CHEM 153A Week 1

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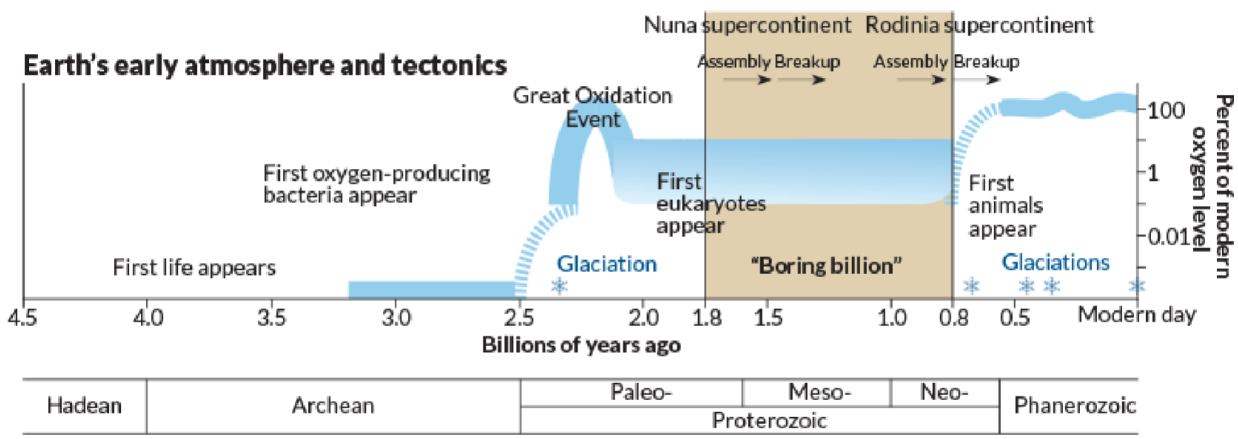
Biochemistry

- It describes in molecular terms the structures, mechanisms, and chemical processes shared by all organisms and **provides organization principles** that underlie life in all its diverse forms.

How Molecular Processes Evolved

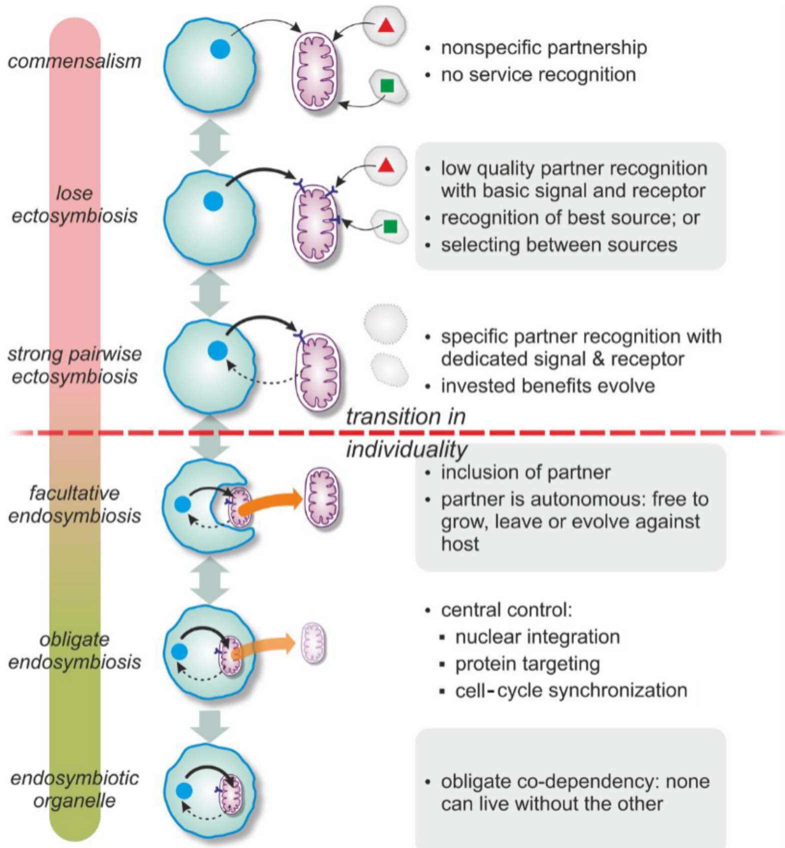
The Great Oxidation Event (2.4-2.1B years ago)



During this event, a few things happened:

- Lots of species went extinct because of the change in atmosphere
- Animals can now exist, since aerobic respiration became possible
- Mitochondria began appearing.

