Physical Biology

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For Ginette, Mike, Sean, Peter, Mia, James, Dylan, and Christopher

Contents

Preface *page* iv

1 Atoms and Molecules 1
- 1.1 Atoms 1
- 1.2 Bonds between atoms 1
- 1.3 Oxidation and reduction 5
- 1.4 Molecules in cells 6
- 1.5 Sugars 6
- 1.6 Hydrocarbons, fatty acids, and fats 8
- 1.7 Nucleotides 9
- 1.8 Amino acids 16
- 1.9 Proteins 18

Exercises 19

2 Metabolism 22
- 2.1 Glycolysis 22
- 2.2 The citric-acid cycle 22

3 Molecular devices 26
- 3.1 Transport 26

4 Probability and statistics 27
- 4.1 Mean and variance 27
- 4.2 The binomial distribution 28
- 4.3 Random walks 31
- 4.4 Diffusion 32
- 4.5 The Poisson distribution 33
- 4.6 The gaussian distribution 34
- 4.7 The error function erf 36
- 4.8 The Maxwell-Boltzmann distribution 37
- 4.9 Characteristic functions 39

4.10 Central limit theorem 40
Exercises 42

5 Statistical Mechanics 45
5.1 Equilibrium 45
5.2 Entropy 48
5.3 Temperature and entropy 49
5.4 The partition function 50
5.5 The Helmholtz free energy 52
5.6 The Gibbs free energy 53
Exercises 55

6 Liquids 56
6.1 Diffusion 56
6.2 Langevin's Theory of Brownian Motion 58
6.3 The Einstein-Nernst relation 62
6.4 The Poisson-Boltzmann equation 63
6.5 Reynolds number 64
6.6 Fluid mechanics 67

7 Cell structure 68
7.1 Organelles 68
7.2 Membranes 69
7.3 Membrane potentials 71
7.4 Potassium leak channels 73
7.5 The Debye-Hückel equation 74
7.6 The Poisson-Boltzmann equation in one dimension 77
7.7 Neurons 78
Exercises 80

8 Polymers 81
8.1 Freely jointed polymers 81
8.2 Entropic force 82

9 Some Experimental Methods 84
9.1 Time-dependent perturbation theory 84
9.2 FRET 86
9.3 Fluorescence 93
9.4 Some mathematics 97
References 99
Index 100

Preface

Most books on biophysics hide the physics so as to appeal to a wide audience of students. This book describes the physics of biology as simply as possible and is intended for students who have studied college-level physics and mathematics for two or three years. I hope they it easier to read than books of hidden physics.

A list of errata will be maintained at theory.phys.unm.edu/physicalbiology and all the solutions to the exercises will be available to instructors who adopt the book for their courses.

Several friends and colleagues—Elaine Bearer, Roy Glauber, Jooyoung Lee, Keith Lidke, V. Adrian Parsegian, Sudhakar Prasad, ...—have given me valuable advice. Students have helped with questions, ideas, and corrections. Prominent among these were David Amdahl, Hanieh Mazloom Farsibaf, Farzin Farzam, Mohamadreza Fazel, Matthew Koppa, Lei Ma, Gabriel Sandoval, ...

1

Atoms and Molecules

1.1 Atoms

The most important elements of life are hydrogen H, carbon C, nitrogen N, and oxygen O. These four elements together with calcium Ca and phosphorus P make up 99 percent of the mass of the human body. Potassium K, sulfur S, chlorine Cl, sodium Na, and magnesium Mg constitute another 3/4 of 1 percent. Trace amounts of manganese Mn, iron, Fe, cobalt Co, copper Cu, zinc Zn, iodine I, selenium Se, bromine Br, and molybdenum Mo make up the remaining 1/4 of 1 percent of the mass of the human body. These 17 elements are among the most abundant elements on the surface of the Earth. Elements heavier than lithium Li were made in stars that later exploded.

1.2 Bonds between atoms

Electrostatic interactions form four kinds of bonds between atoms: ionic, hydrogen, van der Waals, and covalent.

The simplest is the **ionic bond** which occurs when atoms have opposite charges. The potential energy between two atoms carrying charges q and q' and separated by a distance r in the vacuum is

$$V(r) = \frac{q\,q'}{4\pi\epsilon_0 r} \tag{1.1}$$

in which ϵ_0 is the **electric constant** $\epsilon_0 = 8.854 \times 10^{-12}$ F/m. The resulting force

$$\boldsymbol{F} = -\boldsymbol{\nabla} V(r) \tag{1.2}$$

is attractive when the charges have opposite signs and repulsive when they

have the same sign. Many crystals are arrangements of ions of opposite charge in solid lattices. Table salt, NaCl, is a common example.

A typical ionic bond in vacuum is 0.25 nm long and has an energy of 3.47 eV or 80 kcal/mol. This energy is the kinetic energy an electron gets from a potential difference of 3.47 V; it also is the energy that when given to Avogadro's number ($N_A = 6.022 \times 10^{23}$) of water molecules would raise the temperature of a liter of water by 80°C.

Example 1.1 (Units of energy)**.** An **electron Volt eV** is the energy that an electron gets when falling through a potential difference of one Volt. Since the charge of an electron is $e = 1.60217662 \times 10^{-19}$ of a Coulomb C this energy is 1.602×10^{-19} of a Joule J so 1 eV = 1.602×10^{-19} J. The **kilocalorie, kcal** is the energy (4,184 J) that raises 1 kilogram kg of water or 1 liter of water by 1 degree centigrade or Kelvin at a pressure of 1 atmosphere. A **mol** of a given molecule is **Avogadro's number** 6.0221367×10^{23} of those molecules. So 1 eV = $6.0221367 \times 10^{23} \times 1.602 \times 10^{-19}/4184 = 23.06$ kcal/mol = $6.0221367 \times 10^{23} \times 1.602 \times 10^{-19} = 96.485$ kJ/mol. A Dalton (Da) is one gram per mole or 1.66×10^{-27} kg. An atom of oxygen has a mass of 16 Da. □

Biology does not normally take place in a vacuum. The potential energy of two atoms of charges q and q' separated by a distance r in water is

$$V(r) = \frac{q\,q'}{4\pi\epsilon r} \tag{1.3}$$

in which the **permittivity** ϵ of water is $\epsilon = 80.1\,\epsilon_0$ at 20°C and $74.16\,\epsilon_0$ at 37°C. This drop of permittivity with temperature means that the electrostatic interactions become stronger as the temperature rises, which may partly explain why cells are so sensitive to temperature. Because ionic bonds are so short, their energies in water drop from their vacuum values by a factor of 27 rather than by a factor of 80, to about 3 kcal/mol.

A hydrogen atom that is bonded to an atom of nitrogen or oxygen loses part of its electron cloud to the nitrogen or oxygen atom. The hydrogen atom therefore carries a small positive charge, and the atom of nitrogen or oxygen a small negative charge. The resulting ionic bond between a positive hydrogen atom bonded to an atom of nitrogen or oxygen and a negative nitrogen or an oxygen atom is called a **hydrogen bond**. Hydrogen bonds are about 0.3 nm long and have an energy of 4 kcal/mol in vacuum and 1 kcal/mol in water.

The **van der Waals bond** is about 0.35 nm long and has an energy of about 0.1 kcal/mol in vacuum and in water. It arises because two neutral

atoms in their ground states attract each other weakly. This electrostatic attraction is simplest in the case of two hydrogen atoms.

Example 1.2 (The van der Waals bond)**.** Let R be the distance between two nuclei one at the origin and the other at $R\hat{\boldsymbol{z}}$ so that the electrons are at $\boldsymbol{r}_1$ and at $R\hat{\boldsymbol{z}} + \boldsymbol{r}_2$. Then the hamiltonian H for the two atoms is $H = H_{01} + H_{02} + V$ in which the electrostatic potential is

$$V = \frac{e^2}{4\pi\epsilon_0}\left[\frac{1}{R} + \frac{1}{\sqrt{(R\hat{\boldsymbol{z}} + \boldsymbol{r}_2 - \boldsymbol{r}_1)^2}} - \frac{1}{\sqrt{(\boldsymbol{r}_1 - R\hat{\boldsymbol{z}})^2}} - \frac{1}{\sqrt{(R\hat{\boldsymbol{z}} + \boldsymbol{r}_2)^2}}\right] \tag{1.4}$$

in SI units. If the distance R between the atoms is much bigger than the distances r_1 and r_2 of the electrons from their nuclei, then one can expand the square-roots in powers of $1/R$ and approximate (exercise 1.1) the potential as

$$V \approx \frac{e^2}{4\pi\epsilon_0 R^3}\left(x_1 x_2 + y_1 y_2 - 2 z_1 z_2\right) \tag{1.5}$$

Since hydrogen atoms are spherically symmetric in their ground states, the mean value of this potential vanishes. But second-order perturbation theory gives the change in the energy of the two atoms as a sum over all the states of the two atoms except the ground state $|0\rangle$

$$\Delta E(R) = -\sum_{n>0} \frac{|\langle n|V|0\rangle|^2}{E_n - E_0}. \tag{1.6}$$

Since the potential V goes as $1/R^3$, we see that the energy $\Delta E(R)$ varies with the distance between the atoms as $1/R^6$. Since $E_n - E_0 \geq E_2 - E_0$ and since $\langle 0|V|0\rangle = 0$, we have

$$\begin{aligned} \Delta E(R) &\leq -\frac{1}{E_2 - E_0}\sum_n |\langle n|V|0\rangle|^2 \\ &\leq -\frac{1}{E_2 - E_0}\sum_n \langle 0|V|n\rangle\langle n|V|0\rangle \\ &\leq -\frac{\langle 0|V^2|0\rangle}{E_2 - E_0}. \end{aligned} \tag{1.7}$$

A detailed computation shows that the van der Waals potential between two hydrogen atoms is

$$\Delta E(R) \approx -6.5\,\frac{e^2 a_0^5}{4\pi\epsilon_0 R^6} \tag{1.8}$$

in which $a_0 = 4\pi\epsilon_0\hbar^2/me^2 = 5.292 \times 10^{-11}$ m is the Bohr radius of the hydrogen atom (Schiff, 1968). □

As two neutral atoms approach each other more closely than a few nanometers, the van der Waals interaction can turn into a **covalent bond**. Electrons are several thousand times lighter than nuclei, and so they quickly go where the attractive force of the nuclei of the approaching atoms pulls them. They go between the two nuclei and form a negative charge that attracts the nuclei toward them. This attraction of the electrons to the nuclei and of the nuclei to the electrons holds the atoms in a tight covalent bond about 0.15 nm apart. The energy of covalent bonds is of the order of a few electron volts or 90 kcal/mol and is the same in vacuum as in water.

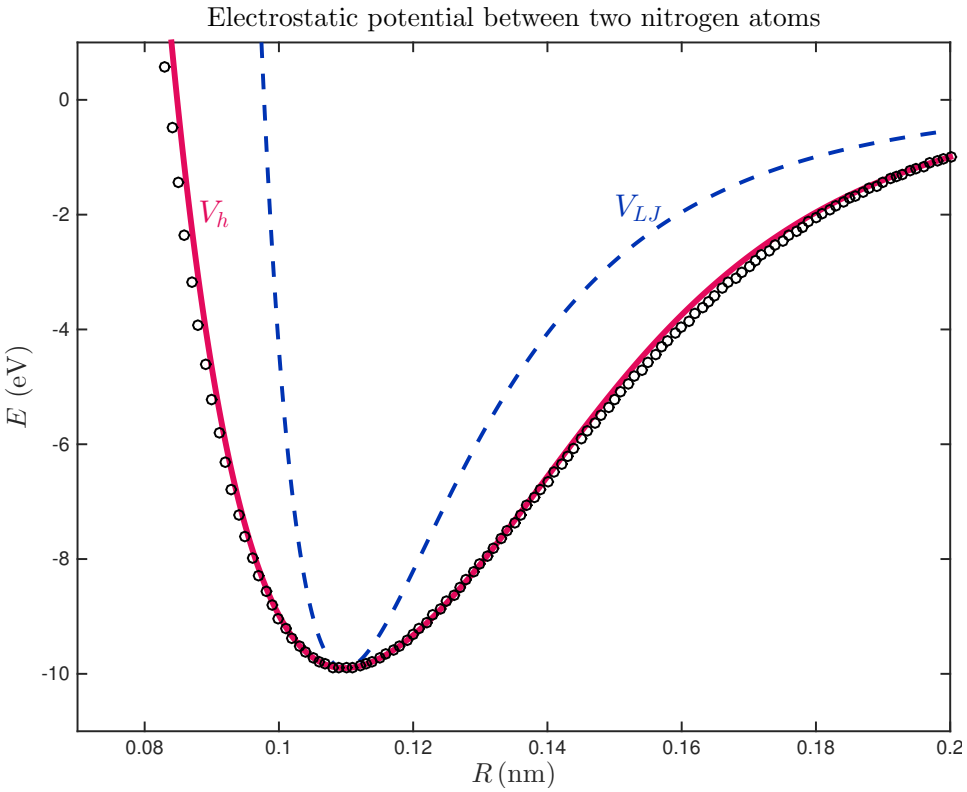

Figure 1.1 The hybrid potential $V_h(R)$ (1.9, red solid line) fits the potential between two nitrogen atoms obtained from spectroscopy (black circles) better than the Lennard-Jones potential $V_{LJ}(R)$ (1.10, blue dashes). The binding of N_2 is unusually strong because of its triple bond N≡N, which is why nitrogen is used in explosives.

One can approximate the electrostatic potential between two neutral atoms

by the hybrid potential

$$V_h(R) = ae^{-bR}(1 - cR) - \frac{C_6}{R^6 + dR^{-6}} \tag{1.9}$$

which combines the Rydberg formula of spectroscopy with the London formula for pairs of atoms. Formulas exist that relate the parameters a, b, c, and d to the internuclear separation R_0, the depth E_0, curvature k of the potential at its minimum, and the van der Waals coefficient C_6 of the pair (Cahill, 2007). In 1924, John Lennard-Jones introduced as a teaching device the simple potential

$$V_{LJ} = E_0 \left[\left(\frac{R_0}{R} \right)^{12} - 2 \left(\frac{R_0}{R} \right)^{6} \right] \tag{1.10}$$

in which R_0 is the distance between the nuclei at which the potential energy assumes its minimum value $-E_0$ (Lennard-Jones, 1924). The hybrid potential is more accurate than the Lennard-Jones potential as illustrated by the figure (1.1) for the case of two nitrogen atoms.

1.3 Oxidation and reduction

Atoms bind electrons more tightly are said to be more **electronegative**. On Linus Pauling's scale, the electronegativities of the main atoms that occur in the human body are listed in Table 1.1. Among them, oxygen is the most

Table 1.1 *Electonegativities*

K	Na	Ca	Mg	P	H	C	S	N	Cl	O
0.82	0.93	1.00	1.31	2.19	2.20	2.55	2.58	3.04	3.16	3.44

electronegative with an electonegativity of 3.44. Thus oxygen tends to steal electrons from other atoms and molecules, a process called **oxidation**. The term oxidation also is used to describe any process that raises the electric charge of an atom or molecule. Hydrogen is less electronegative than C, S, N, Cl, and O. It tends to lend its electron to other atoms or molecules. So when a molecule loses a hydrogen atom, it also loses the electron it was borrowing from the hydrogen atom. So the loss of an atom of hydrogen also is called an oxidation.

Reduction is the gain of electrons or the lowering of the charge on an atom or molecule.

1.4 Molecules in cells

Water molecules make up about 70 percent of the mass of a living cell. This molecule H_2O is an electric dipole: the two hydrogen atoms carry a small positive charge equal to one-half of the negative charge on the oxygen atom. Its dipole moment is $d = 6.2 \times 10^{-30}$ mC or 1.85 D, a unit named after Debye (1 D $= 3.34 \times 10^{-30}$mC). It is this huge electric dipole moment that increases the permittivity of water from that of vacuum by a factor of about 80.

Macromolecules make up about 26 percent of the mass of a cell. These are mainly proteins, nucleic acids, and polysaccharides.

Sugars, amino acids, nucleotides, fatty acids, their precursors, and other small molecules make up the remaining 4 percent of the mass of a living cell.

1.5 Sugars

Sugars are carbohydrates, that is, they are molecules made from carbon and water.

Example 1.3 (Sugar and sulfuric acid)**.** If you pour some concentrated sulfuric acid H_2SO_4 into a beaker of sugar and stir, the acid will draw the water from the sugar, and a column of black carbon will rise from the beaker in a cloud of steam and acid. Do this experiment outside, not in a closed classroom. □

Simple monosaccharides $(CH_2O)_n$ are chains of $n \geq 3$ carbon atoms, including one **carbonyl** C=O group, $n-1$ **hydroxyl** OH groups, and $n+1$ hydrogen atoms. A carbonyl group at one end of the chain forms an **aldehyde** aldehyde H−C=O group $^{\text{H}}>$C=O, and the sugar is an **aldose**. A carbonyl group in the middle of the chain is a **ketone** group >C=O, and the sugar is a **ketose**. The simplest sugars are **glyceraldehyde** and **dihydroxyacetone**, both $(CH_2O)_3$. Two important aldoses are **ribose** $C_5H_{10}O_5$, which has 5 carbon atoms and 5 water molecules, and **glucose** $C_6H_{12}O_6$. **Fructose** is an $n = 6$ ketose $C_6H_{12}O_6$.

A monosaccharide's linear chain of carbon atoms can form a ring when its carbonyl group reacts with one of the hydroxyl groups so that its carbonyl carbon atom binds both to its oxygen and to the oxygen of the hydroxyl group, as illustrated the figure (1.2). The carbon atom thus bound to two oxygen atoms can then react with a hydroxyl group on a second sugar expelling a water molecule and forming a **glycosidic bond** C−O−C between

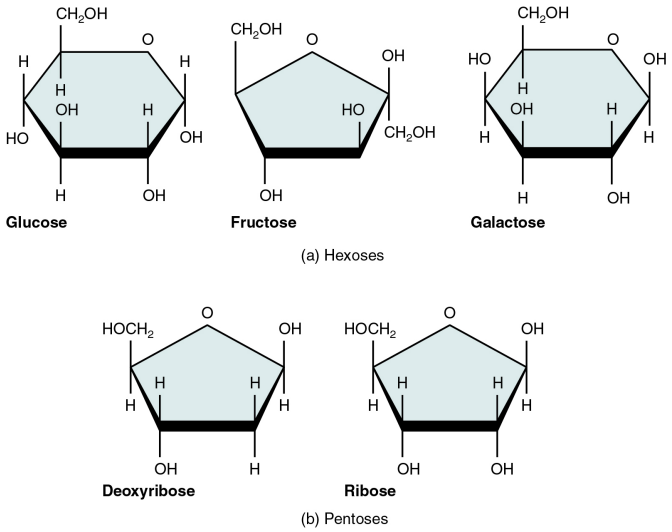

Figure 1.2 In these diagrams of five of the most important simple sugars, the unlabeled vertices denote carbon atoms. Thus ribose has five carbon atoms and glucose has six. From Anatomy & Physiology, Connexions Web site.

the two sugars. This joining of two sugars to form a **disaccharide** is called a **condensation reaction**.

Monosaccharides $(CH_2O)_n$ with the same number n of carbon-water units differ by where the carbonyl group is and in their ring forms by where the hydroxyl groups are. Some of these **isomers** are related by spatial reflexion. In cells right-handed sugars like D-glucose are more common than their left-handed isomers such as L-glucose. Two D-glucoses can form 11 different disaccharides.

Any number of monosaccharides can condense forming linear or branched polymers. Sugars can form huge numbers of different branched and unbranched polymers. A sugar polymer with only a few sugars is called an **oligosaccharide**. A sugar polymer with many sugars is a **polysaccharide**. **Glycogen** and starch are polysaccharides of glucose that cells use as sources of energy. **Glycosaminoglycans** (**GAGs**) are long unbranched chains of the same disaccharide, typically an **amino** sugar (a sugar in which an amine group replaces its terminal hydroxyl group, $C-OH \longrightarrow C-NH_2$) and a **uronic** sugar (a sugar in which an carboxyl group replaces a hydroxyl group, $C-OH \longrightarrow C-COOH$). **Cellulose** is an unbranched chain of glucose used in the cell walls of plants; **chitin** is a linear polysaccharide used

in the exoskeletons of insects. Sugars bound to proteins are **glycoproteins**; sugars bound to fats are **glycolipids**.

1.6 Hydrocarbons, fatty acids, and fats

Saturated hydrocarbons are mainly polymers of CH_2 groups. The shortest ones are methane CH_4, ethane H_3C-CH_3, propane $H_3C-CH_2-CH_3$, and butane C_4H_{10}. They are gases at room temperature. Longer polymers from pentane C_5H_{12} to pristane $C_{19}H_{40}$ are liquids at room temperature. Hydrocarbon polymers as long as eicosane $C_{20}H_{42}$ or longer are solids at room temperature, like wax. A saturated hydrocarbon has single bonds between adjacent carbon atoms and a maximal number of hydrogen atoms in each molecule; it is saturated with hydrogen. These molecules have a zigzag shape, but they are basically straight, like several v's vvvvvvv.

Unsaturated hydrocarbons have double bonds between some carbon atoms. These molecules are crooked like the fatty acids of the unsaturated fat in figure 1.5.

Hydrocarbons are a source of energy for cells as for industry.

