

5.5.1 Entropy and Hydrophobicity

To gain a little more practice in the use of the entropy idea, we consider a toy model of one of the most important molecular driving forces in biological systems, namely, the hydrophobic effect. The qualitative idea is that when a hydrophobic molecule is placed in water, it prevents the water molecules in its vicinity from participating in some of the hydrogen bonds that they would have in the hydrophobic molecule's absence. An example of the highly idealized hydrogen bonding network in water is illustrated in Figure 5.27.

Hydrophobicity Results from Depriving Water Molecules of Some of Their Configurational Entropy

The objective of the present section is to make an estimate of the magnitude of these hydrophobic effects. The basic thrust of the argument will be to describe how nonpolar molecules in solution deprive water molecules of the capacity to engage in hydrogen bonding and thereby take away part of their orientational entropy. This simple model borrows from a model originally formulated by Pauling (1935) to capture the entropy of ice. With this mechanism in hand, we then carry out numerical estimates of the size of this effect.

The structural idea suggested by Figure 5.27 is that the oxygen atoms of neighboring water molecules form a tetrahedral network. As further suggested by Figure 5.27, these water molecules form a dynamic network of hydrogen bonds, where each oxygen, on average, makes hydrogen bonds with two of the four water molecules surrounding it. A useful conceptual framework for thinking about hydrophobicity is that when nonpolar molecules are placed in solution, the water molecules that neighbor the nonpolar molecule of interest have a restricted set of choices for effecting such hydrogen bonding. We can coarse grain the continuum of possible orientations available to a water molecule to the six distinct orientations shown in Figure 5.28. As a result, it is possible to estimate the entropic

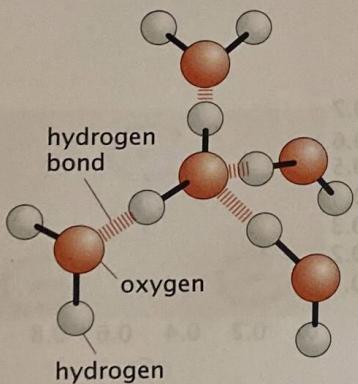


Figure 5.27: The hydrogen bonding network in water. Water molecules participate in hydrogen bonding (illustrated by the striped lines joining adjacent water molecules). A given water molecule can be idealized as having neighbors arranged in a tetrahedral structure.

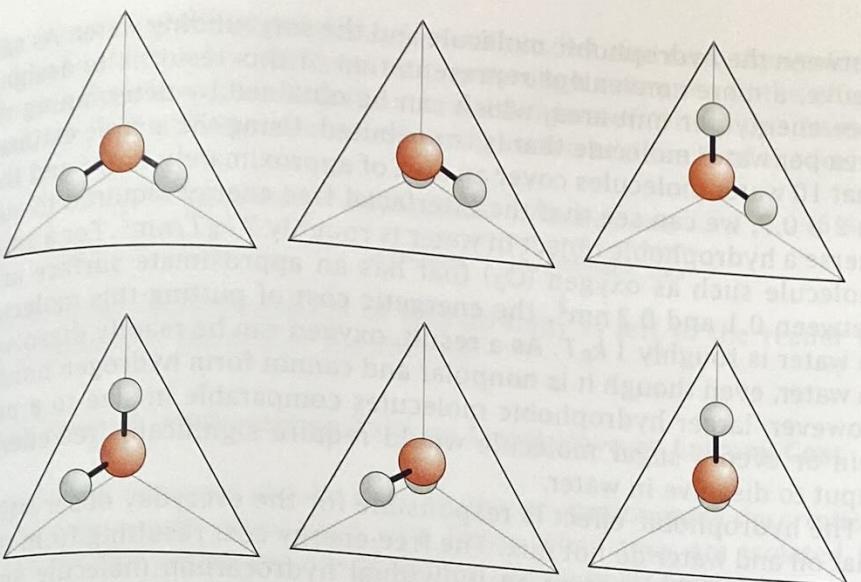


Figure 5.28: Orientations of water molecules in a tetrahedral network. Each image shows a different arrangement of the water molecule that permits the formation of hydrogen bonds with neighboring water molecules. The hydrogen bonds are in the directions of the vertices that are *not* occupied by hydrogens in the figure (Adapted from K. Dill and S. Bromberg, Molecular Driving Forces, 2nd ed., Garland Science, 2011.)

disadvantage associated with the presence of nonpolar molecules (see Dill and Bromberg (2011) for a clear description of this effect).