Endosymbiotic Theory

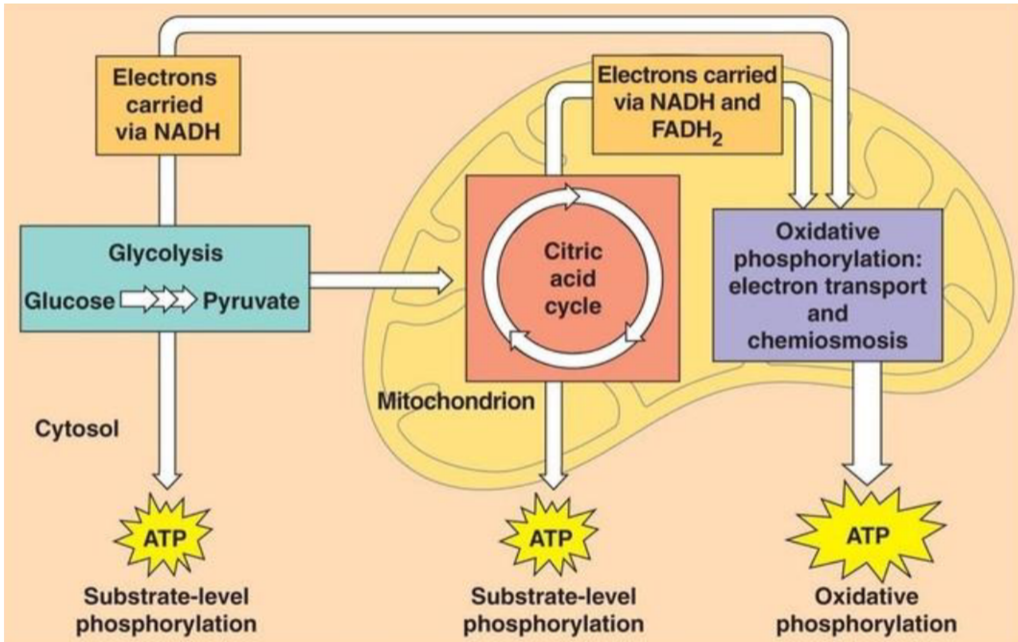


Zachar & Boza, 2020

https://doi.org/10.1007/s00018-020-03462-6

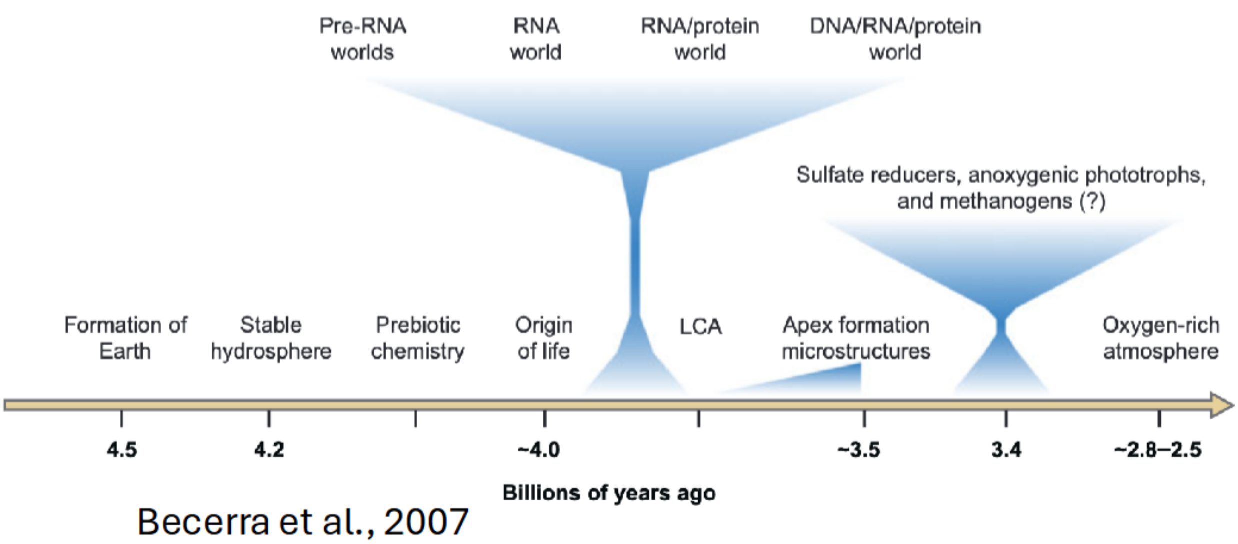
- Mitochondria used to be separate cells, rather than an organelle.
- At some point, one cell engulfed the other, and evolution occured.