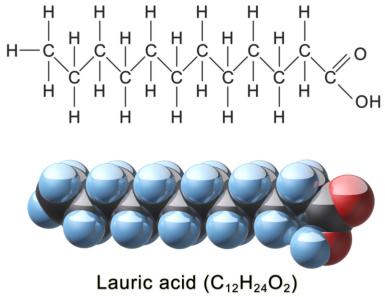

Figure 1.3 Lauric acid is a saturated fatty acid. (Courtesy of Bruce Blaus.)

An organic acid has a **carboxylic group** $O=C-OH$ which in pH 7 water loses a proton and becomes $O=C-O^-$. A **fatty acid** is a hydrocarbon with a carboxylic-acid group COOH instead of a methyl CH_3 group at one end ($-CH_2-CH_3 \longrightarrow -CH_2-COOH$). Figure 1.3 displays Lauric acid, a saturated fatty acid.

A molecule $X-O-H$ is an **oxoacid** if the group X is sufficiently **elec-**

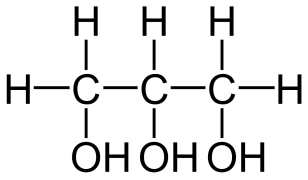

Figure 1.4 *Enzymes attach fatty acids and phosphate groups to the three hydroxyl groups of this glycerol or glycerin molecule to make triacylglycerides and phospholipids. (Courtesy of NEUROtiker.)*

tronegative as to attract electrons from the oxygen atom releasing a proton when in water, $\mathrm{X{-}O{-}H} \longrightarrow \mathrm{X{-}O^-} + \mathrm{H^+}$. An **acyl** group (aka, an **alkanoyl** group) is what's left when the hydroxyl group OH is removed from an oxoacid. An acyl group formed from a carboxylic acid $\mathrm{R{-}COOH}$ has a double-bonded oxygen atom $\mathrm{R{-}C{=}O}$ and a carbon atom that can form a single bond with something else.

Cells store fatty acids by connecting them in groups of three to **glycerol** $\mathrm{HO{-}CH_2{-}CHOH{-}CH_2{-}OH}$ (figure 1.4) through **ester linkages**

$$\mathrm{R{-}C{-}OH + COOH{-}(CH_2)_nCH_3} \longrightarrow \mathrm{R{-}C{-}O{-}COO{-}(CH_2)_nCH_3 + H_2O} \tag{1.11}$$

forming **triacylglycerides** also known as **triglycerides** and more simply as fats. In the image of the very unsaturated triacylglyceride in figure 1.5, the vertices represent carbon atoms, the hydrogen atoms are omitted (except for the methyl $\mathrm{CH_3}$ groups), the glycerol molecule is black, and the three unsaturated fatty acids are red, blue, and green. The saturated fatty acids of saturated fats are nearly straight, and so the fats can pack themselves into hard, dense arrays that stick to dinner plates and to the insides of one's arteries. Unsaturated fatty acids are crooked and so are softer and have lower melting points than saturated fats.

1.7 Nucleotides

A **nucleotide** is a molecule made up of a **purine or pyrimidine base** attached by a glycosidic bond to a five-carbon sugar, itself bonded to one or more negatively charged phosphate $\mathrm{PO_4}$ groups as in figure 1.6. The bases are single or double rings of carbon and nitrogen atoms. The single

rings are **cytosine** C, **thymine** T, and **uracil** U; all three are derived from a six-atom, **pyrimidine** ring of four carbon atoms and two nitrogen atoms. The double rings are the **purines adenine** A and **guanine** G. The pyrimidines C, T, and U and the purines A and G are called *bases* because their amine groups absorb protons under acidic conditions. In **ribonucleotides**, the five-carbon sugar is ribose, the bottom-right sugar in figure 1.2. In **deoxyribonucleotides**, the five-carbon sugar is deoxyribose, or ribose with a missing oxygen atom, the bottom-left sugar in that figure.

In a nucleotide with three phosphate groups, the outer phosphate $PO_4{}^{2-}$ is doubly charged, and the two inner phosphates $2\,PO_4{}^{-}$ each carry a single negative charge. By **Gauss's law**, $\boldsymbol{\nabla}\cdot\boldsymbol{D} = \rho$, these four negative charges, all within a nanometer, generate an electric field $\boldsymbol{E} = \boldsymbol{D}/\epsilon$ whose electrostatic energy

$$W = \frac{1}{2}\int \boldsymbol{D}\cdot\boldsymbol{E}\; d^3r \tag{1.12}$$

releases 12 kcal/mol of usable energy when the terminal phosphate group is hydrolysed in the reaction $ATP^{4-} + H_2O \longrightarrow ADP^{3-} + P_i{}^{2-} + H^+$ in which $P_i{}^{2-} = HOPO_3{}^{2-}$ is **inorganic phosphate**. This energy powers chemical reactions and keeps animals warm. The **permittivity** ϵ is $K\epsilon_0$ in which the relative permittivity K is unity for vacuum, 2 for fat, and 80 for water. The nucleotide **adenine triphosphate** ATP is one of the main ways in which a cell stores and uses energy. In a **eucaryotic cell** cell (a cell with a nucleus), **mitochondria** use oxygen and glucose to turn ADP into ATP. The nucleotides **guanine triphosphate** GTP and diphosphate GDP play similar roles but in fewer reactions.

Cells use linear chains of the **monophosphate nucleotides** AMP, CMP,

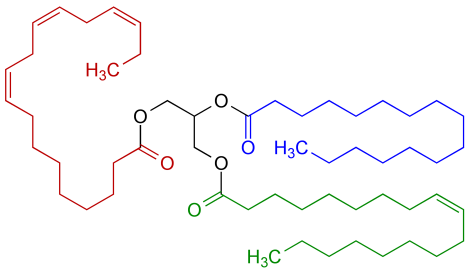

Figure 1.5 In this image of a very unsaturated triacylglyceride, the vertices represent carbon atoms, the hydrogen atoms are omitted (except for the methyl CH_3 groups), the glycerol molecule is black, and the three unsaturated fatty acids are red, blue, and green.(Courtesy of Jü.)

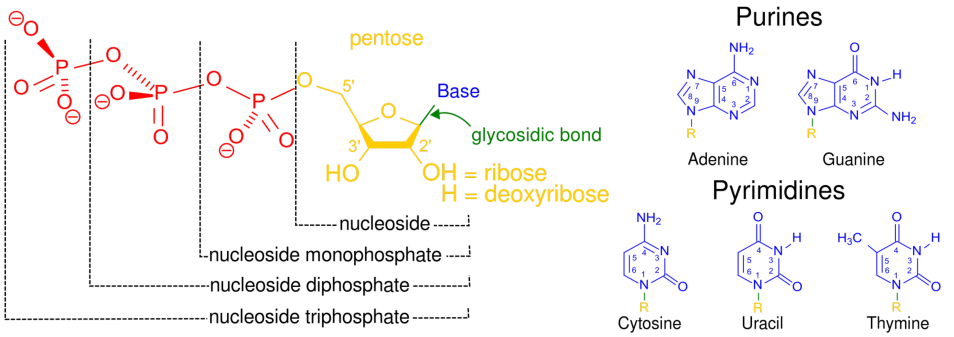

Figure 1.6 The figure shows the structure of nucleotides with one, two, and three phosphate groups and the five possible bases, the purines adenine A and guanine G, and the pyrimidines cytosine C, uracil U, and thymine T. (Courtesy of Wikipedia.)

GMP, TMP, and UMP to make the genome and many molecular devices. Ribose is a pentagon made of one oxygen atom and four carbon atoms, denoted $1'$, ... $4'$, with a fifth carbon atom $5'$ bound to the $4'$ carbon as in figure 1.7. In **RNA** (ribonucleic acid), a **phosphodiester bond** links the

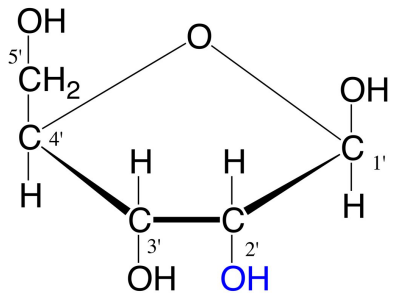

Figure 1.7 Ribose with the carbon atoms labeled. In deoxyribose, the $2'$ OH is replaced by H. (Courtesy of chronoxphya and flickr.)

$5'$ carbon atom of a ribose to a phosphate group PO_4^- which is linked to the $3'$ carbon atom of the next ribose by another phosphodiester bond as in figure 1.8. (It is an acid because **phosphoric acid**, $(HO)_3P{=}O$, loses two protons when it joins with a ribose and a base to form a nucleotide.) RNA is made of the monophosphate ribonucleotides CMP, GMP, AMP, and UMP. **DNA**, deoxyribonucleic acid, is made of the monophosphate deoxyribonucleotides CMP, GMP, AMP, and TMP.

The bases have oxygen and nitrogen atoms and amine and hydroxyl groups

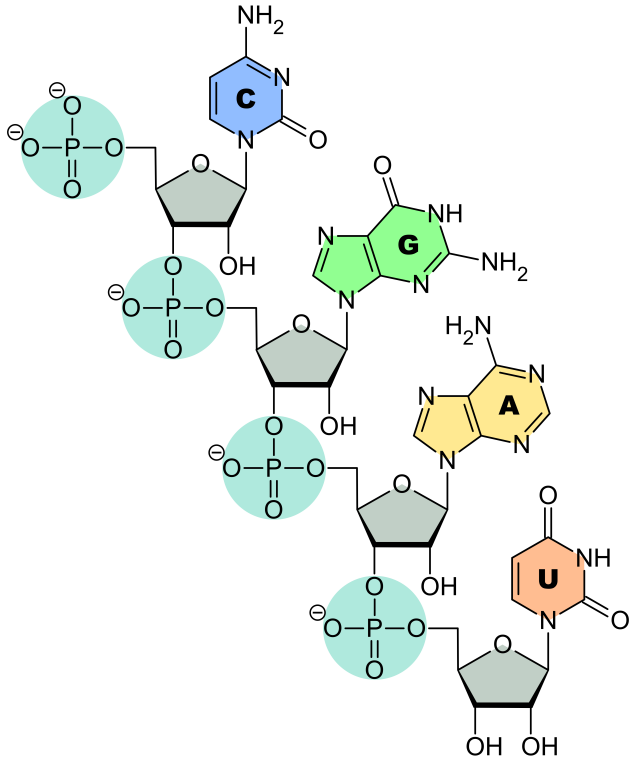

Figure 1.8 A very short strand of RNA which is a linear chain of CMP, GMP, AMP, and UMP. (Courtesy of Sponk and Wikimedia.)

that can form hydrogen bonds (section **??**) between pairs of bases. As shown in figure 1.9, guanine forms three hydrogen bonds with cytosine C, while adenine A forms only two with uracil in RNA and with thymine T in DNA. These Crick-Watson base pairs contribute to the structure of molecules of RNA and DNA.

Cells use RNA to do many things. Long strands of **messenger RNA**, mRNA, carry the protein recipes as sequences of **codons** (triplets of nucleotides) each codon denoting a specific amino acid. A **ribosome** is a 2.5 MDa molecular machine that is one-third protein and two-thirds **ribosomal RNA**, rRNA, and that reads mRNA and links the correct amino acids in a chain to make the protein specified by the mRNA. There are about 20,000 ribosomes in an *E. coli* cell and as many as 10 million in a mammalian cell.

Transfer RNA, tRNA, are small molecules of RNA that embody the ge-

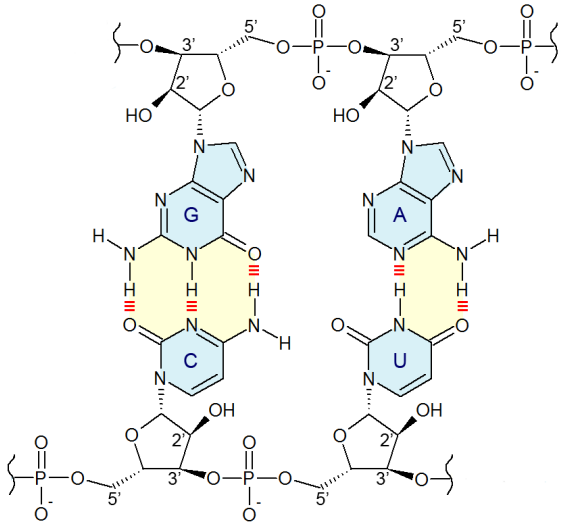

Figure 1.9 In RNA, guanine G forms three hydrogen bonds with cytosine C, and adenine A forms two with uracil U. (Courtesy if Wikipedia.)

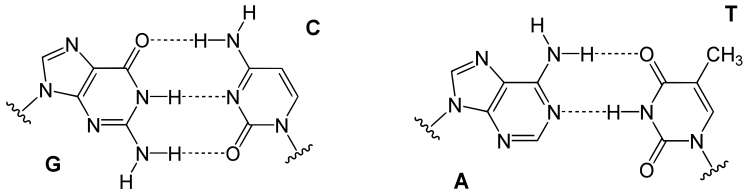

Figure 1.10 In DNA, guanine G forms three hydrogen bonds with cytosine C, and adenine A forms two with thymine T. (Courtesy of Wikipedia.)

netic code of figure 1.16. Figure 1.12 shows a bacterial tRNA without its amino acid. Each tRNA molecule has an amino acid at one end and the anticodon that specifically binds to the codon of mRNA that asks for that amino acid. For instance, suppose RNA polymerase reads the codon in DNA 5′TTC3′ and translates it to the mRNA codon 5′UUC3′. Then a tRNA molecule with the anticodon 3′AAG5′ will bind to this mRNA codon 5′UUC3′. That tRNA molecule will carry at its 3′ end, attached to an adenine by its carboxylic-acid group, the amino acid F, Phe, Phenylalanine, as required by the genetic code (figure 1.16). Most cells have 20 **synthetases**, one for each amino acid, that attach the right amino acid to the tRNA molecule that has its anticodon. An *E. coli* cell has some 200,000 tRNAs.

A **micro RNA**, miRNA, is a short (21–26 nucleotide) strand of RNA that controls how many protein molecules the cells ribosomes will make from the

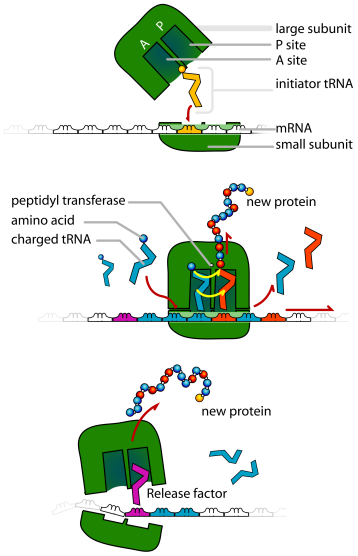

Figure 1.11 Cartoon of a ribosome using mRNA and tRNA's to make a protein. (Courtesy of LadyofHats and Wikimedia.)

mRNA for that protein. **Small nuclear RNA**s (**snRNA**s) help cells to process mRNA in the nucleus, and **small cytoplasmic RNA**s (**scRNA**s) play other roles in the cytoplasm. Cells surely use RNA for other purposes as yet undiscovered.

Cells use the Crick-Watson base pairs shown in figure 1.10 to store genetic information in DNA. DNA uses thymine instead of uracil because cytosine sometimes loses its amine group, gains an oxygen, and turns into uracil, $C + H_2O \longrightarrow U + NH_3$. So by using thymine instead of uracil in DNA, cells can identify uracil in DNA as a mistake due to the decay of cytosine, and then correct that error by replacing the uracil with cytosine. When a cell divides into two daughter cells, the enzyme **DNA polymerase** duplicates the DNA of the cell. Its error rate is less than 10^{-7} per base pair. Repair enzymes correct 99% of these errors for a net error rate of less than 10^{-9} per base pair (McCulloch and Kunkel, 2008).

To make a protein, the enzyme **RNA polymerase II** copies the $5'$ to $3'$ strand of DNA onto a $5'$ to $3'$ strand of mRNA which is then exported from the nucleus of the cell. The **ribosome**, which is made of rRNA and protein, draws the strand of mRNA through it, starting at the $5'$ end and proceeding to the $3'$ end. (Carl Friedrich Gauss 1777-1855, Francis Crick 1916-2004, James Watson 1928-)

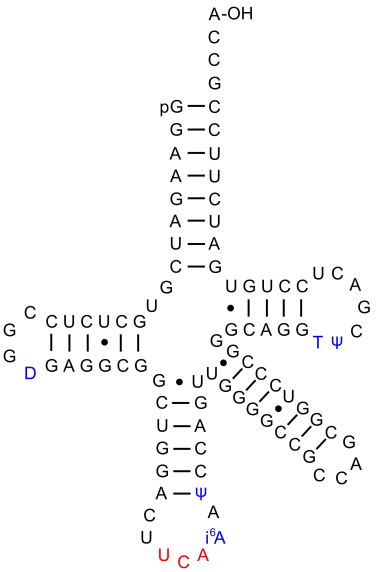

Figure 1.12 A tRNA of the bacterium *E. Coli* without its amino acid. (Courtesy of Yikrazuul and Wikimedia.)

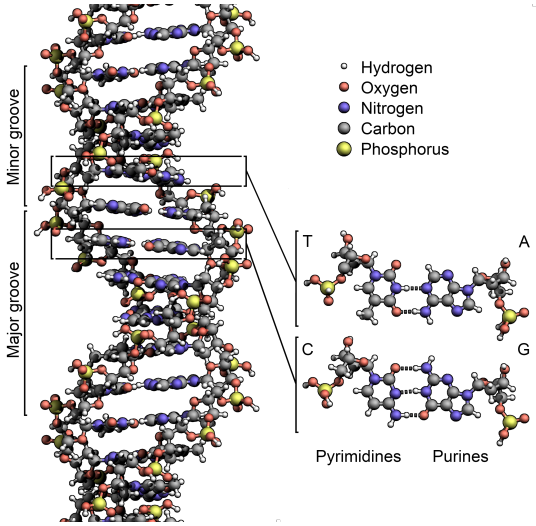

Figure 1.13 DNA.

1.8 Amino acids

An amino acid has an N–C–C backbone. In vaccum, the nitrogen atom is bonded to two hydrogen atoms forming an **amine group** NH_2 and to the first carbon atom, called the **alpha carbon**, as illustrated by the left side of figure 1.14. The alpha carbon is bonded to that amine group, to a hydrogen atom, to the second carbon atom, which is part of a **carboxylic-acid group** HO–C=O, and to a side group represented as R in the figure (1.14). The 20 different amino acids differ by their side groups R. The second carbon atom

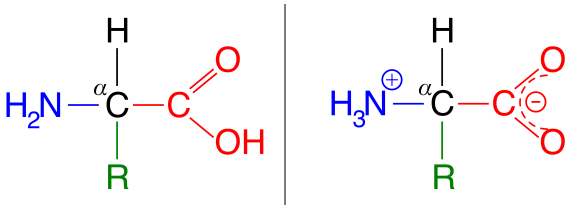

Figure 1.14 On the left is an amino acid with a side chain R in vacuum. On the right is an amino acid in water at pH 7.4. Its amine group has added a proton, and its carbolic acid group has lost a proton, leaving it with an extra electron which its two oxygen atoms share (Courtesy of Yassine Mrabet.)

is bound to the alpha carbon, to a hydroxyl group, and by a double bond to an oxygen atom, forming the carboxylic-acid group. Under physiological conditions, the carboxylic acid group of an amino acid loses a proton and the amine group gains a proton, as shown on the right side of the figure (1.14).

What are physiological conditions? The hydrogen-ion concentration of blood is $c_{H^+} \approx 10^{-7.4}$ moles/liter (M). Its negative logarithm to the base 10 is the **pH**, so the pH of blood is about $7.4 = -\ln_{10} c_{H^+}$. The term **physiological conditions** means a pH near 7.4 and normal concentrations of **electrolytes** such as Ca^{2+}, Cl^-, Mg^{2+}, K^+, Na^+, and so forth.

The **genetic code** uses 64 codons, each of three nucleotides, to redundantly specify the 20 amino acids and the stop signal as beautifully illustrated in figure 1.16.

Eight of the 20 amino acids have hydrocarbon side chains that are **nonpolar**, that is, they are not electric dipoles unless polarized by an electric field. Because water molecules are permanent electric dipoles, they attract each other like magnets and shove aside nonpolar molecules. Amino acids with nonpolar side chains are said to be **hydrophobic** or "water fearing." The 8 hydrophobic amino acids, shown in yellow in the figure (1.16), are alanine Ala A, isoleucine Ile I, leucine Leu L, methionine Met M, phenylalanine Phe

F, tryptophan Trp W, proline Pro P, and valine Val V. The side chain of proline loops around and forms a covalent bond with the amine group of its backbone.

Five of the 20 amino acids are **charged**. Because an amine group can add a proton, arginine Arg R, lysine Lys K, and histidine His H carry positive charges, that of H being smaller. When they take protons from a solution, they raise its pH. The side chains of these three positive amino acids therefore behave as bases and are blue in the figure (1.16).

Because a carboxylic group can lose the proton of its hydroxyl group leaving its electron stuck to the oxygen atom, aspartic acid Asp D and glutamic acid Glu E carry negative charges. They add protons to a solution. The side chains of these two negative amino acids therefore are acids are shown in rose in the figure. The five charged amino acids strongly attract and are attracted by water molecules. They tend to be on the outside of rather than on the inside of globular proteins.