The six orientations that a water molecule can assume derive from the six ways of choosing to point the hydrogen atoms associated with the water molecule of interest towards the vertices of a tetrahedron. If one of the four water molecules in its immediate vicinity is replaced by a nonpolar molecule, then the number of available orientations drops to three since one of the possible hydrogen bonding partners is now gone. For example, if we assume that the neighboring water molecule in the direction of the lower right-hand vertex of Figure 5.28 is removed, this means that hydrogen bonds can no longer be formed with the oxygen on the water shown in the figure and the hydrogen atoms on the missing water molecule. As a result, the three configurations in the bottom of Figure 5.28 are now forbidden. This simple model predicts that the presence of the nonpolar molecule deprives each neighboring water molecule of half of its possible orientations as a participant in the hydrogen bonding network. The entropy change of each such water molecule is given by

$$\Delta S_{\text{hydrophobic}} = \frac{k_B \ln 3}{\text{constrained H}_2\text{O}} - \frac{k_B \ln 6}{\text{unconstrained H}_2\text{O}} = -k_B \ln 2. \quad (5.40)$$

Thus far, we have determined the entropy loss per water molecule. To make our estimate useful, we now need to estimate the number of water molecules that are impacted by the presence of the nonpolar (that is, hydrophobic) molecule of interest.

We can obtain a quantitative description of the hydrophobic cost to place a hydrophobic molecule in water as

$$\Delta G_{\text{hydrophobic}}(n) = n k_B T \ln 2, \quad (5.41)$$

where n is the number of water molecules adjacent to the nonpolar molecule of interest. Here we have accounted only for the entropic contribution to the free energy cost, which is given by $-T \Delta S_{\text{hydrophobic}}$. One particularly useful way of characterizing our result is to say that the presence of hydrophobic molecules incurs some free-energy cost per unit area ($\gamma_{\text{hydrophobic}}$) and hence that the free-energy cost to embed a given hydrophobic molecule in water is obtained as $\Delta G_{\text{hydrophobic}} = \gamma A$, where A is the effective area of the interface

between the hydrophobic molecule and the surrounding water. As said above, a more convenient representation of this result is to assign a free energy per unit area, which can be obtained by determining the area per water molecule that is contributed. Using the simple estimate that 10 water molecules cover an area of approximately 1 nm^2 and that $\ln 2 \approx 0.7$, we can see that the interfacial free energy required to submerge a hydrophobic object in water is roughly $7 k_B T/\text{nm}^2$. For a small molecule such as oxygen (O_2) that has an approximate surface area between 0.1 and 0.2 nm^2 , the energetic cost of putting this molecule in water is roughly $1 k_B T$. As a result, oxygen can be readily dissolved in water, even though it is nonpolar and cannot form hydrogen bonds. However, larger hydrophobic molecules comparable in size to a protein or even a sugar molecule would require significant free-energy input to dissolve in water.

The hydrophobic effect is responsible for the everyday observation that oil and water do not mix. The free-energy cost resulting from this simple model for putting an individual hydrocarbon molecule such as octane into a watery environment is of the order of $15 k_B T$. Each addition of a new molecule of octane to water costs the same amount of free energy additively. However, if the octane molecules clump together, the total surface area of the clump may be much less than the sum of their individual surface areas. In water at room temperature, where individual molecules can jiggle around rapidly, it usually takes no more than a few seconds for the molecules to sort themselves out such that the interfacial surface is minimized.

Amino Acids Can Be Classified According to Their Hydrophobicity

The energies associated with the hydrophobic effect are extremely important at both the molecular and cellular scales in dictating the formation of structures. For example, consider a protein that contains a variety of amino acid side chains, some of which are hydrophilic (able to form hydrogen bonds with water) and others of which are hydrophobic. From the argument outlined above, it is clear that there must be a free-energy cost for the hydrophobic side chains to exist in an aqueous environment. As a first approximation, the folding of proteins into defined three-dimensional structures can be thought of as an application of the principle of the separation of oil and water. The protein is made up of an elastic backbone from which dangle a mixture of hydrophobic and hydrophilic amino acid side chains. As described above, the entropic demands of the system will tend to force the hydrophobic side chains to gather together in a sequestered internal oil droplet at the heart of the protein. Hydrophilic amino acid side chains will tend to remain on the protein surface where they can form hydrogen bonds with water. This concept was illustrated in Figure 5.8 (p. 203).

To make an accurate quantitative model describing the role of the hydrophobic effect in protein folding, we would have to know the relative free-energy cost for water exposure for each of the 20 amino acids. However, as a useful simplified strategy for building intuition, we will start by simply dividing the amino acids into two broad groups, one that includes all hydrophobic residues (H) and the other that includes all hydrophilic or polar residues (P). As we will explore in more detail in Chapter 8, this drastically oversimplified model provides useful estimates for many aspects of structure.