Mitochondria

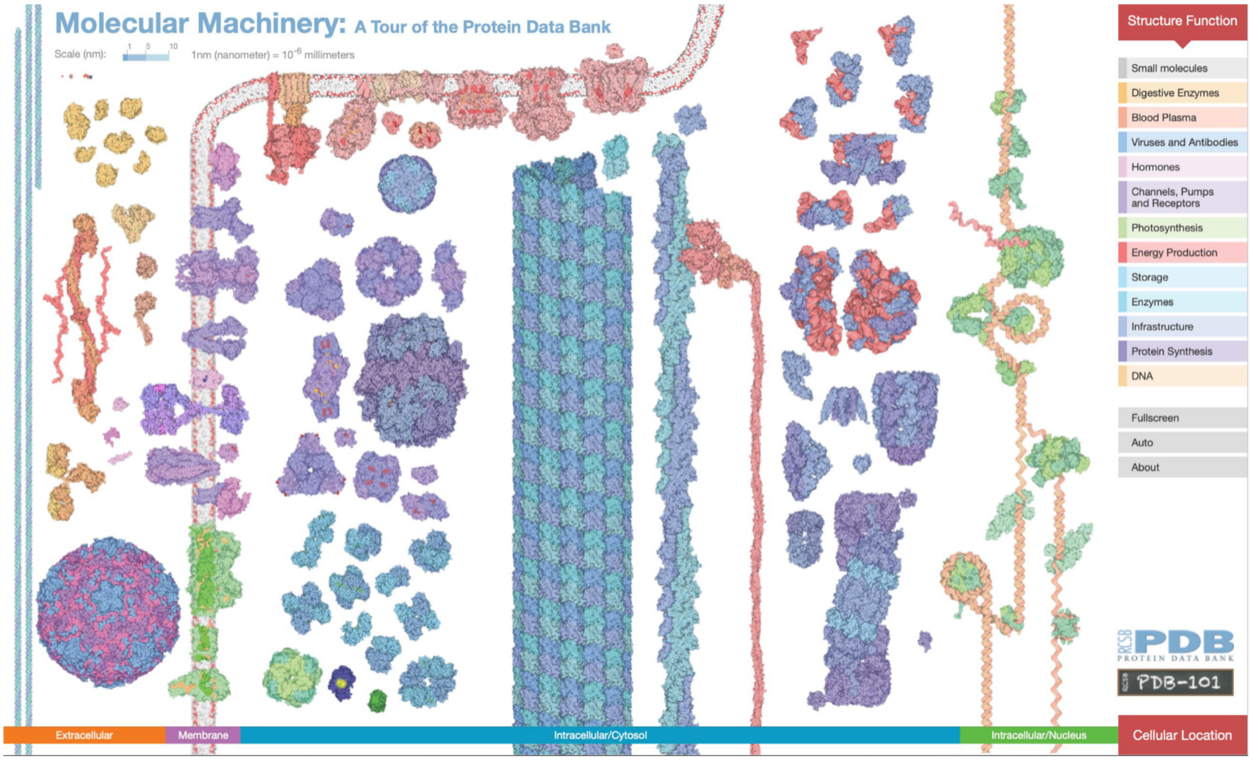


Evolution of Metabolism

- This example alone demonstrates the transformative impact of oxygen in life
- **Biochemistry can be divided into two eras: one before oxygen, and one after**
- Modern processes depend on oxygen, while older, more ancient pathways functioned in its absence.