The remaining 7 amino acids, shown in green in the figure, are serine Ser S, threonine Thr T, tyrosine Tyr Y, asparagine Asn N, and glutamine Gln Q, cysteine Cys C, and glycine Gly G. They are **polar** molecules, that is, they are permanent electric dipoles. Serine, threonine, and tyrosine have hydroxyl groups to which **kinases** can attach **phosphate groups** $PO_4{}^{3-}$ and to which other enzymes can attach sugars though a glycosidic bond. Asparagine and glutamine have **amide** $H_2N-C=O$ groups. Glycine with only a hydrogen atom as its side chain carries the intrinsic polarity of any amino acid in a protein: the hydrogen atom of its amine group is slightly positive and the oxygen atom of its carboxylic group is slightly negative.

The seventh polar amino acid cysteine has a side chain that ends in a **thiol group** SH, which is similar to a hydroxyl group. Two cysteines, located anywhere in the chain of amino acids that constitutes a protein, can form a disulfide bond as illustrated in figure 1.15. The disulfide bond locks the cysteines together and turns the linear chain into a loop that joins parts of the protein that otherwise would be widely separated.

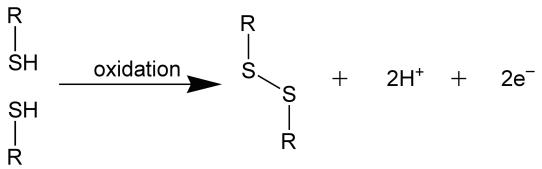

Figure 1.15 The thiol groups of two cysteines can form a disulfide bond releasing two protons and two electrons in an **oxidation** reaction.

As explained in section 1.3, an atom or molecule is **oxidized** if its charge increases; it is **reduced** if its charge decreases. Oxygen atoms tend to grab electrons from other atoms and molecules; they are highly **electronegative**. When an oxygen atom grabs electrons from a molecule, that molecule is said to be **oxidized**. The charge on the molecule becomes more positive. The successive oxidations of a carbon atom from methane CH_4 to methanol CH_3OH to formaldehyde $CH_2{=}O$ to formic acid $HO{-}CH{=}O$ to carbon dioxide $O{=}C{=}O$, transfer negative charge from the carbon atom to oxygen and hydrogen atoms. The charge on the carbon atom becomes more positive. The disulfide reaction $2\,SH \longrightarrow S{-}S + 2\,H$ is an **oxidation** of the sulfur atoms because the electron clouds that the hydrogen atoms had shared with the sulfur atoms leave them and go off with the two hydrogen atoms or as two protons and two electrons. The charge on the sulfur atoms becomes more positive. The opposite reactions from CO_2 to CH_4 add negative charge to the carbon atom and so **reduce** its positive charge. Similarly, the breaking of a disulfide bond $S{-}S + 2\,H \longrightarrow 2\,SH$ is a **reduction**.

1.9 Proteins

Ribosomes join amino acids together by means of **peptide bonds** as in the figure 1.17.

A chain of a few amino acids is an **oligopeptide**; a chain of several amino acids is a **polypeptide**; a long chain is a **protein**. Proteins are most of a cell's dry mass. They do most of the things cells need done. They form the filaments that give a cell its structure. They catalyze its huge numbers of chemical reactions. They form the channels and pumps in the cell's plasma membrane that control the flow of small molecules into and out of the cell. They relay signals across the plasma membrane. They pull membrane-enclosed sacs of molecules along microtubules. They untie tangles of DNA. They function as antibodies, hormones, toxins, ropes, and so forth.

Most proteins are globular. Under physiological conditions, a protein assumes its **native state** of minimal **Giggs free energy**, $G(p,T) = U + pV - TS$ in which U is the internal energy and S is the entropy (explained in chapter 4). In its native state, a globular protein has a density nearly as high as that of a crystal and a specific form that permits it to do its work. One kind of globular protein, an **enzyme**, makes a specific chemical reaction run much faster than it otherwise would. Another kind, a **kinase**, adds a phosphate group to another protein. Another kind, a **phosphatase**, removes

a phosphate group from another molecule. **Synthases** bind two molecules together. **Proteases** break up proteins by hydrolyzing their peptide bonds.

The smallest side group is a single hydrogen atom. That amino acid is called glycine abbreviated as Gly or G. Because the side group is a single hydrogen atom, G is very flexible—it can rotate freely about the N-C bond and about the C-C bond.

Exercises

1.1 Derive the dipole approximation (1.5) from the quadrupole potential (1.4).

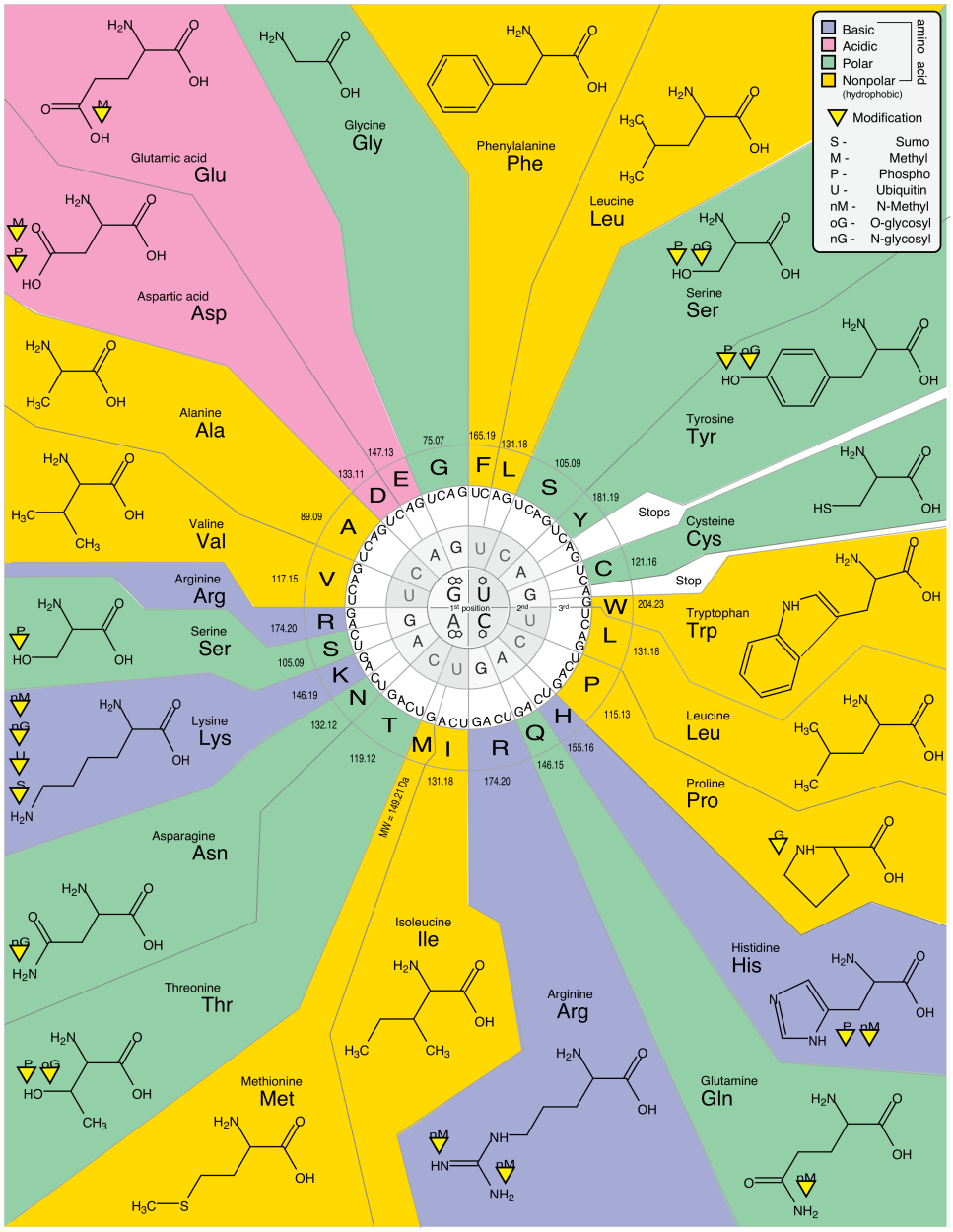

Figure 1.16 A codon is a triplet of the four nucleotides A, C, G, and T of DNA or of the four nucleotides A, C, G, and U of RNA. The 64 different codons redundantly specify 20 amino acids and 3 stop codons. For instance, the codon AUG specifies methionine, which also serves as a start codon. (Courtesy of Seth Miller and Kosi Gramatikoff.)

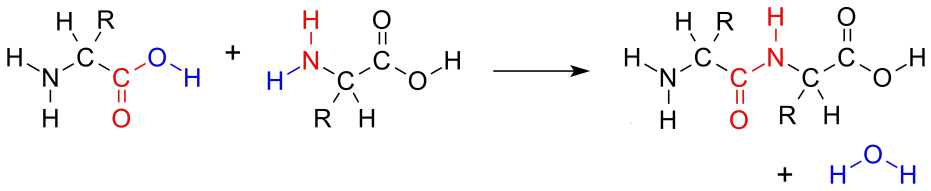

Figure 1.17 A peptide bond joins the carboxylic carbon of one amino acid to the nitrogen of the amino group of another amino acid. The four atoms O=C–N–H (red) lie in the same plane, whereas rotations occur around the N–C_α and C_α–C bonds. (Courtesy of V8rik at en.wikipedia.)

2

Metabolism

2.1 Glycolysis

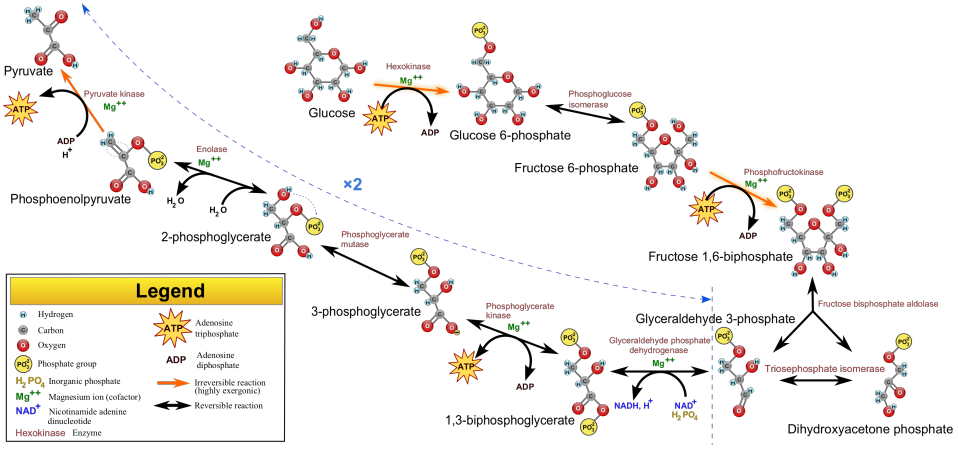

Figure 2.1 Glycolysis

2.2 The citric-acid cycle

Hundreds of different chemical reactions take place in a living cell. These reactions swap inputs and outputs and form a robust system that keeps the cell alive, enables it to adapt to its environment, and to divide when appropriate.

Some of these reactions are **cycles** in that they produce some of the molecules that they use. One of the most important cycles is the **citric-acid cycle**, also known as as the **tricarboxylic-acid cycle** (or **TCA** cycle)

and as the **Krebs cycle**. Citric acid has three carboxylic-acid groups as in figure 2.2.

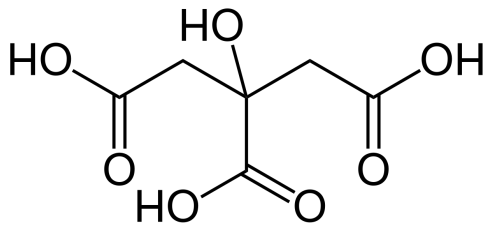

Figure 2.2 Citric acid. The unlabeled vertices are carbon atoms with as many hydrogens as needed to attach to the four bonds of each carbon atom. (Courtesy of Neurotiker via Wikimedia Commons)

It is a cycle because it consumes and regenerates citrate. The citric-acid cycle oxidizes acetate to make **NADH** which cells use to make ATP. The acetate comes in the form of **acetyl-CoA** from carbohydrates, fats, and proteins. The cycle adds a **hydride** ion H^- to NAD^+ thereby **reducing** it to the **reducing agent NADH** and **succinate** which the **oxidative phosphorylation** or **electron transport** pathway uses to make ATP. The TCA cycle also makes precursors of various amino acids and CO_2 as a waste product.

In eukaryotic cells, mitochondria perform the citric-acid cycle; in prokaryotic cells, the cycle occurs in the cytosol.

Acetyl-coA has three phosphate groups and one purine nucleotide. It ends in a sulfur atom which can bind to an acetyl group $COCH_3$.

$NADH^+$ is nicotinamide adenine dinucleotide, a derivative of vitamin B3 (niacin).

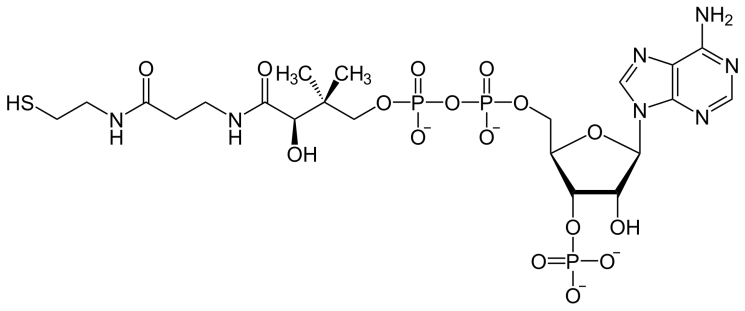

Figure 2.3 Coenzyme-A. An acetyl group $COCH_3$ binds to the sulfur atom at the far left. (Courtesy of Wikipedia)

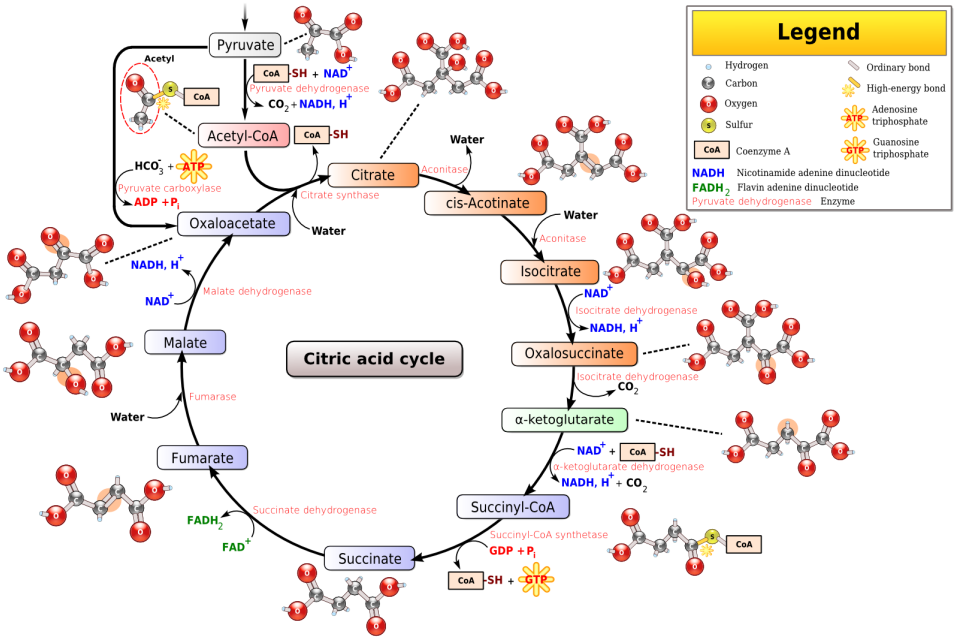

Figure 2.4 The citric-acid cycle. (Courtesy of Wikipedia)

3

Molecular devices

RNA polymerase II transcribes the nucleotide sequence of the DNA of a gene into the same sequence of **pre-messenger RNA** (**pre-mRNA**). RNA polymerase II reads the DNA in the $5'$ to $3'$ direction, terms illustrated by the mRNA figures (1.7) and (1.9), and so the nose of the pre-mRNA is the $5'$ end. Several enzymes then fashion and attach a **cap** to the $5'$ end of the pre-mRNA and add a **poly-A tail** of some 200 adenosine nucleotides to the $3'$ end. A **spliceosome** then deletes most **introns** and some **exons** from the pre-mRNA and so makes one of several possible mRNA transcripts from the same gene according to the immediate needs of the cell, a process known as **alternative splicing**. Introns contain special sequences of nucleotides that tell the spliceosome to cut them out. Proteins that bind to the pre-mRNA tell the spliceosome which exons to delete and which to keep. The production of these proteins is an important control mechanism. The nucleus exports mature mRNAs through its pores into the cytosol but inside the endoplasmic reticulum where **ribosomes translate** the mRNA into many copies of the needed protein. A **micro RNA** (**miRNA**) determines how many copies of protein ribosomes make from an mRNA by binding to a **seed** in its a sequence of nucleotides that lies in the tail of the mRNA between the code for the protein and the poly-A tail. This region is the $3'$ untranslated region ($3'$ **UTR**). The miRNA is some 21 nucleotides long and binds to the six-nucleotide seed by AU and GC Crick-Watson pairing.

3.1 Transport

Eukaryotic cells are too big to rely upon diffusion.

4

Probability and statistics

4.1 Mean and variance

In roulette and many other games, N outcomes x_j can occur with probabilities P_j that sum to unity

$$\sum_{j=1}^{N} P_j = 1. \tag{4.1}$$

The **expected value** $E[x]$ of the outcome x is its **mean** μ or **average** value $\langle x \rangle = \overline{x}$

$$E[x] = \mu = \langle x \rangle = \overline{x} = \sum_{j=1}^{N} x_j \, P_j. \tag{4.2}$$

The **expected value** $E[x]$ also is called the **expectation** of x or **expectation value** of x.

The $\boldsymbol{\ell}$**th moment** is

$$E[x^\ell] = \mu_\ell = \langle x^\ell \rangle = \sum_{j=1}^{N} x_j^\ell P_j \tag{4.3}$$

and the $\boldsymbol{\ell}$**th central moment** is

$$E[(x-\mu)^\ell] = \nu_\ell = \sum_{j=1}^{N} (x_j - \mu)^\ell P_j \tag{4.4}$$

where always $\mu_0 = \nu_0 = 1$ and $\nu_1 = 0$ (exercise 4.1).

The **variance** $V[x]$ is the second central moment ν_2

$$V[x] \equiv E[(x - \langle x \rangle)^2] = \nu_2 = \sum_{j=1}^{N} (x_j - \langle x \rangle)^2 \; P_j \tag{4.5}$$

which one may write as (exercise 4.1)

$$V[x] = \langle x^2 \rangle - \langle x \rangle^2 \tag{4.6}$$

and the standard deviation σ is its square-root

$$\sigma = \sqrt{V[x]}. \tag{4.7}$$

If the values of x are distributed continuously according to a **probability distribution** or **density** $P(x)$ normalized to unity

$$\int P(x)\, dx = 1 \tag{4.8}$$

then the mean value is

$$E[x] = \mu = \langle x \rangle = \int x\, P(x)\, dx \tag{4.9}$$

and the ℓth moment is

$$E[x^\ell] = \mu_\ell = \langle x^\ell \rangle = \int x^\ell\, P(x)\, dx. \tag{4.10}$$

The ℓth central moment is

$$E[(x - \mu)^\ell] = \nu_\ell = \int (x - \mu)^\ell\, P(x)\, dx. \tag{4.11}$$

The variance of the distribution is the second central moment

$$V[x] = \nu_2 = \int (x - \langle x \rangle)^2 \; P(x)\, dx = \mu_2 - \mu^2 \tag{4.12}$$

and the standard deviation σ is its square-root $\sigma = \sqrt{V[x]}$.