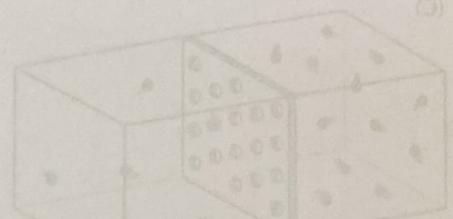
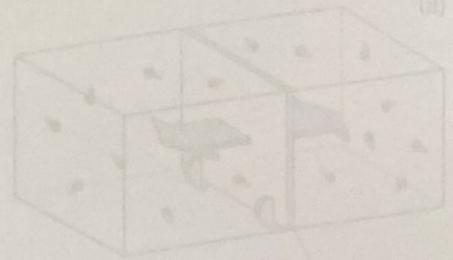
As a result of the arguments given above, we can rank the various hydrophobic amino acids most simply through reference to the effective area that they present to the surrounding water. Within this framework, the hydrophobic cost of exposing such a residue is of the form

$$\Delta G_{\text{hydrophobic}} \approx \frac{\gamma_{\text{hydrophobic}}}{\text{cost/area}} \cdot \frac{A_{\text{hydrophobic}}}{\text{hydrophobic area}} \quad (5.42)$$

The detailed implementation of this strategy is left to the reader in the problems at the end of the chapter.

When in Water, Hydrocarbon Tails on Lipids Have an Entropy Cost

These same ideas can also be used to give an approximate description of the free energy associated with lipids when they are isolated in solution. Lipid molecules are characterized by polar head groups that are attached to long, fatty acid tails that are hydrophobic. The simple and useful idea in this case is to consider each such tail as though it presents a cylinder of hydrophobic material and to assign a free-energy cost to isolated lipids given by the product of the hydrophobic free-energy cost per unit area computed above and the area presented by the "cylinder" from the lipid tails. The free-energy cost associated with isolated lipids leads to the key driving force resulting in the formation of lipid bilayers.



Overview: In which the behavior of salty solutions is described using electrostatics and statistical mechanics

The macromolecules of life inhabit a watery medium. The charge state of DNA and proteins is largely controlled by the ionic character of the surrounding solution. Lipid molecules form ordered bilayers as a result of the unfavorable interactions of their tails with water. In this chapter, we explore the electrostatics of charges in water and how the energetics of such charges plays a role in dictating the binding and assembly reactions that are so central to biology. The culmination of this discussion is the Poisson–Boltzmann theory, which unites simple ideas from electrostatics with the central features of statistical mechanics. These ideas will be explored particularly through case studies in viral packing and assembly.

9.1 Water as Life's Aether

All life on Earth depends on water. Denial of water to cells and organisms rapidly leads to death. In Chapter 12, we will discuss some of the special mechanical properties of water that cells and organisms experience. A second and even more important aspect of water as the medium for life is its unusual ability to interact with charged molecules ranging from individual ions such as K^+ and Na^+ to enormous charged macromolecules such as DNA. Charge interactions play a very special role in the function of biological molecules because they can act over long distances. We have frequently discussed binding reactions between various macromolecules as a result of the binding energy between those molecules. However, biological function usually requires specificity. That is, a macromolecule will bind to some very specific partners but will not bind to others of similar shape and size. In many cases, binding specificity arises because of complementary patterns of charge distribution on the surface of the two macromolecules involved in the interaction.

“
Hic rhodus, hic
salta.”

Aesop's Fables



ESTIMATE

One of the special properties of the H₂O molecule is that it can dissociate into H⁺ and OH⁻. For pure water, on average 1 out of every 10⁷ molecules will undergo this separation. However, the likelihood of separation can be influenced by the presence of other molecules that have the tendency to bind either H⁺ or OH⁻. When in water solution, molecules with this property are said to alter the solution's pH. pH is defined via $pH = -\log_{10}[H^+]$ in a water-based solution. Because proteins contain many amino acid side chains that can either accept or donate H⁺ ions to the water solution, their overall structure is strongly dependent on pH. Cells frequently take advantage of the pH dependence of protein structure as a regulatory mechanism and therefore feature many pathways for modulating local and global pH. For example, in the human body, blood pH is very tightly regulated at a normal value of around 7.3 and an increase or decrease in blood pH by a single unit can cause death. However, some compartments within cells may have very different pH's. For example, lysosomal compartments involved in protein degradation usually maintain a pH below 4. Cells manipulate pH by actively transporting H⁺ ions across membranes. Other effects of charge transport across membranes will be discussed in Chapter 17.

Estimate: The Eighth Continent It has been said that more is known about our nearby celestial neighbors than about our own mysterious oceans. These giant liquid reservoirs have been the scene for some of life's greatest evolutionary stories ranging from the tiny world of microbes and their viruses to the majestic whales that are the largest animals on the planet. Indeed, the subject of biogeography has made much of the biodiversity of the different continents, though the Earth's great oceans harbor some of the weirdest organisms of all, making them perhaps the greatest "continent" of them all.