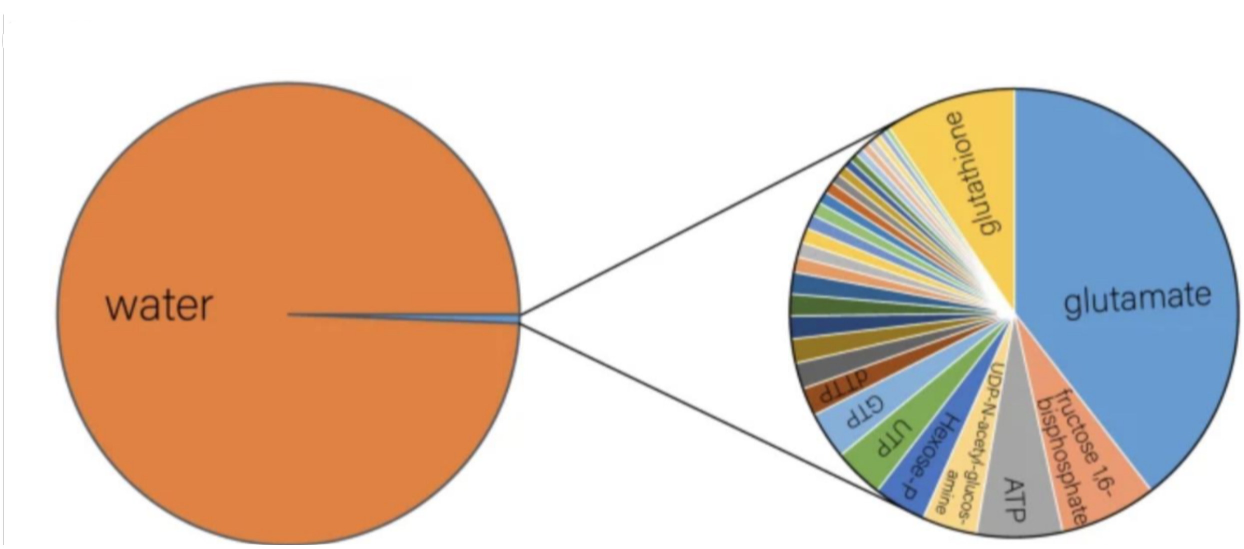


Proteins



- The above diagram shows proteins, an important part of cells and metabolism.
- This class aims to study the metabolic pathways in cells, many of which are catalyzed by proteins (specifically enzymes).
- RNA can also be a catalyst. (RNA is not a protein)

Water



- Water is a dominant metabolite in biochemistry, accounting for 99.4% by molarity of metabolites within an *E. coli.* bacteria. Water in an *E. coli* cell is around 40 M. The sum of the concentrations of all other metabolites is 240 mM.

Proteins Exist in Aqueous Environments

- Our first major topic in this class is **protein synthesis and structure**
  - The **amino acids** of proteins are affected by the **pH** of aqueous environments (protonation state!)
  - These amino acids often form different **intermolecular interactions** amongst themselves and with their environment
  - The folding of proteins is a **thermodynamic** problem

Importance of Water

- Physical and chemical properties of water influence every biochemical interaction
  - The medium for most biochemical reactions
  - Participates directly in many biochemical reactions
  - Affects folding (structure) of biomolecules

Aside: Quantifying the amount of substance dissolved in a solvent

- Concentration measures how much **solute** (the substance being dissolved) is present in a certain volume of **solvent** (usually water)
- Use Molarity (M).
  - Definition: Moles of solute per liter of solution
  - Formula: $M = \frac{\text{Moles solute}}{\text{Liters solution}}$
  - Example: A 1M NaCl solution contains 1 mole of NaCl in 1 liter of water.
  - Square brackets are used in chemistry to represent the concentration of a substance.

Our Watery Origins

Water as Essential but Problematic

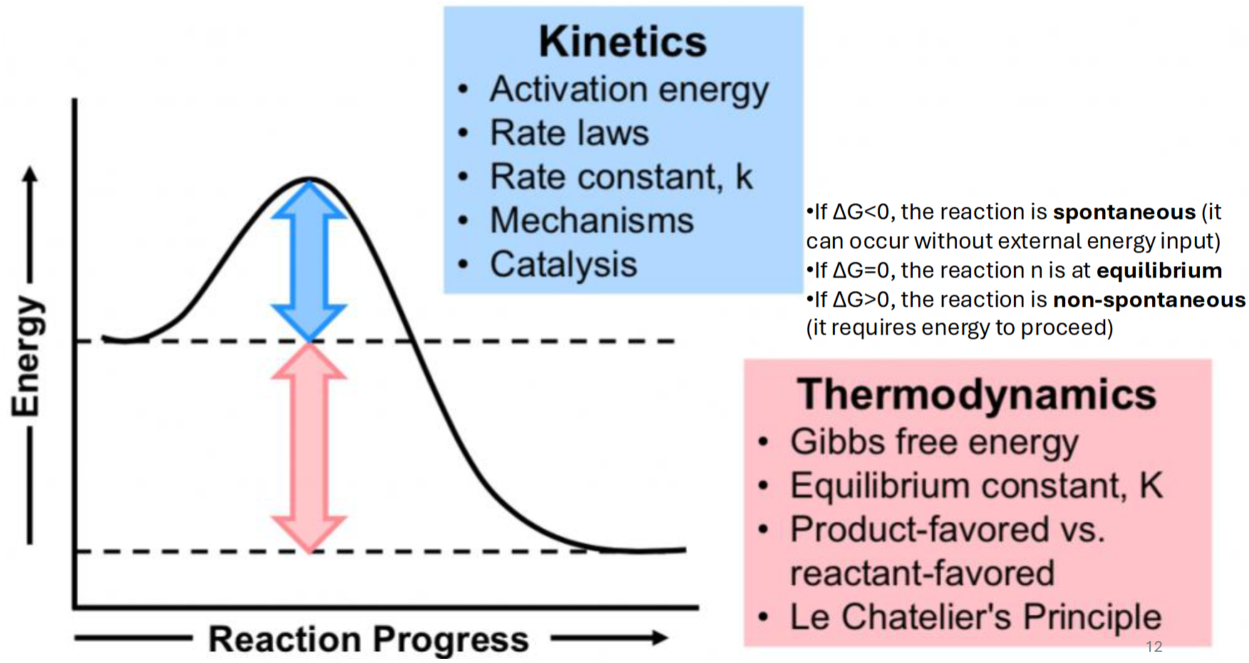
- **Essential for Life:** Water is crucial for life because it acts as a solvent, facilitates biochemical reactions, and is involved in virtually all life processes
- **Problematic for Life's Origins:** Paradoxically, water can hinder the formation of important biomolecules, such as proteins and nucleic acids, because both are **condensation polymers**. This means that their formation involves reactions that produce water as a byproduct. In an aqueous environment, water tends to promote the reverse reaction, hydrolysis, which breaks down these polymers
- The key to overcoming this challenge lies in **balancing thermodynamic activation** (making the formation of polymers energetically favorable) with **kinetic stability** (preventing them from breaking down too easily)