4.2 The binomial distribution

If the probability of success is p on each try, then we expect that in N tries the mean number of successes will be

$$\langle n \rangle = N\, p. \tag{4.13}$$

The probability of failure on each try is $q = 1 - p$. So the probability of a particular sequence of successes and failures, such as n successes followed by $N - n$ failures is $p^n\, q^{N-n}$. There are $N!/n!\,(N-n)!$ different sequences

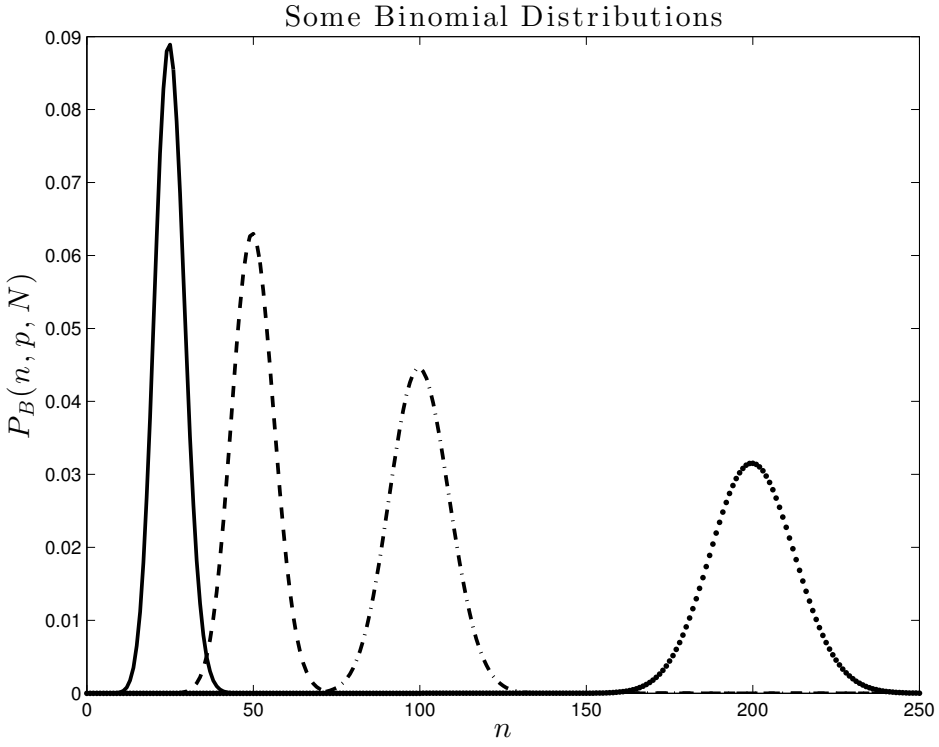

Figure 4.1 If the probability of success on any try is p, then the probability $P_B(n, p, N)$ of n successes in N tries is given by equation (4.14). For $p = 0.2$, this binomial probability distribution $P_B(n, p, N)$ is plotted against n for $N = 125$ (solid), 250 (dashes), 500 (dot dash), and 1000 tries (dots).

of n successes and $N - n$ failures, all with the same probability $p^n\, q^{N-n}$. So the probability of n successes (and $N - n$ failures) in N tries is

$$P_b(n, p, N) = \frac{N!}{n!\,(N-n)!}\, p^n\, q^{N-n} = \binom{N}{n} p^n\, (1-p)^{N-n}. \tag{4.14}$$

This **binomial distribution** also is called **Bernoulli's distribution** (Jacob Bernoulli, 1654–1705).

The sum of the probabilities $P_b(n, p, N)$ for all possible values of n is unity

$$\sum_{n=0}^{N} P_b(n, p, N) = (p + 1 - p)^N = 1. \tag{4.15}$$

In figure 4.1, the probabilities $P_B(n, p, N)$ for $0 \leq n \leq 250$ and $p = 0.2$ are plotted for $N = 125, 250, 500$, and 1000 tries.

The mean number of successes

$$\mu = \langle n \rangle_b = \sum_{n=0}^{N} n\, P_B(n,p,N) = \sum_{n=0}^{N} n \binom{N}{n} p^n q^{N-n} \tag{4.16}$$

is a partial derivative with respect to p with q held fixed

$$\begin{aligned} \langle n \rangle_b &= p\, \frac{\partial}{\partial p} \sum_{n=0}^{N} \binom{N}{n} p^n q^{N-n} \\ &= p\, \frac{\partial}{\partial p}\, (p+q)^N = Np\,(p+q)^{N-1} = Np \end{aligned} \tag{4.17}$$

which verifies the estimate (4.13). The second moment is

$$\begin{aligned} \langle n^2 \rangle_b &= \sum_{n=0}^{N} n^2 \binom{N}{n} p^n q^{N-n} = \left(p\, \frac{\partial}{\partial p}\right)^2 \sum_{n=0}^{N} \binom{N}{n} p^n q^{N-n} \\ &= \left(p\, \frac{\partial}{\partial p}\right)^2 (p+q)^N = p\, \frac{\partial}{\partial p} Np\,(p+q)^{N-1} = Np + N(N-1)p^2. \end{aligned} \tag{4.18}$$

Thus the variance of the binomial distribution is

$$\sigma_b^2 = \langle (n - \langle n \rangle)^2 \rangle = p\,(1-p)\,N. \tag{4.19}$$

Its standard deviation is the square-root of its variance

$$\sigma_b = \sqrt{V_b} = \sqrt{p\,(1-p)\,N}. \tag{4.20}$$

The ratio of the width to the mean

$$\frac{\sigma_b}{\langle n \rangle_B} = \frac{\sqrt{p\,(1-p)\,N}}{Np} = \sqrt{\frac{1-p}{Np}} \tag{4.21}$$

decreases with N as $1/\sqrt{N}$.

Example 4.1 (Avogadro's number)**.** A mole of gas is Avogadro's number $N_A = 6 \times 10^{23}$ of molecules. If the gas is in a cubical box, then the chance that each molecule will be in the left half of the cube is $p = 1/2$. The mean number of molecules there is $\langle n \rangle_B = pN_A = 3 \times 10^{23}$, and the uncertainty in n is $\sigma_B = \sqrt{p\,(1-p)\,N} = \sqrt{3 \times 10^{23}/4} = 3 \times 10^{11}$. So the numbers of gas molecules in the two halves of the box are equal to within $\sigma_B / \langle n \rangle_B = 10^{-12}$ or to 1 part in 10^{12}. □

Example 4.2 (Counting fluorescent molecules)**.** Molecular biologists can insert the DNA that codes for a fluorescent protein next to the DNA that

codes for a natural protein in the genome of a bacterium so that the natural protein produces light of a specific color when suitably illuminated by a laser. The intensity I of the light is proportional to the number n of labeled protein molecules $I = \alpha\, n$, and one can find the constant of proportionality α by measuring the light given off as the bacteria divide. When a bacterium divides, it randomly separates the total number N of fluorescent proteins into its two daughter bacteria, giving one n fluorescent molecules and the other $N - n$. The variance of the difference is

$$\langle (n - (N - n))^2 \rangle = \langle (2n - N)^2 \rangle = 4 \langle n^2 \rangle - 4 \langle n \rangle N + N^2. \tag{4.22}$$

The mean number (4.17) is $\langle n \rangle = pN$, and our variance formula (4.19) tells us that

$$\langle n^2 \rangle = \langle n \rangle^2 + p(1-p)N = (pN)^2 + p(1-p)N. \tag{4.23}$$

Since the probability $p = 1/2$, the variance of the difference is

$$\langle (n - (N - n))^2 \rangle = (2p - 1)^2 N^2 + 4p(1-p)N = N. \tag{4.24}$$

Thus the unknown constant of proportionality α is the ratio of the variance of the difference of daughters' intensities to the intensity of the parent bacterium (Phillips et al., 2012)

$$\alpha = \frac{\langle (I_n - I_{N-n})^2 \rangle}{\langle I_N \rangle}. \tag{4.25}$$

□

4.3 Random walks

Suppose that in each time step τ a particle moves forward by a distance a with probability p and backward a distance a with probability $q = 1 - p$. Then in N time steps the probability that the particle moves forward by na is given by the binomial distribution

$$P(n, p, N) = \binom{N}{n} p^n\, q^{N-n}. \tag{4.26}$$

The mean displacement then is

$$\langle x \rangle = \sum_{n=0}^{N} P(n, p, N)\, (na - (N - n)a) = a \sum_{n=0}^{N} \binom{N}{n} p^n\, q^{N-n}\, (2n - N)\,. \tag{4.27}$$

We can generate the factor of n by differentiating p^n with respect to p keeping q fixed and multiplying by p. Then since $p+q=1$, we get

$$\begin{aligned}\langle x\rangle &= 2a\left[p\frac{\partial}{\partial p}\sum_{n=0}^{N}\binom{N}{n}p^n\,q^{N-n}\right]-Na\\ &= 2a\left[p\frac{\partial}{\partial p}(p+q)^N\right]-Na = Na(2p-1).\end{aligned}\tag{4.28}$$

If $p=1/2$, then this random walk is unbiased, and the mean displacement $\langle x\rangle$ is zero.

The mean value of x^2 is the sum

$$\begin{aligned}\langle x^2\rangle &= a^2\sum_{n=0}^{N}\binom{N}{n}p^n\,q^{N-n}\,(2n-N)^2\\ &= a^2\sum_{n=0}^{N}\binom{N}{n}p^n\,q^{N-n}\left(4n^2-4nN+N^2\right).\end{aligned}\tag{4.29}$$

Iterating the same trick and using the sum rules (4.15) and (4.28), we find

$$\begin{aligned}\langle x^2\rangle &= 4a^2\left(p\frac{\partial}{\partial p}\right)^2(p+q)^N-4Na^2\,p\frac{\partial}{\partial p}(p+q)^N+N^2a^2\\ &= 4a^2\left[N^2p^2+Np(1-p)\right]-4N^2p^2+N^2a^2\\ &= a^2\left[N^2(p-q)^2+4Npq\right].\end{aligned}\tag{4.30}$$

In an unbiased random walk, $p=q=1/2$, so $p-q=0$, and the mean value of the square of the displacement is

$$\langle x^2\rangle = N\,a^2.\tag{4.31}$$

After N random steps in each of three dimensions, the mean value of the square of the displacement $\boldsymbol{r}$ is

$$\langle \boldsymbol{r}^2\rangle = \langle x^2+y^2+z^2\rangle = 3N\,a^2.\tag{4.32}$$

4.4 Diffusion

Diffusion is the movement of particles in unbiased random walks in any number of dimensions. If τ is the time that elapses when a particle takes a step of $\pm a$ in each direction, then the **diffusion constant** D is the ratio

$$D \equiv \frac{a^2}{2\tau}.\tag{4.33}$$

The number N of steps is the elapsed time t divided by the time τ taken per step

$$N = \frac{t}{\tau}. \tag{4.34}$$

So the number N of steps times the squared step size a^2 in each direction is

$$N\,a^2 = \frac{t}{\tau}\,a^2 = 2\,D\,t. \tag{4.35}$$

The mean value (4.31) of the square of the displacement in an unbiased random walk in one dimension is $\langle x^2 \rangle = N\,a^2$. It increases with the time t as

$$\langle x^2 \rangle = N\,a^2 = \frac{t\,a^2}{\tau} = 2\,D\,t. \tag{4.36}$$

The mean value of the square of the displacement in an unbiased random walk in two dimensions is

$$\langle r^2 \rangle = \langle x^2 + y^2 \rangle = 2N\,a^2. \tag{4.37}$$

It increases with the time t as

$$\langle r^2 \rangle = 2N\,a^2 = 2\frac{t\,a^2}{\tau} = 4\,D\,t. \tag{4.38}$$

In three dimensions, the mean value of the square of the displacement in an unbiased random walk is (4.32)

$$\langle \boldsymbol{r}^2 \rangle = \langle x^2 + y^2 + z^2 \rangle = 3N\,a^2. \tag{4.39}$$

It increases with the time t as

$$\langle \boldsymbol{r}^2 \rangle = 3N\,a^2 = 3\frac{t\,a^2}{\tau} = 6\,D\,t. \tag{4.40}$$

In an unbiased random walk in any number n of dimensions, the square root of the mean value of the square of the displacement increases as the square root of the time

$$\sqrt{\langle x_1^2 + \cdots + x_n^2 \rangle} = \sqrt{2n\,D\,t}. \tag{4.41}$$

4.5 The Poisson distribution

Poisson started from the binomial distribution (4.26)

$$P(n, p, N) = \binom{N}{n} p^n\,q^{N-n} \tag{4.42}$$

and took the limit $N \to \infty$ with $\langle n \rangle = p\,N$ held fixed. So we let N and $N - n$, but not n, tend to infinity, and apply Sterling's approximation

$$m! \approx \sqrt{2\pi m}\,\left(\frac{m}{e}\right)^m \tag{4.43}$$

to the probability $P(n, p, N)$ of n successes in N trials. In the limit $N \to \infty$ with $\langle n \rangle = p\,N$ held fixed, the binomial probability (4.42) in Sterling's approximation (4.43) is

$$\begin{aligned} P(n, p, N) &\approx \sqrt{\frac{N}{N-n}}\,\frac{N^N}{(N-n)^{N-n}}\,\frac{p^n\,q^{N-n}}{n!} \\ &\approx \frac{1}{\sqrt{1-n/N}}\,(pN)^n\,\frac{1}{(1-n/N)^{N-n}}\,\frac{q^{N-n}}{n!} \\ &\approx (pN)^n\,\frac{q^{N-n}}{n!} = \langle n \rangle^n\,\frac{q^{N-n}}{n!}. \end{aligned} \tag{4.44}$$

Now $q = 1 - p = 1 - \langle n \rangle / N$, and so for any fixed n we have

$$\lim_{N\to\infty} q^{N-n} = \lim_{N\to\infty} \left(1 - \frac{\langle n \rangle}{N}\right)^N \left(1 - \frac{\langle n \rangle}{N}\right)^{-n} = e^{-\langle n \rangle}. \tag{4.45}$$

Thus as $N \to \infty$ with pN fixed at $\langle n \rangle$, the binomial distribution becomes the Poisson distribution

$$P_P(n, \langle n \rangle) = \frac{\langle n \rangle^n}{n!}\,e^{-\langle n \rangle}. \tag{4.46}$$

The variance of Poisson's distribution is the same as its mean

$$\sigma^2 = \langle (n - \langle n \rangle)^2 \rangle = \mu = \langle n \rangle. \tag{4.47}$$

(Siméon-Denis Poisson, 1781–1840)

4.6 The gaussian distribution

Gauss considered the binomial distribution in the limit $N \to \infty$ with the probability p fixed. In this limit, the binomial probability

$$P_b(n, p, N) = \frac{N!}{n!\,(N-n)!}\,p^n\,q^{N-n} \tag{4.48}$$

is very tiny unless n is near pN which means that $n \approx pN$ and $N - n \approx (1 - p)N = qN$ are comparable. So the limit $N \to \infty$ effectively is one in which n and $N - n$ also tend to infinity. Using Sterling's approximation

(4.43) as N, $N-n$, and n all increase without limit that the binomial probability approaches

$$P_b(n,p,N) \approx \sqrt{\frac{N}{2\pi n(N-n)}}\,\left(\frac{pN}{n}\right)^n\,\left(\frac{qN}{N-n}\right)^{N-n}. \tag{4.49}$$

This probability $P_b(n,p,N)$ is negligible unless $n \approx pN$ and $qN = (1-p)N \approx N-n$. So we set $y = n - pN$ and treat y/n as small. Since $n = pN + y$ and $N - n = (1-p)N + pN - n = qN - y$, we may write the square-root as

$$\begin{aligned}\sqrt{\frac{N}{2\pi\, n\,(N-n)}} &= \frac{1}{\sqrt{2\pi\, N\,[(pN+y)/N]\,[(qN-y)/N]}} \\ &= \frac{1}{\sqrt{2\pi\, pqN\,(1+y/pN)\,(1-y/qN)}}.\end{aligned} \tag{4.50}$$

And because y remains finite as $N \to \infty$, we get in this limit

$$\lim_{N\to\infty} \sqrt{\frac{N}{2\pi\, n\,(N-n)}} = \frac{1}{\sqrt{2\pi\, pqN}}. \tag{4.51}$$

Substituting $pN + y$ for n and $qN - y$ for $N - n$ in (4.49), we find

$$\begin{aligned}P_b(n,p,N) &\approx \frac{1}{\sqrt{2\pi\, pqN}}\,\left(\frac{pN}{pN+y}\right)^{pN+y}\,\left(\frac{qN}{qN-y}\right)^{qN-y} \\ &= \frac{1}{\sqrt{2\pi\, pqN}}\,\left(1+\frac{y}{pN}\right)^{-(pN+y)}\,\left(1-\frac{y}{qN}\right)^{-(qN-y)}\end{aligned} \tag{4.52}$$

which implies that

$$\ln\left[P_b(n,p,N)\sqrt{2\pi\, pqN}\right] \approx -(pN+y)\ln\left[1+\frac{y}{pN}\right] - (qN-y)\ln\left[1-\frac{y}{qN}\right]. \tag{4.53}$$

The first two terms of the power series for $\ln(1+\epsilon)$ are

$$\ln(1+\epsilon) \approx \epsilon - \frac{1}{2}\epsilon^2. \tag{4.54}$$

So applying this expansion to the two logarithms and using the relation $1/p + 1/q = (p+q)/pq = 1/pq$, we get

$$\begin{aligned}\ln\left(P_b(n,p,N)\sqrt{2\pi\, pqN}\right) &\approx -(pN+y)\left[\frac{y}{pN} - \frac{1}{2}\left(\frac{y}{pN}\right)^2\right] \\ &\quad - (qN-y)\left[-\frac{y}{qN} - \frac{1}{2}\left(\frac{y}{qN}\right)^2\right] \approx -\frac{y^2}{2pqN}.\end{aligned} \tag{4.55}$$

Thus since $y = n - pN$, Gauss's approximation to the binomial probability distribution is

$$P_{BG}(n,p,N) = \frac{1}{\sqrt{2\pi pqN}}\,\exp\left(-\frac{(n-pN)^2}{2pqN}\right). \tag{4.56}$$

Extending the integer n to a continuous variable x, we have

$$P_G(x,p,N) = \frac{1}{\sqrt{2\pi pqN}}\,\exp\left(-\frac{(x-pN)^2}{2pqN}\right) \tag{4.57}$$

which is (exercise 4.4) a normalized probability distribution with mean $\langle x\rangle = \mu = pN$ and variance $\langle (x-\mu)^2\rangle = \sigma^2 = pqN$. Replacing pN by μ and pqN by σ^2, we get the standard form of **Gauss's distribution**

$$P_G(x,\mu,\sigma) = \frac{1}{\sigma\sqrt{2\pi}}\,\exp\left(-\frac{(x-\mu)^2}{2\sigma^2}\right). \tag{4.58}$$

This distribution occurs so often in mathematics and in Nature that it is often called **the normal distribution**.

Its central moments

$$\nu_k = \int (x-\mu)^k\, P_G(x,\mu,\sigma)dx \tag{4.59}$$

vanish for odd $k = 2n+1$, and its even ones are $\nu_{2n} = (2n-1)!!\,\sigma^{2n}$.

4.7 The error function erf

The probability that a random variable x distributed according to Gauss's distribution (4.58) has a value between $\mu - \delta$ and $\mu + \delta$ is

$$\begin{aligned} P(|x-\mu|<\delta) &= \int_{\mu-\delta}^{\mu+\delta} P_G(x,\mu,\sigma)\,dx = \frac{1}{\sigma\sqrt{2\pi}}\int_{\mu-\delta}^{\mu+\delta}\exp\left(-\frac{(x-\mu)^2}{2\sigma^2}\right)dx \\ &= \frac{1}{\sigma\sqrt{2\pi}}\int_{-\delta}^{\delta}\exp\left(-\frac{x^2}{2\sigma^2}\right)dx = \frac{2}{\sqrt{\pi}}\int_0^{\delta/\sigma\sqrt{2}} e^{-t^2}\,dt. \end{aligned} \tag{4.60}$$

The last integral is the error function

$$\operatorname{erf}(x) = \frac{2}{\sqrt{\pi}}\int_0^x e^{-t^2}dt \tag{4.61}$$

so in terms of it the probability that x lies within δ of the mean μ is

$$P(|x-\mu|<\delta) = \operatorname{erf}\left(\frac{\delta}{\sigma\sqrt{2}}\right). \tag{4.62}$$

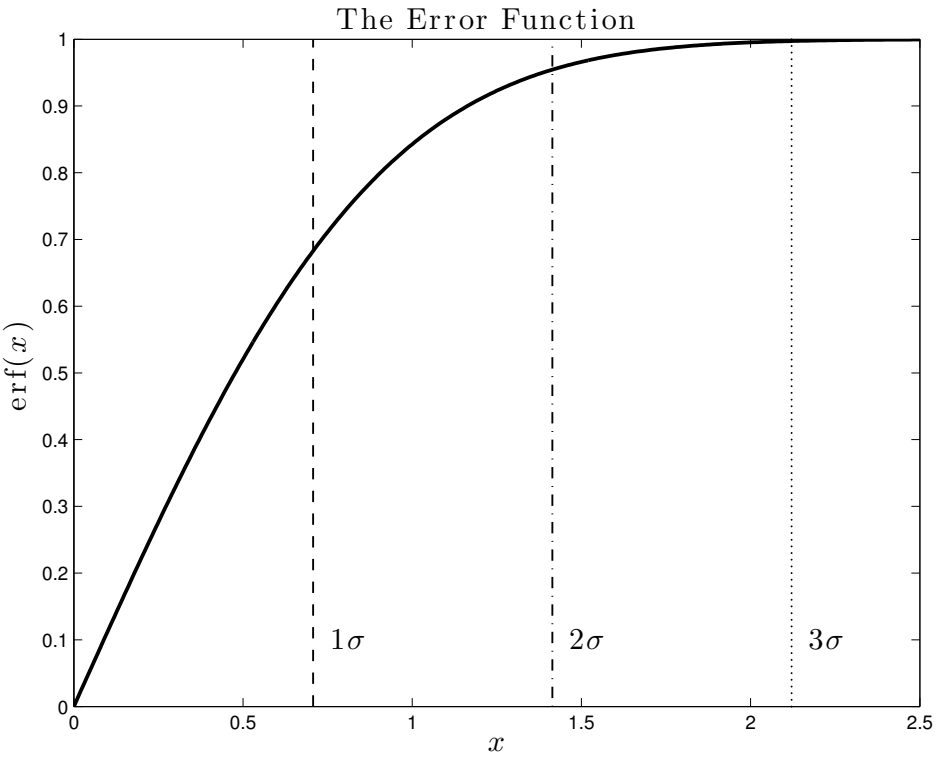

Figure 4.2 The error function $\mathrm{erf}\,(x)$ is plotted for $0 < x < 2.5$. The vertical lines are at $x = \delta/(\sigma\sqrt{2})$ for $\delta = \sigma$, 2σ, and 3σ with $\sigma = 1/\sqrt{2}$.

