + 6H^+ \rightleftharpoons 3I_3^- + 3H_2O \qquad \textbf{(15-18)}$$

Freshly acidified iodate plus iodide can be used to standardize thiosulfate. I_3^- must be used immediately or it will be oxidized by air. The disadvantage of KIO_3 is its low molecular mass relative to the number of electrons it accepts, giving a larger-than-desirable relative weighing error in preparing solutions.

Use of Sodium Thiosulfate

Sodium thiosulfate is the almost universal titrant for triiodide. In neutral or acidic solution, triiodide oxidizes thiosulfate to tetrathionate:



(15-19)

In basic solution, I_3^- disproportionates to I^- and HOI, which can oxidize $S_2O_3^{2-}$ to SO_4^{2-}. Reaction 15-19 should be carried out below pH 9. The common form of thiosulfate, $Na_2S_2O_3 \cdot 5H_2O$, is not pure enough to be a primary standard. Instead, thiosulfate is usually standardized by reaction with a fresh solution of I_3^- prepared from KIO_3 plus KI.

Anhydrous, primary standard $Na_2S_2O_3$ can be prepared from the pentahydrate.[24]

A stable solution of $Na_2S_2O_3$ can be prepared by dissolving the reagent in high-quality, freshly boiled distilled water. Dissolved CO_2 makes the solution acidic and promotes disproportionation of $S_2O_3^{2-}$:

$$S_2O_3^{2-} + H^+ \rightleftharpoons \underset{\text{Bisulfite}}{HSO_3^-} + \underset{\text{Sulfur}}{S(s)} \qquad \textbf{(15-20)}$$

and metal ions catalyze atmospheric oxidation of thiosulfate:

$$2Cu^{2+} + 2S_2O_3^{2-} \rightarrow 2Cu^+ + S_4O_6^{2-}$$

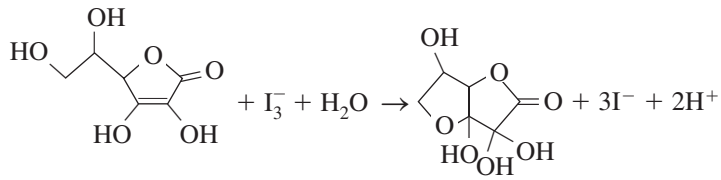
$$2Cu^+ + \frac{1}{2}O_2 + 2H^+ \rightarrow 2Cu^{2+} + H_2O$$

Thiosulfate solutions should be stored in the dark. Addition of 0.1 g of sodium carbonate per liter maintains the pH in an optimum range for stability of the solution. Three drops of chloroform should also be added to each bottle of thiosulfate solution to help prevent bacterial growth. An acidic solution of thiosulfate is unstable, but the reagent can be used to titrate I_3^- in acidic solution because the reaction with triiodide is faster than Reaction 15-20.

Analytical Applications of Iodine

Reducing agent $+I_3^- \rightarrow 3I^-$

Reducing agents can be titrated directly with standard I_3^- in the presence of starch, until reaching the intense blue starch-iodine end point (Table 15-4). An example is the iodimetric determination of vitamin C:



Ascorbic acid (vitamin C) — Dehydroascorbic acid[25]

Oxidizing agent $+3I^- \rightarrow I_3^-$

Oxidizing agents can be treated with excess I^- to produce I_3^- (Table 15-5, Box 15-3). The iodometric analysis is completed by titrating the liberated I_3^- with standard thiosulfate. Starch is not added until just before the end point.

TABLE 15-4 Titrations with standard triiodide (iodimetric titrations)

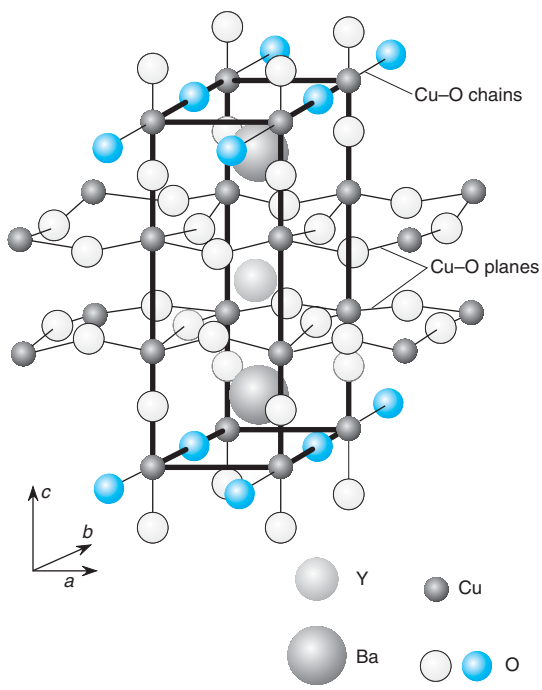
Species analyzed	Oxidation reaction	Notes
As^{3+}	$H_3AsO_3 + H_2O \rightleftharpoons H_3AsO_4 + 2H^+ + 2e^-$	Titrate directly in $NaHCO_3$ solution with I_3^-.
Sn^{2+}	$SnCl_4^{2-} + 2Cl^- \rightleftharpoons SnCl_6^{2-} + 2e^-$	Sn(IV) is reduced to Sn(II) with granular Pb or Ni in 1 M HCl and titrated in the absence of oxygen.
N_2H_4	$N_2H_4 \rightleftharpoons N_2 + 4H^+ + 4e^-$	Titrate in $NaHCO_3$ solution.
SO_2	$SO_2 + H_2O \rightleftharpoons H_2SO_3$ $H_2SO_3 + H_2O \rightleftharpoons SO_4^{2-} + 4H^+ + 2e^-$	Add SO_2 (or H_2SO_3 or HSO_3^- or SO_3^{2-}) to excess standard I_3^- in dilute acid and back-titrate unreacted I_3^- with standard thiosulfate.
H_2S	$H_2S \rightleftharpoons S(s) + 2H^+ + 2e^-$	Add H_2S to excess I_3^- in 1 M HCl and back-titrate with thiosulfate.
Zn^{2+}, Cd^{2+}, Hg^{2+}, Pb^{2+}	$M^{2+} + H_2S \rightarrow MS(s) + 2H^+$ $MS(s) \rightleftharpoons M^{2+} + S + 2e^-$	Precipitate and wash metal sulfide. Dissolve in 3 M HCl with excess standard I_3^- and back-titrate with thiosulfate.
Cysteine, glutathione, thioglycolic acid, mercaptoethanol	$2RSH \rightleftharpoons RSSR + 2H^+ + 2e^-$	Titrate the sulfhydryl compound at pH 4–5 with I_3^-.
HCN	$I_2 + HCN \rightleftharpoons ICN + I^- + H^+$	Titrate in carbonate-bicarbonate buffer, using *p*-xylene as an extraction indicator.
$H_2C{=}O$	$H_2CO + 3OH^- \rightleftharpoons HCO_2^- + 2H_2O + 2e^-$	Add excess I_3^- plus NaOH to the unknown. After 5 min, add HCl and back-titrate with thiosulfate.
Glucose (and other reducing sugars)	$RC(=O)H + 3OH^- \rightleftharpoons RCO_2^- + 2H_2O + 2e^-$	Add excess I_3^- plus NaOH to the sample. After 5 min, add HCl and back-titrate with thiosulfate.
Ascorbic acid (vitamin C)	Ascorbate $+ H_2O \rightleftharpoons$ dehydroascorbate $+ 2H^+ + 2e^-$	Titrate directly with I_3^-.
H_3PO_3	$H_3PO_3 + H_2O \rightleftharpoons H_3PO_4 + 2H^+ + 2e^-$	Titrate in $NaHCO_3$ solution.

BOX 15-3 Iodometric Analysis of High-Temperature Superconductors

An important application of superconductors is in powerful electromagnets needed for medical magnetic resonance imaging. Ordinary conductors in such magnets require a huge amount of electric power. Because electricity moves through a superconductor with no resistance, the voltage can be removed from the electromagnetic coil once the current has started. Current continues to flow with no power consumption.

A breakthrough in superconductor technology came with the discovery[26] of yttrium barium copper oxide, $YBa_2Cu_3O_7$, whose crystal structure is shown here. When heated, the material readily loses oxygen atoms from the Cu—O chains, and any composition between $YBa_2Cu_3O_7$ and $YBa_2Cu_3O_6$ is observable.

When high-temperature superconductors were discovered, the oxygen content in the formula $YBa_2Cu_3O_x$ was unknown. $YBa_2Cu_3O_7$ represents an unusual set of oxidation states. Common states of yttrium and barium are Y^{3+} and Ba^{2+}, and the common states of copper are Cu^{2+} and Cu^{+}. If all the copper were Cu^{2+}, the formula of the superconductor would be $(Y^{3+})(Ba^{2+})_2(Cu^{2+})_3(O^{2-})_{6.5}$, with a cation charge of +13 and an anion charge of −13. The composition $YBa_2Cu_3O_7$ requires Cu^{3+}, which is rather rare. Formally, $YBa_2Cu_3O_7$ can be thought of as $(Y^{3+})(Ba^{2+})_2(Cu^{2+})_2(Cu^{3+})(O^{2-})_7$ with a cation charge of +14 and an anion charge of −14.



Structure of $YBa_2Cu_3O_7$. One-dimensional Cu—O chains (shown in color) run along the crystallographic *b*-axis and two-dimensional Cu—O sheets lie in the *a*–*b* plane. Loss of colored oxygen atoms from the chains at elevated temperature results in $YBa_2Cu_3O_6$. [From G. F. Holland and A. M. Stacy, "Physical Properties of the Quaternary Oxide Superconductor $YBa_2Cu_3O_x$," *Acc. Chem. Res.* **1988**, *21*, 8.]

Redox titrations proved to be the most reliable way to measure the oxidation state of copper and thereby deduce the oxygen content of $YBa_2Cu_3O_x$.[27] An iodometric method includes two experiments.

In *Experiment A*, $YBa_2Cu_3O_x$ is dissolved in dilute acid, in which Cu^{3+} is converted into Cu^{2+}. For simplicity, we write reactions for $YBa_2Cu_3O_7$, but you could balance these equations for $x \neq 7$.[28]

$$YBa_2Cu_3O_7 + 13H^+ \rightarrow$$
$$Y^{3+} + 2Ba^{2+} + 3Cu^{2+} + \frac{13}{2}H_2O + \frac{1}{4}O_2 \qquad (1)$$

The total copper content is measured by treatment with iodide

$$Cu^{2+} + \frac{5}{2}I^- \rightarrow CuI(s) + \frac{1}{2}I_3^- \qquad (2)$$

and titration of the liberated triiodide with standard thiosulfate by Reaction 15-19. Each mole of Cu in $YBa_2Cu_3O_7$ is equivalent to 1 mol of $S_2O_3^{2-}$ in Experiment A.

In *Experiment B*, $YBa_2Cu_3O_x$ is dissolved in dilute acid containing I^-. Each mole of Cu^{2+} produces 0.5 mol of I_3^- by Reaction (2) and each mole of Cu^{3+} produces 1 mol of I_3^-:

$$Cu^{3+} + 4I^- \rightarrow CuI(s) + I_3^- \qquad (3)$$

The moles of $S_2O_3^{2-}$ required in Experiment A equal the total moles of Cu in the superconductor. The difference in $S_2O_3^{2-}$ required between Experiments B and A gives the Cu^{3+} content. From this difference, you can find x in the formula $YBa_2Cu_3O_x$.[29]

Although we can balance cation and anion charges in the formula $YBa_2Cu_3O_7$ by including Cu^{3+} in the formula, there is no evidence for discrete Cu^{3+} ions in the crystal. There is also no evidence that some of the oxygen is in the form of peroxide, O_2^{2-}, which also would balance the cation and anion charges. The best description of the valence state in the solid crystal involves electrons and holes delocalized in the Cu—O planes and chains. Nonetheless, the formal designation of Cu^{3+} and Reactions 1 through 3 accurately describe the redox chemistry of $YBa_2Cu_3O_7$. Problem 15-35 describes titrations that separately measure oxidation numbers of Cu and Bi in the superconductor $Bi_2Sr_2(Ca_{0.8}Y_{0.2})Cu_2O_{8.295}$.

TABLE 15-5 Titration of I_3^- produced by analyte (iodometric titrations)

Species analyzed	Reaction	Notes
Cl_2	$Cl_2 + 3I^- \rightleftharpoons 2Cl^- + I_3^-$	Reaction in dilute acid.
$HOCl$	$HOCl + H^+ + 3I^- \rightleftharpoons Cl^- + I_3^- + H_2O$	Reaction in 0.5 M H_2SO_4.
Br_2	$Br_2 + 3I^- \rightleftharpoons 2Br^- + I_3^-$	Reaction in dilute acid.
BrO_3^-	$BrO_3^- + 6H^+ + 9I^- \rightleftharpoons Br^- + 3I_3^- + 3H_2O$	Reaction in 0.5 M H_2SO_4.
IO_3^-	$2IO_3^- + 16I^- + 12H^+ \rightleftharpoons 6I_3^- + 6H_2O$	Reaction in 0.5 M HCl.
IO_4^-	$2IO_4^- + 22I^- + 16H^+ \rightleftharpoons 8I_3^- + 8H_2O$	Reaction in 0.5 M HCl.
O_2	$O_2 + 4Mn(OH)_2 + 2H_2O \rightleftharpoons 4Mn(OH)_3$ $2Mn(OH)_3 + 6H^+ + 3I^- \rightleftharpoons 2Mn^{2+} + I_3^- + 6H_2O$	The sample is treated with Mn^{2+}, NaOH, and KI. After 1 min, it is acidified with H_2SO_4, and the I_3^- is titrated.
H_2O_2	$H_2O_2 + 3I^- + 2H^+ \rightleftharpoons I_3^- + 2H_2O$	Reaction in 1 M H_2SO_4 with NH_4MoO_3 catalyst.
O_3[a]	$O_3 + 3I^- + 2H^+ \rightleftharpoons O_2 + I_3^- + H_2O$	O_3 is passed through neutral 2 wt% KI solution. Add H_2SO_4 and titrate.
NO_2^-	$2HNO_2 + 2H^+ + 3I^- \rightleftharpoons 2NO + I_3^- + 2H_2O$	The nitric oxide is removed (by bubbling CO_2 generated in situ) prior to titration of I_3^-.
As^{5+}	$H_3AsO_4 + 2H^+ + 3I^- \rightleftharpoons H_3AsO_3 + I_3^- + H_2O$	Reaction in 5 M HCl.
$S_2O_8^{2-}$	$S_2O_8^{2-} + 3I^- \rightleftharpoons 2SO_4^{2-} + I_3^-$	Reaction in neutral solution. Then acidify and titrate.
Cu^{2+}	$2Cu^{2+} + 5I^- \rightleftharpoons 2CuI(s) + I_3^-$	NH_4HF_2 is used as a buffer.
$Fe(CN)_6^{3-}$	$2Fe(CN)_6^{3-} + 3I^- \rightleftharpoons 2Fe(CN)_6^{4-} + I_3^-$	Reaction in 1 M HCl.
MnO_4^-	$2MnO_4^- + 16H^+ + 15I^- \rightleftharpoons 2Mn^{2+} + 5I_3^- + 8H_2O$	Reaction in 0.1 M HCl.
MnO_2	$MnO_2(s) + 4H^+ + 3I^- \rightleftharpoons Mn^{2+} + I_3^- + 2H_2O$	Reaction in 0.5 M H_3PO_4 or HCl.
$Cr_2O_7^{2-}$	$Cr_2O_7^{2-} + 14H^+ + 9I^- \rightleftharpoons 2Cr^{3+} + 3I_3^- + 7H_2O$	Reaction in 0.4 M HCl requires 5 min for completion and is particularly sensitive to air oxidation.
Ce^{4+}	$2Ce^{4+} + 3I^- \rightleftharpoons 2Ce^{3+} + I_3^-$	Reaction in 1 M H_2SO_4.

a. The pH must be $\gtrsim 7$ when O_3 is added to I^-. In acidic solution, each O_3 produces 1.25 I_3^-, not 1 I_3^-. [N. V. Klassen, D. Marchington, and H. C. E. McGowan, Anal. Chem. ***1994****, 66, 2921.]*

Terms to Understand

amalgam
disproportionation
preoxidation
prereduction
redox indicator
redox titration

Summary

Redox titrations are based on an oxidation-reduction reaction between analyte and titrant. Sometimes a quantitative chemical preoxidation (with reagents such as $S_2O_8^{2-}$, AgO, $NaBiO_3$, or H_2O_2) or prereduction (with reagents such as $SnCl_2$, $CrCl_2$, SO_2, H_2S, or a metallic reductor column) is necessary to adjust the oxidation state of the analyte prior to analysis. The end point of a redox titration is commonly detected by potentiometry or with a redox indicator. A useful indicator must have a transition range ($= E°$(indicator) $\pm$ 0.059 16/n V) that overlaps the abrupt change in potential of the titration curve.

The greater the difference in reduction potential between analyte and titrant, the sharper will be the end point. Plateaus before and after the equivalence point are centered near $E°$(analyte) and $E°$(titrant). Prior to the equivalence point, the half-reaction involving analyte is used to find the voltage because the concentrations of both the oxidized and the reduced forms of analyte are known. After the equivalence point, the half-reaction involving titrant is employed. At the equivalence point, both half-reactions are used to find the voltage.

Common oxidizing titrants include $KMnO_4$, Ce^{4+}, and $K_2Cr_2O_7$. Many procedures are based on oxidation with I_3^- or titration of I_3^- liberated in a chemical reaction.

Exercises

15-A. A 20.0-mL solution of 0.005 00 M Sn^{2+} in 1 M HCl was titrated with 0.020 0 M Ce^{4+} to give Sn^{4+} and Ce^{3+}. Calculate the potential (versus S.C.E.) at the following volumes of Ce^{4+}: 0.100, 1.00, 5.00, 9.50, 10.00, 10.10, and 12.00 mL. Sketch the titration curve.