> **Prebiotic chemistry** could bypass fully hydrolyzed monomers and use energy-rich intermediates for polymer formation
>
> Example: **ATP**, though thermodynamically unstable in water, remains kinetically stable enough to drive biochemical reactions

- Liquid water is an extraordinary molecule that plays a central role in the chemistry of life due to its unique properties.
- The most important among them probably are the ability to establish hydrogen bonds, a high polarity and a high dielectric constant

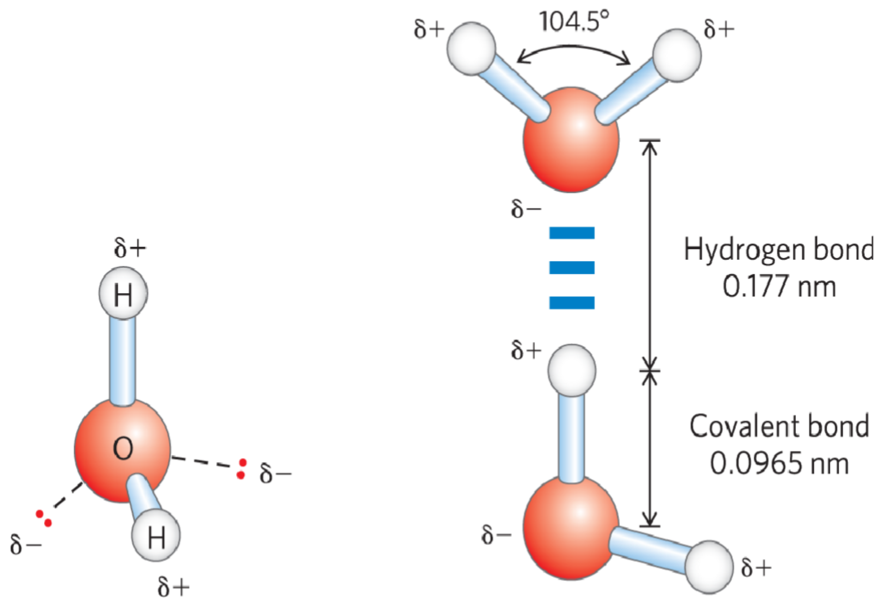
Kinetic vs. Thermodynamic Stability

- **Thermodynamic Stability:** Determines whether a reaction will be energetically favorable, or spontaneous, based on the overall energy of the system. A thermodynamically stable molecule is one that is in a lower energy state compared to its potential products
- **Kinetic Stability:** Refers to how quickly (or slowly) a reaction proceeds. A kinetically stable molecule is one that reacts very slowly, even if the reaction would be favorable (thermodynamically stable).