In particular, the probabilities that x falls within one, two, or three standard deviations of μ are

$$\begin{aligned} P(|x-\mu| < \sigma) &= \mathrm{erf}\,(1/\sqrt{2}) = 0.6827 \\ P(|x-\mu| < 2\sigma) &= \mathrm{erf}\,(2/\sqrt{2}) = 0.9545 \\ P(|x-\mu| < 3\sigma) &= \mathrm{erf}\,(3/\sqrt{2}) = 0.9973. \end{aligned} \tag{4.63}$$

The error function $\mathrm{erf}\,(x)$ is plotted in Fig. 4.2 in which the vertical lines are at $x = \delta/(\sigma\sqrt{2})$ for $\delta = \sigma$, 2σ, and 3σ.

4.8 The Maxwell-Boltzmann distribution

It is a small jump from Gauss's distribution (4.58) to the Maxwell-Boltzmann distribution of velocities of molecules in a gas. We start in one dimension and focus on a single molecule that is being hit fore and aft with equal probabilities by other molecules. If each hit increases or decreases its speed

by dv, then after n aft hits and $N-n$ fore hits, the speed v_x of a molecule initially at rest would be

$$v_x = ndv - (N-n)dv = (2n-N)dv. \tag{4.64}$$

The probability of this speed is given by Gauss's approximation (4.56) to the binomial distribution $P_b(n, \frac{1}{2}, N)$ as

$$P_{bG}(n, \tfrac{1}{2}, N) = \sqrt{\frac{2}{\pi N}}\, \exp\left(-\frac{(2n-N)^2}{2N}\right) = \sqrt{\frac{2}{\pi N}}\, \exp\left(-\frac{v_x^2}{2N dv^2}\right). \tag{4.65}$$

This argument applies to any physical variable subject to unbiased random fluctuations. It is why Gauss's distribution describes statistical errors and why it occurs so often in Nature as to be called the normal distribution.

We now write the argument of the exponential in terms of the temperature T and Boltzmann's constant k by setting $N = kT/(m\,dv^2)$ so that

$$-\frac{\frac{1}{2}v_x^2}{N dv^2} = -\frac{\frac{1}{2}mv_x^2}{mN dv^2} = -\frac{\frac{1}{2}mv_x^2}{kT}. \tag{4.66}$$

Then with $dv_x = 2dv$, we have

$$P_G(v_x)dv_x = \sqrt{\frac{2m}{\pi kT}}\, dv\, \exp\left(-\frac{\frac{1}{2}mv_x^2}{kT}\right) = \sqrt{\frac{m}{2\pi kT}}\, dv_x\, \exp\left(-\frac{\frac{1}{2}mv_x^2}{kT}\right). \tag{4.67}$$

Gauss's distribution is normalized to unity because it is the limit of the binomial distribution (4.15)

$$\int_{-\infty}^{\infty} \sqrt{\frac{m}{2\pi kT}}\, \exp\left(-\frac{\frac{1}{2}mv_x^2}{kT}\right)\, dv_x = 1 \tag{4.68}$$

as you may verify by explicit integration.

In three space dimensions, the Maxwell-Boltzmann distribution $P_{MB}(\boldsymbol{v})$ is the product

$$P_{MB}(\boldsymbol{v})d^3v = P_G(v_x)\, P_G(v_y)\, P_G(v_z)d^3v = \left(\frac{m}{2\pi kT}\right)^{3/2}\, e^{-\frac{1}{2}m\boldsymbol{v}^2/(kT)} 4\pi v^2 dv. \tag{4.69}$$

The mean value of the velocity of a Maxwell-Boltzmann gas vanishes

$$\langle \boldsymbol{v} \rangle = \int \boldsymbol{v}\, P_{MB}(\boldsymbol{v})d^3v = \boldsymbol{0} \tag{4.70}$$

but the mean value of the square of the velocity $\boldsymbol{v}^2 = \boldsymbol{v}\cdot\boldsymbol{v}$ is the sum of the

three variances $\sigma_x^2 = \sigma_y^2 = \sigma_z^2 = kT/m$

$$\langle v^2 \rangle = V[\boldsymbol{v}^2] = \int \boldsymbol{v}^2 \, P_{MB}(\boldsymbol{v}) \, d^3v = 3kT/m \tag{4.71}$$

which is the familiar statement

$$\frac{1}{2} m \langle v^2 \rangle = \frac{3}{2} \, kT \tag{4.72}$$

that each degree of freedom gets $kT/2$ of energy.

4.9 Characteristic functions

The Fourier transform of a probability distribution $P(x)$ is its **characteristic function** $\tilde{P}(k)$ sometimes written as $\chi(k)$

$$\tilde{P}(k) \equiv \chi(k) \equiv E[e^{ikx}] = \int e^{ikx} \, P(x) \, dx. \tag{4.73}$$

The probability distribution $P(x)$ is the inverse Fourier transform

$$P(x) = \int e^{-ikx} \, \tilde{P}(k) \, \frac{dk}{2\pi}. \tag{4.74}$$

Example 4.3 (Gauss)**.** The characteristic function of the gaussian

$$P_G(x, \mu, \sigma) = \frac{1}{\sigma\sqrt{2\pi}} \, \exp\left(-\frac{(x-\mu)^2}{2\sigma^2} \right) \tag{4.75}$$

is by

$$\begin{aligned} \tilde{P}_G(k, \mu, \sigma) &= \frac{1}{\sigma\sqrt{2\pi}} \int \exp\left(ikx - \frac{(x-\mu)^2}{2\sigma^2} \right) dx \qquad (4.76) \\ &= \frac{e^{ik\mu}}{\sigma\sqrt{2\pi}} \int \exp\left(ikx - \frac{x^2}{2\sigma^2} \right) dx = \exp\left(i\mu k - \frac{1}{2}\sigma^2 k^2 \right). \end{aligned}$$

□

Example 4.4 (Poisson)**.** The Poisson distribution (4.46)

$$P_P(n, \langle n \rangle) = \frac{\langle n \rangle^n}{n!} \, e^{-\langle n \rangle} \tag{4.77}$$

has the characteristic function

$$\chi(k) = \sum_{n=0}^{\infty} e^{ikn} \, \frac{\langle n \rangle^n}{n!} \, e^{-\langle n \rangle} = e^{-\langle n \rangle} \sum_{n=0}^{\infty} \frac{(\langle n \rangle e^{ik})^n}{n!} = \exp\left[\langle n \rangle \left(e^{ik} - 1 \right) \right]. \tag{4.78}$$

□

4.10 Central limit theorem

We have seen in sections (4.8 & 6.1) that unbiased fluctuations tend to distribute the position and velocity of molecules according to Gauss's distribution (4.58). Gaussian distributions occur very frequently. The **central limit theorem** suggests why they occur so often.

Let $x_1, \ldots, x_N$ be N **independent** random variables described by probability distributions $P_1(x_1), \ldots, P_N(x_N)$ with finite means μ_j and finite variances σ_j^2. The P_j's may be all different. The central limit theorem says that as $N \to \infty$ the probability distribution $P^{(N)}(y)$ for the average of the x_j's

$$y = \frac{1}{N}\left(x_1 + x_2 + \cdots + x_N\right) \tag{4.79}$$

tends to a gaussian in y quite independently of what the underlying probability distributions $P_j(x_j)$ happen to be.

Because expected values are linear, the mean value of the average y is the average of the N means

$$\begin{aligned}\mu_y = E[y] = E[\left(x_1 + \cdots + x_N\right)/N] &= \frac{1}{N}\left(E[x_1] + \cdots + E[x_N]\right) \\ &= \frac{1}{N}\left(\mu_1 + \cdots + \mu_N\right).\end{aligned} \tag{4.80}$$

Similarly, the variance of a linear combination of *independent* variables is the sum of their variances, and so the variance of the average y is

$$\sigma_y^2 = V[\left(x_1 + \cdots + x_N\right)/N] = \frac{1}{N^2}\left(\sigma_1^2 + \cdots + \sigma_N^2\right). \tag{4.81}$$

The independence of the random variables $x_1, x_2, \ldots, x_N$ implies that their joint probability distribution factorizes

$$P(x_1, \ldots, x_N) = P_1(x_1)P_2(x_2)\cdots P_N(x_N). \tag{4.82}$$

We can use a delta function to write the probability distribution $P^{(N)}(y)$ for the average $y = (x_1 + x_2 + \cdots + x_N)/N$ of the x_j's as

$$P^{(N)}(y) = \int P(x_1, \ldots, x_N)\, \delta((x_1 + x_2 + \cdots + x_N)/N - y)\, d^N x \tag{4.83}$$

where $d^N x = dx_1 \ldots dx_N$. Its characteristic function

$$\begin{aligned}\tilde{P}^{(N)}(k) &= \int e^{iky}\, P^{(N)}(y)\, dy \\ &= \int e^{iky} \int P(x_1, \ldots, x_N)\, \delta((x_1 + x_2 + \cdots + x_N)/N - y)\, d^N x\, dy \\ &= \int \exp\left[\frac{ik}{N}(x_1 + x_2 + \cdots + x_N)\right] P(x_1, \ldots, x_N)\, d^N x \qquad (4.84) \\ &= \int \exp\left[\frac{ik}{N}(x_1 + x_2 + \cdots + x_N)\right] P_1(x_1) P_2(x_2) \cdots P_N(x_N)\, d^N x\end{aligned}$$

is then the product

$$\tilde{P}^{(N)}(k) = \tilde{P}_1(k/N)\, \tilde{P}_2(k/N) \cdots \tilde{P}_N(k/N) \qquad (4.85)$$

of the characteristic functions

$$\tilde{P}_j(k/N) = \int e^{ikx_j/N}\, P_j(x_j)\, dx_j \qquad (4.86)$$

of the probability distributions $P_1(x_1), \ldots, P_N(x_N)$.

The Taylor series for each characteristic function is

$$\tilde{P}_j(k/N) = \sum_{n=0}^{\infty} \frac{(ik)^n}{n!\, N^n}\, \mu_{nj} \qquad (4.87)$$

and so for big N we can use the approximation

$$\tilde{P}_j(k/N) \approx 1 + \frac{ik}{N}\, \mu_j - \frac{k^2}{2N^2}\, \mu_{2j} \qquad (4.88)$$

in which $\mu_{2j} = \sigma_j^2 + \mu_j^2$ by the formula (4.6) for the variance. So we have

$$\tilde{P}_j(k/N) \approx 1 + \frac{ik}{N}\, \mu_j - \frac{k^2}{2N^2}\, (\sigma_j^2 + \mu_j^2) \qquad (4.89)$$

or for large N

$$\tilde{P}_j(k/N) \approx \exp\left(\frac{ik}{N}\mu_j - \frac{k^2}{2N^2}\sigma_j^2\right). \qquad (4.90)$$

Thus as $N \to \infty$, the characteristic function (4.85) for the variable y converges to

$$\begin{aligned}\tilde{P}^{(N)}(k) = \prod_{j=1}^{N} \tilde{P}_j(k/N) \;&= \prod_{j=1}^{N} \exp\left(\frac{ik}{N}\mu_j - \frac{k^2}{2N^2}\sigma_j^2\right) \\ = \exp\left[\sum_{j=1}^{N}\left(\frac{ik}{N}\mu_j - \frac{k^2}{2N^2}\sigma_j^2\right)\right] &= \exp\left(i\mu_y k - \frac{1}{2}\sigma_y^2 k^2\right)\end{aligned} \qquad (4.91)$$

which is the characteristic function (4.76) of a gaussian (4.75) with mean and variance

$$\mu_y = \frac{1}{N}\sum_{j=1}^{N}\mu_j \quad \text{and} \quad \sigma_y^2 = \frac{1}{N^2}\sum_{j=1}^{N}\sigma_j^2. \tag{4.92}$$

An inverse Fourier transform now gives the probability distribution $P^{(N)}(y)$ for the average $y = (x_1 + x_2 + \cdots + x_N)/N$ as

$$P^{(N)}(y) = \int_{-\infty}^{\infty} e^{-iky}\,\tilde{P}^{(N)}(k)\,\frac{dk}{2\pi} \tag{4.93}$$

which in view of (4.91) and (4.76) tends as $N \to \infty$ to Gauss's distribution $P_G(y, \mu_y, \sigma_y)$

$$\begin{aligned}\lim_{N\to\infty} P^{(N)}(y) &= \int_{-\infty}^{\infty} e^{-iky}\lim_{N\to\infty}\tilde{P}^{(N)}(k)\,\frac{dk}{2\pi} \\ &= \int_{-\infty}^{\infty} e^{-iky}\,\exp\left(i\mu_y k - \frac{1}{2}\sigma_y^2 k^2\right)\,\frac{dk}{2\pi} \\ &= P_G(y,\mu_y,\sigma_y) = \frac{1}{\sigma_y\sqrt{2\pi}}\exp\left[-\frac{(y-\mu_y)^2}{2\sigma_y^2}\right]\end{aligned} \tag{4.94}$$

with mean μ_y and variance σ_y^2 as given by (4.92). The sense in which $P^{(N)}(y)$ converges to $P_G(y, \mu_y, \sigma_y)$ is that for all a and b the probability $\Pr_N(a < y < b)$ that y lies between a and b as determined by $P^{(N)}(y)$ converges as $N \to \infty$ to the probability that y lies between a and b as determined by the gaussian $P_G(y, \mu_y, \sigma_y)$

$$\lim_{N\to\infty}\Pr_N(a < y < b) = \lim_{N\to\infty}\int_a^b P^{(N)}(y)\,dy = \int_a^b P_G(y,\mu_y,\sigma_y)\,dy. \tag{4.95}$$

This type of convergence is called **convergence in probability** (Feller, 1966, pp. 231, 241–248).

Exercises

4.1 Show that the zeroth moment μ_0 and the zeroth central moment ν_0 always are unity, and that the first central moment ν_1 always vanishes.

4.2 Show that the variance of the binomial distribution (4.14) is given by (4.19).

4.3 Show that the variance σ^2 of the Poisson distribution is the same as its mean μ as stated by equation 4.47.

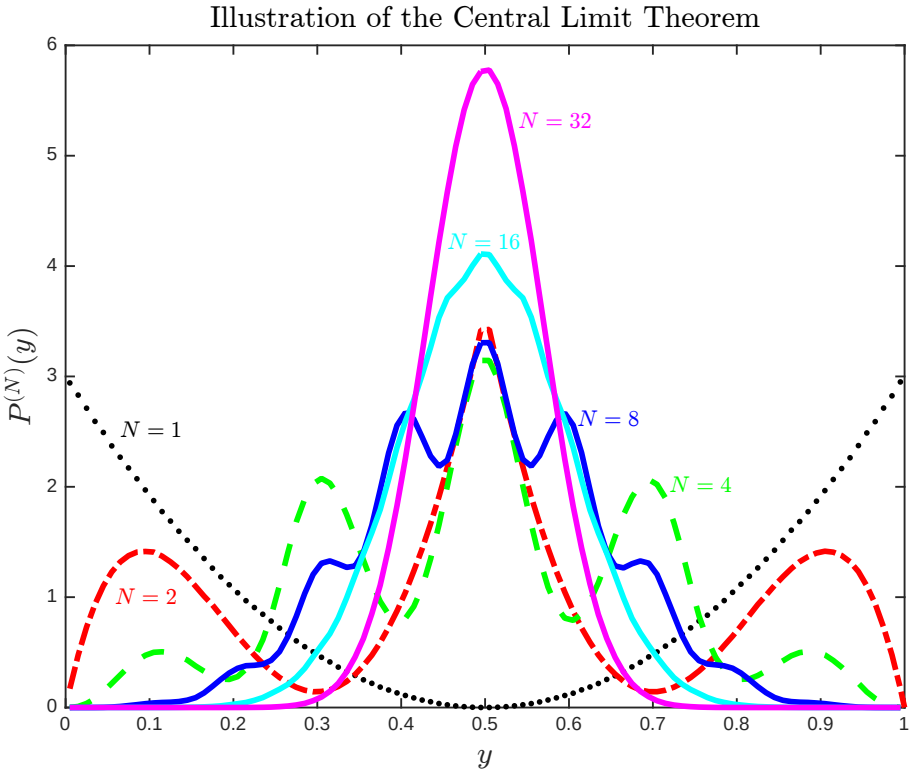

Figure 4.3 The combination of N independent, identical parabolic probability distributions $P_j^{(N)}(x_j) = 12(x_j - 1/2)^2$ gives for the average $y = (x_1 + x_2 \cdots + x_N)/N$ a distribution $P^{(N)}(y)$ that approaches a gaussian probability distribution as $N \to \infty$ and is very close by $N = 32$.

4.4 Show that the Gaussian distribution (4.57) is a normalized probability distribution with mean $\langle x \rangle = \mu = pN$ and variance $\langle (x - \mu)^2 \rangle = \sigma^2 = pqN$.

4.5 Derive equation (6.53) for the variance of the position $\boldsymbol{r}$ about its mean $\langle \boldsymbol{r}(t) \rangle$. You may assume that $\langle \boldsymbol{r}(0) \rangle = \langle \boldsymbol{v}(0) \rangle = 0$ and that $\langle (\boldsymbol{v} - \langle \boldsymbol{v}(t) \rangle)^2 \rangle = 3kT/m$.

4.6 Derive equation (6.53) for the variance of the position $\boldsymbol{r}$ about its mean $\langle \boldsymbol{r}(t) \rangle$. You may assume that $\langle \boldsymbol{r}(0) \rangle = \langle \boldsymbol{v}(0) \rangle = 0$ and that $\langle (\boldsymbol{v} - \langle \boldsymbol{v}(t) \rangle)^2 \rangle = 3kT/m$.

5

Statistical Mechanics

5.1 Equilibrium

Imagine a vast number $N \gg 10^{10}$ of particles of a fluid in a stationary container or box with walls that do not allow energy to enter or leave the fluid. After a very long time, the liquid or gas in the box is in a state of **equilibrium**. The N particles of the fluid at equilibrium assume vast numbers of different configurations as time passes. We seek a probabilistic description of this system at equilibrium.

Let us say that the fluid and its box are in a specific quantum state $|\psi\rangle$

$$|\psi\rangle = \sum_{f,b} |f,b\rangle\langle f,b|\psi\rangle \tag{5.1}$$

in which the quantum numbers $f = f_1, f_2, \ldots$ describe the fluid and the quantum numbers $b = b_1, b_2, \ldots$ describe the box and its heat bath. Any observable F that describes only the fluid and acts only on its quantum numbers f must have matrix elements $\langle f', b'|F|f, b\rangle = \delta_{b,b'}\langle f'|F|f\rangle$ that are diagonal in the quantum numbers b of the box and its heat bath. The mean value $\langle\psi|F|\psi\rangle$ of such an observable then is

$$\begin{aligned}
\langle\psi|F|\psi\rangle &= \sum_{f,b,f',b'} \langle\psi|f',b'\rangle\langle f',b'|F|f,b\rangle\langle f,b|\psi\rangle \\
&= \sum_{f,b,f',b'} \langle\psi|f',b'\rangle\langle f'|F|f\rangle\delta_{b,b'}\langle f,b|\psi\rangle \\
&= \sum_{f,b,f'} \langle\psi|f',b\rangle\langle f'|F|f\rangle\langle f,b|\psi\rangle \\
&= \sum_{f,f'} \langle f'|F|f\rangle\langle f|\rho|f'\rangle = \mathrm{Tr}(F\rho)
\end{aligned} \tag{5.2}$$

in which the matrix elements of the **density operator** ρ are

$$\langle f|\rho|f'\rangle = \sum_b \langle f, b|\psi\rangle\langle\psi|f', b\rangle, \tag{5.3}$$

and the trace is over the quantum numbers f, f' of the fluid.