The backdrop for life in the ocean is a salty environment characterized by roughly 1 mole of salt for every kilogram of water. Given that there are 18 g of water per mole and 1000 g of water in each such kilogram, this means that the number of moles of water is

$$\text{moles of water in a kilogram} = \frac{1000 \text{ g/L}}{18 \text{ g/mol}} \approx 55.5 \text{ M.} \quad (9.1)$$

What this means in turn is that the mole fraction of salt in the ocean is

$$\text{mole fraction of salt} = 1/55.5 \approx 0.018. \quad (9.2)$$

More extreme examples such as Mono Lake in California and the Great Salt Lake in Utah are characterized by concentrations of salt between 3 and 8 times higher than that found in the ocean, with these high concentrations placing special demands on the living occupants of these lakes.

In Section 6.2.3, we already saw the significance of these kinds of salt concentrations for osmotic pressure and we may use the relation $\Delta\Pi = ck_B T$ to derive a simple rule of thumb that a concentration difference of 100 mM corresponds to a

pressure difference of

$$\frac{100 \times 10^{-3} \times 6 \times 10^{23}}{1000 \text{ cm}^3} \times \frac{10^6 \text{ cm}^3}{1 \text{ m}^3} \times 4 \times 10^{-21} \text{ J}$$

$$\approx 24 \times 10^4 \frac{\text{N}}{\text{m}^2} = 2.4 \text{ atm.} \quad (9.3)$$

When seen in this way, it is clear that the salt content of life's watery medium can lead to large osmotic pressures.

The utility of pH regulation of protein structure is vividly illustrated during the invasion of host cells by influenza virus. Influenza virus is surrounded by a membrane containing many copies of a protein called hemagglutinin (HA) that is capable of mediating membrane fusion. When the virus is outside a host cell, for example when it is being scattered in the sneeze droplets of an infected person, HA is in an inactive conformation. Only after being taken up by a cell into a compartment with low pH does the HA protein change into a form that can fuse with the membrane as shown in Figure 9.1. In this way, the virus takes advantage of the host cell's preference to regulate pH within certain cellular compartments as a clue to let the virus know that it has been taken up by an unsuspecting cell and should initiate its program of replication and destruction.

The present chapter examines water, animated by the view that water is the medium of biochemical life. The reader is reminded of Figure 2.4 (p. 42), in which we carried out the single-molecule census of a typical bacterium. From our present perspective, what is particularly important about the numbers quoted there is that they reveal the enormous quantity of both water molecules and their attendant ions. Using the rough estimate that 70% by mass of a typical cell is water, we found that there are roughly 2×10^{10} water molecules in each bacterium. Similarly, estimates of the concentrations (mM) of ions such as K^+ and Na^+ tell us that there are roughly 10^7 ions populating a typical bacterium.

In addition to the interesting mechanical questions that can be raised about biological fluids in motion to be taken up in Chapter 12, it is also of interest to examine the way in which water serves as a kind of aether for biochemical action. One of our key points in undertaking

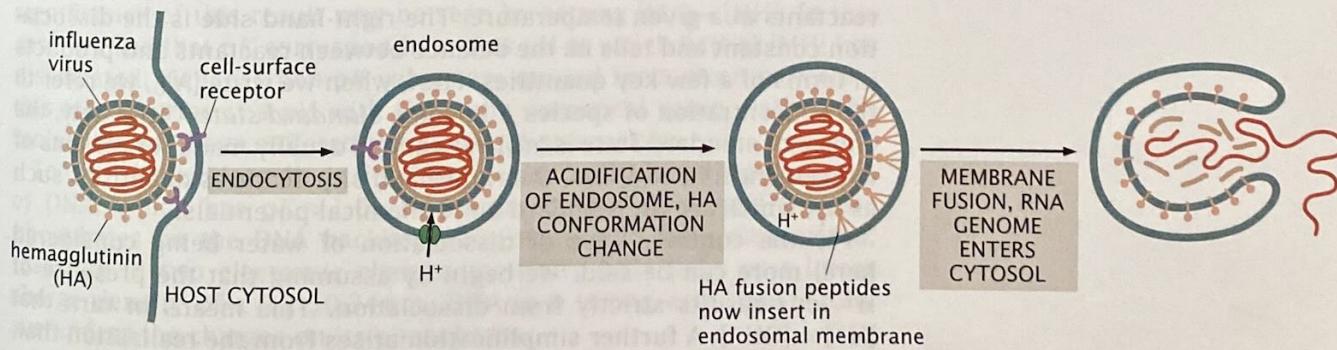


Figure 9.1: Influenza virus uptake. This diagram shows the pH-dependent process by which the nucleocapsid of the influenza virus is delivered into the cytoplasm of a mammalian host cell. The virus binds to receptors on the cell surface and is taken up by receptor-mediated endocytosis. After endocytosis, specialized proton pumps are added to the endosomal membrane, transporting H^+ ions from the cytoplasm, consequently causing a drop in pH. The pH decrease causes a dramatic conformational change in the influenza envelope protein, HA. The extended, low-pH form of the protein catalyzes fusion of the viral membrane with the endosomal membrane, releasing the virus contents into the cytoplasm of the cell. (Adapted from B. Alberts et al., Molecular Biology of the Cell, 5th ed., Garland Science, 2008.)