15-B. Would indigo tetrasulfonate be a suitable redox indicator for the titration of $Fe(CN)_6^{4-}$ with Tl^{3+} in 1 M HCl? (*Hint:* The potential at the equivalence point must be between the potentials for each redox couple.)

15-C. Compute the titration curve for Demonstration 15-1, in which 400.0 mL of 3.75 mM Fe^{2+} are titrated with 20.0 mM MnO_4^- at a *fixed pH* of 0.00 in 1 M H_2SO_4. Calculate the potential versus S.C.E. at titrant volumes of 1.0, 7.5, 14.0, 15.0, 16.0, and 30.0 mL and sketch the titration curve.

15-D. A titration of 50.0 mL of unknown Fe^{2+} with 0.100 M Ce^{4+} at 25°C, monitored with Pt and calomel electrodes, gave data in the following table.[8] Prepare a Gran plot and decide which data lie on a straight line. Find the *x*-intercept of this line, which is the equivalence volume. Calculate the molarity of Fe^{2+} in the unknown.

Titrant volume, *V* (mL)	*E* (volts)
6.50	0.635
8.50	0.651
10.50	0.669
11.50	0.680
12.50	0.696

15-E. A solid mixture weighing 0.054 85 g contained only ferrous ammonium sulfate and ferrous chloride. The sample was dissolved in 1 M H_2SO_4, and the Fe^{2+} required 13.39 mL of 0.012 34 M Ce^{4+} for complete oxidation to Fe^{3+}. Calculate the weight percent of Cl in the original sample.

$FeSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$	$FeCl_2 \cdot 6H_2O$
Ferrous ammonium sulfate	Ferrous chloride
FM 392.13	FM 234.84

Problems

Shape of a Redox Titration Curve

15-1. Consider the titration in Figure 15-2.

(a) Write a balanced titration reaction.

(b) Write two different half-reactions for the indicator electrode.

(c) Write two different Nernst equations for the cell voltage.

(d) Calculate *E* at the following volumes of Ce^{4+}: 10.0, 25.0, 49.0, 50.0, 51.0, 60.0, and 100.0 mL. Compare your results with Figure 15-2.

15-2. Consider the titration of 100.0 mL of 0.010 0 M Ce^{4+} in 1 M $HClO_4$ by 0.040 0 M Cu^{+} to give Ce^{3+} and Cu^{2+}, using Pt and saturated Ag | AgCl electrodes to find the end point.

(a) Write a balanced titration reaction.

(b) Write two different half-reactions for the indicator electrode.

(c) Write two different Nernst equations for the cell voltage.

(d) Calculate *E* at the following volumes of Cu^{+}: 1.00, 12.5, 24.5, 25.0, 25.5, 30.0, and 50.0 mL. Sketch the titration curve.

15-3. Consider the titration of 25.0 mL of 0.010 0 M Sn^{2+} by 0.050 0 M Tl^{3+} in 1 M HCl, using Pt and saturated calomel electrodes to find the end point.

(a) Write a balanced titration reaction.

(b) Write two different half-reactions for the indicator electrode.

(c) Write two different Nernst equations for the cell voltage.

(d) Calculate *E* at the following volumes of Tl^{3+}: 1.00, 2.50, 4.90, 5.00, 5.10, and 10.0 mL. Sketch the titration curve.

15-4. Ascorbic acid (0.010 0 M) was added to 10.0 mL of 0.020 0 M Fe^{3+} in a solution buffered to pH 0.30, and the potential was monitored with Pt and saturated Ag | AgCl electrodes.

$$\text{Dehydroascorbic acid} + 2H^+ + 2e^- \rightleftharpoons \text{ascorbic acid} + H_2O \qquad E^\circ = 0.390\ \text{V}$$

(a) Write a balanced equation for the titration reaction.

(b) Using $E^\circ = 0.767$ V for the $Fe^{3+} \mid Fe^{2+}$ couple, calculate the cell voltage when 5.0, 10.0, and 15.0 mL of ascorbic acid have been added. (*Hint:* Refer to the calculations in Demonstration 15-1.)

15-5. Consider the titration of 25.0 mL of 0.050 0 M Sn^{2+} with 0.100 M Fe^{3+} in 1 M HCl to give Fe^{2+} and Sn^{4+}, using Pt and calomel electrodes.

(a) Write a balanced titration reaction.

(b) Write two half-reactions for the indicator electrode.

(c) Write two Nernst equations for the cell voltage.

(d) Calculate *E* at the following volumes of Fe^{3+}: 1.0, 12.5, 24.0, 25.0, 26.0, and 30.0 mL. Sketch the titration curve.

Finding the End Point

15-6. Select indicators from Table 15-2 that would be suitable for finding the end point in Figure 15-3. What color changes would be observed?

15-7. Would tris(2,2′-bipyridine)iron be a useful indicator for the titration of Sn^{2+} with $Mn(EDTA)^-$? (*Hint:* The potential at the equivalence point must be between the potentials for each redox couple.)

Adjustment of Analyte Oxidation State

15-8. Explain what we mean by *preoxidation* and *prereduction*. Why is it important to be able to destroy the reagents used for these purposes?

15-9. Write balanced reactions for the destruction of $S_2O_8^{2-}$, Ag^{2+}, and H_2O_2 by boiling.

15-10. What is a Jones reductor and what is it used for?

15-11. Why don't Cr^{3+} and TiO^{2+} interfere in the analysis of Fe^{3+} when a Walden reductor, instead of a Jones reductor, is used for prereduction?

Redox Reactions of $KMnO_4$, Ce(IV), and $K_2Cr_2O_7$

15-12. From information in Table 15-3, explain how you would use $KMnO_4$ to find the content of $(NH_4)_2S_2O_8$ in a solid mixture with $(NH_4)_2SO_4$. What is the purpose of phosphoric acid in the procedure?

15-13. Write balanced half-reactions in which MnO_4^- acts as an oxidant at **(a)** pH = 0; **(b)** pH = 10; **(c)** pH = 15.

15-14. When 25.00 mL of unknown were passed through a Jones reductor, molybdate ion (MoO_4^{2-}) was converted into Mo^{3+}. The filtrate required 16.43 mL of 0.010 33 M $KMnO_4$ to reach the purple end point.

$$MnO_4^- + Mo^{3+} \rightarrow Mn^{2+} + MoO_2^{2+}$$

A blank required 0.04 mL. Balance the reaction and find the molarity of molybdate in the unknown.

15-15. A 25.00-mL volume of commercial hydrogen peroxide solution was diluted to 250.0 mL in a volumetric flask. Then 25.00 mL

of the diluted solution were mixed with 200 mL of water and 20 mL of 3 M H_2SO_4 and titrated with 0.021 23 M $KMnO_4$. The first pink color was observed with 27.66 mL of titrant. A blank prepared from water in place of H_2O_2 required 0.04 mL to give visible pink color. Using the H_2O_2 reaction in Table 15-3, find the molarity of the commercial H_2O_2.

15-16. Two possible reactions of MnO_4^- with H_2O_2 to produce O_2 and Mn^{2+} are

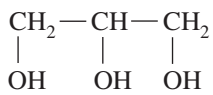
$$\text{Scheme 1:} \quad MnO_4^- \rightarrow Mn^{2+}$$
$$H_2O_2 \rightarrow O_2$$
$$\text{Scheme 2:} \quad MnO_4^- \rightarrow O_2 + Mn^{2+}$$
$$H_2O_2 \rightarrow H_2O$$

(a) Complete the half-reactions for both schemes by adding e^-, H_2O, and H^+ and write a balanced net equation for each scheme.

(b) Sodium peroxyborate tetrahydrate, $NaBO_3 \cdot 4H_2O$ (FM 153.86), produces H_2O_2 when dissolved in acid: $BO_3^- + 2H_2O \rightarrow H_2O_2 + H_2BO_3^-$. To decide whether Scheme 1 or Scheme 2 occurs, students at the U.S. Naval Academy[30] weighed 1.023 g $NaBO_3 \cdot 4H_2O$ into a 100-mL volumetric flask, added 20 mL of 1 M H_2SO_4, and diluted to the mark with H_2O. Then they titrated 10.00 mL of this solution with 0.010 46 M $KMnO_4$ until the first pale pink color persisted. How many mL of $KMnO_4$ are required in Scheme 1 and in Scheme 2? (The Scheme 1 stoichiometry was observed.)

15-17. A 50.00-mL sample containing La^{3+} was treated with sodium oxalate to precipitate $La_2(C_2O_4)_3$, which was washed, dissolved in acid, and titrated with 18.04 mL of 0.006 363 M $KMnO_4$. Calculate the molarity of La^{3+} in the unknown.

15-18. An aqueous glycerol solution weighing 100.0 mg was treated with 50.0 mL of 0.083 7 M Ce^{4+} in 4 M $HClO_4$ at 60°C for 15 min to oxidize the glycerol to formic acid:



Glycerol
FM 92.095

HCO_2H

Formic acid

The excess Ce^{4+} required 12.11 mL of 0.044 8 M Fe^{2+} to reach a ferroin end point. What is the weight percent of glycerol in the unknown?

15-19. Nitrite (NO_2^-) can be determined by oxidation with excess Ce^{4+}, followed by back titration of the unreacted Ce^{4+}. A 4.030-g sample of solid containing only $NaNO_2$ (FM 68.995) and $NaNO_3$ was dissolved in 500.0 mL. A 25.00-mL sample of this solution was treated with 50.00 mL of 0.118 6 M Ce^{4+} in strong acid for 5 min, and the excess Ce^{4+} was back-titrated with 31.13 mL of 0.042 89 M ferrous ammonium sulfate.

$$2Ce^{4+} + NO_2^- + H_2O \rightarrow 2Ce^{3+} + NO_3^- + 2H^+$$
$$Ce^{4+} + Fe^{2+} \rightarrow Ce^{3+} + Fe^{3+}$$

Calculate the weight percent of $NaNO_2$ in the solid.

15-20. Calcium fluorapatite ($Ca_{10}(PO_4)_6F_2$, FM 1 008.6) laser crystals were doped with chromium to improve their efficiency. It was suspected that the chromium could be in the +4 oxidation state.

1. To measure the total oxidizing power of chromium in the material, a crystal was dissolved in 2.9 M $HClO_4$ at 100°C, cooled to 20°C, and titrated with standard Fe^{2+}, using Pt and Ag | AgCl electrodes to find the end point. Chromium oxidized above the +3 state should oxidize an equivalent amount of Fe^{2+} in this step. That is, Cr^{4+} would consume one Fe^{2+}, and each atom of Cr^{6+} in $Cr_2O_7^{2-}$ would consume three Fe^{2+}:

$$Cr^{4+} + Fe^{2+} \rightarrow Cr^{3+} + Fe^{3+}$$
$$\frac{1}{2}Cr_2O_7^{2-} + 3Fe^{2+} \rightarrow Cr^{3+} + 3Fe^{3+}$$

2. In a second step, the total chromium content was measured by dissolving a crystal in 2.9 M $HClO_4$ at 100°C and cooling to 20°C. Excess $S_2O_8^{2-}$ and Ag^+ were then added to oxidize all chromium to $Cr_2O_7^{2-}$. Unreacted $S_2O_8^{2-}$ was destroyed by boiling, and the remaining solution was titrated with standard Fe^{2+}. In this step, each Cr in the original unknown reacts with three Fe^{2+}.

$$Cr^{x+} \xrightarrow{S_2O_8^{2-}} Cr_2O_7^{2-}$$
$$\frac{1}{2}Cr_2O_7^{2-} + 3Fe^{2+} \rightarrow Cr^{3+} + 3Fe^{3+}$$

In step 1, 0.437 5 g of laser crystal required 0.498 mL of 2.786 mM Fe^{2+} (prepared by dissolving $Fe(NH_4)_2(SO_4)_2 \cdot 6H_2O$ in 2 M $HClO_4$). In step 2, 0.156 6 g of crystal required 0.703 mL of the same Fe^{2+} solution. Find the average oxidation number of Cr in the crystal and find the total micrograms of Cr per gram of crystal.

15-21. Primary-standard-grade arsenic(III) oxide (As_4O_6) is a useful (but carcinogenic) reagent for standardizing oxidants including MnO_4^- and I_3^-. To standardize MnO_4^-, As_4O_6 is dissolved in base and then titrated with MnO_4^- in acid. A small amount of iodide (I^-) or iodate (IO_3^-) catalyzes the reaction between H_3AsO_3 and MnO_4^-.

$$As_4O_6 + 8OH^- \rightleftharpoons 4HAsO_3^{2-} + 2H_2O$$
$$HAsO_3^{2-} + 2H^+ \rightleftharpoons H_3AsO_3$$
$$5H_3AsO_3 + 2MnO_4^- + 6H^+ \rightarrow 5H_3AsO_4 + 2Mn^{2+} + 3H_2O$$

(a) A 3.214-g aliquot of $KMnO_4$ (FM 158.034) was dissolved in 1.000 L of water, heated to cause any reactions with impurities to occur, cooled, and filtered. What is the theoretical molarity of this solution if no MnO_4^- was consumed by impurities?

(b) What mass of As_4O_6 (FM 395.68) would be just sufficient to react with 25.00 mL of the $KMnO_4$ solution in part **(a)**?

(c) It was found that 0.146 8 g of As_4O_6 required 29.98 mL of $KMnO_4$ solution for the faint color of unreacted MnO_4^- to appear. In a blank titration, 0.03 mL of MnO_4^- was required to produce enough color to be seen. Calculate the molarity of the permanganate solution.

Methods Involving Iodine

15-22. Why is iodine almost always used in a solution containing excess I^-?

15-23. State two ways to make standard triiodide solution.

15-24. In which technique, iodimetry or iodometry, is starch indicator not added until just before the end point? Why?

15-25. (a) Potassium iodate solution was prepared by dissolving 1.022 g of KIO_3 (FM 214.00) in a 500-mL volumetric flask. Then 50.00 mL of the solution were pipetted into a flask and treated with excess KI (2 g) and acid (10 mL of 0.5 M H_2SO_4). How many moles of I_3^- are created by the reaction?

(b) The triiodide from part **(a)** reacted with 37.66 mL of $Na_2S_2O_3$ solution. What is the concentration of the $Na_2S_2O_3$ solution?

(c) A 1.223-g sample of solid containing ascorbic acid and inert ingredients was dissolved in dilute H_2SO_4 and treated with 2 g of KI and 50.00 mL of KIO_3 solution from part **(a)**. Excess triiodide required 14.22 mL of $Na_2S_2O_3$ solution from part **(b)**. Find the weight percent of ascorbic acid (FM 176.13) in the unknown.

(d) Does it matter whether starch indicator is added at the beginning or near the end point in the titration in part **(c)**?

15-26. A 3.026-g portion of a copper(II) salt was dissolved in a 250-mL volumetric flask. A 50.0-mL aliquot was analyzed by adding 1 g of KI and titrating the liberated iodine with 23.33 mL of 0.046 68 M $Na_2S_2O_3$. Find the weight percent of Cu in the salt. Should starch indicator be added to this titration at the beginning or just before the end point?

15-27. H_2S was measured by slowly adding 25.00 mL of aqueous H_2S to 25.00 mL of acidified standard 0.010 44 M I_3^- to precipitate elemental sulfur. (If $[H_2S] > 0.01$ M, then precipitated sulfur traps some I_3^- solution, which is not subsequently titrated.) The remaining I_3^- was titrated with 14.44 mL of 0.009 336 M $Na_2S_2O_3$. Find the molarity of the H_2S solution. Should starch indicator be added to this titration at the beginning or just before the end point?

15-28. From the following reduction potentials

$$I_2(s) + 2e^- \rightleftharpoons 2I^- \qquad E^\circ = 0.535\ \text{V}$$
$$I_2(aq) + 2e^- \rightleftharpoons 2I^- \qquad E^\circ = 0.620\ \text{V}$$
$$I_3^- + 2e^- \rightleftharpoons 3I^- \qquad E^\circ = 0.535\ \text{V}$$

(a) Calculate the equilibrium constant for $I_2(aq) + I^- \rightleftharpoons I_3^-$.

(b) Calculate the equilibrium constant for $I_2(s) + I^- \rightleftharpoons I_3^-$.

(c) Calculate the solubility (g/L) of $I_2(s)$ in water.

15-29. The Kjeldahl analysis in Section 10-8 is used to measure the nitrogen content of organic compounds, which are digested in boiling sulfuric acid to decompose to ammonia, which, in turn, is distilled into standard acid. The remaining acid is then back-titrated with base. Kjeldahl himself had difficulty in 1880 discerning by lamplight the methyl red indicator end point in the back titration. He could have refrained from working at night, but instead he chose to complete the analysis differently. After distilling the ammonia into standard sulfuric acid, he added a mixture of KIO_3 and KI to the acid. The liberated iodine was then titrated with thiosulfate, using starch for easy end-point detection—even by lamplight.[31] Explain how the thiosulfate titration is related to the nitrogen content of the unknown. Derive a relationship between moles of NH_3 liberated in the digestion and moles of thiosulfate required for titration of iodine.

15-30. Some people have an allergic reaction to the food preservative sulfite (SO_3^{2-}). Sulfite in wine was measured by the following procedure: To 50.0 mL of wine were added 5.00 mL of solution containing (0.804 3 g KIO_3 + 5 g KI)/100 mL. Acidification with 1.0 mL of 6.0 M H_2SO_4 quantitatively converted IO_3^- into I_3^-. The I_3^- reacted with SO_3^{2-} to generate SO_4^{2-}, leaving excess I_3^- in solution. The excess I_3^- required 12.86 mL of 0.048 18 M $Na_2S_2O_3$ to reach a starch end point.

(a) Write the reaction that occurs when H_2SO_4 is added to KIO_3 + KI and explain why 5 g KI were added to the stock solution. Is it necessary to measure out 5 g very accurately? Is it necessary to measure 1.0 mL of H_2SO_4 very accurately?

(b) Write a balanced reaction between I_3^- and sulfite.