The density operator is **hermitian** $\rho^\dagger = \rho$ because

$$\langle f|\rho|f'\rangle^* = \sum_b \langle f, b|\psi\rangle^*\langle\psi|f', b\rangle^* = \sum_b \langle f', b|\psi\rangle\langle\psi|f, b\rangle = \langle f'|\rho|f\rangle. \tag{5.4}$$

Its diagonal matrix element $\langle f|\rho|f\rangle$ in any state $|f\rangle$ of the fluid is the probability that the system is in that state $|f\rangle$ because

$$\langle f|\rho|f\rangle = \sum_b \langle f, b|\psi\rangle\langle\psi|f, b\rangle = \sum_b |\langle f, b|\psi|^2. \tag{5.5}$$

Since probabilities are nonnegative, the density operator is **nonnegative**, that is $\langle f|\rho|f\rangle \geq 0$ for every state $|f\rangle$ of the fluid. Since the system must be in some state, the sum of these probabilities over any complete orthonormal set of states must be unity

$$\sum_f \langle f|\rho|f\rangle = \mathrm{Tr}(\rho) = 1. \tag{5.6}$$

We now focus upon the fluid after it has reached equilibrium with itself and its box. We will use $n = n_1, n_2, \ldots$ as the quantum numbers of the fluid at equilibrium. Once the fluid is in equilibrium, the probabilities $\langle n|\rho|n\rangle$ do not vary with time. They therefore must be functions of physical quantities that do not change with time. There are seven conserved quantities: energy E, momentum $\boldsymbol{P}$, and angular momentum $\boldsymbol{J}$. Because our system is in a stationary box, the mean values of the momentum and angular momentum are zero. So the equilibrium probabilities $\langle n|\rho|n\rangle$ can depend only upon the energy E_n of the state $|n\rangle$

$$\langle n|\rho|n\rangle = P(E_n). \tag{5.7}$$

The equilibrium density operator is time independent, and so it commutes with the hamiltonian H of the system

$$[\rho, H] = 0. \tag{5.8}$$

Because they commute, the operators ρ and H are **compatible**, and so the eigenstates $|n\rangle$ of the density operator ρ

$$\rho|n\rangle = \langle n|\rho|n\rangle|n\rangle \tag{5.9}$$

may be chosen to be eigenstates of the hamiltonian H

$$H|n\rangle = E_n|n\rangle. \tag{5.10}$$

Now consider two independent subsystems that we may describe either by means of their density operators ρ_1 and ρ_2 or by means of their joint density operator ρ_{12}. Since these subsystems are independent, the joint probability $\langle n, n'|\rho_{12}|n, n'\rangle$ must be the product of the two probabilities

$$\langle n, n'|\rho_{12}|n, n'\rangle = \langle n|\rho_1|n\rangle\langle n'|\rho_2|n'\rangle. \tag{5.11}$$

And since these probabilities depend upon the energies E_n and $E_{n'}$, we must have

$$\langle n, n'|\rho_{12}|n, n'\rangle = P_{12}(E_n + E_{n'}) = P_1(E_n)P_2(E_{n'}) = \langle n|\rho_1|n\rangle\langle n'|\rho_2|n'\rangle. \tag{5.12}$$

The derivatives of $P(E_n + E_{n'})$ with respect either to E_n or to $E_{n'}$ are the same and so

$$P'_{12}(E_n + E_{n'}) = P'_1(E_n)P_2(E_{n'}) = P_1(E_n)P'_2(E_{n'}) \tag{5.13}$$

which implies

$$\frac{P'_1(E_n)}{P_1(E_n)} = \frac{P'_2(E_{n'})}{P_2(E_{n'})} = -\beta \tag{5.14}$$

or

$$P_1(E_n) = a_1\, e^{-\beta E_n} \quad \text{and} \quad P_2(E_{n'}) = a_2\, e^{-\beta E_{n'}} \tag{5.15}$$

in which β at this point is just an arbitrary constant, the same for both probability distributions. Since these probabilities must sum to unity (5.6), they form a **Boltzmann distribution**

$$\langle n|\rho_1|n\rangle = P_1(E_n) = \frac{e^{-\beta E_n}}{\sum_n e^{-\beta E_n}}. \tag{5.16}$$

Similar formulas apply to the second system and to the combined system. The density operator that describes a quantum system in equilibrium is

$$\rho = \frac{e^{-\beta H}}{\mathrm{Tr}(e^{-\beta H})}. \tag{5.17}$$

The eigenstates $|n\rangle$ of both the hamiltonian H and the density operator ρ are direct-product states

$$|n\rangle = |n_1, n_2, \ldots, n_N\rangle \tag{5.18}$$

where the quantum numbers n_1, n_2 and so forth denote the energy levels

of the various subsystems, which may be individual particles. The identity operator for the system is

$$I = \sum_n |n\rangle\langle n|. \tag{5.19}$$

In terms of its eigenstates $|n\rangle = |n_1, n_2, \ldots, n_N\rangle$ (5.18), the density operator is

$$\rho = \rho I = \frac{\sum_n |n\rangle e^{-\beta E_n}\langle n|}{\sum_n e^{-\beta E_n}}. \tag{5.20}$$

One may define the **absolute temperature** of the system described by this density operator as

$$T = \frac{1}{k\beta} \tag{5.21}$$

in which k is Boltzmann's constant $k = 1.3806488(13) \times 10^{-23}$ J/K. Thus the parameter β is $1/kT$. At body temperature $T_b = 310$ K, the quantity kT is

$$kT_b = 4.28 \text{ pN nm} = 4.28 \times 10^{-21} \text{ J} = 0.0267 \text{ eV} = 1/37.4 \text{ eV}. \tag{5.22}$$

(Ludwig Boltzmann 1844-1906)

5.2 Entropy

The **entropy** S of a system described by a density operator ρ is the trace

$$S = -k \operatorname{Tr}(\rho \ln \rho) = -k \sum_n \langle n|\rho|n\rangle \ln\langle n|\rho|n\rangle. \tag{5.23}$$

The entropy S_c of classical physics is the logarithm of the total number N of states

$$S_c = -k \ln N. \tag{5.24}$$

At equilibrium, the entropy, like the density operator, is a function $S(E)$ of the energy of the system.

The mean value E of the energy of the fluid is the trace

$$E = \langle H\rangle = \operatorname{Tr}(H\rho). \tag{5.25}$$

Let us find the density operator that maximizes the entropy while keeping

the mean value E of the energy and the trace of the density operator fixed. We use two Lagrange multipliers and seek the stationary points of

$$L(\rho, \lambda_1, \lambda_2) = -k \sum_n \rho_n \ln \rho_n - \lambda_1 \left[\sum_n \rho_n - 1 \right] - \lambda_2 \left[\sum_n \rho_n E_n - E \right] \quad (5.26)$$

when we vary the probabilities ρ_n and the multipliers λ_1 and λ_2. One may show (exercise 5.1) that the density operator that maximizes the entropy S (5.23) for a fixed average energy E is the Boltzmann density operator (5.20)

$$\rho = \frac{e^{-\beta H}}{\sum_n e^{-\beta E_n}} \quad (5.27)$$

which describes the fluid in equilibrium. It follows therefore that the **entropy S increases** as the system approaches equilibrium and reaches its maximum possible value when it is at equilibrium and so is described by the Boltzmann density operator (5.27). This is the **second law of thermodynamics**.

The entropy of two independent subsystems of a system at equilibrium described by the density operators ρ_1, ρ_2, and by the joint density operator $\rho_{12} = \rho_1 \otimes \rho_2$ is the sum of the entropies of the two subsystems

$$\begin{aligned} S_{12} =& -k \operatorname{Tr}(\rho_{12} \ln \rho_{12}) = -k \operatorname{Tr}(\rho_{12} \ln \rho_1 \otimes \rho_2) \\ =& -k \operatorname{Tr}(\rho_1 \otimes \rho_2 (\ln \rho_1 + \ln \rho_2)) \\ =& -k \operatorname{Tr}(\rho_1 \otimes \rho_2 \ln \rho_1) - k \operatorname{Tr}(\rho_1 \otimes \rho_2 \ln \rho_2) \\ =& -k \operatorname{Tr}(\rho_1 \ln \rho_1) \operatorname{Tr}(\rho_2) - k \operatorname{Tr}(\rho_1) \operatorname{Tr}(\rho_2 \ln \rho_2) \\ =& -k \operatorname{Tr}(\rho_1 \ln \rho_1) - k \operatorname{Tr}(\rho_2 \ln \rho_2) = S_1 + S_2. \end{aligned} \quad (5.28)$$

Entropy is **additive** or **extensive**.

5.3 Temperature and entropy

Let's imagine dividing our system at equilibrium into two subsystems with energies E_1 and E_2. Since the whole system is at equilibrium, its total energy $E = E_1 + E_2$ is constant. The entropy $S(E)$ of the whole system is the sum of the entropies of its two parts $S(E) = S_1(E_1) + S_2(E_2)$, and written as $S(E_1) = S_1(E_1) + S_2(E - E_1)$, may be considered to be a function E_1. Its derivative with respect to E_1 must vanish because the entropy is maximal at equilibrium

$$\frac{dS}{dE_1} = \frac{dS_1}{dE_1} + \frac{dS_2}{dE_2}\frac{dE_2}{dE_1} = \frac{dS_1}{dE_1} - \frac{dS_2}{dE_2} = 0. \quad (5.29)$$

Thus these derivatives are equal

$$\frac{dS_1}{dE_1} = \frac{dS_2}{dE_2}. \tag{5.30}$$

At equilibrium, the derivative of the entropy of a subsystem with respect to its energy is the same for all subsystems. For a system is in equilibrium inside a box of fixed size, shape, and position, this derivative is at constant volume V and it provides another definition of the **absolute temperature** as

$$\frac{1}{T} = \left.\frac{\partial S}{\partial E}\right|_V \quad \text{or as} \quad T = \left.\frac{\partial E}{\partial S}\right|_V . \tag{5.31}$$

This definition is a postulate of classical thermodynamics; in statistical mechanics, it holds when the system is in equilibrium and so is described by the Boltzmann density operator (5.27).

5.4 The partition function

The normalization factor in the denominator of the Boltzmann density operator (5.27) is the **partition function**

$$Z(\beta) = \sum_n e^{-\beta E_n}. \tag{5.32}$$

In terms of it, the Boltzmann density operator is

$$\rho = \frac{e^{-\beta H}}{Z(\beta)}. \tag{5.33}$$

The mean value of the energy is

$$E = \langle H \rangle = \mathrm{Tr}(H\rho) = \frac{\mathrm{Tr}(He^{-\beta H})}{Z(\beta)} \tag{5.34}$$

the logarithmic derivative of the partition function

$$E = \langle H \rangle = -\frac{d \ln Z(\beta)}{d\beta}. \tag{5.35}$$

The partition function gives the pressure as

$$p = \langle p \rangle = \frac{1}{\beta}\frac{\partial \ln Z}{\partial V}. \tag{5.36}$$

In terms of the Boltzmann density operator (5.27), the entropy (5.23) is

$$\begin{aligned} S = & -k\mathrm{Tr}(\rho \ln \rho) = -k \sum_n \left[e^{-\beta E_n} Z(\beta)^{-1} \ln(e^{-\beta E_n} Z(\beta)^{-1}) \right] \\ = & -k \sum_n \left[e^{-\beta E_n} Z(\beta)^{-1} (-\beta E_n - \ln Z(\beta)) \right] = \frac{E}{T} + k \ln Z(\beta). \end{aligned} \tag{5.37}$$

Example 5.1 (Partition function for an ideal gas)**.** An **ideal gas** is N noninteracting identical point molecules in a volume V. Simple quantum mechanics says that each point molecule occupies a volume $d^3q d^3p$ of phase space equal to the cube h^3 of Planck's constant. The nonrelativistic energy of a molecule of momentum $\boldsymbol{p}$ and mass m is $\boldsymbol{p}^2/2m$. If we numbered the N particles, then we'd have $N!$ different ways of assigning points $\boldsymbol{q}, \boldsymbol{p}$ in phase space to the $N!$ molecules. But since the molecules don't care what we call them, these $N!$ different configurations represent the same state, and so we must divide by $N!$ as well as by h^{3N}

$$\begin{aligned} Z(\beta) &= \frac{1}{N!\, h^{3N}} \int \exp\left(-\beta \sum_{i=1}^{N} \frac{\boldsymbol{p}_i^2}{2m} \right) dq^{3N} dp^{3N} \\ &= \frac{V^N}{N!\, h^{3N}} \left[4\pi \int \exp\left(-\beta \frac{p^2}{2m} \right) p^2 dp \right]^N \\ &= \frac{V^N}{N!\, h^{3N}} \left(\frac{2\pi m}{\beta} \right)^{3N/2} = \frac{V^N}{N!\, h^{3N}} \left(2\pi m\, kT \right)^{3N/2}. \end{aligned} \tag{5.38}$$

If c is the part of $\ln Z(\beta)$ that does not depend upon β, then the energy (5.35) of the gas is

$$E = -\frac{d \ln Z(\beta)}{d\beta} = -\frac{d}{d\beta} \left(c - \frac{3N}{2} \ln \beta \right) = \frac{3N}{2\,\beta} = \frac{3}{2} N\, kT. \tag{5.39}$$

Similarly, if c' is the part of $\ln Z(\beta)$ that does not depend upon V, then the pressure (5.36) is

$$p = \frac{1}{\beta} \frac{\partial \ln Z}{\partial V} = \frac{1}{\beta} \frac{\partial}{\partial V} \left(c' + N \ln V \right) = \frac{N}{V\,\beta} = \frac{N\, kT}{V} \tag{5.40}$$

which is the ideal-gas law. Its entropy (5.37) is

$$\begin{aligned} S &= \frac{E}{T} + k \ln Z(\beta) \\ &= \frac{3}{2} Nk + k \left[N \ln V + \frac{3}{2} N \ln kT + \frac{3}{2} N \ln \frac{2\pi m}{h^2} - \ln N! \right]. \end{aligned} \tag{5.41}$$

We now can verify the definition (5.31) of the inverse temperature as

$$\frac{1}{T} = \left.\frac{\partial S}{\partial E}\right|_V = \frac{\partial (3/2)Nk \ln kT}{\partial (3/2)NkT} = k\frac{\partial \ln kT}{\partial kT} = \frac{1}{T} \tag{5.42}$$

at least for an ideal gas. □

Example 5.2 (Van der Waals's gas law)**.** In his 1873 doctoral thesis, van der Waals proposed the more accurate formula

$$\left[P + \left(\frac{N}{V}\right)^2 a'\right]\left(V - Nb'\right) = NkT \tag{5.43}$$

in which a' represents the mutual attraction of the molecules and has the dimensions of energy times volume and b' is the effective volume of a single molecule. (Johannes van der Waals 1837–1923) □

5.5 The Helmholtz free energy

The **Helmholtz free energy** F is

$$F = -kT \ln Z(\beta) = E - TS. \tag{5.44}$$

If the energy of a tiny part of a large system, held at constant energy E and at a constant temperature T, changes by ΔE, then the energy of the rest of the system must change by $-\Delta E$. By the definition (5.31) of temperature, the change in the entropy of the rest of the system is $\Delta S_r = -\Delta E/T$. Thus as the tiny part of the system comes into equilibrium with the rest of the system, the change in the entropy of the whole system, that of the tiny part ΔS and that of the rest of the system ΔS_r, must be positive or zero

$$-\frac{\Delta E}{T} + \Delta S \geq 0 \tag{5.45}$$

because entropy always increases. Thus the Helmholtz free energy F of the tiny part decreases

$$\Delta F = \Delta E - T\Delta S \leq 0 \tag{5.46}$$

as it comes into equilibrium with the rest of the system. It reaches its minimum value at equilibrium.

The Boltzmann distribution gives the ratio of the probabilities of a system being in state 1 or state 2 as

$$\frac{p_1}{p_2} = \frac{e^{-\beta E_1}}{e^{-\beta E_2}}. \tag{5.47}$$

Suppose however that the system has n_1 states of energy E_1 and n_2 states of energy E_2. Then the ratio of the probabilities is

$$\frac{p_1}{p_2} = \frac{n_1\, e^{-\beta E_1}}{n_2\, e^{-\beta E_2}} = \frac{e^{-\beta E_1 + \ln n_1}}{e^{-\beta E_2 + \ln n_2}}. \tag{5.48}$$

The combination $-\beta E + \ln n$ appearing in these exponentials is Helmholtz's free energy at least classically because the classical entropy S_c is $k \ln n$

$$-\beta E + \ln n = -\beta(E - kT \ln n) = -\beta(E - TS_c) = -\beta F_c. \tag{5.49}$$

So for complex systems having many states of the same or nearly the same energy, the ratio of probabilities is

$$\frac{p_1}{p_2} = \frac{e^{-\beta F_1}}{e^{-\beta F_2}}. \tag{5.50}$$

(Hermann von Helmholtz 1821-1894)

5.6 The Gibbs free energy

When we derived the Boltzmann density operator (5.27), we assumed that the number of particles in our system was fixed at N, and so we did not consider how the density operator ρ might vary with that number N. If instead we focus on a part of the fluid that can exchange particles and energy with the whole fluid, then we must let the probability of a state $|n\rangle$ of the fluid depend not only upon its energy E_n like the probability (5.7) but also upon its particle number N_n

$$\langle n|\rho|n\rangle = P(E_n, N_n). \tag{5.51}$$

If we now repeat the argument (exercise 5.2) that led from the functional dependence (5.7) of $\langle n|\rho|n\rangle$ upon the energy E_n to the equilibrium density operator (5.17), then we arrive at the **Gibbs density operator**

$$\rho = \frac{e^{-\beta(H - \mu N)}}{\sum_n e^{-\beta(E_n - \mu N_n)}} = \frac{e^{-\beta(H-\mu N)}}{Z_G(\beta, \mu)} \tag{5.52}$$

in which μ is the **chemical potential**, and E_n and N_n are the energy and particle-number eigenvalues of the hamiltonian and the particle-number operator

$$H|n\rangle = E_n|n\rangle \quad \text{and} \quad N|n\rangle = N_n|n\rangle. \tag{5.53}$$

The Gibbs density operator (5.52) is the **grand canonical ensemble**, and the **Gibbs partition function**

$$Z_G(\beta,\mu) = \sum_n e^{-\beta(E_n-\mu N_n)} \tag{5.54}$$

is known also as the **grand partition function**.

One may show (exercise 5.3) that the Gibbs density operator is the one that maximizes the entropy while respecting the three constraints

$$\overline{E} = \mathrm{Tr}(H\rho), \quad \overline{N} = \mathrm{Tr}(N\rho), \quad \text{and} \quad 1 = \mathrm{Tr}(\rho). \tag{5.55}$$

The entropy of the Gibbs density operator is

$$\begin{aligned} S =& -\frac{k}{Z_G(\beta,\mu)} \sum_n \left[-\beta E_n + \beta\mu N_n) - \ln Z_G\right] e^{-\beta(E_n-\mu N_n)} \\ =& \frac{\overline{E}-\mu\overline{N}}{T} + k\ln Z_G. \end{aligned} \tag{5.56}$$

Thus we arrive at the **Gibbs potential**

$$K(\beta,\mu) = -kT\ln Z_G(\beta,\mu) = E - TS - \mu N \tag{5.57}$$

also known as the **grand canonical potential**.

One may show that the Gibbs potential K is just

$$K = -kT\ln Z_G(\beta,\mu) = -pV \tag{5.58}$$

in which p is the pressure. First

$$K(T,\mu,\lambda V) = \lambda K(T,\mu,V) \tag{5.59}$$

so

$$\left.\frac{\partial K(T,\mu,\lambda V)}{\partial\lambda}\right|_{\lambda=1} = V\frac{\partial K(T,\mu,V)}{\partial V} = \left.\frac{\partial \lambda K(T,\mu,V)}{\partial\lambda}\right|_{\lambda=1} = K(T,\mu,V). \tag{5.60}$$

Since the pressure is

$$p = kT\frac{\partial \ln Z}{\partial V} = -\frac{\partial K}{\partial V} \tag{5.61}$$

we have

$$p = -\frac{K}{V}. \tag{5.62}$$

The Gibbs enthalpy is

$$G = F + pV = E - TS + pV. \tag{5.63}$$

(Josiah Willard Gibbs 1839-1903)

Exercises

5.1 Show that the density operator that maximizes the entropy S (5.23) for a fixed average energy E is the Boltzmann density operator (5.27).

5.2 Fill in the steps to derive the formula (5.52) for the Gibbs density operator from the dependence (5.51) of the probabilities upon the energy and particle-number eigenvalues.

5.3 Use three Lagrange multipliers to show that the Gibbs density operator (5.52) is the one that maximizes the entropy while respecting the three constraints (5.55).

6

Liquids

6.1 Diffusion

We may apply the same reasoning as in the section (4.8) on the Maxwell-Boltzmann distribution to the diffusion of particles in a gas or a liquid treated as a random walk with step size dx. In one dimension, after n steps forward and $N-n$ steps backward, a particle starting at $x=0$ is at $x=(2n-N)dx$. Thus as in (4.65), the probability of being at x is given by Gauss's approximation (4.56) to the binomial distribution $P_b(n,\frac{1}{2},N)$ as

$$P_{bG}(n,\tfrac{1}{2},N)=\sqrt{\frac{2}{\pi N}}\,\exp\left(-\frac{(2n-N)^2}{2N}\right)=\sqrt{\frac{2}{\pi N}}\,\exp\left(-\frac{x^2}{2Ndx^2}\right). \tag{6.1}$$

In terms of the diffusion constant

$$D=\frac{Ndx^2}{2t} \tag{6.2}$$

this distribution is

$$P_G(x)=\left(\frac{1}{4\pi Dt}\right)^{1/2}\exp\left(-\frac{x^2}{4Dt}\right) \tag{6.3}$$

when normalized to unity on $(-\infty,\infty)$.

In three dimensions, this gaussian distribution is the product

$$P(\boldsymbol{r},t)=P_G(x)\,P_G(y)\,P_G(z)=\left(\frac{1}{4\pi Dt}\right)^{3/2}\exp\left(-\frac{\boldsymbol{r}^2}{4Dt}\right). \tag{6.4}$$

The variance $\sigma^2=2Dt$ gives the average of the squared displacement of each of the three coordinates. Thus the mean of the squared displacement

$\langle \boldsymbol{r}^2 \rangle$ rises **linearly** with the time as

$$\langle \boldsymbol{r}^2 \rangle = V[\boldsymbol{r}] = 3\sigma^2 = \int \boldsymbol{r}^2 \, P(\boldsymbol{r}, t) \, d^3r = 6 \, D \, t. \tag{6.5}$$

The distribution $P(\boldsymbol{r}, t)$ satisfies the **diffusion equation**

$$\dot{P}(\boldsymbol{r}, t) = D \, \nabla^2 P(\boldsymbol{r}, t) \tag{6.6}$$

in which the dot means time derivative.