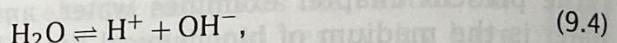
an examination of the role of water as the seat of biochemical action will be a recognition of the central importance of charges that both are free in solution and can be liberated from their macromolecular hosts. In particular, we will examine how these issues are central to questions such as the salt dependence of DNA-protein interactions and the assembly of viruses.

9.2 The Chemistry of Water

9.2.1 pH and the Equilibrium Constant

Dissociation of Water Molecules Reflects a Competition Between the Energetics of Binding and the Entropy of Charge Liberation

To examine pH from a quantitative perspective requires that we consider the interplay of energetic and entropic effects in dictating charge separation. In particular, the competition between energy minimization (bound water molecules) and entropy maximization (ionic dissociation of water) sets the stage for many biological reactions and is a compelling and enlightening example of the uses of the law of mass action developed in Section 6.3 (p. 267). The reaction of interest can be written as



with the idea being that we are interested in finding out what fraction of the water molecules in a sample of water are in a dissociated state. For the purposes of notational simplicity, we replace the v_i favored in the general derivation of Equation 6.104 (p. 269) with $v_{\text{H}_2\text{O}}$, v_{H^+} , and v_{OH^-} , with the further realization that for this reaction we have $v_{\text{H}_2\text{O}} = -1$, $v_{\text{H}^+} = 1$, and $v_{\text{OH}^-} = 1$. Using these definitions, the law of mass action (see Section 6.3 on p. 267) for the problem of dissociation becomes

$$\frac{[\text{H}^+][\text{OH}^-]}{[\text{H}_2\text{O}]} = \frac{[\text{H}^+]_0[\text{OH}^-]_0}{[\text{H}_2\text{O}]_0} \exp\left(-\frac{\mu_{\text{H}^+}^0 + \mu_{\text{OH}^-}^0 - \mu_{\text{H}_2\text{O}}^0}{k_B T}\right). \quad (9.5)$$

What this equation tells us may be understood as follows. The left-hand side tells us the ratio of the concentrations of products to reactants at a given temperature. The right-hand side is the dissociation constant and tells us the balance between reactants and products in terms of a few key quantities. First, when we write $[A]_0$, we refer to the concentration of species A in some *standard state*. Ultimately, the choice of standard state is arbitrary and is usually made for reasons of convenience. In addition, the right-hand side features quantities such as μ_i^0 , which are the standard state chemical potentials.

For the concrete case of dissociation of water being considered here, more can be said. We begin by assuming that the presence of H^+ ions results strictly from dissociation. This means in turn that $[\text{H}^+] = [\text{OH}^-]$. A further simplification arises from the realization that, for all practical purposes, $[\text{H}_2\text{O}] = [\text{H}_2\text{O}]_0$. This claim results from the fact that the reaction in Equation 9.4 leads to so little product that it barely perturbs the initial concentration of water, $[\text{H}_2\text{O}]_0 = 55 \text{ M}$. As a result, we can assume $[\text{H}_2\text{O}] = [\text{H}_2\text{O}]_0$ in Equation 9.5. This means that $[\text{H}^+]_0 = [\text{OH}^-]_0 = 1 \text{ M}$ and using the fact that the measured energy change in the reaction is $\mu_{\text{H}^+}^0 + \mu_{\text{OH}^-}^0 - \mu_{\text{H}_2\text{O}}^0 \approx 79.9 \text{ kJ/mol}$, we find

$[\text{H}^+][\text{OH}^-] = [\text{H}^+]^2 = 1.0 \times 10^{-14} \text{ M}^2$, and hence $[\text{H}^+] = 1.0 \times 10^{-7} \text{ M}$. Recalling that the definition of pH is

$$\text{pH} = -\log_{10}[\text{H}^+], \quad (9.6)$$

where $[\text{H}^+]$ is in molar units, we see that we have recovered $\text{pH} = 7$ for water under standard conditions. To gain further intuition about pH, in Figure 9.2 we plot the average distance between H^+ ions as a function of the pH as another way of viewing the significance of the pH concept.