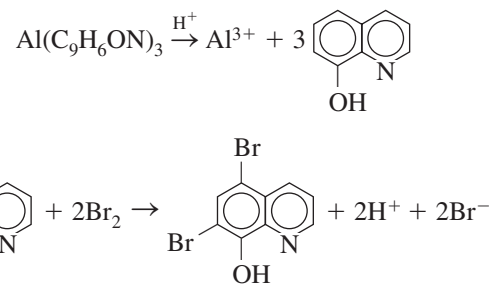
(c) Find the concentration of sulfite in the wine. Express your answer in mol/L and in mg SO_3^{2-} per liter.

(d) *t test.* Another wine was found to contain 277.7 mg SO_3^{2-}/L with a standard deviation of ±2.2 mg/L for three determinations by the iodimetric method. A spectrophotometric method gave 273.2 ± 2.1 mg/L in three determinations. Are these results significantly different at the 95% confidence level?

15-31. Potassium bromate, $KBrO_3$, is a primary standard for the generation of Br_2 in acidic solution:

$$BrO_3^- + 5Br^- + 6H^+ \rightleftharpoons 3Br_2(aq) + 3H_2O$$

The Br_2 can be used to analyze many unsaturated organic compounds. Al^{3+} was analyzed as follows: An unknown was treated with 8-hydroxyquinoline (oxine) at pH 5 to precipitate aluminum oxinate, $Al(C_9H_6ON)_3$. The precipitate was washed, dissolved in warm HCl containing excess KBr, and treated with 25.00 mL of 0.020 00 M $KBrO_3$.



The excess Br_2 was reduced with KI, which was converted into I_3^-. The I_3^- required 8.83 mL of 0.051 13 M $Na_2S_2O_3$ to reach a starch end point. How many milligrams of Al were in the unknown?

15-32. *Iodometric analysis of high-temperature superconductor.* The procedure in Box 15-3 was carried out to find the effective copper oxidation state, and therefore the number of oxygen atoms, in the formula $YBa_2Cu_3O_{7-z}$, where z ranges from 0 to 0.5.

(a) In Experiment A of Box 15-3, 1.00 g of superconductor required 4.55 mmol of $S_2O_3^{2-}$. In Experiment B, 1.00 g of superconductor required 5.68 mmol of $S_2O_3^{2-}$. Calculate the value of z in the formula $YBa_2Cu_3O_{7-z}$ (FM 666.246 – 15.999 4z).

(b) *Propagation of uncertainty.* In several replications of Experiment A, the thiosulfate required was 4.55 (±0.10) mmol of $S_2O_3^{2-}$ per gram of $YBa_2Cu_3O_{7-z}$. In Experiment B, the thiosulfate required was 5.68 (±0.05) mmol of $S_2O_3^{2-}$ per gram. Calculate the uncertainty of x in the formula $YBa_2Cu_3O_x$.

15-33. Here is a description of an analytical procedure for superconductors containing unknown quantities of Cu(I), Cu(II), Cu(III), and peroxide (O_2^{2-}):[32] "The possible trivalent copper and/or peroxide-type oxygen are reduced by Cu(I) when dissolving the sample (*ca.* 50 mg) in deoxygenated HCl solution (1 M) containing a known excess of monovalent copper ions (*ca.* 25 mg CuCl). On the other hand, if the sample itself contained monovalent copper, the amount of Cu(I) in the solution would increase upon dissolving the sample. The excess Cu(I) was then determined by coulometric back-titration . . . in an argon atmosphere." The abbreviation "*ca.*" means "approximately." *Coulometry* is an electrochemical method in which the electrons liberated in the reaction $Cu^+ \rightarrow Cu^{2+} + e^-$ are measured from the charge flowing through an electrode. Explain with your own words and equations how this analysis works.

15-34. $Li_{1+y}CoO_2$ is an anode for lithium batteries. Cobalt is present as a mixture of Co(III) and Co(II). Most preparations also contain inert lithium salts and moisture. To find the stoichiometry, Co was measured by atomic absorption and its average oxidation state was measured by a potentiometric tritration.[33] For the titration, 25.00 mg of solid were dissolved under N_2 in 5.000 mL containing 0.100 0 M Fe^{2+} in 6 M H_2SO_4 plus 6 M H_3PO_4 to give a clear pink solution:

$$Co^{3+} + Fe^{2+} \rightarrow Co^{2+} + Fe^{3+}$$

Unreacted Fe^{2+} required 3.228 mL of 0.015 93 M $K_2Cr_2O_7$ for complete titration.

(a) How many mmol of Co^{3+} are contained in 25.00 mg of the material?

(b) Atomic absorption found 56.4 wt% Co in the solid. What is the average oxidation state of Co?

(c) Find y in the formula $Li_{1+y}CoO_2$.

(d) What is the theoretical quotient wt% Li/wt% Co in the solid? The observed quotient, after washing away inert lithium salts, was 0.138 8 ± 0.000 6. Is the observed quotient consistent with the average cobalt oxidation state?

15-35. *Warning! The Surgeon General has determined that this problem is hazardous to your health.* The oxidation numbers of Cu and Bi in high-temperature superconductors of the type $Bi_2Sr_2(Ca_{0.8}Y_{0.2})Cu_2O_x$ (which could contain Cu^{2+}, Cu^{3+}, Bi^{3+}, and Bi^{5+}) can be measured by the following procedure.[34] In Experiment A, the superconductor is dissolved in 1 M HCl containing excess 2 mM CuCl. Bi^{5+} (written as BiO_3^-) and Cu^{3+} consume Cu^+ to make Cu^{2+}:

$$BiO_3^- + 2Cu^+ + 4H^+ \rightarrow BiO^+ + 2Cu^{2+} + 2H_2O \qquad \textbf{(1)}$$

$$Cu^{3+} + Cu^+ \rightarrow 2Cu^{2+} \qquad \textbf{(2)}$$

The excess, unreacted Cu^+ is then titrated by *coulometry* (described in Chapter 16). In Experiment B, the superconductor is dissolved in 1 M HCl containing excess 1 mM $FeCl_2 \cdot 4H_2O$. Bi^{5+} reacts with the Fe^{2+} but Cu^{3+} does not react with Fe^{2+}.[35]

$$BiO_3^- + 2Fe^{2+} + 4H^+ \rightarrow BiO^+ + 2Fe^{3+} + 2H_2O \qquad \textbf{(3)}$$

$$Cu^{3+} + \frac{1}{2}H_2O \rightarrow Cu^{2+} + \frac{1}{4}O_2 + H^+ \qquad \textbf{(4)}$$

The excess, unreacted Fe^{2+} is then titrated by coulometry. The total oxidation number of Cu + Bi is measured in Experiment A, and the oxidation number of Bi is determined in Experiment B. The difference gives the oxidation number of Cu.

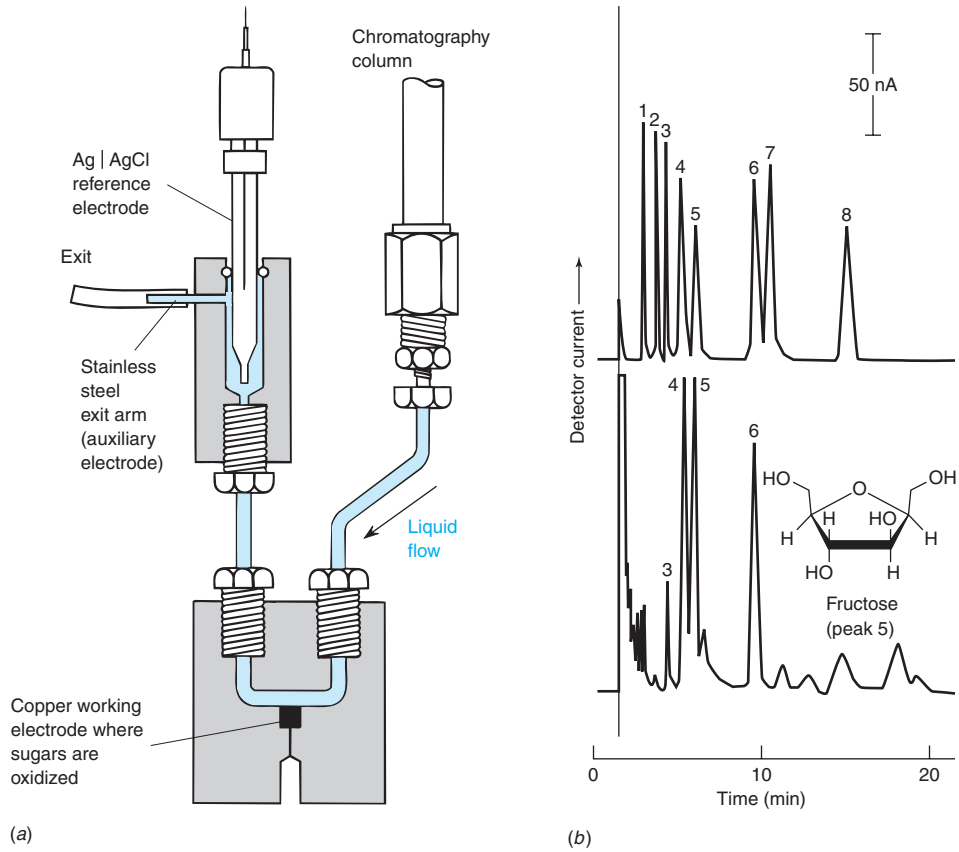
(a) In Experiment A, a sample of $Bi_2Sr_2CaCu_2O_x$ (FM 760.37 + 15.999 4x) (containing no yttrium) weighing 102.3 mg was dissolved in 100.0 mL of 1 M HCl containing 2.000 mM CuCl. After reaction with the superconductor, coulometry detected 0.108 5 mmol of unreacted Cu^+ in the solution. In Experiment B, 94.6 mg of superconductor were dissolved in 100.0 mL of 1 M HCl containing 1.000 mM $FeCl_2 \cdot 4H_2O$. After reaction with the superconductor, coulometry detected 0.057 7 mmol of unreacted Fe^{2+}. Find the average oxidation numbers of Bi and Cu in the superconductor and the oxygen stoichiometry coefficient, x.

(b) Find the uncertainties in the oxidation numbers and x if the quantities in Experiment A are 102.3 (±0.2) mg and 0.108 5 (±0.000 7) mmol and the quantities in Experiment B are 94.6 (±0.2) mg and 0.057 7 (±0.000 7) mmol. Assume negligible uncertainty in other quantities.

16 Electroanalytical Techniques

HOW SWEET IT IS!

(*a*) Electrochemical detector measures sugars emerging from a chromatography column. Sugars are oxidized at the Cu electrode, whose potential is regulated with respect to the Ag | AgCl reference electrode. Reduction ($H_2O + e^- \rightarrow \frac{1}{2}H_2 + OH^-$) occurs at the stainless steel exit arm, and electric current is measured between Cu and steel. [Adapted from Bioanalytical Systems, West Lafayette, IN.] (*b*) Anion-exchange separation of sugars in 0.1 M NaOH with CarboPac PA1 column. Upper chromatogram shows a standard mixture of (1) fucose, (2) methylglucose, (3) arabinose, (4) glucose, (5) fructose, (6) lactose, (7) sucrose, and (8) cellobiose. Lower chromatogram was obtained with Bud Dry beer diluted by a factor of 100 with water and filtered through a 0.45-μm membrane to remove particles. [From P. Luo, M. Z. Luo, and R. P. Baldwin, "Determination of Sugars in Food Products," *J. Chem. Ed.* **1993**, *70*, 679.]



You can measure sugars in your favorite beverage by separating the sugars by anion-exchange chromatography (Chapter 25) in strongly basic solution and detecting them with an electrode as they emerge from the column.[1] The —OH groups of sugars such as fructose, whose structure is shown in the chromatogram, partially dissociate to $—O^-$ anions in 0.1 M NaOH. Anions are separated from one another when they pass through a column that has fixed positive charges. As sugars emerge from the column, they are detected by oxidation at a Cu electrode poised at a potential of +0.55 V versus Ag | AgCl. The chromatogram is a graph of detector current versus time. Each sugar gives a peak whose area is proportional to the moles exiting the column.

	Sugar concentration (g/L)			
Brand	**Glucose**	**Fructose**	**Lactose**	**Maltose**
Budweiser	0.54	0.26	0.84	2.05
Bud Dry	0.14	0.29	0.46	—
Coca-Cola	45.1	68.4	—	1.04
Pepsi	44.0	42.9	—	1.06
Diet Pepsi	0.03	0.01	—	—

Electrolytic production of aluminum by the Hall-Héroult process consumes ~5% of the electrical output of the United States! Al^{3+} in a molten solution of Al_2O_3 and cryolite (Na_3AlF_6) is reduced to Al at the cathode of a cell that typically draws 250 kA. This process was invented by Charles Hall in 1886 when he was 22 years old, just after graduating from Oberlin College.[2]

Charles Martin Hall. [Courtesy of Alcoa.]

Convention: *cathodic current* is considered *positive*.

Previous chapters dealt with *potentiometry*—in which voltage was measured in the absence of significant current. Now we consider electroanalytical methods in which current is essential.[3] Techniques in this chapter are all examples of **electrolysis**—the process in which a chemical reaction is forced to occur at an electrode by an imposed voltage (Demonstration 16-1). The home glucose monitor described in this chapter, with sales of more than $3 billion in 2007, is the single largest electroanalytical application.

16-1 Fundamentals of Electrolysis

Suppose we dip Cu and Pt electrodes into a solution of Cu^{2+} and force electric current through to deposit copper metal at the cathode and to liberate O_2 at the anode.

Cathode: $$Cu^{2+} + 2e^- \rightleftharpoons Cu(s)$$

Anode: $$H_2O \rightleftharpoons \frac{1}{2}O_2(g) + 2H^+ + 2e^-$$

Net reaction: $$H_2O + Cu^{2+} \rightleftharpoons Cu(s) + \frac{1}{2}O_2(g) + 2H^+ \qquad (16\text{-}1)$$

Figure 16-1 shows how we might conduct the experiment. The potentiometer measures the voltage applied by the power source. The ammeter measures the current flowing through the circuit.

The electrode at which the reaction of interest occurs is called the **working electrode.** In Figure 16-1, we happen to be interested in reduction of Cu^{2+}, so Cu is the working electrode. The other electrode is called the *counter electrode*. We adopt the convention that *current is positive if reduction occurs at the working electrode*.

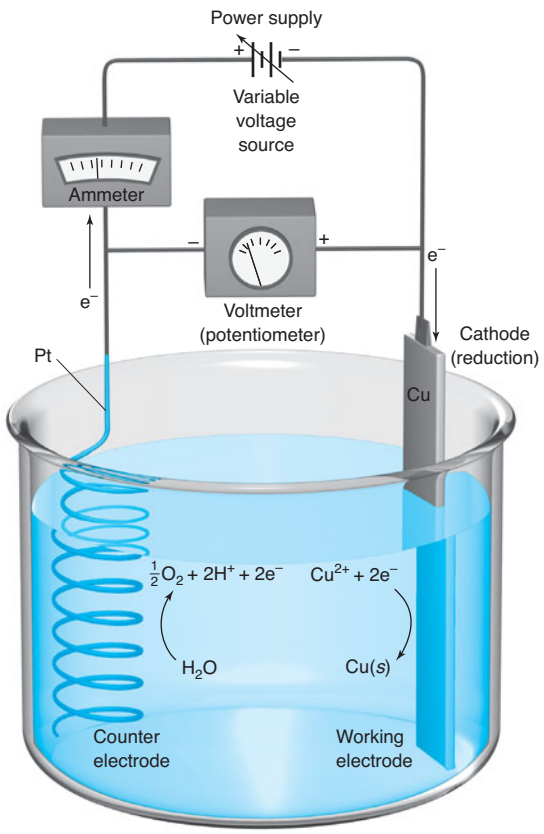


FIGURE 16-1 Electrolysis experiment. The power supply is a variable voltage source. The potentiometer measures voltage and the ammeter measures current.

Current Measures the Rate of Reaction

If a current I flows for a time t, the charge q passing any point in the circuit is

Relation of charge to current and time: $$q = I \cdot t \qquad (16\text{-}2)$$

Coulombs Amperes · Seconds

An *ampere* is an electric current of 1 coulomb per second.

A *coulomb* contains $6.241\ 5 \times 10^{18}$ electrons.

The number of moles of electrons is

$$\text{Moles of } e^- = \frac{\text{coulombs}}{\text{coulombs/mole}} = \frac{I \cdot t}{F}.$$

Faraday constant:
$F = 9.648\,5 \times 10^4$ C/mol

moles of electrons $= \dfrac{I \cdot t}{F}$

If a reaction requires n electrons per molecule, the quantity reacting in time t is

Relation of moles to current and time:

$$\text{Moles reacted} = \frac{I \cdot t}{nF} \qquad \textbf{(16-3)}$$

EXAMPLE **Relating Current, Time, and Amount of Reaction**

If a current of 0.17 A flows for 16 min through the cell in Figure 16-1, how many grams of Cu(s) will be deposited?

Solution We first calculate the moles of e^- flowing through the cell:

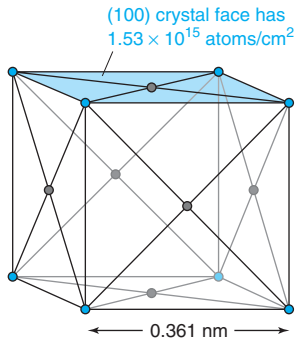
$$\text{Moles of } e^- = \frac{I \cdot t}{F} = \frac{\left(0.17\,\frac{\text{C}}{\text{s}}\right)(16\text{ min})\left(60\,\frac{\text{s}}{\text{min}}\right)}{96\,485\left(\frac{\text{C}}{\text{mol}}\right)} = 1.6_9 \times 10^{-3}\text{ mol}$$

The cathode half-reaction requires $2e^-$ for each Cu deposited. Therefore,

$$\text{Moles of Cu}(s) = \frac{1}{2}(\text{moles of } e^-) = 8.4_5 \times 10^{-4}\text{ mol}$$

The mass of Cu(s) deposited is $(8.4_5 \times 10^{-4}\text{ mol})(63.546\text{ g/mol}) = 0.054$ g.