Another way of understanding diffusion is to consider the flow rate $\boldsymbol{J}$ (per unit area, per unit time) of a fixed number of randomly moving particles, such as molecules of a gas or a liquid. This flow rate $\boldsymbol{J}$ is proportional to the negative gradient of their concentration $c(\boldsymbol{x}, t)$

$$\boldsymbol{J}(\boldsymbol{x}, t) = -D \nabla c(\boldsymbol{x}, t) \tag{6.7}$$

where D is the diffusion constant, an equation known as **Fick's law** (Adolf Fick 1829–1901). Since the number of particles is conserved, the 4-vector $J = (c, \boldsymbol{J})$ obeys the conservation law

$$\frac{\partial}{\partial t} \int c(\boldsymbol{x}, t) \, d^3\boldsymbol{x} = - \oint \boldsymbol{J}(\boldsymbol{x}, t) \cdot \boldsymbol{da} = - \int \nabla \cdot \boldsymbol{J}(\boldsymbol{x}, t) d^3\boldsymbol{x} \tag{6.8}$$

which with Fick's law (6.7) gives the diffusion equation (6.6)

$$\dot{c}(\boldsymbol{x}, t) = -\nabla \cdot \boldsymbol{J}(\boldsymbol{x}, t) = D \nabla^2 c(\boldsymbol{x}, t) \quad \text{or} \quad \left(D\nabla^2 - \partial_t \right) c(\boldsymbol{x}, t) = 0. \tag{6.9}$$

Fourier had in mind such equations when he invented his transform.

If we write the density $c(\boldsymbol{x}, t)$ as the transform

$$c(\boldsymbol{x}, t) = \int e^{i\boldsymbol{k}\cdot\boldsymbol{x} + i\omega t} \tilde{c}(\boldsymbol{k}, \omega) \, d^3\boldsymbol{k} d\omega \tag{6.10}$$

then the diffusion equation becomes

$$\left(D\nabla^2 - \partial_t \right) c(\boldsymbol{x}, t) = \int e^{i\boldsymbol{k}\cdot\boldsymbol{x} + i\omega t} \left(-D\boldsymbol{k}^2 - i\omega \right) \tilde{c}(\boldsymbol{k}, \omega) \, d^3\boldsymbol{k} d\omega = 0 \tag{6.11}$$

which implies the algebraic equation

$$\left(D\boldsymbol{k}^2 + i\omega \right) \tilde{c}(\boldsymbol{k}, \omega) = 0. \tag{6.12}$$

As explained in (Cahill, 2013, section 3.13), the solution of this homogeneous equation is

$$c(\boldsymbol{x}, t) = \int e^{i\boldsymbol{k}\cdot\boldsymbol{x} + i\omega t} \delta \left(-D\boldsymbol{k}^2 - i\omega \right) h(\boldsymbol{k}, \omega) \, d^3\boldsymbol{k} d\omega \tag{6.13}$$

in which $h(\boldsymbol{k}, \omega)$ is an arbitrary function. Dirac's delta function requires ω

to be imaginary $\omega = iD\boldsymbol{k}^2$, with $D\boldsymbol{k}^2 > 0$. So the ω-integration is up the imaginary axis. It is a Laplace transform, and we have

$$c(\boldsymbol{x}, t) = \int_{-\infty}^{\infty} e^{i\boldsymbol{k}\cdot\boldsymbol{x} - D\boldsymbol{k}^2 t}\, \tilde{c}(\boldsymbol{k})\, d^3\boldsymbol{k} \tag{6.14}$$

in which $\tilde{c}(\boldsymbol{k}) \equiv h(\boldsymbol{k}, iD\boldsymbol{k}^2)$. Thus the function $\tilde{c}(\boldsymbol{k})$ is the Fourier transform of the initial density $c(\boldsymbol{x}, 0)$

$$c(\boldsymbol{x}, 0) = \int_{-\infty}^{\infty} e^{i\boldsymbol{k}\cdot\boldsymbol{x}} \tilde{c}(\boldsymbol{k})\, d^3\boldsymbol{k}. \tag{6.15}$$

So if the initial density $c(\boldsymbol{x}, 0)$ is concentrated at $\boldsymbol{y}$

$$c(\boldsymbol{x}, 0) = \delta(\boldsymbol{x} - \boldsymbol{y}) = \int_{-\infty}^{\infty} e^{i\boldsymbol{k}\cdot(\boldsymbol{x}-\boldsymbol{y})}\, \frac{d^3\boldsymbol{k}}{(2\pi)^3} \tag{6.16}$$

then its Fourier transform $\tilde{c}(\boldsymbol{k})$ is

$$\tilde{c}(\boldsymbol{k}) = \frac{e^{-i\boldsymbol{k}\cdot\boldsymbol{y}}}{(2\pi)^3} \tag{6.17}$$

and at later times the density $c(\boldsymbol{x}, t)$ is given by (6.14) as

$$c(\boldsymbol{x}, t) = \int_{-\infty}^{\infty} e^{i\boldsymbol{k}\cdot(\boldsymbol{x}-\boldsymbol{y}) - D\boldsymbol{k}^2 t}\, \frac{d^3\boldsymbol{k}}{(2\pi)^3}. \tag{6.18}$$

The Fourier transform of a gaussian, and we find doing the integral

$$c(\boldsymbol{x}, t) = \frac{1}{(4\pi Dt)^{3/2}}\, e^{-(\boldsymbol{x}-\boldsymbol{y})^2/(4Dt)}. \tag{6.19}$$

Since the diffusion equation is linear, it follows that an arbitrary initial distribution $c(\boldsymbol{y}, 0)$ evolves to the distribution

$$c(\boldsymbol{x}, t) = \frac{1}{(4\pi Dt)^{3/2}} \int e^{-(\boldsymbol{x}-\boldsymbol{y})^2/(4Dt)}\, c(\boldsymbol{y}, 0)\, d^3\boldsymbol{y}. \tag{6.20}$$

at time t. Such **convolutions** often occur in physics.

6.2 Langevin's Theory of Brownian Motion

Einstein made the first theory of brownian motion in 1905, but Langevin's approach (Langevin, 1908) is simpler. A tiny particle of colloidal size and mass m in a fluid is buffeted by a force $\boldsymbol{F}(t)$ due to the 10^{21} collisions per second it suffers with the molecules of the surrounding fluid. Its equation of motion is

$$m\, \frac{d\boldsymbol{v}(t)}{dt} = \boldsymbol{F}(t). \tag{6.21}$$

Langevin suggested that the force $\boldsymbol{F}(t)$ is the sum of a viscous drag $-\boldsymbol{v}(t)/B$ and a rapidly fluctuating part $\boldsymbol{f}(t)$

$$\boldsymbol{F}(t) = -\boldsymbol{v}(t)/B + \boldsymbol{f}(t) \tag{6.22}$$

so that

$$m\,\frac{d\boldsymbol{v}(t)}{dt} = -\frac{\boldsymbol{v}(t)}{B} + \boldsymbol{f}(t). \tag{6.23}$$

The parameter B is called the **mobility**. The **ensemble average** (the average over the set of particles) of the fluctuating force $\boldsymbol{f}(t)$ is zero

$$\langle \boldsymbol{f}(t) \rangle = \boldsymbol{0}. \tag{6.24}$$

Thus the ensemble average of the velocity satisfies

$$m\,\frac{d\langle \boldsymbol{v} \rangle}{dt} = -\frac{\langle \boldsymbol{v} \rangle}{B} \tag{6.25}$$

whose solution with $\tau = mB$ is

$$\langle \boldsymbol{v(t)} \rangle = \langle \boldsymbol{v(0)} \rangle\, e^{-t/\tau}. \tag{6.26}$$

The instantaneous equation (6.23) divided by the mass m is

$$\frac{d\boldsymbol{v}(t)}{dt} = -\frac{\boldsymbol{v}(t)}{\tau} + \boldsymbol{a}(t) \tag{6.27}$$

in which $\boldsymbol{a}(t) = \boldsymbol{f}(t)/m$ is the acceleration. The ensemble average of the scalar product of the position vector $\boldsymbol{r}$ with this equation is

$$\left\langle \boldsymbol{r} \cdot \frac{d\boldsymbol{v}}{dt} \right\rangle = -\frac{\langle \boldsymbol{r} \cdot \boldsymbol{v} \rangle}{\tau} + \langle \boldsymbol{r} \cdot \boldsymbol{a} \rangle. \tag{6.28}$$

But since the ensemble average $\langle \boldsymbol{r} \cdot \boldsymbol{a} \rangle$ of the scalar product of the position vector $\boldsymbol{r}$ with the random, fluctuating part $\boldsymbol{a}$ of the acceleration vanishes, we have

$$\left\langle \boldsymbol{r} \cdot \frac{d\boldsymbol{v}}{dt} \right\rangle = -\frac{\langle \boldsymbol{r} \cdot \boldsymbol{v} \rangle}{\tau}. \tag{6.29}$$

Now

$$\frac{1}{2}\frac{d\,\boldsymbol{r}^2}{dt} = \frac{1}{2}\frac{d}{dt}\,(\boldsymbol{r} \cdot \boldsymbol{r}) = \boldsymbol{r} \cdot \boldsymbol{v} \tag{6.30}$$

and so

$$\frac{1}{2}\frac{d^2\boldsymbol{r}^2}{dt^2} = \boldsymbol{r} \cdot \frac{d\boldsymbol{v}}{dt} + \boldsymbol{v}^2. \tag{6.31}$$

The ensemble average of this equation gives us

$$\frac{d^2\langle \boldsymbol{r}^2\rangle}{dt^2} = 2\left\langle \boldsymbol{r}\cdot\frac{d\boldsymbol{v}}{dt}\right\rangle + 2\langle \boldsymbol{v}^2\rangle \tag{6.32}$$

or in view of (6.29)

$$\frac{d^2\langle \boldsymbol{r}^2\rangle}{dt^2} = -2\frac{\langle \boldsymbol{r}\cdot\boldsymbol{v}\rangle}{\tau} + 2\langle \boldsymbol{v}^2\rangle. \tag{6.33}$$

We now use (6.30) to replace $\langle \boldsymbol{r}\cdot\boldsymbol{v}\rangle$ with half the first time derivative of $\langle \boldsymbol{r}^2\rangle$ so that we have

$$\frac{d^2\langle \boldsymbol{r}^2\rangle}{dt^2} = -\frac{1}{\tau}\frac{d\langle \boldsymbol{r}^2\rangle}{dt} + 2\langle \boldsymbol{v}^2\rangle. \tag{6.34}$$

If the fluid is in equilibrium, then the ensemble average of $\boldsymbol{v}^2$ is given by the Maxwell-Boltzmann value (4.72)

$$\langle \boldsymbol{v}^2\rangle = \frac{3kT}{m} \tag{6.35}$$

and so the acceleration (6.34) is

$$\frac{d^2\langle \boldsymbol{r}^2\rangle}{dt^2} + \frac{1}{\tau}\frac{d\langle \boldsymbol{r}^2\rangle}{dt} = \frac{6kT}{m}. \tag{6.36}$$

which we can integrate.

The general solution to a second-order linear inhomogeneous differential equation is the sum of any particular solution to the inhomogeneous equation plus the general solution of the homogeneous equation (Cahill, 2013, section 6.1). The function $\langle \boldsymbol{r}^2(t)\rangle_{pi} = 6kTt\tau/m$ is a particular solution of the inhomogeneous equation. The general solution to the homogeneous equation is $\langle \boldsymbol{r}^2(t)\rangle_{gh} = U + W\exp(-t/\tau)$ where U and W are constants. So $\langle \boldsymbol{r}^2(t)\rangle$ is

$$\langle \boldsymbol{r}^2(t)\rangle = U + W\,e^{-t/\tau} + 6kT\tau t/m \tag{6.37}$$

where U and W make $\langle \boldsymbol{r}^2(t)\rangle$ fit the boundary conditions. If the individual particles start out at the origin $\boldsymbol{r} = \boldsymbol{0}$, then one boundary condition is

$$\langle \boldsymbol{r}^2(0)\rangle = 0 \tag{6.38}$$

which implies that

$$U + W = 0. \tag{6.39}$$

And since the particles start out at $\boldsymbol{r} = \boldsymbol{0}$ with an isotropic distribution of initial velocities, the formula (6.30) for $\dot{r}^2$ implies that at $t = 0$

$$\left.\frac{d\,\langle \boldsymbol{r}^2\rangle}{dt}\right|_{t=0} = 2\langle \boldsymbol{r}(0)\cdot\boldsymbol{v}(0)\rangle = 0. \tag{6.40}$$

This boundary condition means that our solution (6.37) must satisfy

$$\left.\frac{d\,\langle \boldsymbol{r}^2(t)\rangle}{dt}\right|_{t=0} = -\frac{W}{\tau} + \frac{6kT\tau}{m} = 0. \tag{6.41}$$

Thus $W = -U = 6kT\tau^2/m$, and so our solution (6.37) is

$$\langle \boldsymbol{r}^2(t)\rangle = \frac{6kT\tau^2}{m}\left[\frac{t}{\tau} + e^{-t/\tau} - 1\right]. \tag{6.42}$$

At times short compared to τ, the first two terms in the power series for the exponential $\exp(-t/\tau)$ cancel the terms $-1 + t/\tau$, leaving

$$\langle \boldsymbol{r}^2(t)\rangle = \frac{6kT\tau^2}{m}\left[\frac{t^2}{2\tau^2}\right] = \frac{3kT}{m}\,t^2 = \langle v^2\rangle\, t^2. \tag{6.43}$$

But at times long compared to τ, the exponential vanishes, leaving

$$\langle \boldsymbol{r}^2(t)\rangle = \frac{6kT\tau}{m}\,t = 6\,B\,kT\,t. \tag{6.44}$$

The **diffusion constant** D is defined by

$$\langle \boldsymbol{r}^2(t)\rangle = 6\,D\,t \tag{6.45}$$

and so we arrive at **Einstein's relation**

$$D = B\,kT \tag{6.46}$$

which often is written in terms of the **viscous-friction coefficient** ζ

$$\zeta \equiv \frac{1}{B} = \frac{m}{\tau} \tag{6.47}$$

as

$$\zeta\, D = kT. \tag{6.48}$$

This equation expresses Boltzmann's constant k in terms of three quantities ζ, D, and T that were accessible to measurement in the first decade of the 20th century. It enabled scientists to measure Boltzmann's constant k for the first time. And since Avogadro's number N_A was the known gas constant R divided by k, the number of molecules in a mole was revealed to be $N_A = 6.022 \times 10^{23}$. Chemists could then divide the mass of a mole of any pure substance by 6.022×10^{23} and find the mass of the molecules that composed it. Suddenly the masses of the molecules of chemistry became known, and molecules were recognized as real particles and not tricks for balancing chemical equations. (Paul Langevin 1872–1946, Albert Einstein 1879–1955)

6.3 The Einstein-Nernst relation

If a particle of mass m carries an electric charge q and is exposed to an electric field $\boldsymbol{E}$, then in addition to viscosity $-\boldsymbol{v}/B$ and random buffeting $\boldsymbol{f}$, the constant force $q\boldsymbol{E}$ acts on it

$$m\,\frac{d\boldsymbol{v}}{dt} = -\frac{\boldsymbol{v}}{B} + q\boldsymbol{E} + \boldsymbol{f}. \tag{6.49}$$

The mean value of its velocity will then satisfy the differential equation

$$\left\langle \frac{d\boldsymbol{v}}{dt} \right\rangle = -\frac{\langle \boldsymbol{v} \rangle}{\tau} + \frac{q\boldsymbol{E}}{m} \tag{6.50}$$

where $\tau = mB$. A particular solution of this inhomogeneous equation is

$$\langle \boldsymbol{v}(t) \rangle_{pi} = \frac{q\tau \boldsymbol{E}}{m} = qB\boldsymbol{E}. \tag{6.51}$$

The general solution of its homogeneous version is $\langle \boldsymbol{v}(t) \rangle_{gh} = \boldsymbol{A}\, \exp(-t/\tau)$ in which the constant $\boldsymbol{A}$ is chosen to give $\langle \boldsymbol{v}(0) \rangle$ at $t = 0$. So as explained in (Cahill, 2013, section 6.1), the general solution $\langle \boldsymbol{v}(t) \rangle$ to equation (6.50) is (exercise 4.5) the sum of $\langle \boldsymbol{v}(t) \rangle_{pi}$ and $\langle \boldsymbol{v}(t) \rangle_{gh}$

$$\langle \boldsymbol{v}(t) \rangle = qB\boldsymbol{E} + [\langle \boldsymbol{v}(0) \rangle - qB\boldsymbol{E}]\; e^{-t/\tau}. \tag{6.52}$$

By applying the tricks of the previous section (6.2), one may show (exercise 4.6) that the variance of the position $\boldsymbol{r}$ about its mean $\langle \boldsymbol{r}(t) \rangle$ is

$$\left\langle (\boldsymbol{r} - \langle \boldsymbol{r}(t) \rangle)^2 \right\rangle = \frac{6kT\tau^2}{m} \left(\frac{t}{\tau} - 1 + e^{-t/\tau} \right) \tag{6.53}$$

where $\langle \boldsymbol{r}(t) \rangle = (q\tau^2 \boldsymbol{E}/m) \left(t/\tau - 1 + e^{-t/\tau} \right)$ if $\langle \boldsymbol{r}(0) \rangle = \langle \boldsymbol{v}(0) \rangle = 0$. So for times $t \gg \tau$, this variance is

$$\left\langle (\boldsymbol{r} - \langle \boldsymbol{r}(t) \rangle)^2 \right\rangle = \frac{6kT\tau t}{m}. \tag{6.54}$$

Since the diffusion constant D is defined by (6.45) as

$$\left\langle (\boldsymbol{r} - \langle \boldsymbol{r}(t) \rangle)^2 \right\rangle = 6\, D\, t \tag{6.55}$$

we arrive at the Einstein-Nernst relation

$$D = BkT = \frac{\mu}{q} kT \tag{6.56}$$

in which the electric mobility is $\mu = qB$.

The general solution (6.52) tells us that at times $t \gg \tau$, an electric field $\boldsymbol{E}$ changes Fick's law (6.7) to

$$\boldsymbol{J} = -D\nabla c + qB\boldsymbol{E}c = -D\nabla c + \frac{q\boldsymbol{E}c}{\zeta}. \tag{6.57}$$

Useing Einstein's formula $\zeta = kT/D$ (6.48) for the viscous-friction coefficient, we get the **Nernst-Planck formula**

$$\boldsymbol{J} = D\left(-\nabla c + \frac{q\boldsymbol{E}c}{kT}\right). \tag{6.58}$$

(Walther Nernst 1864–1941, Max Planck 1858–1947)

Example 6.1 (Potential across a cell membrane)**.** At equilibrium, the current density vanishes, $\boldsymbol{J} = 0$, and we can integrate the Nernst-Planck formula (6.58)

$$\frac{1}{c(z)}\frac{d}{dz}c(z) = \frac{q\boldsymbol{E}}{kT} \tag{6.59}$$

across the (5 nm) thin plasma membrane of a eukaryotic cell and find that the concentrations of (positively) charged ions inside $c(-)$ and outside $c(+)$ the cell membrane are related to the change in voltage across the membrane

$$\ln\frac{c(+)}{c(-)} = \frac{q(V(+) - V(-))}{kT}. \tag{6.60}$$

At room temperature, the thermal energy kT is about

$$kT = \frac{1}{40}\ \text{eV} \tag{6.61}$$

so $kT/e = 1/40$ V. So if $\ln c(+)/c(-) \approx \ln(10) = 2.3$, then the voltage rise across the membrane is 58 mV, which is typical. The electric field $\boldsymbol{E}$ points into the cell and is about 10^7 V/m in the lipid bilayer which is only 5 nm thick. □

6.4 The Poisson-Boltzmann equation

Gauss's law equates the divergence of the **electric displacement** $\boldsymbol{D}$

$$\boldsymbol{\nabla}\cdot\boldsymbol{D} = \rho \tag{6.62}$$

to the density ρ of **free charges** (charges that are free to move in or out of the dielectric medium—as opposed to those that are part of the medium and bound to it by molecular forces). In a **linear isotropic dielectric**,

the electric displacement $\boldsymbol{D} = \epsilon_m \boldsymbol{E}$ is proportional to the electric field $\boldsymbol{E}$ in which the **permittivity** $\epsilon_m = K_m \epsilon_0$ of the dielectric is a multiple K_m of the **electric constant** $\epsilon_0 = 8.85418782 \times 10^{-12}$ F/m.