9.2.2 The Charge on DNA and Proteins

The Charge State of Biopolymers Depends upon the pH of the Solution

We have already noted that the charge state of macromolecules is a critical factor in determining both their structure and function. To investigate the way that this charge state is tuned, we consider the generic reaction



where M is the macromolecule of interest. From our earlier discussion of the law of mass action (see Section 6.3 on p. 267), we note that there is a dissociation constant for this reaction given by

$$K_d = \frac{[\text{H}^+][\text{M}^-]}{[\text{HM}]} \quad (9.8)$$

A useful measure of the tendency of a particular molecule to undergo the dissociation reaction is known as the pK and is defined by

$$\text{pK} = -\log_{10} K_d. \quad (9.9)$$

If we take the logarithm of both sides of Equation 9.8, we are left with

$$-\log_{10} K_d = -\log_{10}[\text{H}^+] - \log_{10}[\text{M}^-] + \log_{10}[\text{MH}]. \quad (9.10)$$

Recalling the definitions of both pK and pH we see that this may be rewritten as

$$\text{pH} = \text{pK} + \log_{10} \frac{[\text{M}^-]}{[\text{MH}]}, \quad (9.11)$$

a result known as the Henderson-Hasselbalch equation. The physical significance of this result may be seen by setting $[\text{M}^-] = [\text{MH}]$. In this case, we see that pK corresponds to that pH at which half of $[\text{MH}]$ has dissociated. Hence, when pK values are quoted for a given molecule, this tells us that at a pH with the same numerical value, half of the molecules will have suffered the dissociation reaction.

To see these ideas in action, we begin by considering the case of DNA, which has $\text{pK} \approx 1.0$. This tells us that at normal pH, the phosphates on the DNA backbone are essentially fully dissociated, resulting in two electronic charges for every base pair, or a linear charge density of $\lambda = 2e/0.34 \text{ nm}$. DNA is a strong acid and readily surrenders the charges on its phosphates.

Different Amino Acids Have Different Charge States

A more compelling application of these ideas is to the charge state of proteins since different side groups have different dissociation tendencies, resulting in the fact that at different pHs, different side groups will be in different states of dissociation (we already saw this

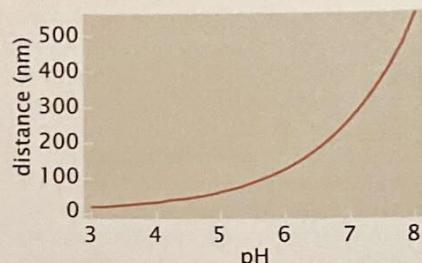


Figure 9.2: Distance between H^+ ions as a function of pH.

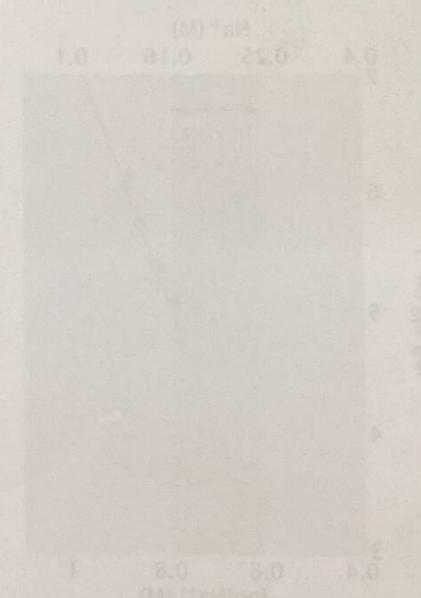


Figure 9.10: Methanesulfonic acid ionizes in water. The ionization of methanesulfonic acid is shown as a function of pH. The x-axis is labeled "pH" and ranges from 0.0 to 14.0. The y-axis is labeled "QH (%)" and ranges from 0 to 100. The curve starts at (0, 0) and rises sharply, reaching 100% ionization at approximately pH 1.3. A vertical dashed line is drawn at pH 1.3, labeled "pK".

in the titration curve in Figure 5.9 on p. 204). In Chapter 10, we will discuss the spontaneous self-assembly of the nucleosome as DNA segments wrap onto histone octamers. We will see that the lysine and arginine residues on the histones present positive charges that interact favorably with the negative charges on the DNA and make it possible to overcome the steep elastic cost of bending the DNA to fit on the histones. More generally, the interplay of protein charge and pH is one of the primary ways that the repertoire of protein responses is extended.

9.2.3 Salt and Binding

Many events in the lives of biological molecules involve specific recognition of one molecule by another. Some examples we have considered (see Chapter 6) include RNA polymerase binding to DNA specifically at promoter sites and receptors binding their specific ligands. The surface distribution of charges on these macromolecules plays a critical role in determining the specificity of these recognition events as well as their strength. The importance of electrostatics in macromolecular binding is easily observed in the laboratory because nearly all such binding interactions are strongly dependent on the concentration of ions in the solution in which they are measured.