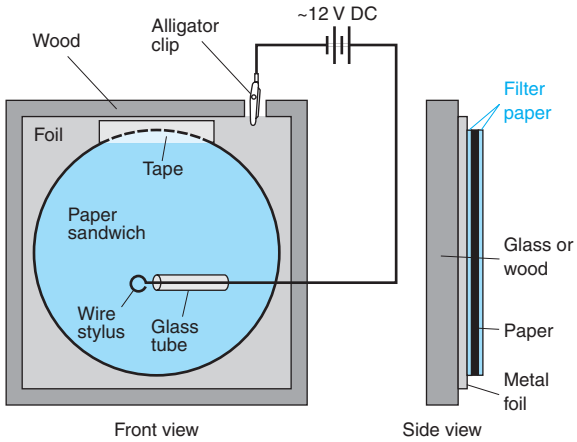
Test Yourself A *monolayer* (single layer of atoms) of Cu on the crystal face shown in the margin has 1.53×10^{15} atoms/cm^2 $= 2.54 \times 10^{-9}$ mol/cm^2. What current can deposit one layer of Cu atoms on 1 cm^2 in 1 s? (***Answer:*** 0.490 mA)



Face-centered cubic crystal

DEMONSTRATION 16-1 **Electrochemical Writing**[4]

Approximately 7% of electric power in the United States goes into electrolytic chemical production. The electrolysis apparatus pictured here consists of a sheet of Al foil taped or cemented to a wood surface. Any size will work, but an area of 15 cm on a side is convenient for a classroom demonstration. Tape to the metal foil (at one edge only) a sandwich consisting of filter paper, printer paper, and another sheet of filter paper. Make a stylus from Cu wire (18 gauge or thicker) looped at one end and passed through a length of glass tubing.



Prepare a fresh solution from 1.6 g of KI, 20 mL of water, 5 mL of 1 wt% starch solution, and 5 mL of phenolphthalein indicator solution. (If the solution darkens after several days, decolorize it with a few drops of dilute $Na_2S_2O_3$.) Soak the three layers of paper with the KI-starch-phenolphthalein solution. Connect the stylus and foil to a 12 V DC power source, and write on the paper with the stylus.

When the stylus is the cathode, water is reduced to H_2 plus OH^- and pink color appears from the reaction of OH^- with phenolphthalein.

$$\text{Cathode:} \qquad H_2O + e^- \rightarrow \frac{1}{2}H_2(g) + OH^-$$

When the polarity is reversed and the stylus is the anode, I^- is oxidized to I_2; a black (very dark blue) color appears from the reaction of I_2 with starch.

$$\text{Anode:} \qquad I^- \rightarrow \frac{1}{2}I_2 + e^-$$

Pick up the top sheet of filter paper and the printer paper, and you will discover that the writing appears in the opposite color on the bottom sheet of filter paper (Color Plate 10).

Voltage Changes When Current Flows

Figure 16-1 is drawn with the same conventions as Figures 13-4 and 13-6. The cathode—where reduction occurs—is at the right side of the figure. The positive terminal of the potentiometer is on the right-hand side.

If electric current is negligible, the cell voltage is

$$E = E(\text{cathode}) - E(\text{anode}) \tag{16-4}$$

To use $E = E(\text{cathode}) - E(\text{anode})$, you must write both reactions as *reductions*. $E(\text{cathode}) - E(\text{anode})$ is the *open-circuit* voltage. It is the voltage measured with negligible current flowing between cathode and anode.

The *cathode* is the electrode connected to the *negative* terminal of the power supply.

In Chapter 13, we wrote $E = E_+ - E_-$, where E_+ is the potential of the electrode attached to the positive terminal of the potentiometer and E_- is the potential of the electrode attached to the negative terminal of the potentiometer. Equation 16-4 is equivalent to $E = E_+ - E_-$. The polarity of the potentiometer in Figure 16-1 is the same as in Figures 13-4 and 13-6. In an electrolysis, electrons come from the negative terminal of the power supply into the cathode of the electrolysis cell. $E(\text{cathode})$ is the potential of the electrode connected to the negative terminal of the power supply, and $E(\text{anode})$ is the potential of the electrode connected to the positive terminal of the power supply.

If Reaction 16-1 contains 0.20 M Cu^{2+} and 1.0 M H^+ and liberates O_2 at a pressure of 1.0 bar, we find

$$E = \underbrace{\left\{0.339 - \frac{0.059\,16}{2}\log\left(\frac{1}{[Cu^{2+}]}\right)\right\}}_{E\ (\text{cathode})} - \underbrace{\left\{1.229 - \frac{0.059\,16}{2}\log\left(\frac{1}{P_{O_2}^{1/2}[H^+]^2}\right)\right\}}_{E\ (\text{anode})}$$

$$= \left\{0.339 - \frac{0.059\,16}{2}\log\left(\frac{1}{[0.20]}\right)\right\} - \left\{1.229 - \frac{0.059\,16}{2}\log\left(\frac{1}{(1.0)^{1/2}[1.0]^2}\right)\right\}$$

$$= 0.318 - 1.229 = -0.911\ \text{V}$$

Free energy change for Reaction 16-1:

$$\Delta G = -nFE = -nF(-0.911\ \text{V})$$
$$= -(2)\left(96\,485\ \frac{\text{C}}{\text{mol}}\right)(-0.911\ \text{V})$$
$$= +1.76 \times 10^5\ \text{C}\cdot\text{V/mol}$$
$$= +1.76 \times 10^5\ \text{J/mol} = 176\ \text{kJ/mol}$$

Note that C × V = J

This voltage would be read on the potentiometer in Figure 16-1 if there were negligible current. The voltage is negative because the positive terminal of the potentiometer is connected to the negative side of the power supply. The free energy change computed in the margin is positive because the reaction is not spontaneous. We need the power supply to force the reaction to occur. If current is not negligible, *overpotential*, *ohmic potential*, and *concentration polarization* can change the voltage required to drive the reaction.

Overpotential is the voltage required to overcome the *activation energy* for a reaction at an electrode (Figure 16-2).[5] The faster you wish to drive the reaction, the greater the overpotential that must be applied. Electric current measures the rate of electron transfer. Applying a greater overpotential will sustain a higher *current density* (current per unit area of electrode surface, A/m^2). Table 16-1 shows that the overpotential for liberation of H_2 at a Cu surface must be increased from 0.479 to 1.254 V to increase the current density from 10 A/m^2 to 10 000 A/m^2. Activation energy depends on the nature of the surface. H_2 is evolved at a Pt surface with little overpotential, whereas a Hg surface requires ~1 V to drive the reaction.

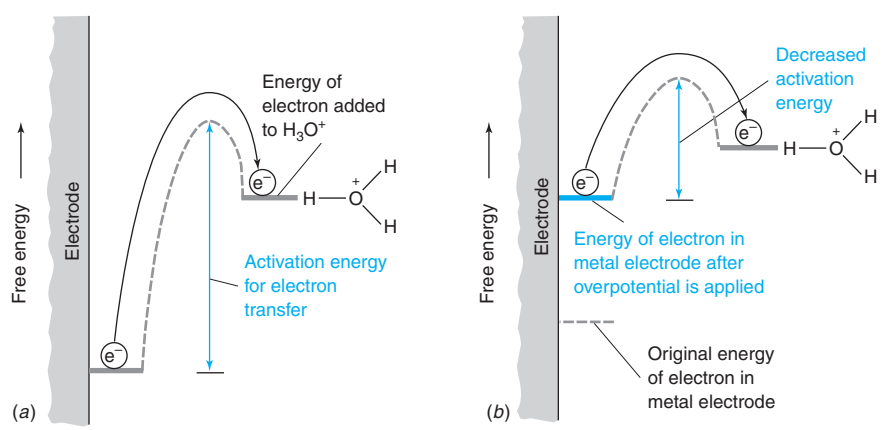


FIGURE 16-2 (*a*) Schematic energy profile for electron transfer from a metal to H_3O^+, leading to liberation of H_2. (*b*) Applying a potential to the metal raises the energy of the electron in the metal and decreases the activation energy for electron transfer.

Ohmic potential is the voltage needed to overcome electrical resistance, R, of the solution in the electrochemical cell when a current, I, is flowing:

Ohmic potential: $$E_{\text{ohmic}} = IR \tag{16-5}$$

TABLE 16-1 Overpotential (V) for gas evolution at various current densities (A/m^2) at 25°C

	10 A/m^2		100 A/m^2		1 000 A/m^2		10 000 A/m^2	
Electrode	H_2	O_2	H_2	O_2	H_2	O_2	H_2	O_2
Platinized Pt	0.015 4	0.398	0.030 0	0.521	0.040 5	0.638	0.048 3	0.766
Smooth Pt	0.024	0.721	0.068	0.85	0.288	1.28	0.676	1.49
Cu	0.479	0.422	0.584	0.580	0.801	0.660	1.254	0.793
Ag	0.475 1	0.580	0.761 8	0.729	0.874 9	0.984	1.089 0	1.131
Au	0.241	0.673	0.390	0.963	0.588	1.244	0.798	1.63
Graphite	0.599 5		0.778 8		0.977 4		1.220 0	
Pb	0.52		1.090		1.179		1.262	
Zn	0.716		0.746		1.064		1.229	
Hg	0.9		1.0		1.1		1.1	

SOURCE: *International Critical Tables*, **1929**, *6, 339. This reference also gives overpotentials for Cl_2, Br_2, and I_2.*

If the cell has a resistance of 2 ohms and a current of 20 mA is flowing, the voltage required to overcome the resistance is $E = (2\ \Omega)(20\ \text{mA}) = 0.040$ V.

Resistance is measured in ohms, whose symbol is capital Greek omega, Ω.

Concentration polarization occurs when the concentrations of reactants or products are not the same at the surface of the electrode as they are in bulk solution. For Reaction 16-1, the Nernst equation should be written

$$E(\text{cathode}) = 0.339 - \frac{0.059\ 16}{2}\log\left(\frac{1}{[Cu^{2+}]_s}\right)$$

Electrodes respond to concentrations of reactants and products adjacent to the electrode, not to concentrations in the bulk solution.

where $[Cu^{2+}]_s$ is the concentration in the solution *at the surface of the electrode*. If reduction of Cu^{2+} occurs rapidly, $[Cu^{2+}]_s$ could be very small because Cu^{2+} cannot diffuse to the electrode as fast as it is consumed. As $[Cu^{2+}]_s$ decreases, E(cathode) becomes more negative.

If $[Cu^{2+}]_s$ were reduced from 0.2 M to 2 μM, E(cathode) would change from 0.318 to 0.170 V.

Overpotential, ohmic potential, and concentration polarization make electrolysis more difficult. They drive the cell voltage more negative, requiring more voltage from the power supply in Figure 16-1 to drive the reaction forward.

$$E = \underbrace{E(\text{cathode}) - E(\text{anode})}_{\text{These terms include the effects of concentration polarization}} - IR - \text{overpotentials} \qquad \textbf{(16-6)}$$

There can be concentration polarization and overpotential at both the cathode and the anode.

EXAMPLE Effects of Ohmic Potential, Overpotential, and Concentration Polarization

Suppose we wish to electrolyze I^- to I_3^- in a 0.10 M KI solution containing 3.0×10^{-5} M I_3^- at pH 10.00 with P_{H_2} fixed at 1.00 bar.

$$3I^- + 2H_2O \rightarrow I_3^- + H_2(g) + 2OH^-$$

(a) Find the cell voltage if no current is flowing. **(b)** Then suppose that electrolysis increases $[I_3^-]_s$ to 3.0×10^{-4} M, but other concentrations are unaffected. Suppose that the cell resistance is 2.0 Ω, the current is 63 mA, the cathode overpotential is 0.382 V, and the anode overpotential is 0.025 V. What voltage is needed to drive the reaction?

Solution **(a)** The open-circuit voltage is E(cathode) − E(anode):

Cathode: $2H_2O + 2e^- \rightarrow H_2(g) + 2OH^-$ $\quad E° = -0.828$ V

Anode: $I_3^- + 2e^- \rightarrow 3I^-$ $\quad E° = 0.535$ V

$$E(\text{cathode}) = -0.828 - \frac{0.059\ 16}{2}\log(P_{H_2}[OH^-]^2)$$

$$= -0.828 - \frac{0.059\ 16}{2}\log[(1.00)(1.0 \times 10^{-4})^2] = -0.591\ \text{V}$$

$$E(\text{anode}) = 0.535 - \frac{0.059\,16}{2}\log\left(\frac{[I^-]^3}{[I_3^-]}\right)$$

$$= 0.535 - \frac{0.059\,16}{2}\log\left(\frac{[0.10]^3}{[3.0 \times 10^{-5}]}\right) = 0.490 \text{ V}$$

$$E = E(\text{cathode}) - E(\text{anode}) = -1.081 \text{ V}$$

We would have to apply −1.081 V to force the reaction to occur.

(b) Now E(cathode) is unchanged but E(anode) changes because $[I_3^-]_s$ is different from $[I_3^-]$ in bulk solution.

$$E(\text{anode}) = 0.535 - \frac{0.059\,16}{2}\log\left(\frac{[0.10]^3}{[3.0 \times 10^{-4}]}\right) = 0.520 \text{ V}$$

$$E = E(\text{cathode}) - E(\text{anode}) - IR - \text{overpotentials}$$

$$= -0.591 \text{ V} - 0.520 \text{ V} - (2.0\ \Omega)(0.063 \text{ A}) - 0.382 \text{ V} - 0.025 \text{ V}$$

$$= -1.644 \text{ V}$$

Instead of −1.081 V, we need to apply −1.644 V to drive the reaction.

Test Yourself Find the voltage in part **(b)** if $[I^-]_s = 0.01$ M. (***Answer:*** −1.732 V)

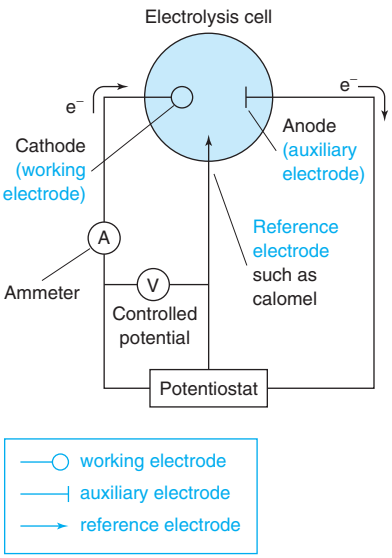


FIGURE 16-3 Circuit used for controlled-potential electrolysis with a three-electrode cell.

Controlled-Potential Electrolysis with a Three-Electrode Cell

An **electroactive species** is one that can be oxidized or reduced at an electrode. We regulate the potential of the working electrode to control which species react and which do not. Metal electrodes are said to be **polarizable,** which means that their potentials are easily changed when small currents flow. A reference electrode such as calomel or Ag | AgCl is said to be **nonpolarizable,** because its potential does not vary much unless a significant current is flowing. Ideally, we want to measure the potential of a polarizable working electrode with respect to a nonpolarizable reference electrode. How can we do this if there is to be significant current at the working electrode and negligible current at the reference electrode?

The answer is to introduce a third electrode (Figure 16-3). The **working electrode** is the one at which the reaction of interest occurs. A calomel or other **reference electrode** is used to measure the potential of the working electrode. The **auxiliary electrode** (also called the *counter electrode*) is the current-supporting partner of the working electrode. Current flows between the working and the auxiliary electrodes. Negligible current flows through the reference electrode, so its potential is unaffected by ohmic potential, concentration polarization, and overpotential. It truly maintains a constant reference potential. In **controlled-potential electrolysis,** the voltage difference between the working and reference electrodes in a three-electrode cell is regulated by an electronic device called a **potentiostat.**

Concentration polarization and overpotential can both occur at the working and auxiliary electrodes. There is an ohmic potential drop between the working and auxiliary electrodes. To obtain the best measurement of the working electrode potential, the reference electrode should be placed as close as possible to the working electrode (Figure 16-4).

Working electrode: where the analytical reaction occurs

Auxiliary electrode: the other electrode needed for current flow

Reference electrode: used to measure the potential of the working electrode

The chromatographic detector at the opening of this chapter has a Cu working electrode, a stainless steel auxiliary electrode, and a Ag | AgCl reference electrode.

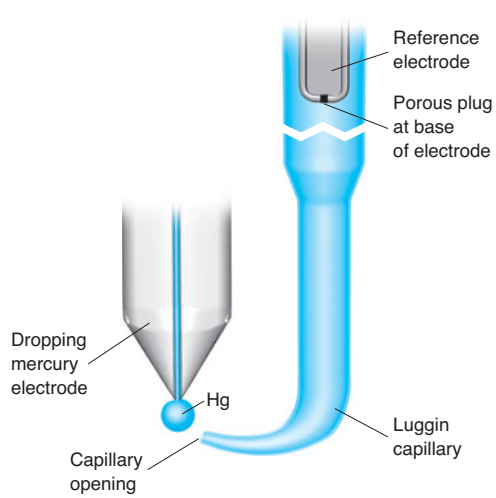


FIGURE 16-4 Use of a Luggin capillary to position a reference electrode as close as possible to the working electrode (shown as a dropping mercury electrode in this illustration). The capillary, with an opening of ~0.2 mm, is filled with the same electrolyte that is in the analyte solution. The reference electrode is in contact with the capillary solution. There is negligible current in the capillary, so there is negligible ohmic loss between the tip of the capillary and the reference electrode.

16-2 Electrogravimetric Analysis

In **electrogravimetric analysis,** analyte is quantitatively deposited on an electrode by electrolysis. The electrode is weighed before and after deposition. The increase in mass tells us how much analyte was deposited. We can measure Cu^{2+} in a solution by reducing it to Cu(*s*) on a clean Pt gauze cathode with a large surface area (Figure 16-5). O_2 is liberated at the counter electrode.