Hydrogen Bonds

- Hydrogen bonds are crucial for the unique properties of water, enabling its role as a solvent and in biochemical reactions.
- Water molecules can form hydrogen bonds because of the polarity in their O-H bonds. Oxygen, being more electronegative, pulls shared electrons closer, creating a partial negative charge on the oxygen and partial positive charges on the hydrogen atoms
- This polarity allows water to generate a cohesive hydrogen-bond network, resulting in phenomena such as high surface tension and capillary action, and enabling it to dissolve many polar substances effectively. Hydrogen bonding also stabilizes biological macromolecules (e.g., proteins, nucleic acids)
- Water has a higher melting point, boiling point, and heat of vaporization than most other common solvents (due to polarity and H-bonds)
- Hydrogen bond (H-bond) = **electrostatic attraction between the oxygen atom of one water molecule and the hydrogen of another**



(a) **(b)**

Strength of Hydrogen Bonds

- Hydrogen bonds are **relatively weak**
  - bond dissociation energy (energy req uired to break a bond) = 23 kJ/mol in liquid H_2O (470 kJ/mol for a covalent O-H bond)
  - 1% covalent, 90% electrostatic
- Hydrogen bonds are fleeting
  - lifetime of each hydrogen bond is just 1 to 20 picoseconds in liquid (1 picosecond = 10^{-12} seconds)
  - when one hydrogen bond breaks, another forms

Number of Hydrogen Bonds Formed

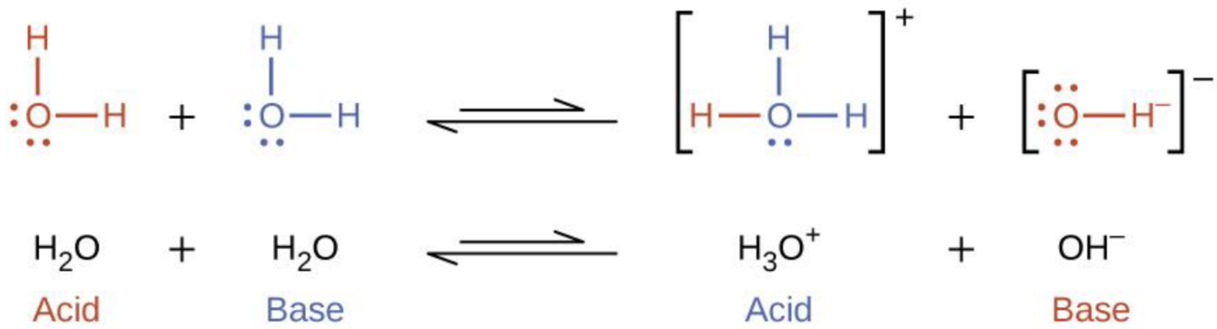
- In liquid, each H_2O molecule forms hydrogen bonds with an average of 3.4 other molecules
- In ice, each H_2O molecule forms 4 hydrogen bonds.

Water and Polar Solutes

- Hydrogen bonds form between:
  - Hydrogen acceptor: Electronegavie atom (e.g., O or N)
  - Hydrogen donor: H covalently bonded to another electronegative atom
- Important note: H atoms bonded to carbon do not participate in hydrogen bonding

Acids and Bases and Water

- The concept of acids and bases is entirely mediated by water.



The **autoionization of water** is the process by which two water molecules interact to form a hydronium ion (H_3O^+) and a hydroxide ion (OH^-). This occurs even in pure water, albeit at a very low rate, leading to an equilibrium concentration of H_3O^+ and OH^- (10^{-7} M each at 25°C, corresponding to a neutral pH of 7)

Acids and Bases: Brønsted-Lowry Definitions

- **Acids** are **proton donors**
- **Bases** are **proton acceptors**
- **Acid-base reactions** are **proton transfers**

Many reactions that occur in nature are ***reversible*** and do not proceed to completion. Instead, they come to an apparent halt or ***equilibrium*** at some point between 0 and 100% completion. ***At equilibrium, the net velocity is zero*** because the absolute velocity in the forward direction exactly equals the absolute velocity in the reverse direction. The position of equilibrium is conveniently described by an equilibrium constant, K_{eq}. For example, consider the dissociation of a weak acid:

Ionization Constants

- the tendency for any acid (HA) to lose a proton and form its conjugate base (A^-) is defined by the equilibrium constant (K_{eq}) for the reversible reaction

$$\mathrm{HA} \rightleftharpoons \mathrm{H}^+ + \mathrm{A}^-$$

for which

$$K_{eq} = \frac{[\mathrm{H}^+][\mathrm{A}^-]}{[\mathrm{HA}]} = K_a$$

The acid dissociation constant (K_a) is a measure of the extent to which an acid dissociates in solution and therefore its **strength**. The less an acid dissociates, the smaller the value of K_a. The stronger the acid, the higher the value of K_a.