One set of examples of salt effects on binding are those related to DNA–protein interactions, and especially the way in which regulatory proteins (transcription factors) bind to DNA. In Section 6.1.2 (p. 244) we examined the binding of RNA polymerase to promoters. We also noted that under most circumstances, the decision to create an mRNA transcript at a gene of interest is dictated by the binding of repressors and activators, which often work by inhibiting or enhancing the binding of polymerase. The case study that will run as a thread through the entire book is that of the *lac* operon, introduced in Figures 4.13 (p. 155) and 4.15 (p. 158). An example of how the affinity of a transcription factor (that is, Lac repressor) for DNA is tuned by the concentration of salt is shown in Figure 9.3.

There are several intuitive ways to begin to think about these results. One of the ideas to be explored in the remainder of the chapter is that the ions in salty solutions assemble in a screening cloud around the macromolecules that have the potential to bind. When this binding reaction occurs, there is a release of the ions in these screening clouds, which results in an entropy increase. A second feature that can be attributed to such binding interactions is that, with increasing ion concentration, the ions can actually interact with the receptor in a way that competes with the ligands. Toy models that explore these effects are presented in the problems at the end of the chapter, though we note that there are many subtleties that these toy models do not even begin to acknowledge.

9.3 Electrostatics for Salty Solutions

As shown above, the use of measured equilibrium (or dissociation) constants can take us a long way toward understanding the charge state of macromolecules in solution. On the other hand, to really examine the microscopic underpinnings of the equilibrium constant, we need to be able to assess electrostatic potentials. Further, a host of problems, such as the energetics of viral DNA packing, the molecular origins of nucleosomal stability, and the nature of membrane potentials, require us to have certain key facts about electrostatics

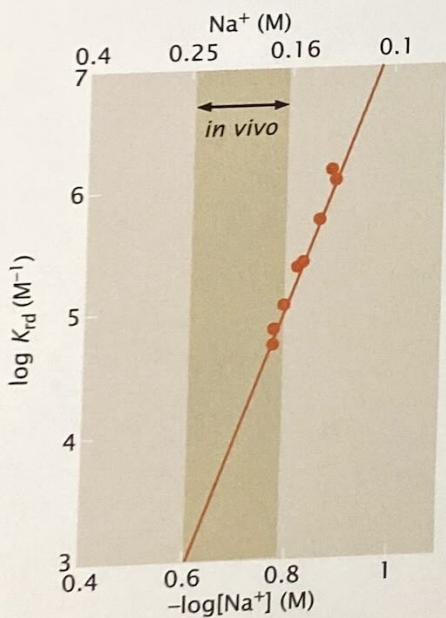


Figure 9.3: Salt dependence of protein–DNA binding. Equilibrium constant for Lac repressor binding to nonspecific DNA as a function of Na^+ concentration. The range of *in vivo* salt concentrations is shaded. (Adapted from Y. Kao-Huang et al., *Proc. Natl Acad. Sci. USA* 74:4228, 1977.)



The Mathematics of Water

12

Overview: In which life's watery medium is studied as a dynamical object

The preceding six chapters have all shared a common assumption that has been both their strength and their weakness. That assumption is that approximate physical descriptions of biological systems can invoke the concept of equilibrium. We have taken pains to delimit the conditions under which this assumption is valid or reasonable. But now it is time to acknowledge the reality that living systems generally exist far from equilibrium and that *dynamic* descriptors such as time, rates, and trajectories are frequently the natural language of physical biology. This chapter undertakes an analysis of the dynamics of life's watery medium. In particular, we will develop the physical and mathematical tools to make estimates of fluid dynamics both for phenomena within cells and for environmental interactions such as swimming.