How do you know when electrolysis is complete? One way is to observe the disappearance of color in a solution from which a colored species such as Cu^{2+} or Co^{2+} is removed. Another way is to expose most, but not all, of the surface of the cathode to the solution during electrolysis. To test whether or not the reaction is complete, raise the beaker or add water so that fresh surface of the cathode is exposed to the solution. After an additional period of electrolysis (15 min, say), see if the newly exposed electrode surface has a deposit. If it does, repeat the procedure. If not, the electrolysis is done. A third method is to remove a drop of solution and perform a qualitative test for analyte.

Tests for completion of the deposition:

- disappearance of color
- no deposition on freshly exposed electrode surface
- qualitative test for analyte in solution

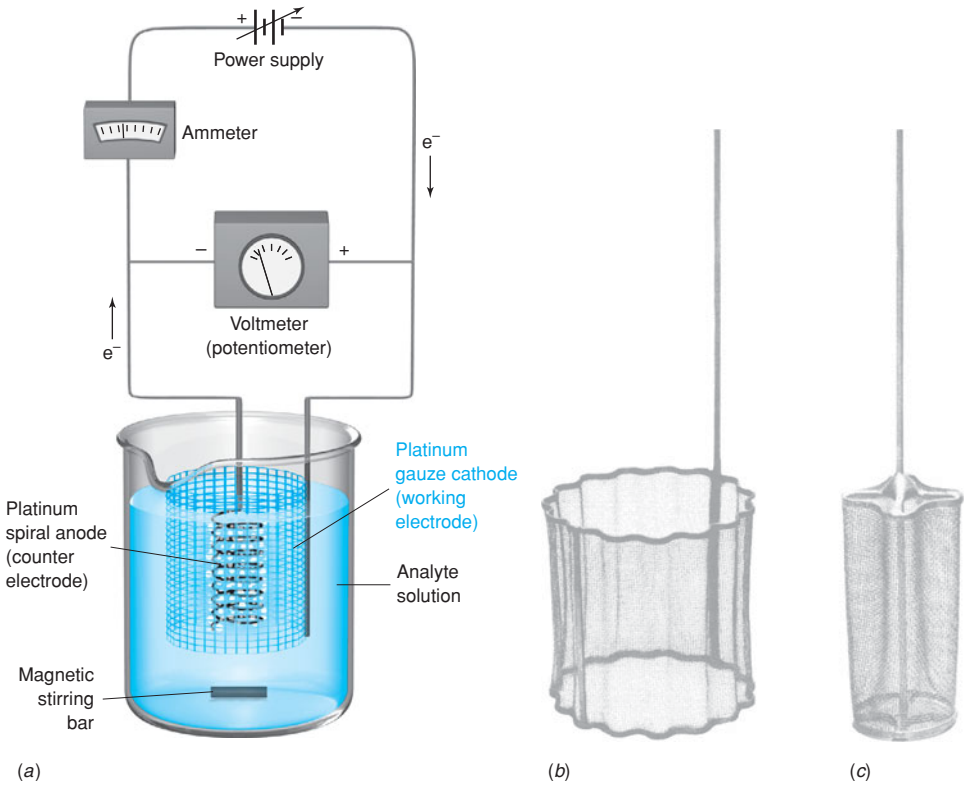


FIGURE 16-5 (*a*) Electrogravimetric analysis. Analyte is deposited on the large Pt gauze electrode. If analyte is to be oxidized, rather than reduced, the polarity of the power supply is reversed so that deposition still occurs on the large electrode. (*b*) Outer Pt gauze electrode. (*c*) Optional inner Pt gauze electrode designed to be spun by a motor in place of magnetic stirring.

In the preceding section, we calculated that −0.911 V needs to be applied between the electrodes to deposit Cu(*s*) on the cathode. The actual behavior of the electrolysis in Figure 16-6 shows that nothing special happens at −0.911 V. Near −2 V, the reaction begins in earnest. At low voltage, a small *residual current* is observed from reduction at the cathode and an equal amount of oxidation at the anode. Reduction might involve traces of dissolved O_2, impurities such as Fe^{3+}, or surface oxide on the electrode.

Table 16-1 shows that an overpotential of ~1 V is required for O_2 formation at the smooth Pt anode. Overpotential is the main reason why not much happens in Figure 16-6 until −2 V is applied. Beyond −2 V, the rate of reaction (the current) increases steadily. Around −4.6 V, the current increases more rapidly with the onset of reduction of H_3O^+ to H_2. Gas bubbles at the working electrode interfere with deposition of solids.

The voltage between the two electrodes is

$$E = E(\text{cathode}) - E(\text{anode}) - IR - \text{overpotentials} \qquad \textbf{(16-6)}$$

Suppose we hold the applied potential at $E = -2.0$ V. As Cu^{2+} is used up, the current decreases and both ohmic and overpotentials decrease in magnitude. E(anode) is fairly

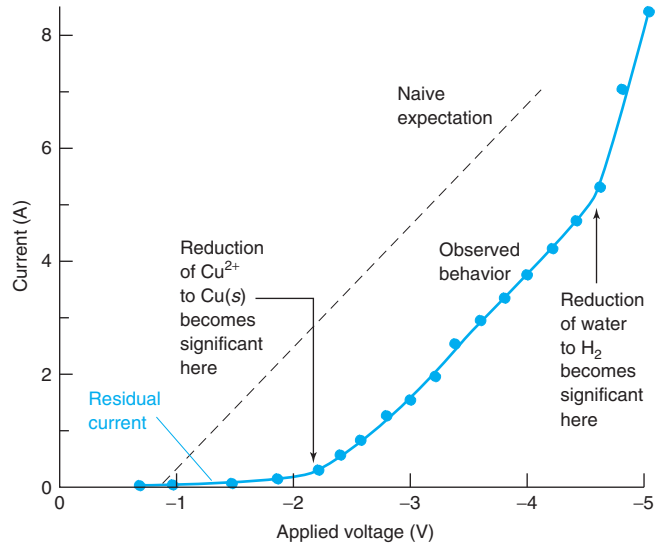


FIGURE 16-6 Observed current-voltage relation for electrolysis of 0.2 M $CuSO_4$ in 1 M $HClO_4$ under N_2, using the apparatus in Figure 16-5.

constant because of the high concentration of solvent being oxidized at the anode ($H_2O \rightarrow \frac{1}{2}O_2 + 2H^+ + 2e^-$). If E and E(anode) are constant and if IR and overpotentials decrease in magnitude, then *E(cathode) must become more negative* to maintain the algebraic equality in Equation 16-6. E(cathode) drops in Figure 16-7 to -0.4 V, at which H_3O^+ is reduced to H_2. As E(cathode) falls from $+0.3$ V to -0.4 V, other ions such as Co^{2+}, Sn^{2+}, and Ni^{2+} can be reduced. In general, then, *when the applied voltage is constant, the cathode potential drifts to more negative values and other solutes might be reduced.*

A *cathodic depolarizer* is reduced in preference to solvent. For *oxidation* reactions, *anodic depolarizers* include N_2H_4 (hydrazine) and NH_2OH (hydroxylamine).

To prevent the cathode potential from becoming so negative that unintended ions are reduced, a cathodic **depolarizer** such as NO_3^- can be added to the solution. The cathodic depolarizer is more easily reduced than H_3O^+:

$$NO_3^- + 10H^+ + 8e^- \rightarrow NH_4^+ + 3H_2O$$

Alternatively, we can use a three-electrode cell (Figure 16-3) with a potentiostat to control the cathode potential and prevent unwanted side reactions.

EXAMPLE Controlled-Potential Electrolysis

What cathode potential is required to reduce 99.99% of 0.10 M Cu^{2+} to Cu(*s*)? Is it possible to remove this Cu^{2+} without reducing 0.10 M Sn^{2+} in the same solution?

$$Cu^{2+} + 2e^- \rightleftharpoons Cu(s) \qquad E^\circ = 0.339 \text{ V} \tag{16-7}$$

$$Sn^{2+} + 2e^- \rightleftharpoons Sn(s) \qquad E^\circ = -0.141 \text{ V} \tag{16-8}$$

Solution If 99.99% of Cu^{2+} were reduced, the concentration of remaining Cu^{2+} would be 1.0×10^{-5} M, and the required cathode potential would be

$$E(\text{cathode}) = 0.339 - \frac{0.059\,16}{2}\log\left(\frac{1}{\underbrace{1.0 \times 10^{-5}}_{[Cu^{2+}]}}\right) = 0.19 \text{ V}$$

The cathode potential required to reduce Sn^{2+} is

$$E(\text{cathode, for reduction of } Sn^{2+}) = -0.141 - \frac{0.059\,16}{2}\log\left(\frac{1}{\underbrace{0.10}_{[Sn^{2+}]}}\right) = -0.17 \text{ V}$$

We do not expect reduction of Sn^{2+} at a cathode potential more positive than -0.17 V. The reduction of 99.99% of Cu^{2+} without reducing Sn^{2+} appears feasible.

Test Yourself Will E(cathode) = 0.19 V reduce 0.10 M SbO^+ at pH 2 by the reaction $SbO^+ + 2H^+ + 3e^- \rightleftharpoons Sb(s) + H_2O$, $E^\circ = 0.208$ V? (***Answer:*** E(cathode) for SbO^+ = 0.11 V, so reduction should not occur at 0.19 V)

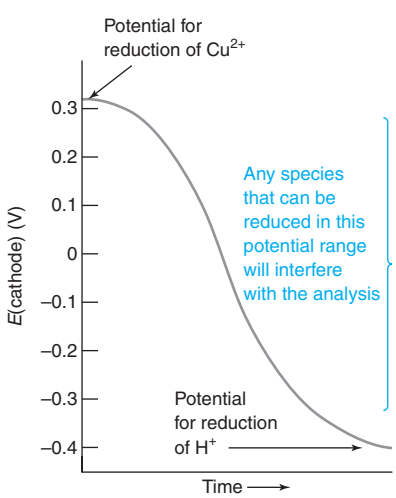
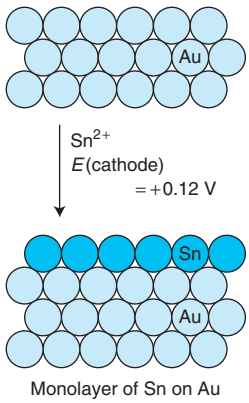


FIGURE 16-7 E(cathode) becomes more negative with time when electrolysis is conducted in a two-electrode cell with a constant voltage between the electrodes.

Underpotential Deposition

When Sn^{2+} in 1 M HCl is electrolyzed at a gold working electrode, reduction is observed at E(cathode) = −0.18 V by the technique of cyclic voltammetry, which we study later in this chapter. From what you know so far, you should not expect that potentials more positive than −0.18 V will reduce Sn^{2+}. Yet, a small current is observed at E(cathode) = +0.12 V. The coulombs required at −0.18 V increase in proportion to $[Sn^{2+}]$. The coulombs required at +0.12 V are just enough to produce 8.7×10^{-10} mol Sn(s) per square centimeter of gold electrode surface.[6] Then no more current flows at E(cathode) = +0.12 V.



Reduction at +0.12 V is called **underpotential deposition.** It occurs at a potential that is not predicted to reduce Sn^{2+} to bulk Sn(s). It is explained by the reaction

$$Sn^{2+} + 2e^- \rightleftharpoons Sn(\textit{monolayer on Au}) \qquad \textbf{(16-9)}$$

in which the product is a one-atom-thick layer of tin on gold. It is thermodynamically more favorable to deposit a layer of tin atoms on gold than it is to deposit a fresh layer of tin on bulk tin metal. Therefore, the potential for Reaction 16-9 is more positive than the potential for Reaction 16-8.

16-3 Coulometry

Coulometry is a chemical analysis based on counting the electrons used in a reaction. For example, cyclohexene can be titrated with Br_2 generated by electrolytic oxidation of Br^-:

Coulometric methods are based on measuring the number of electrons that participate in a chemical reaction.

$$2Br^- \rightarrow Br_2 + 2e^- \qquad \textbf{(16-10)}$$

Cyclohexene *trans*-1,2-Dibromocyclohexane **(16-11)**

The initial solution contains an unknown quantity of cyclohexene and a large amount of Br^-. When Reaction 16-10 has generated just enough Br_2 to react with all the cyclohexene, the moles of electrons liberated in Reaction 16-10 are equal to twice the moles of Br_2 and therefore twice the moles of cyclohexene.

The reaction is carried out *at a constant current* with the apparatus in Figure 16-8. Br_2 generated at the Pt anode at the left reacts with cyclohexene. When cyclohexene is consumed, the concentration of Br_2 suddenly rises, signaling the end of the reaction.

The rise in Br_2 concentration is detected by measuring the current between the two detector electrodes at the right in Figure 16-8. A voltage of 0.25 V applied between these two electrodes is not enough to electrolyze any solute, so only a tiny current of <1 μA flows through

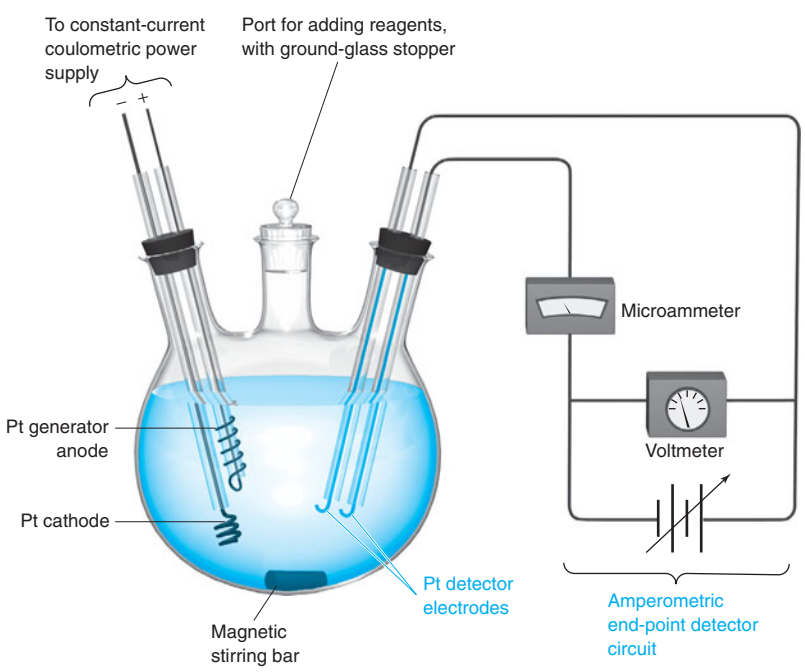


FIGURE 16-8 Apparatus for coulometric titration of cyclohexene with Br_2. The solution contains cyclohexene, 0.15 M KBr, and 3 mM mercuric acetate in a mixed solvent of acetic acid, methanol, and water. Mercuric acetate catalyzes the addition of Br_2 to the olefin. [Adapted from D. H. Evans, "Coulometric Titration of Cyclohexene with Bromine," *J. Chem. Ed.* **1968**, *45*, 88.]

the microammeter. At the equivalence point, cyclohexene is consumed, $[Br_2]$ suddenly increases, and detector current flows by virtue of the reactions:

Both Br_2 and Br^- must be present for the detector half-reactions to occur. Prior to the equivalence point, there is Br^-, but virtually no Br_2.

$$\text{Detector anode:} \quad 2Br^- \rightarrow Br_2 + 2e^-$$
$$\text{Detector cathode:} \quad Br_2 + 2e^- \rightarrow 2Br^-$$

In practice, enough Br_2 is first generated in the absence of cyclohexene to give a detector current of 20.0 μA. When cyclohexene is added, the current decreases to a tiny value because Br_2 is consumed. Br_2 is then generated by the coulometric circuit, and the end point is taken when the detector again reaches 20.0 μA. Because the reaction is begun with Br_2 present, impurities that can react with Br_2 before analyte is added are eliminated.

The electrolysis current (not to be confused with the detector current) for the Br_2-generating electrodes is controlled by a hand-operated switch. As the detector current approaches 20.0 μA, you close the switch for shorter and shorter intervals. This practice is analogous to adding titrant dropwise from a buret near the end of a titration. The switch in the coulometer circuit serves as a "stopcock" for addition of Br_2 to the reaction. Modern instruments automate the entire procedure.

EXAMPLE **Coulometric Titration**

A 2.000-mL volume containing 0.611 3 mg of cyclohexene/mL is to be titrated in Figure 16-8. How much time is required for titration at a constant current of 4.825 mA?

Solution The moles of cyclohexene are

$$\frac{(2.000\text{ mL})(0.611\,3\text{ mg/mL})}{(82.146\text{ mg/mmol})} = 0.014\,88\text{ mmol}$$

In Reactions 16-10 and 16-11, each mole of cyclohexene requires 1 mol of Br_2, which requires 2 mol of electrons. For 0.014 88 mmol of cyclohexene to react, 0.029 76 mmol of electrons must flow. From Equation 16-3,

$$\text{Moles of } e^- = \frac{I \cdot t}{F} \Rightarrow t = \frac{(\text{moles of } e^-)F}{I}$$

$$t = \frac{(0.029\,76 \times 10^{-3}\text{mol})(96\,485\text{ C/mol})}{(4.825 \times 10^{-3}\text{ C/s})} = 595.1\text{ s}$$

It will require just under 10 min to complete the reaction.

Test Yourself How much time is required to titrate 1.000 mg of cyclohexene at 4.000 mA? (***Answer:*** 587.3 s)

Advantages of coulometry:

- precision
- sensitivity
- generation of unstable reagents in situ

The Latin *in situ* means "in place." Reagent is used right where it is generated.

Commercial coulometers deliver electrons with an accuracy of ~0.1%. With extreme care, the Faraday constant has been measured to within several parts per million by coulometry.[7] Automated coulometers commonly generate H^+, OH^-, Ag^+, and I_2 to titrate analytes including CO_2, sulfites in food, and sulfide in wastewater.[8] Unstable reagents such as Ag^{2+}, Cu^+, Mn^{3+}, and Ti^{3+} can be generated and used in situ.