The ionization behavior of water and of weak acids and bases dissolved in water can be represented by one or more equilibrium constants. Most biomolecules are ionizable; their structure and function depend on their ionization state, which is characterized by equilibrium constants.

In general:

$$K = \frac{[\mathrm{P}]}{[\mathrm{R}]}$$

$$aA + bB \rightleftharpoons cC + dD$$

The Ion Product of Water

$$K_w = K_{H_2O} = [H_3O^+][OH^-] = 1 \times 10^{-14} M^2$$

As a consequence, neutral pH = exactly equal concentrations of $H^+$and OH^-as in pure water.

At neutral pH:

$$K_w = [H^+][OH^-] = [H^+]^2 = [OH^-]^2$$
$$[H^+] = \sqrt{K_w} = \sqrt{1.0 \times 10^{-14}\ M^2}$$
$$[H^+] = [OH^-] = 10^{-7} M$$

The pH Scale Designates the $H^+$and OH^-Concentrations

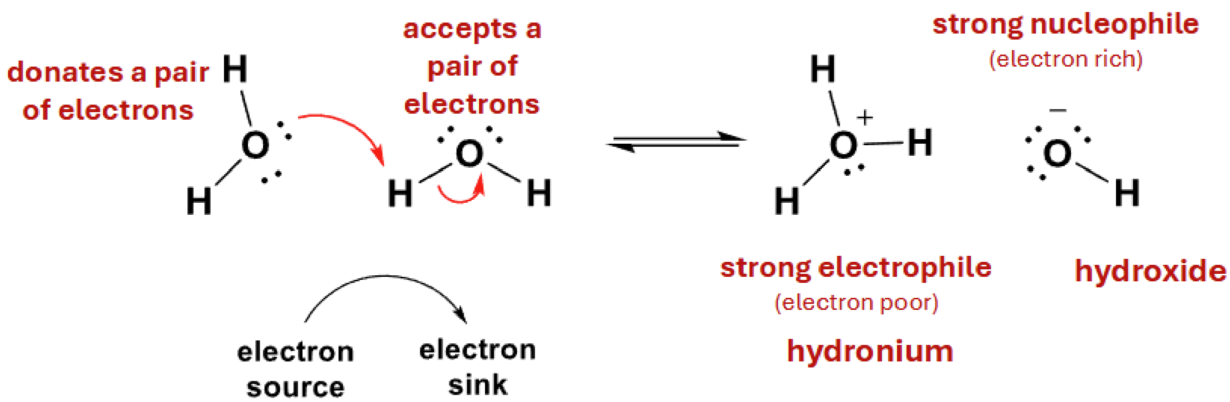
- the pH scale is based on the ion product of water, K_w
- the term pH is defined by the expresson:

$$pH = \log \frac{1}{[H^+]} = -\log [H^+]$$

  where $[H^+] = [OH^-] = 10^{-7}$ M

- for a precisely neutral solution at 25°C, pH = 7.0

The Mechanism of Autoionization

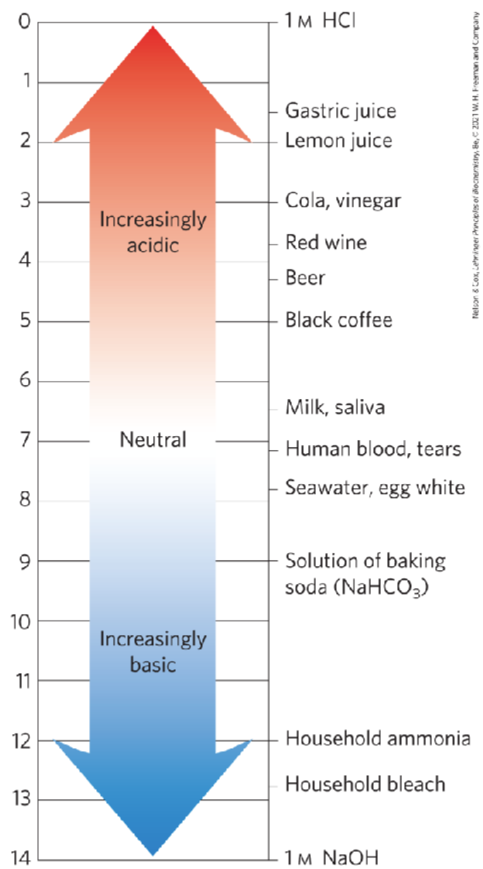


Lewis Acids and Lewis Bases

- **Lewis base** - Any molecule (or ion) that can form a new covalent bond by donating a pair of electrons
  - Also called a **nucleophile** ("nucleus loving")
  - Electron rich (-, δ^-, lone pairs, pi-bonds)
  - Examples: H_2O, OH^-, $H_2C{=}CH_2$
- **Lewis acid** - Any molecule (or ion) that can form a new covalent bond by accepting a pair of electrons
  - Also called an **electrophile** ("electron loving")
  - Electron poor (+, δ^+, unfilled octet)
  - Examples: H_3O^+, $^+CH_3$, $H_3C{-}Cl$