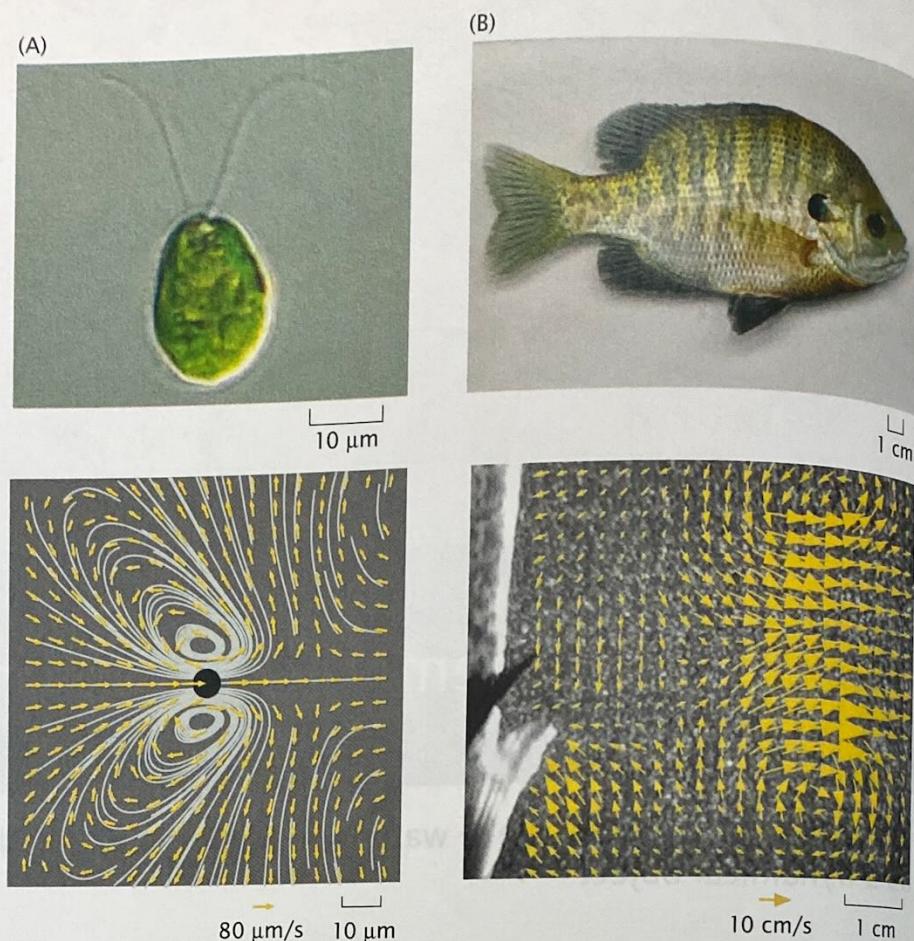
12.1 Putting Water in Its Place

In a Darwinian environment where organisms compete for limited resources, the ability to consume, grow, and reproduce more rapidly than one's rivals may lead to a selectable advantage. In this chapter, we will begin our exploration of biological dynamics with a celebration of water, the medium of life on Earth. Oceans cover 70% of the Earth's surface and humans diving into these oceans are greeted by a rich diversity of living forms. But this panoply of life is nothing in comparison with the teeming masses that are revealed upon glancing through a microscope at a drop of pond water. The many organisms that actively swim through water, chasing prey, avoiding predators, and seeking more favorable environments for life are practical masters at managing fluid dynamics. No vessel yet built by man can move through water with the energetic efficiency of a blue whale, anchovy, or *Paramecium*. Even organisms that have left the ocean and carry

“ There are these two young fish swimming along and they happen to meet an older fish swimming the other way, who nods at them and says ‘Morning, boys. How’s the water?’ And the two young fish swim on for a bit, and then eventually one of them looks over at the other and goes ‘What the hell is water?’ ”

David Foster Wallace

Figure 12.1: Swimming across scales. (A) The single-cell alga *Chlamydomonas reinhardtii* swims with the help of its flagella at about $100 \mu\text{m/s}$. The velocity field of the fluid around it can be visualized using fluorescent beads as tracer particles. (B) Bluegill sunfish swimming at a speed of about 10 cm/s produce a flow field in the surrounding water, which can be visualized in a similar fashion, using fluorescent tracer particles. In this chapter, we explore the physics of fluids in motion and describe the key differences between flows at length and velocity scales associated with microorganisms and fish. (A (top), courtesy of Brian Piasecki, Lawrence University; A (bottom), adapted from J. S. Guasto et al., *Phys. Rev. Lett.* 105:168102, 2010; B (top), courtesy of the Ohio Department of Natural Resources, Division of Wildlife; B (bottom), adapted from E. G. Drucker and G. V. Lauder, *J. Exp. Biol.* 204:431, 2001)



their own water internally require exquisite control over the water's movement as in blood circulation or the rising sap in plants.

Water plays an important part in the living world on scales ranging from a single cell to groups of organisms swimming in schools, as illustrated in Figure 12.1. Its physical and chemical properties are of direct relevance to the structure and function of biomolecules. Therefore, intuition about water, and fluids in general, is of considerable importance when exploring the living world. In this chapter, we investigate the properties of fluids with regards to their motion by developing the model of the Newtonian fluid.

12.2 Hydrodynamics of Water and Other Fluids

12.2.1 Water as a Continuum

Though Fluids Are Composed of Molecules It Is Possible to Treat Them as a Continuous Medium

In order to formulate a mathematical description of a fluid such as water, we must first decide on the proper "coordinates." In this regard, a fluid can be thought of as a "box of molecules" as shown in Figure 12.2. The water molecules are thermally agitated and interact with each other via forces such as the van der Waals force. In this case, the description of a fluid would entail providing a full list of position and momentum coordinates of all the molecules. This is the worldview of molecular dynamics, which we will largely avoid in our search