In Figure 16-8, the reactive species (Br_2) is generated at the anode. The cathode products (H_2 from solvent and Hg from the catalyst) do not interfere with the reaction of Br_2 and cyclohexene. In some cases, however, H_2 or Hg could react with analyte. Then it is desirable to separate the counter electrode from the analyte, using the cell in Figure 16-9. H_2 bubbles innocuously out of the cathode chamber without mixing with the bulk solution.

Types of Coulometry

Coulometry employs either a *constant current* or a *controlled potential*. Constant-current methods, like the preceding Br_2/cyclohexene example, are called **coulometric titrations.** If we know the current and the time of reaction, we know how many coulombs have been delivered from Equation 16-2: $q = I \cdot t$.

Controlled-potential coulometry in a three-electrode cell is more selective than constant-current coulometry. Because the working electrode potential is constant, current decreases exponentially as analyte concentration decreases. Charge is measured by integrating current over the time of the reaction:

The number of coulombs is equal to the area under a curve of current versus time. Problem 16-21 provides an example.

$$q = \int_0^t I\,dt \qquad \textbf{(16-12)}$$

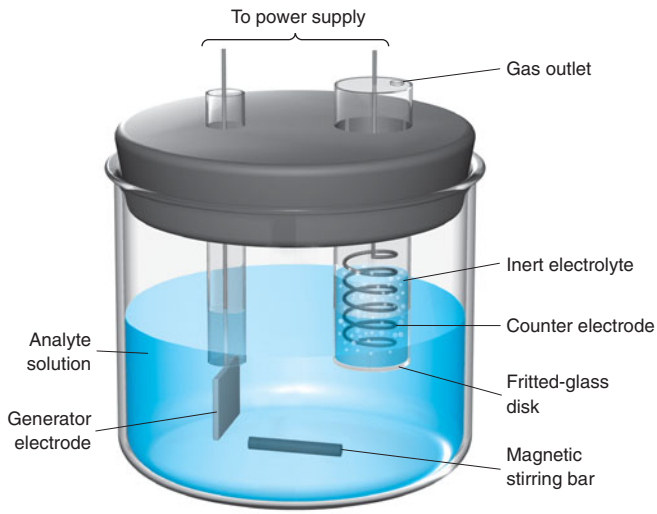


FIGURE 16-9 Isolating the counter electrode from analyte. Ions can flow through the porous fritted-glass disk. The liquid level in the counter electrode compartment should be higher than the liquid in the reactor so that analyte solution does not flow into the compartment.

In controlled-potential coulometry, current decays exponentially. You can approach the equivalence point by letting the current decay to a set value. For example, the current (*above* the residual current) will ideally be 0.1% of its initial value when 99.9% of the analyte has been consumed. Alternatively, the current versus time curve can be extrapolated according to its theoretical behavior after measuring its actual behavior for some time.

16-4 Amperometry

In **amperometry,** we measure the electric current between a pair of electrodes that are driving an electrolysis reaction. One reactant is the intended analyte, and the measured current is proportional to the concentration of analyte. The measurement of dissolved O_2 with the **Clark electrode** in Box 16-1 is based on amperometry. A different kind of sensor based on conductivity—the "electronic nose"—is described in Box 16-2.

Amperometry: Electric current is proportional to the concentration of analyte.

Coulometry: Total number of electrons used for a reaction tells us how much analyte is present.

Box 16-1 Clark Oxygen Electrode

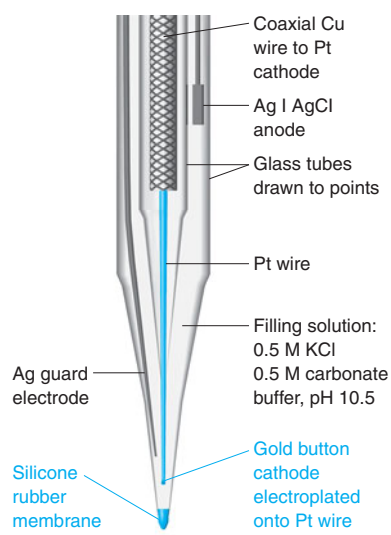
The Clark oxygen electrode[9] is widely used in medicine and biology to measure dissolved oxygen by amperometry. Leland Clark, who invented the electrode, also invented the glucose monitor and the heart-lung machine.

The glass body of the microelectrode in the figure is drawn to a fine point with a 5-μm opening at the base. Inside the opening is a 10- to 40-μm-long plug of silicone rubber, which is permeable to O_2. Oxygen diffuses into the electrode through the rubber and is reduced at the Au tip on the Pt wire, which is held at −0.75 V with respect to the Ag | AgCl reference electrode:

Pt | Au cathode: $O_2 + 4H^+ + 4e^- \rightarrow 2H_2O$

Ag | AgCl anode: $4Ag + 4Cl^- \rightarrow 4AgCl + 4e^-$

A Clark electrode is calibrated by placing it in solutions of known O_2 concentration, and a graph of current versus $[O_2]$ is constructed. The electrode also contains a silver *guard electrode* extending most of the way to the bottom. The guard electrode is kept at a negative potential so that any O_2 diffusing in from the top of the electrode is reduced and does not interfere with measurement of O_2 diffusing in through the silicone membrane at the bottom. Similar electrodes have been designed for detection of NO, H_2S, and CO.[10]

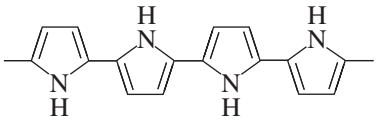


Clark oxygen microelectrode used to measure dissolved O_2 in small volumes. The tip of the cathode is plated with Au, which is less prone than Pt to fouling by adsorption of species from the test solution. [Adapted from N. P. Revsbech, "An Oxygen Microsensor with a Guard Column," *Limnol. Oceanogr.* **1989,** *34*, 474.]

Box 16-2 What Is An "Electronic Nose"?

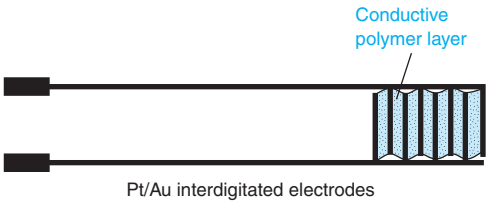
In the "old days," chemists prided themselves on their ability to identify compounds by odor. Smelling unknown chemicals is a bad idea because some vapors are toxic. Chemists are developing "electronic noses" that recognize odors to assess the freshness of meat, to find out if fruit is internally bruised, and to detect adulteration of food products.[11]

One approach to recognizing vapors is to coat interdigitated electrodes with an electronically conductive polymer, such as a derivative of polypyrrole.



Polypyrrole

When gaseous odor molecules are absorbed by the polymer, the electrical conductivity of the polymer changes. Different gases affect conductivity in different ways. Other sensor coatings are polymers containing conductive particles of silver or graphite. When the polymer absorbs small molecules, it swells and the conductivity decreases.



Interdigitated electrodes coated with conductive polymer to create an electronic nose. The conductivity of the polymer changes when it absorbs odor molecules. The spacing between "fingers" is ~0.25 mm.

One commercial "nose" has 32 sets of electrodes, each coated with a different polymer. The sensor yields 32 different responses when exposed to a vapor. The 32 changes are a "fingerprint" of the vapor. The electronic nose must be "trained" by pattern recognition algorithms to recognize an odor by its characteristic fingerprint. Other electronic noses are based on changes in optical absorption of polymers at the tips of optical fibers and on changes at the gates of field effect transistors (Section 14-8).

Enzyme: A protein that catalyzes a biochemical reaction. The enzyme increases the rate of reaction by many orders of magnitude.

Antibody: A protein that binds to a specific target molecule called an *antigen*. Antibodies bind to foreign cells that infect your body to initiate their destruction or identify them for attack by immune system cells.

Biosensors[12,13] use biological components such as *enzymes*, *antibodies*, or DNA for a highly selective response to one analyte. Biosensors that generate electric or optical signals are most common. Examples of amperometric biosensors are those that measure perchlorate in groundwater,[14] adenosine triphosphate (ATP) in biological tissue,[15] attomolar levels of genes,[16] and antibodies at femtomolar levels.[17] We now describe blood glucose monitors, which are, by far, the most widely used biosensors.

Blood Glucose Monitor

Diabetes afflicts approximately 5% of the population. Many people with diabetes must monitor their blood sugar (glucose) several times a day to control their disease through diet and insulin injections. Figure 16-10 shows a home glucose monitor featuring a disposable test strip with two carbon working electrodes and a Ag | AgCl reference electrode. As little as 4 μL of blood applied in the circular opening at the right of the figure is wicked over all three electrodes by a thin *hydrophilic* ("water loving") mesh. A 20-s measurement begins when the liquid reaches the reference electrode.

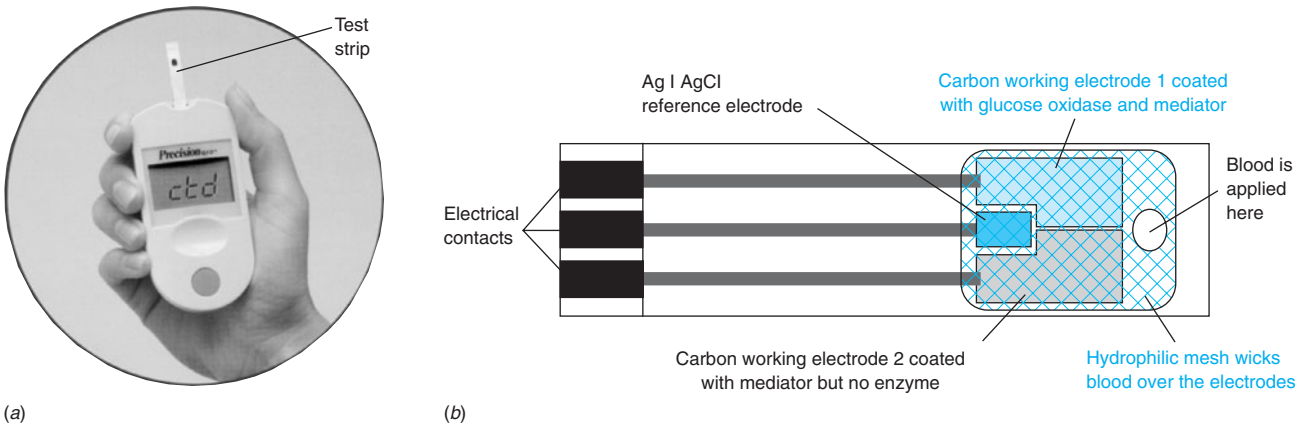
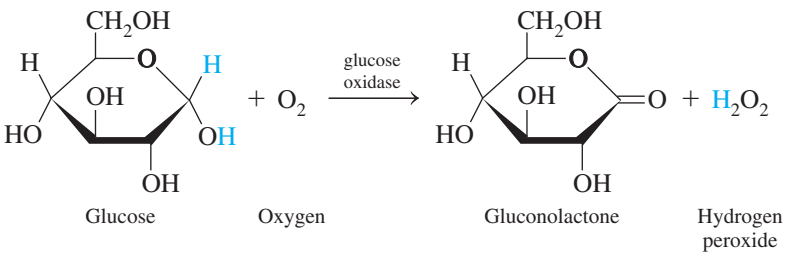


FIGURE 16-10 (*a*) Personal glucose monitor used by diabetics to measure blood sugar level. (*b*) Details of disposable test strip to which a drop of blood is applied. [Courtesy Abbott Laboratories MediSense Products, Bedford, MA.]

Working electrode 1 is coated with the enzyme *glucose oxidase* and a *mediator*, which we describe soon. The enzyme catalyzes the reaction of glucose with O_2:

Reaction in coating above working electrode 1:



(16-13)

In the absence of enzyme, the oxidation of glucose is negligible.

Early glucose monitors measured H_2O_2 from Reaction 16-13 by oxidation at a single working electrode, which was held at +0.6 V versus Ag | AgCl:

Reaction at working electrode 1:

$$H_2O_2 \rightarrow O_2 + 2H^+ + 2e^- \qquad \textbf{(16-14)}$$

The current is proportional to the concentration of H_2O_2, which, in turn, is proportional to the glucose concentration in blood (Figure 16-11).

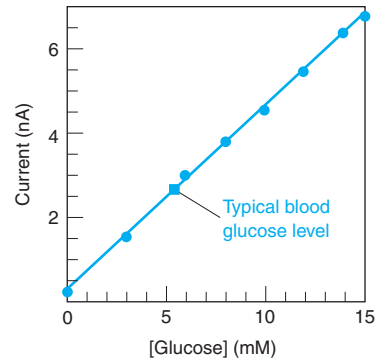


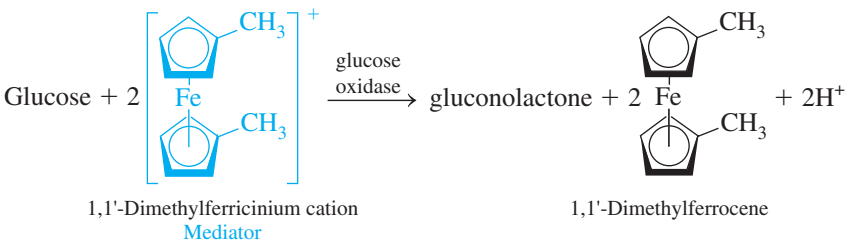
FIGURE 16-11 Response of an amperometric glucose electrode with dissolved O_2 concentration corresponding to an oxygen pressure of 0.027 bar, which is 20% lower than the typical concentration in subcutaneous tissue. [Data from S.-K. Jung and G. W. Wilson, "Polymeric Mercaptosilane-Modified Platinum Electrodes for Elimination of Interferents in Glucose Biosensors," *Anal. Chem.* **1996**, *68*, 591.]

One problem with early glucose monitors is that their response depended on the concentration of O_2 in the enzyme layer, because O_2 participates in Reaction 16-13. If the O_2 concentration is low, the monitor responds as though the glucose concentration were low.

A good way to reduce O_2 dependence is to incorporate into the enzyme layer a species that substitutes for O_2 in Reaction 16-13. A substance that transports electrons between the analyte (glucose, in this case) and the electrode is called a **mediator.**

A *mediator* transports electrons between the analyte and the working electrode. The mediator undergoes no net reaction itself.

Reaction in coating above working electrode 1:

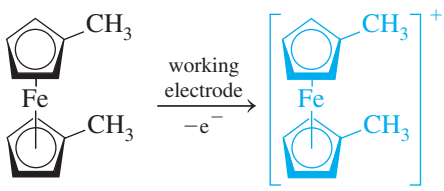


(16-15)

Ferrocene contains flat, five-membered rings, similar to benzene. Each ring formally carries one negative charge, so the oxidation state of Fe, which sits between the rings, is +2. This molecule is called a *sandwich complex.*

The mediator consumed in Reaction 16-15 is then regenerated at the working electrode:

Reaction at working electrode 1:



(16-16)

The mediator lowers the required working electrode potential from 0.6 V to 0.2 V versus Ag | AgCl, thereby improving the stability of the sensor and eliminating some interference by other species in the blood.

The current at the working electrode is proportional to the concentration of ferrocene, which, in turn, is proportional to the concentration of glucose in the blood.

One problem with glucose monitors is that species such as ascorbic acid (vitamin C), uric acid, and acetaminophen (Tylenol) found in blood can be oxidized at the same potential required to oxidize the mediator in Reaction 16-16. To correct for this interference, the test strip in Figure 16-10 has a second indicator electrode coated with mediator, *but not with glucose oxidase*. Interfering species that are reduced at electrode 1 are also reduced at electrode 2. The current due to glucose is the current at electrode 1 *minus* the current at electrode 2 (both measured with respect to the reference electrode). Now you see why the test strip has two working electrodes.

A modified sensor measures glucose at a concentration of 2 fM in a 30-μL volume containing just 36 000 molecules of glucose.[18]

A challenge is to manufacture glucose monitors in such a reproducible manner that they do not require calibration. A user expects to add a drop of blood to the test strip and get a reliable reading without first constructing a calibration curve from known concentrations of glucose in blood. Each lot of test strips is highly reproducible and calibrated at the factory.

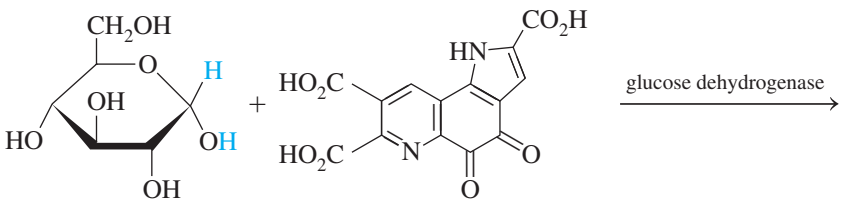
"Electrical Wiring" of Enzymes and Mediators for Blood Glucose Monitor

Demand for glucose monitors provides an economic stimulus for research that continues to improve the performance of home glucose monitors.[19] Noteworthy advances include (1) monitoring the reaction by coulometry instead of amperometry, (2) using a different enzyme to catalyze glucose oxidation, and (3) "electrical wiring" to increase the rate of reaction and to prevent reactants from diffusing away from the working electrode.

In *amperometry*, current flowing during glucose oxidation is measured. In *coulometry*, the number of electrons required to oxidize the glucose in a blood sample is counted. Amperometry measures the *rate of oxidation*. Coulometry measures the *number of molecules that have been oxidized*. The rate of reaction, and therefore the current, depends on temperature, but total charge transferred during oxidation is independent of temperature. Therefore, the coulometric measurement is independent of temperature. Total charge transferred is also insensitive to the activity of the enzyme (how quickly it works) and the mobility of the mediator, both of which affect current. Current is also affected by depletion of glucose during the measurement. In coulometry, the goal is to use up all the glucose.