The pH of Some Aqueous Fluids

- pH values > 7:
  - alkaline or basic
  - concentration of $OH^-$is greater than that of H^+
- pH values < 7:
  - acidic
  - concentration of $H^+$is greater than that of OH^-

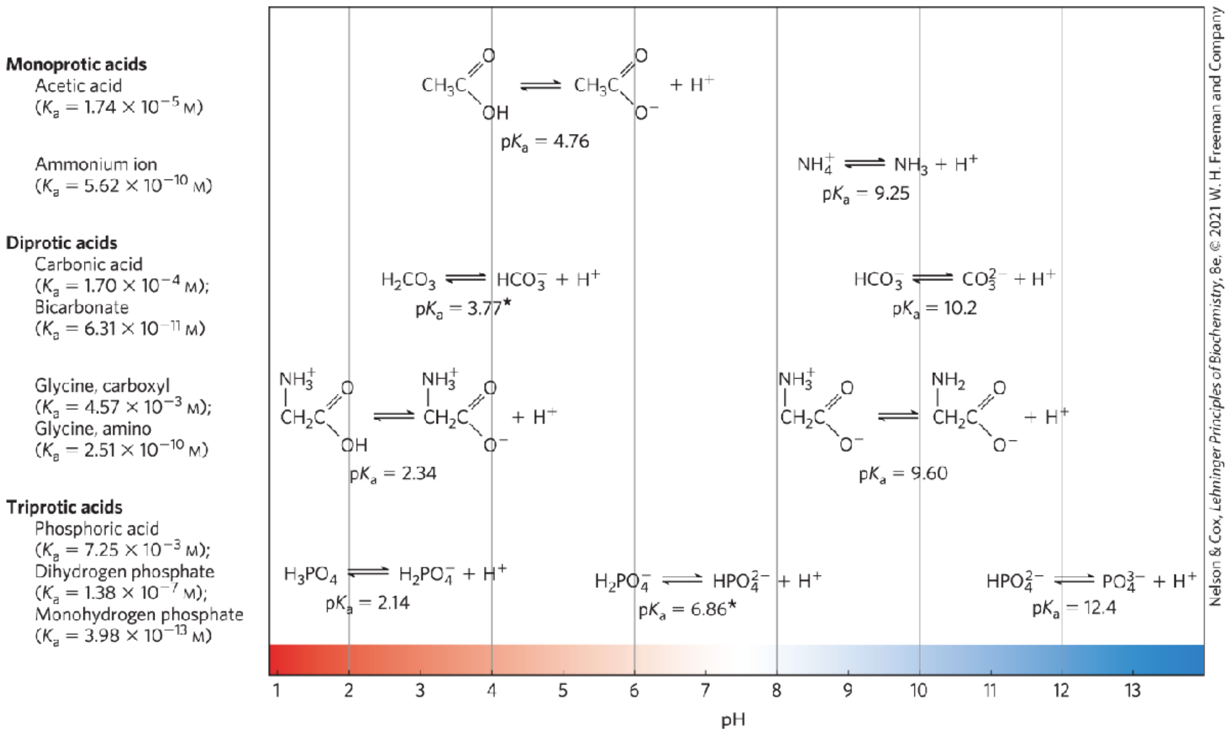


pH and Medical Diagnoses

- acidosis = pH of blood plasma below the normal value of 7.4
  - common in people with severe, uncontrolled diabetes
- alkalosis = pH of blood plasma above the normal value of 7.4
- extreme acidosis or alkalosis can be life-threatening

Conjugate Acid-Base Pairs

- conjugate acid-base pair = a proton donor and its corresponding proton acceptor
- the stronger the acid, the greater its tendency to lose its proton



pK_a

- pK_a = analogous to pH and defined by the equation

$$pK_a = \log \frac{1}{K_a} = -\log K_a$$

- the stronger the tendency to dissociate a proton, the **stronger the acid** and **the lower its pK_a**
- pK_a can be determined experimentally