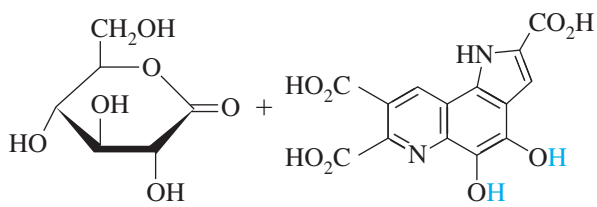
A *cofactor* is a small, nonprotein molecule that is bound to an enzyme and is necessary for the activity of the enzyme.

Replacing the enzyme glucose oxidase with *glucose dehydrogenase* eliminates O_2 as a reactant. A *cofactor* called PQQ, which is bound to glucose dehydrogenase, receives $2H^+ + 2e^-$ during the oxidation.



Glucose

Pyrroloquinoline quinone (PQQ) cofactor in glucose dehydrogenase



Gluconolactone

$PQQH_2$

(16-17)

Unlike Reaction 16-13, O_2 is not involved in Reaction 16-17. Therefore, there is no dependence of the response to dissolved O_2.

In an "electrically wired" polymer gel on the surface of a carbon electrode (Figure 16-12), the enzyme and an osmium mediator are tethered to a polymer backbone. The $PQQH_2$ product of Reaction 16-17 is oxidized back to $PQQ + 2H^+$ by a nearby Os^{3+}. Os^{3+} is reduced to Os^{2+} in the process. Os^{2+} can exchange an electron with another Os^{3+}. Electrons are transported rapidly from Os to Os until they reach a carbon anode. Electrons then flow through a circuit to the Ag | AgCl counter electrode where AgCl is reduced to $Ag + Cl^-$.

"Electrical wiring" of the enzyme and the osmium mediators increases the current by a factor of 10 to 100 compared with an enzyme/mediator layer deposited onto an electrode. Increased current provides larger signal and a faster measurement. Covalent attachment of osmium to the polymer prevents the mediator from diffusing to the counter electrode, where it would react and create a large background current. Ligands for osmium are chosen so that the mildest possible potential (+0.1 V versus Ag | AgCl) can be applied to the electrode to oxidize glucose. At this potential, common oxidizable interferents produce acceptably small errors in glucose measurement.

The newest glucose monitor test strips require only 0.3 μL of blood for a measurement, significantly reducing the pain experienced by people who need to measure their glucose several times each day. Glucose in the entire volume is oxidized in about 1 min, and current is measured as a function of time. Integrating current versus time (Equation 16-12) gives the total charge required to reduce glucose.

Rotating Disk Electrode

A molecule has three ways to reach the surface of an electrode: (1) *diffusion* through a concentration gradient; (2) *convection*, which is the movement of bulk fluid by physical means

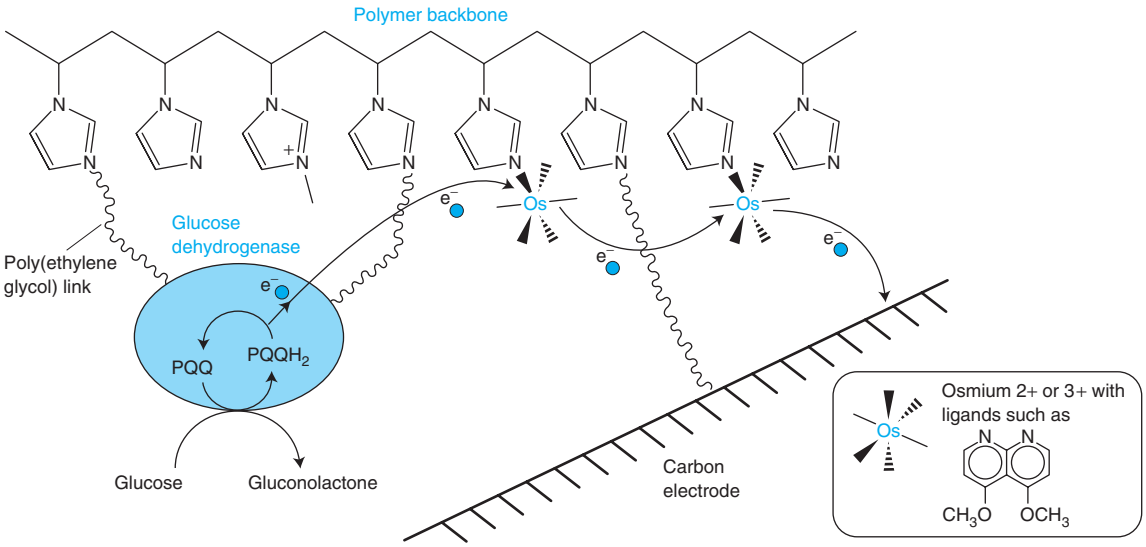


FIGURE 16-12 "Electrically wired" glucose dehydrogenase. The enzyme catalyzes the oxidation of glucose, reducing PQQ to $PQQH_2$. $PQQH_2$ is oxidized back to PQQ + $2H^+$ by Os^{3+}. Electrons move through successive osmium atoms until they reach the carbon anode. All members of the redox chain are bound to a polymer backbone.

such a stirring or boiling; and (3) *migration*, which is the attraction or repulsion of an ion by a charged surface. A common working electrode for amperometry is the **rotating disk electrode,** for which convection and diffusion control the flux of analyte to the electrode.[20]

Three ways for analyte to reach an electrode:

- diffusion
- convection
- migration

When the electrode in Figure 16-13a is spun at ~1 000 revolutions per minute, a vortex is established that brings analyte near the electrode rapidly by convection. If the potential is great enough, analyte reacts rapidly at the electrode, thereby reducing the concentration of analyte at the surface to near 0. The resulting concentration gradient is shown schematically in Figure 16-13b. Analyte must traverse the final, short distance (~10–100 μm) by diffusion alone.

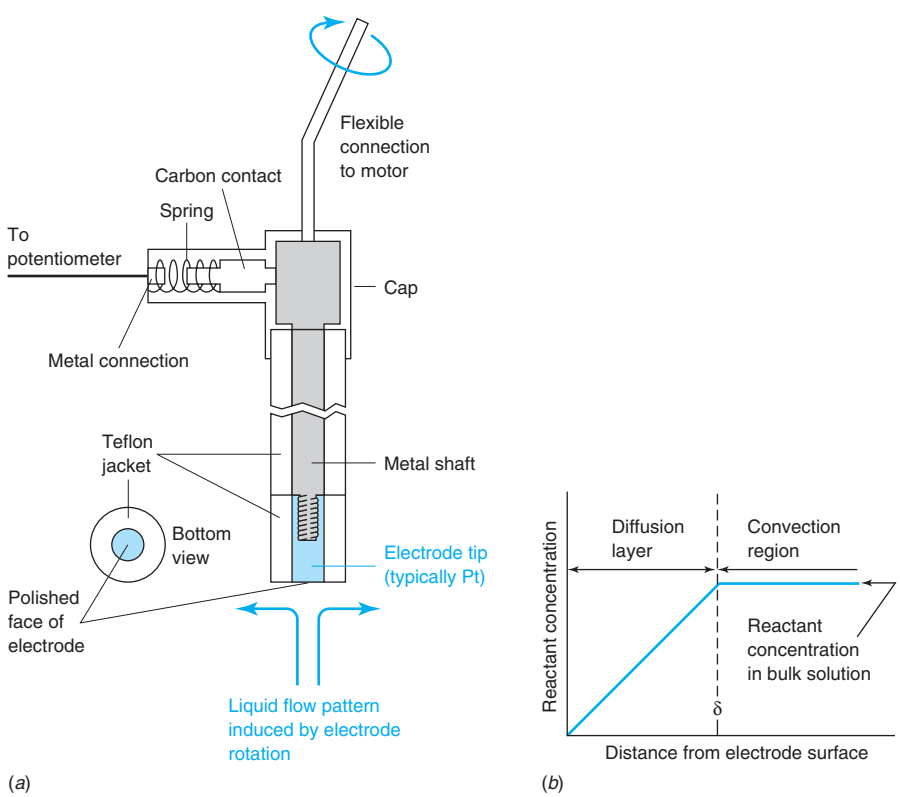


FIGURE 16-13 (*a*) Rotating disk electrode. Only the polished bottom surface of the electrode, which is typically 5 mm in diameter, contacts the solution. (*b*) Schematic concentration profile of analyte near the surface of the rotating disk electrode when the potential is great enough to reduce the concentration of analyte to 0 at the electrode surface.

The rate at which analyte diffuses from bulk solution to the surface of the electrode is proportional to the concentration difference between the two regions:

The symbol $\propto$ means "is proportional to."

$$\text{Current} \propto \text{rate of diffusion} \propto [C]_0 - [C]_s \tag{16-18}$$

where $[C]_0$ is the concentration in bulk solution and $[C]_s$ is the concentration at the surface of the electrode. At sufficiently great potential, the rate of reaction at the electrode is so fast that $[C]_s \ll [C]_0$ and Equation 16-18 reduces to

$$\text{Limiting current} = \text{diffusion current} \propto [C]_0 \tag{16-19}$$

The limiting current is called the **diffusion current** because it is governed by the rate at which analyte can diffuse to the electrode. The proportionality of diffusion current to bulk-solute concentration is the basis for quantitative analysis by amperometry and, in the next section, voltammetry.

The faster a rotating disk electrode spins, the thinner is the diffusion layer in Figure 16-13b and the greater is the diffusion current. A rapidly rotating Pt electrode can measure 20 nM H_2O_2 in rainwater.[21] H_2O_2 is oxidized to O_2 at +0.4 V (versus S.C.E.) at the Pt surface, and the current is proportional to $[H_2O_2]$ in the rainwater.

16-5 Voltammetry

Voltammetry is a collection of techniques in which the relation between current and voltage is observed during electrochemical processes.[22] The **voltammogram** in Figure 16-14a is a graph of current versus working electrode potential for a mixture of ferricyanide and ferrocyanide being oxidized or reduced at a rotating disk electrode. By convention, current is positive when analyte is reduced at the working electrode. The limiting (diffusion) current for oxidation of $Fe(CN)_6^{4-}$ is observed at potentials above +0.5 V (versus S.C.E.).

$$\underset{\substack{\text{Ferrocyanide}\\ \text{Fe(II)}}}{Fe(CN)_6^{4-}} \rightarrow \underset{\substack{\text{Ferricyanide}\\ \text{Fe(III)}}}{Fe(CN)_6^{3-}} + e^-$$

In this region, current is governed by the rate at which $Fe(CN)_6^{4-}$ diffuses to the electrode. Diffusion current is proportional to the bulk concentration of $Fe(CN)_6^{4-}$ (Figure 16-14b) just as it is for the rotating disk electrode in Equation 16-19. Below 0 V, there is another plateau corresponding to the diffusion current for reduction of $Fe(CN)_6^{3-}$, whose concentration is constant in all the solutions.

Polarography has been largely replaced by voltammetry with electrodes that do not present the toxicity hazard of Hg. Mercury is still the electrode of choice for stripping analysis, which is the most sensitive voltammetric technique. For cleaning up Hg spills, see note 23.

Polarography

Voltammetry conducted with a **dropping-mercury electrode** is called **polarography** (Figure 16-15). The dispenser suspends one drop of mercury from the bottom of the capillary. After current and voltage are measured, the drop is mechanically dislodged. Then a

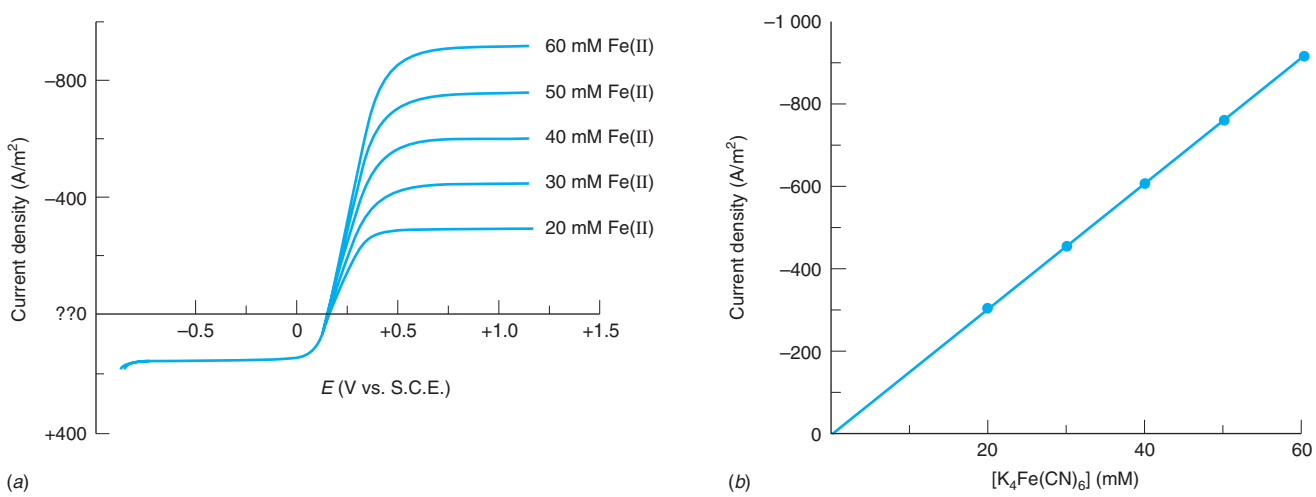


FIGURE 16-14 (*a*) Voltammograms for a mixture of 10 mM $K_3Fe(CN)_6$ and 20–60 mM $K_4Fe(CN)_6$ in 0.1 M Na_2SO_4 at a glassy carbon rotating electrode. Rotation speed = 2 000 revolutions/min and voltage sweep rate = 5 mV/s. (*b*) Dependence of limiting current on $K_4Fe(CN)_6$ concentration. [From J. Nikolic, E. Expósito, J. Iniesta, J. González-Garcia, and V. Montiel, "Theoretical Concepts and Applications of a Rotating Disk Electrode," *J. Chem. Ed.* **2000**, *77*, 1191.]

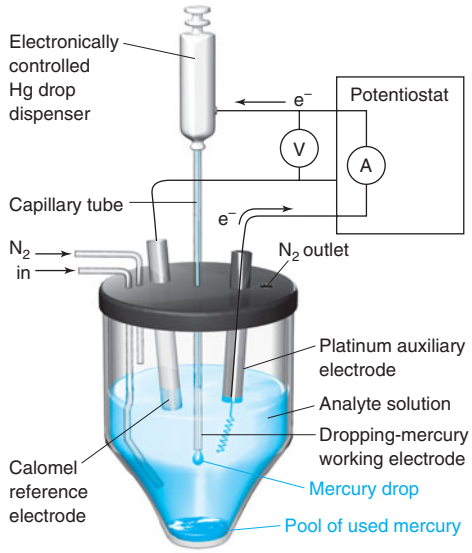


FIGURE 16-15 Polarography apparatus featuring a dropping-mercury working electrode. Polarography was invented by J. Heyrovský in 1922, for which he received the Nobel Prize in 1959.

fresh drop is suspended and the next measurement is made. Freshly exposed Hg yields reproducible current-potential behavior. The current for other electrodes, such as Pt, depends on surface condition.

Most reactions studied with the Hg electrode are reductions. At a Pt surface, reduction of H^+ competes with reduction of many analytes:

$$2H^+ + 2e^- \rightarrow H_2(g) \qquad E^\circ = 0$$

Table 16-1 showed that there is a large *overpotential* for reduction of H^+ at the Hg surface. Reactions that are thermodynamically less favorable than reduction of H^+ can be carried out without competitive reduction of H^+. In neutral or basic solutions, even alkali metal (Group 1) cations are reduced more easily than H^+. Furthermore, reduction of a metal into a mercury *amalgam* is more favorable than reduction to the solid state:

An **amalgam** is anything dissolved in Hg.

$$K^+ + e^- \rightarrow K(s) \qquad E^\circ = -2.936\ \text{V}$$
$$K^+ + e^- + Hg \rightarrow K(in\ Hg) \qquad E^\circ = -1.975\ \text{V}$$

Mercury is not useful for studying oxidations because Hg is oxidized in noncomplexing media near +0.25 V (versus S.C.E.). If the concentration of Cl^- is 1 M, Hg is oxidized near 0 V because Hg(II) is stabilized by Cl^-:

$$Hg(l) + 4Cl^- \rightleftharpoons HgCl_4^{2-} + 2e^-$$

For oxidations, Pt, Au, C, or diamond working electrodes in appropriate solvents provide a range of accessible potentials (Table 16-2). Boron-doped chemical-vapor-deposited diamond (Figure 16-16) is an exceptionally inert carbon electrode with a wide potential window, low background current,[24] and visible and infrared transparency.

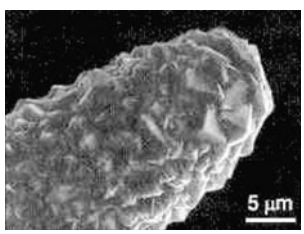


FIGURE 16-16 Boron-doped diamond coating on Pt electrode. [From J. Cvačka et al., *Anal. Chem.* **2003,** *75*, 2678. Courtesy G. M. Swain, Michigan State University.]

TABLE 16-2 Approximate working electrode potential range in 1 M H_2SO_4

Electrode	Potential range (V vs. S.C.E.)
Pt	−0.2 to +0.9 V
Au	−0.3 to +1.4 V
Hg	−1.3 to +0.1 V
Glassy carbon	−0.8 to +1.1 V
B-doped diamond[a]	−1.5 to +1.7 V
Fluorinated B-doped diamond[b]	−2.5 to +2.5 V

a. A. E. Fischer, Y. Show, and G. M. Swain, "Electrochemical Performance of Diamond Thin-Film Electrodes from Different Commercial Sources," Anal. Chem. ***2004,*** *76, 2553; Y. Dai, G. M. Swain, M. D. Porter, and J. Zak, "Optically Transparent Carbon Electrodes," Anal. Chem.* ***2008,*** *80, 14; J. Stotter, Y. Show, S. Wang, and G. Swain, "Comparison of Electrical, Optical, and Electrochemical Properties of Diamond and Indium Tin Oxide Thin-Film Electrodes," Chem. Mater.* ***2005,*** *17, 4880.*

b. S. Ferro and A. De Battisti, "The 5-V Window of Polarizability of Fluorinated Diamond Electrodes in Aqueous Solution," Anal. Chem. ***2003,*** *75, 7040.*

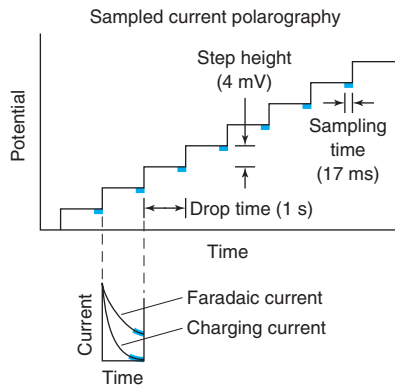


FIGURE 16-17 *Staircase voltage profile* used in *sampled current polarography*. Current is measured only during the intervals shown by heavy, colored lines. Potential is scanned toward more negative values as the experiment progresses. Lower graph shows that charging current decays more rapidly than faradaic current after each voltage step.

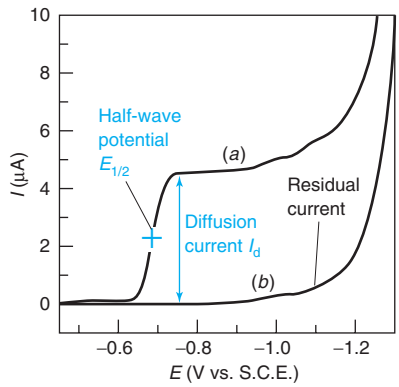


FIGURE 16-18 *Sampled current polarograms* of (*a*) 5 mM Cd^{2+} in 1 M HCl and (*b*) 1 M HCl alone.

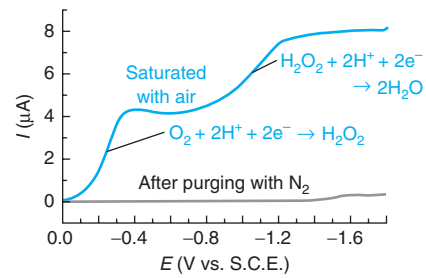


FIGURE 16-19 Sampled current polarogram of 0.1 M KCl, saturated with air or purged (bubbled) with N_2 to remove O_2.

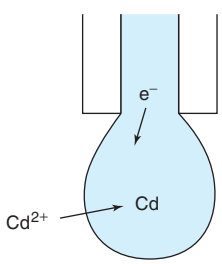
Polarograms in the older literature have large oscillations superimposed on the wave in Figure 16-18a. For the first 50 years of polarography, current was measured continuously as Hg flowed from a capillary tube. Each drop grew until it fell off and was replaced by a new drop. The current oscillated from a low value when the drop was small to a high value when the drop was big.

One way to conduct a measurement is by **sampled current polarography** with the *staircase voltage ramp* in Figure 16-17. After each drop of Hg is dispensed, the potential is made more negative by 4 mV. After waiting almost 1 s, current is measured during the last 17 ms of the life of each Hg drop. The **polarographic wave** in Figure 16-18a results from reduction of Cd^{2+} analyte to form an amalgam:

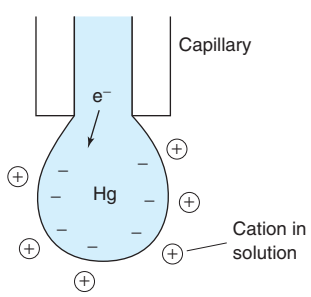
$$Cd^{2+} + 2e^- \rightarrow Cd(in\ Hg)$$

The potential at which half the maximum current is reached in Figure 16-18a, called the **half-wave potential** ($E_{1/2}$), is characteristic of a given analyte in a given medium and can be used for qualitative analysis. For electrode reactions in which reactants and products are both in solution, such as $Fe^{3+} + e^- \rightleftharpoons Fe^{2+}$, $E_{1/2}$ (expressed with respect to S.H.E.) is nearly equal to E° for the half-reaction.

Faradaic current: due to redox reaction at the electrode



Charging current: due to electrostatic attraction or repulsion of ions in solution and electrons in the electrode



Faradaic current is the signal of interest. Charging current obscures the signal of interest, so we seek to minimize charging current.

For quantitative analysis, the *diffusion current* in the plateau region is proportional to the concentration of analyte. Diffusion current is measured from the baseline recorded without analyte in Figure 16-18b. **Residual current** in the absence of analyte is due to reduction of impurities in solution and on the surface of the electrodes. Near −1.2 V in Figure 16-18, current increases rapidly as reduction of H^+ to H_2 commences.

For quantitative analysis, the limiting current should be controlled by the rate at which analyte can diffuse to the electrode. We minimize convection by using an unstirred solution. We minimize migration (electrostatic attraction of analyte) by using a high concentration of *supporting electrolyte*, such as 1 M HCl in Figure 16-18.

Oxygen must be absent because O_2 gives two polarographic waves when it is reduced to H_2O_2 and then to H_2O (Figure 16-19). Typically, N_2 is bubbled through analyte solution for 10 min to remove O_2.[25] Then N_2 flow in the gas phase is continued to keep O_2 out. The liquid should not be purged with N_2 during a measurement, because we do not want convection of analyte to the electrode.

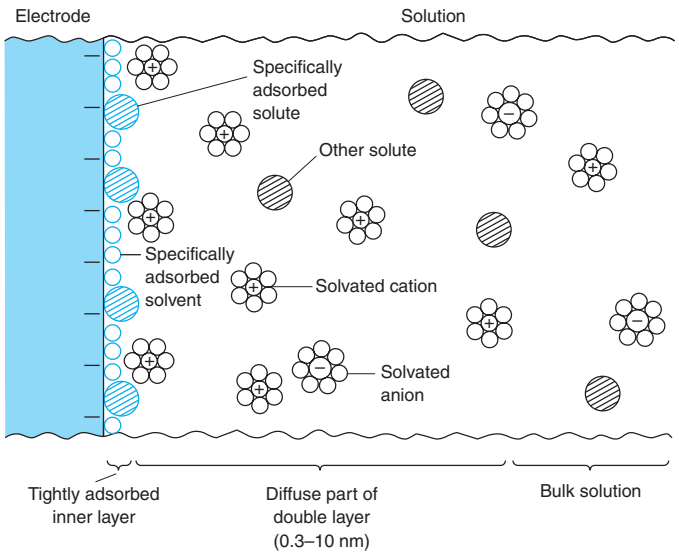
Faradaic and Charging Currents

The current we seek to measure in voltammetry is **faradaic current** due to reduction or oxidation of analyte at the working electrode. In Figure 16-18a, faradaic current comes from reduction of Cd^{2+} at the Hg electrode. Another current, called **charging current** (or *capacitor current* or *condenser current*) interferes with every measurement. We step the working electrode to a more negative potential by forcing electrons into the electrode from the potentiostat. In response, cations in solution flow toward the electrode, and anions flow away from the electrode (Box 16-3). This flow of ions and electrons, called *charging current*, is not from redox reactions. We try to minimize charging current, which obscures faradaic current. Charging current usually controls the detection limit in voltammetry.

The bottom of Figure 16-17 shows the behavior of faradaic and charging currents after each potential step. Faradaic current decays because analyte cannot diffuse to the electrode

BOX 16-3 The Electric Double Layer

When a power supply pumps electrons into or out of an electrode, the charged surface of the electrode attracts ions of opposite charge. The charged electrode and the oppositely charged ions next to it constitute the **electric double layer.**



Electrode-solution interface. The tightly adsorbed inner layer (also called the *compact, Helmholtz,* or *Stern* layer) may include solvent and any solute molecules. Cations in the inner layer do not completely balance the charge of the electrode. Therefore, excess cations are required in the *diffuse part of the double layer* for charge balance.

A given solution has a *potential of zero charge* at which there is no excess charge on the electrode. This potential is −0.58 V (versus a calomel electrode containing 1 M KCl) for a mercury electrode immersed in 0.1 M KBr. It shifts to −0.72 V for the same electrode in 0.1 M KI.

The first layer of molecules at the surface of the electrode is *specifically adsorbed* by van der Waals and electrostatic forces. The adsorbed solute could be neutral molecules, anions, or cations. Iodide is more strongly adsorbed than bromide, so the potential of zero charge for KI is more negative than for KBr: A more negative potential is required to expel adsorbed iodide from the electrode surface.

The next layer beyond the specifically adsorbed layer is rich in cations attracted by the negative electrode. The excess of cations decreases with increasing distance from the electrode. This region, whose composition is different from that of bulk solution, is called the *diffuse part of the double layer* and is typically 0.3–10 nm thick. The thickness is controlled by the balance between attraction toward the electrode and randomization by thermal motion.

When a species is created or destroyed by an electrochemical reaction, its concentration near the electrode is different from its concentration in bulk solution (Figure 16-13b and Color Plate 11). The region containing excess product or decreased reactant is called the *diffusion layer* (not to be confused with the diffuse part of the double layer).

fast enough to sustain the high reaction rate. Charging current decays even faster because ions near the electrode redistribute themselves rapidly. A second after each potential step, faradaic current is still significant and charging current is small.

Square Wave Voltammetry

The most efficient voltage profile for voltammetry, called **square wave voltammetry,** uses the waveform in Figure 16-20, which consists of a square wave superimposed on a staircase.[26] During each cathodic pulse, analyte is reduced at the electrode surface. During the anodic

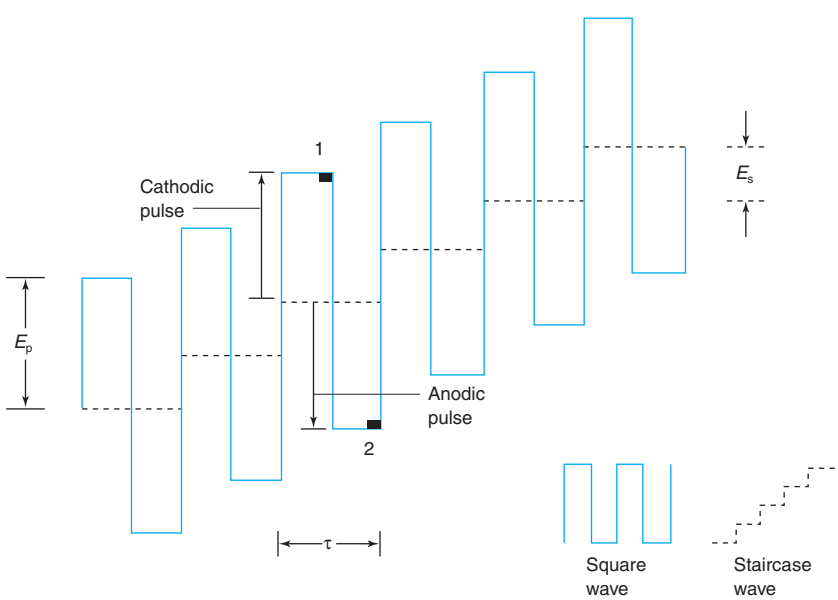


FIGURE 16-20 Waveform for square wave voltammetry. Typical parameters are pulse height (E_p) = 25 mV, step height (E_s) = 10 mV, and pulse period (τ) = 5 ms. Current is measured in regions 1 and 2. Optimum values are $E_p = 50/n$ mV and $E_s = 10/n$ mV, where n is the number of electrons in the half-reaction.

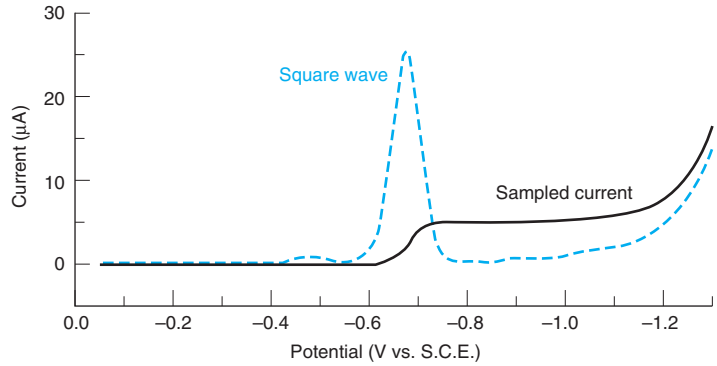


FIGURE 16-21 Comparison of polarograms of 5 mM Cd^{2+} in 1 M HCl. Waveforms are shown in Figures 16-17 and 16-20. Sampled current: drop time = 1 s, step height = 4 mV, sampling time = 17 ms. Square wave: drop time = 1 s, step height = 4 mV, pulse period = 67 ms, pulse height = 25 mV, sampling time = 17 ms.

pulse, analyte that was just reduced is reoxidized. The square wave polarogram in Figure 16-21 is the *difference* in current between intervals 1 and 2 in Figure 16-20. Electrons flow from the electrode to analyte at point 1 and in the reverse direction at point 2. Because the two currents have opposite signs, their difference is larger than either current alone. When the difference is plotted, the shape of the square wave polarogram in Figure 16-21 is essentially the derivative of the sampled current polarogram.

Advantages of square wave voltammetry:

- increased signal
- derivative (peak) shape permits better resolution of neighboring signals
- faster measurement

The signal in square wave voltammetry is increased relative to a sampled current voltammogram and the wave becomes peak shaped. Signal is increased because reduced product from each cathodic pulse is right at the surface of the electrode waiting to be oxidized by the next anodic pulse. Each anodic pulse provides a high concentration of reactant at the surface of the electrode for the next cathodic pulse. The detection limit is reduced from ~10^{-5} M for sampled current voltammetry to ~10^{-7} M in square wave voltammetry. Because it is easier to resolve neighboring peaks than neighboring waves, square wave voltammetry can resolve species whose half-wave potentials differ by ~0.05 V, whereas potentials must differ by ~0.2 V to be resolved in sampled current voltammetry. Square wave voltammetry is faster than other voltammetric techniques. The square wave polarogram in Figure 16-21 was recorded in one-fifteenth of the time required for the sampled current polarogram. In principle, the shorter the pulse period, τ, in Figure 16-20, the greater the current that will be observed. With $\tau = 5$ ms (a practical lower limit) and $E_s = 10$ mV, an entire square wave polarogram with a 1-V width is obtained with *one drop of Hg in 0.5 s*. Such rapid sweeps allow voltammograms to be recorded on individual components as they emerge from a chromatography column.

Anodic stripping analysis:

1. Concentrate analyte onto electrode by reduction
2. Reoxidize analyte by scanning to more positive potential
3. Peak current during oxidation is proportional to analyte concentration

Stripping Analysis

In **stripping analysis,** analyte from a dilute solution is concentrated into a thin film of Hg or other electrode material, usually by electroreduction. The electroactive species is then *stripped* from the electrode by reversing the direction of the voltage sweep. The potential becomes more *positive*, *oxidizing* the species back into solution. Peak current measured during oxidation is proportional to the quantity of analyte that was deposited. Figure 16-22 shows an anodic stripping voltammogram of Cd, Pb, and Cu from honey.

Stripping is the most sensitive voltammetric technique (Table 16-3), because analyte is concentrated from a dilute solution. The longer the period of concentration, the more sensitive

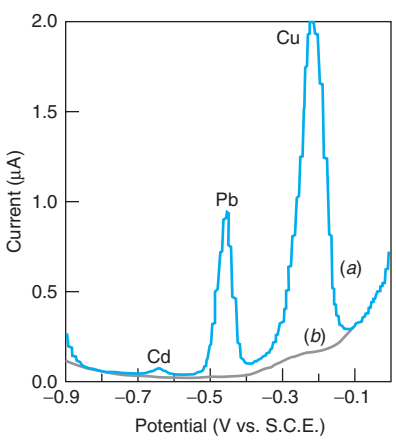


FIGURE 16-22 (*a*) Anodic stripping voltammogram of honey dissolved in water and acidified to pH 1.2 with HCl. Cd, Pb, and Cu were reduced from solution into a thin film of Hg for 5 min at −1.4 V (versus S.C.E.) prior to recording the voltammogram. (*b*) Voltammogram obtained without 5-min reduction step. The concentrations of Cd and Pb in the honey were 7 and 27 ng/g (ppb), respectively. Precision was 2–4%. [From Y. Li, F. Wahdat, and R. Neeb, "Digestion-Free Determination of Heavy Metals in Honey," *Fresenius J. Anal. Chem.* **1995,** *351*, 678.]

TABLE 16-3 Detection limits for stripping analysis

Analyte	Stripping mode	Detection limit
Ag^+	Anodic	2×10^{-12} M[a]
Testosterone	Anodic	2×10^{-10} M[b]
I^-	Cathodic	1×10^{-10} M[c]
DNA or RNA	Cathodic	2–5 pg/mL[d]
Fe^{3+}	Cathodic	1×10^{-11} M[e]

a. S. Dong and Y. Wang, Anal. Chim. Acta ***1988,*** *212, 341.*

b. J. Wang, "Adsorptive Stripping Voltammetry." EG&G Princeton Applied Research Application Note A-7 (1985).

c. G. W. Luther III, C. Branson Swartz, and W. J. Ullman, Anal. Chem. ***1988,*** *60, 1721.* I^- *is deposited onto the mercury drop by anodic oxidation:* $Hg(l) + I^- \rightleftharpoons \frac{1}{2}Hg_2I_2(adsorbed\ on\ Hg) + e^-$.

d. S. Reher, Y. Lepka, and G. Schwedt, Fresenius J. Anal. Chem. ***2000,*** *368, 720; J. Wang, Anal. Chim. Acta* ***2003,*** *500, 247.*

e. C. M. G. van den Berg, Anal. Chem. ***2006,*** *78, 156.*