If the fluid is in equilibrium, then the charge density ρ should be proportional to the Boltzmann factor

$$\rho = \rho_0 \, e^{-qV/kT}. \tag{6.63}$$

If the fluid is an linear isotropic dielectric with a constant permittivity ϵ_m, then Gauss's law (6.62) is

$$\boldsymbol{\nabla} \cdot \boldsymbol{D} = \epsilon_m \boldsymbol{\nabla} \cdot \boldsymbol{E} = \rho. \tag{6.64}$$

Equilibrium implies time independence, and so the electric field is related to the gradient of the scalar potential V

$$\boldsymbol{E} = \, - \boldsymbol{\nabla} V. \tag{6.65}$$

Putting these equations (6.63–6.65) together, we arrive at the **Poisson-Boltzmann equation**

$$- \epsilon_m \, \boldsymbol{\nabla} \cdot \boldsymbol{\nabla} \, V = \rho_0 \, e^{-qV/kT}. \tag{6.66}$$

A more general form of the Poisson-Boltzmann equation applies when there are several kinds of ions of charge q_i and a fixed charge distribution ρ_f

$$- \epsilon_m \, \boldsymbol{\nabla}^2 \, V = \rho_f + \sum_i \rho_{i,0} \, e^{-q_i V/kT}. \tag{6.67}$$

This nonlinear partial differential equation is hard to solve analytically. Gouy and Chapman, however, found an exact solution for problems in one dimension (Gouy, 1910; Chapman, 1913), which we'll use in section 7.6. (Louis Gouy 1854-1926, David Chapman 1869-1958)

6.5 Reynolds number

Engineers mean two very different things by *stress* and *strain* which have similar meanings in everyday English. Consider a fluid between two large parallel plates of area A separated by a distance L in the vertical z-direction. Suppose a force F moves the top plate slowly in the x direction at a constant speed v, while the bottom plate remains stationary. The **shear stress** τ is the force applied to the top plate divided by its area,

$$\tau = \frac{F}{A} \qquad \text{shear stress.} \tag{6.68}$$

If the speed v is slow enough and the separation z big enough, then the liquid adjacent to and adsorbed by the upper plate moves at the speed of the upper plate, and the liquid adjacent to and adsorbed by the lower plate is stationary like the lower plate. The **shear strain** of the fluid at height z is the derivative of the displacement Δx in the x-direction with respect to the height

$$\gamma = \frac{d\Delta x}{dz} \qquad \text{shear strain.} \tag{6.69}$$

The displacement Δx is proportional to the time t, and its time derivative is the speed at height z

$$v(z) = \frac{d\Delta x}{dt}. \tag{6.70}$$

The **shear rate** is the z-derivative of $v(z)$. In **newtonian liquids**, the shear stress is proportional to the shear rate

$$\tau = \frac{F}{A} = \eta \frac{dv(z)}{dz}, \tag{6.71}$$

and the constant of proportionality is the **viscosity** η.

The **viscosity** η of water runs from 0.001003 kg/m·s at 20° C to 0.000692 kg/m·s at 37° C; that of corn syrup is $\eta = 1.3806$ kg/m·s at 25°C. (One kg/m·s = 1 Pa·s.) Stokes related the viscosity η of a fluid of particles of radius r to the viscous-friction coefficient ζ of the fluid

$$\eta = \frac{\zeta}{6\pi r}. \tag{6.72}$$

The dimensionless ratio of the mass ρAL times v^2/L, which has the same dimensions as acceleration, to the force F

$$\mathcal{R} = \frac{\rho AL v^2/L}{F} = \frac{\rho AL v^2/L}{\eta A v/L} = \frac{\rho L v}{\eta} \tag{6.73}$$

is the **Reynolds number** of a process. In numerous experiments, Reynolds showed that a process that has a Reynolds number $\mathcal{R} \gtrsim 10^3$ is turbulent, while one with a small Reynolds number $\mathcal{R} \ll 10^3$ flows smoothly in layers, a process called **laminar flow**. (Osborne Reynolds 1842–1912)

A pressure p forces a newtonian fluid of mass density ρ and viscosity η through a cylindrical pipe of radius R and length L (in the absence of gravity). The speed $v(r)$ is fastest in the center of the pipe, $r = 0$, and vanishes at the inner surface of the pipe, $r = R$. In laminar flow, the fluid does not accelerate, so the force $p2\pi r dr$ applied by the pressure to an annulus of width dr must equal the frictional force or drag due to the viscosity η.

That drag is the difference between the frictional force forward due to the faster fluid at r minus the frictional force forward due to the slower fluid at $r + dr$. Using our definition (6.71) of the viscosity (with $z \to r$), we find that the drag is $2\pi\eta L\, d(r dv(r)/dr)$. Equating the two forces and dividing by $2\pi\eta L\, dr$, we get

$$\frac{d}{dr}\left(r\,\frac{dv(r)}{dr}\right) = \frac{p}{\eta L}\,r. \tag{6.74}$$

This second-order inhomogeneous differential equation for $v(r)$ is a first-order differential equation for $V(r) = rv'(r)$ in which the prime means r-derivative

$$\frac{d}{dr}V(r) = \frac{p}{\eta L}r. \tag{6.75}$$

Since $V(0) = 0$, the solution to this equation is

$$V(r) = \int_0^r \frac{p}{\eta L}r'dr' = \frac{p}{2\eta L}\,r^2. \tag{6.76}$$

Integrating once more and applying the boundary condition $v(R) = 0$, we find

$$-\,v(r) = v(R) - v(r) = -\int_r^R v'(r')\,dr' = \int_r^R \frac{p}{2\eta L}\,r'\,dr'. \tag{6.77}$$

So the speed $v(r)$ of the fluid at radius r is

$$v(r) = \frac{p}{4\eta L}\left(R^2 - r^2\right). \tag{6.78}$$

The flow rate Q through the pipe is the integral of the speed $v(r)$ of the fluid over the circular cross-section of the pipe

$$Q = \int_0^R \frac{p}{4\eta L}\left(R^2 - r'^2\right)2\pi r'\,dr' = \frac{\pi}{8\eta L}\,p\,R^4 \tag{6.79}$$

which is the **Hagen-Poiseuille** formula. So to the extent that blood is a newtonian fluid, the blood pressure needed for a given rate of flow varies as the inverse fourth power $1/R^4$ of the radius R of the artery.

Example 6.2 (Laminar flow)**.** Suppose we slowly stir corn syrup in which we carefully placed drops of acrylic dyes of different colors mixed with the corn syrup. The speed v is about 0.02 m/s. The length $L = 0.1$ m. The density of corn syrup is $\rho = 1.38 \times 10^3$ kg/m^3, and its viscosity is $\eta = 1.3806$ kg/m·s. So the Reynolds number for this event is

$$\mathcal{R} = \frac{vL\rho}{\eta} \approx \frac{0.02\text{ m/s} \times 0.1\text{ m} \times 1.38 \times 10^3\text{ kg/m}^3}{1.38\text{ kg/m·s}} = 2. \tag{6.80}$$

And indeed we can slowly stir the mixture backwards and recover the separated drops of colored dye. The demo is on YouTube (`https://www.youtube.com/watch?v=p08_KlTKP50`). Had we used water instead of corn syrup, the Reynolds number of the event would have been $\mathcal{R} \approx 2 \times 10^3$ which is within the range of turbulent flow. This is why one can't stir cream into one's coffee and then separate the cream by stirring it backwards. □

6.6 Fluid mechanics

The **conservation law** for a fluid of mass density ρ moving with velocity $\boldsymbol{v}$ is

$$\frac{\partial \rho}{\partial t} = -\boldsymbol{\nabla} \cdot (\rho \boldsymbol{v}) = -\rho \boldsymbol{\nabla} \cdot \boldsymbol{v} - \boldsymbol{v} \cdot \boldsymbol{\nabla} \rho. \tag{6.81}$$

The total time derivative of the density then is

$$\frac{d\rho}{dt} = \frac{\partial \rho}{\partial t} + \boldsymbol{v} \cdot \boldsymbol{\nabla} \rho = -\rho \boldsymbol{\nabla} \cdot \boldsymbol{v}. \tag{6.82}$$

An **incompressible fluid** is one for which both sides of this continuity equation vanish

$$\frac{d\rho}{dt} = 0 \quad \text{and} \quad \boldsymbol{\nabla} \cdot \boldsymbol{v} = 0. \tag{6.83}$$

The force $\boldsymbol{F}$ acting on a tiny volume dV of a fluid due to a pressure p is the integral over the surface $\boldsymbol{dA}$ of dV

$$-\oint p \, \boldsymbol{dA} = -\int \boldsymbol{\nabla} p \, dV. \tag{6.84}$$

in which $\boldsymbol{dA}$ is the outward normal to the surface. Equating this force per unit volume to the density times the acceleration, we find

$$\rho \frac{d\boldsymbol{v}}{dt} = \rho \left(\frac{\partial \boldsymbol{v}}{\partial t} + (\boldsymbol{v} \cdot \boldsymbol{\nabla}) \, \boldsymbol{v} \right) = -\boldsymbol{\nabla} p \tag{6.85}$$

which is Euler's equation for an **ideal fluid**, that is, a fluid without viscosity or thermal conductivity. (Leonhard Euler 1707–1783)

An incompressible fluid with a constant viscosity η obeys the **Navier-Stokes equation**

$$\rho \left(\frac{\partial \boldsymbol{v}}{\partial t} + (\boldsymbol{v} \cdot \boldsymbol{\nabla}) \, \boldsymbol{v} \right) = -\boldsymbol{\nabla} p + \eta \, \boldsymbol{\nabla}^2 \boldsymbol{v}. \tag{6.86}$$

(Claude-Louis Navier 1785–1836, George Stokes 1819–1903)

7

Cell structure

7.1 Organelles

A **prokaryotic** cell is a bag of salty water, DNA, RNA, proteins, sugars, and so forth between 0.1 and 5 μm in diameter surrounded by a tough cell wall. Prokaryotic cells have no internal structure or transport mechanism. They rely upon diffusion to move their molecules around.

Eukaryotic cells have diameters between 10 and 100 μm, and nerve cells can be as long as one meter. A eukaryotic cell has a **nucleus** that contains the cell's DNA, is about 5 μm in diameter, and constitutes one-tenth of the volume of the cell. A plasma membrane surrounds the nucleus in a double layer that extends into the cytosol as the **endoplasmic reticulum**. Inside the nucleus, the **nucleolus** is a factory that makes ribosomes.

RNA polymerase II transcribes a nucleotide sequence from DNA into **pre-mRNA** inside the nucleus. A **spliceosome** (made of snRNAs and proteins) then excises **intron** segments and redundant **exons** from the pre-mRNA. An **exportin** protein then transports the resulting mRNA through a **nuclear pore complex** into the cytosol.

The endoplasmic reticulum and the **Golgi apparatus** use ribosomes and other molecular devices to make and decorate proteins and glycosaminoglycans (GAGs, long chains of disacharides) which the cell then moves to the plasma membrane in membrane-enclosed sacs that bud from the endoplasmic reticulum and from the Golgi apparatus and then fuse with the membranes of other organelles or with the plasma membrane. Ribosomes in the cytosol also translate mRNAs into proteins.

A **mitochondrion** is an organelle with an outer membrane and an inner membrane on which **ATP synthase** uses **pyruvate** and **NADH** (both made from glucose in the cytosol) to turn ADP into ATP. A red blood cell has no nucleus nor any mitochondria, but a liver cell can have 2000 mito-

chondria. Most animals inherit their mitochondria only from their mothers; mechanisms destroy the mitochondria of sperm after fertilization (Zhou et al., 2016).

Endosomes are membrane sacs that enclose external material that the cell has just swallowed by **endocytosis**. Endosomes pass much of this material to **lysosomes** which use acids and enzymes to digest this material and surplus cytosolic macromolecules into elementary molecules that the cell reuses. Cells oxidize toxic molecules in **peroxisomes**. **Proteasomes** are organelles that use **proteases** to dissolve the peptide bonds of proteins, decomposing them into reusable amino acids.

Because eukaryotic cells have volumes that are between 8 and 10^9 times bigger than prokaryotic cells, they can't rely upon diffusion to move molecules and bags of molecules around. They use three families of protein filaments: **Intermediate filaments** give structure and flexibility (they can stretch and contract) to the **cytoskeleton**, are 10 nm in diameter, and are dimers of dimers. Oriented **microtubules** (made of dimers of the proteins α-tubulin and β-tubulin) position the membrane-enclosed organelles, are 25 nm in diameter, and are the cell's Fedex. The motor proteins **dynein** and **kinesin** use ATP to drag membrane-enclosed sacs of molecules along microtubules toward their (+) and (-) ends. Oriented **actin filaments** are made of the globular protein G-actin and are 7 nm in diameter. They can rapidly become longer by polymerization or shorter by depolymerization, and so enable the cell to change its shape and to move.

7.2 Membranes

The plasma membrane of an animal cell and the membranes of the endoplasmic reticulum, the Golgi apparatus, the endosomes, and other membrane-enclosed organelles are lipid bilayers about 5-nm thick studded with proteins. The lipid constituents are mainly phospholipids, sterols, and glycolipids.

There are four main phospholipids in membranes. Three of them are neutral: phosphatidylethanolamine (PE), phosphatidylcholine (PC), and sphingolipids (SL) have polar but neutral head groups. Phosphatidylserine (PS), has a negatively charged head group. In a living cell, **flippases** use ATP to move PS and to a lesser degree PE to the cytosolic layer of the plasma membrane, while **floppases** use ATP to move PC and SL to the outer layer. **Scramblases** help these phospholipids move in the opposite directions (Clark, 2011).

The lipid interior of a cell membrane is a barrier to ions and to polar molecules bigger than water, but not to hydrophobic molecules such as O_2,

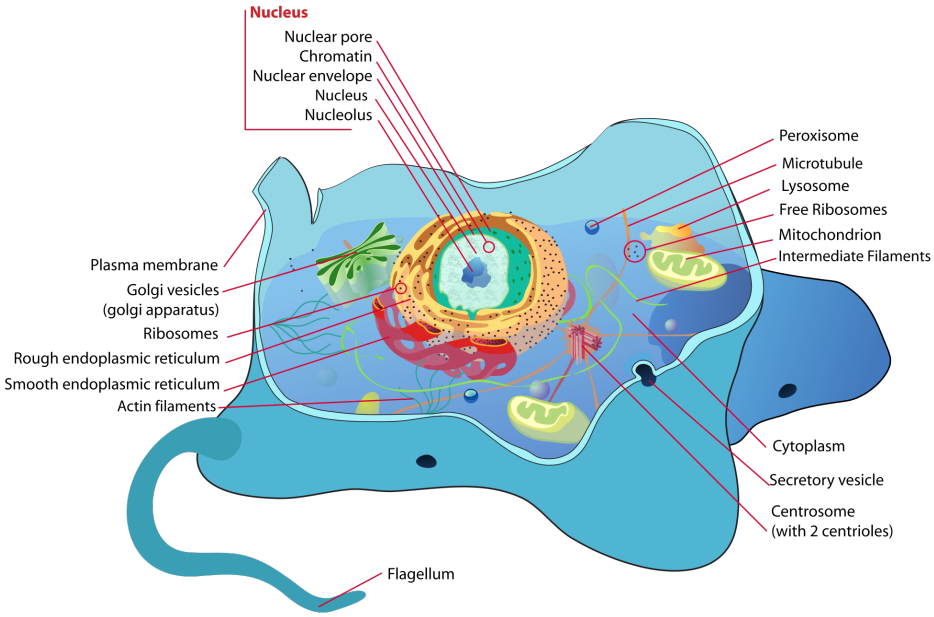

Figure 7.1 Cartoon of a eukaryotic cell. (Courtesy of Wikipedia.)

CO_2, N_2, and steroid hormones. **Transporters** and **channels**, the two classes of **membrane transport proteins**, control the passage of ions and big polar molecules across cell membranes. Transporters bind specific molecules and move them across the membrane. For instance, **Na^+–K^+ pumps** use ATP to drive 3 Na^+ ions out of a cell in each cycle while putting 2 K^+ ions into it. These **P-type transport ATPases** maintain the intracellular concentration of potassium 28 times higher than its extracellular concentration and that of sodium about 14 times lower than its extracellular concentration, as listed in table 7.1. In the cytosol, negative ions such as Cl^-, $HCO_3{}^-$, $PO_4{}^{3-}$, amino acids, proteins, nucleic acids, and metabolites carrying carboxyl or phosphate groups balance the positive charges of the 140 mM K^+.

Water channels or **aquaporins** pass 10^9 water molecules per second while blocking ions. **K^+ leak channels** let potassium ions leak out of a cell. **Gated ion channels** open and close so as to allow specific ions Na^+, K^+, Ca^{2+}, or Cl^- to pass at up to 10^8 ions per second when needed. The Na^+–K^+ pumps and the K^+ leak channels largely determine the concentra-

Ion	Intracellular concentration (mM)	Extracellular concentration (mM)
K^+	140	5
Na^+	5-15	145
Cl^-	5-15	110
Ca^{2+}	10^{-4}	1-2
Mg^{2+}	0.5	1-2
H^+	$7 \times 10^{-5} = 10^{-7.2}$ M (pH 7.2)	$4 \times 10^{-5} = 10^{-7.4}$ M (pH 7.4)

Table 7.1 *Intracellular and extracellular concentrations (mM) of some ions in and near a typical mammalian cell (Alberts et al., 2008, chap. 11).*

tion gradients of Na^+ and K^+ and the 20–120 mV drop of the membrane potential across the plasma membrane.

7.3 Membrane potentials

Gauss's law $\boldsymbol{\nabla} \cdot \boldsymbol{D} = \rho$ says the divergence of the **electric displacement** $\boldsymbol{D}$ is equal to the density ρ of **free charges** (as opposed to those of polar molecules). In electrostatic problems, Maxwell's equations reduce to Gauss's law and the static form $\boldsymbol{\nabla} \times \mathbf{E} = 0$ of Faraday's law which implies that the electric field $\boldsymbol{E}$ is the gradient of an electrostatic potential $\boldsymbol{E} = -\boldsymbol{\nabla} V$. (James Maxwell 1831–1879, Michael Faraday 1791–1867)

Across an interface with normal vector $\hat{\boldsymbol{n}}$ between two dielectrics, the tangential electric field is continuous while the normal electric displacement jumps by the surface density of free charge σ

$$\hat{\boldsymbol{n}} \times (\boldsymbol{E}_2 - \boldsymbol{E}_1) = 0 \quad \text{and} \quad \sigma = \hat{\boldsymbol{n}} \cdot (\boldsymbol{D}_2 - \boldsymbol{D}_1)\,. \tag{7.1}$$

In a **linear isotropic dielectric**, the electric displacement $\boldsymbol{D}$ is proportional to the electric field $\boldsymbol{D} = \epsilon_m \boldsymbol{E}$, where the **permittivity** $\epsilon_m = K_m \epsilon_0$ of the material differs from that of the vacuum ϵ_0 by the **relative permittivity** K_m. The permittivity of the vacuum is the **electric constant** $\epsilon_0 = 8.854 \times 10^{-12}$ F/m.

Example 7.1 (Membrane potential)**.** The plasma membrane is a phospholipid bilayer about 5 nm thick. If the potential drop across it is $V_i - V_e = -50$

mV, then the electric field in the bilayer is $-50\,\mathrm{mV}/5\,\mathrm{nm} = -10^7$ V/m. This very strong electric field points into the cell. □

Example 7.2 (Charge density on and near inner leaflet)**.** The field across the plasma mambrane is mainly due to a negative surface charge density σ that lies on or near the cytosolic leaflet of the bilayer. If we apply Gauss's law (7.1) to a box whose top surface is in the middle of the bilayer, and whose bottom surface at a depth in the cytosol where $\boldsymbol{D} = 0$, then we find that that this charge density σ is equal to the electric displacement D on the top surface. In a lipid, $D = \epsilon_m E \approx 2\,\epsilon_0 E$, so

$$\sigma \approx -2 \times 8.85 \times 10^{-12} \times 10^7 = -1.77 \times 10^{-4}\,\mathrm{C/m^2}. \tag{7.2}$$

The number of negative ions of charge $-e$ per square meter that make up the surface charge density σ on or near the inner leaflet then is

$$n = \frac{\sigma}{-e} = \frac{-1.77 \times 10^{-4}}{-1.602 \times 10^{-19}} = 1.1 \times 10^{15} \tag{7.3}$$

or 1100 per square micron.

If we apply Gauss's law to the whole cell apart from the exterior leaflet of the plasma membrane, then we find that the net charge of a typical mammalian cell of radius 10 μm is

$$Q = -1100\,4\pi 10^2\,e = -1.4 \times 10^6\,e = -2.2 \times 10^{-13}\,\mathrm{C} \tag{7.4}$$

or -0.22 pC. If we were to assume that the net negative charge of a spherical cell were located in its nucleus, where most of the nucleotides are, then we would estimate the electric field at a distance r from the center of the cell as

$$E = \frac{Q}{4\pi K_c \epsilon_0 r^2} \tag{7.5}$$

in which the relative permittivity of the cytosol is $K_c \approx 80$. At $r = 5\,\mu$m, the electric field would be

$$E = -\frac{2.2 \times 10^{-13}}{4\pi 80 \times 8.854 \times 10^{-12} \times 25 \times 10^{-12}} = -10^6\,\mathrm{V/m}. \tag{7.6}$$

If the positive ions, the **cations**, screened the negative ions, the **anions**, then the net charge density would be uniform $\rho = Q/(4\pi R^3/3)$ and inversely proportional to the radius R of the cell. The electric field then would be

$$E = \frac{Qr}{4\pi K_c \epsilon_0 R^3} \tag{7.7}$$

which at $r = 5\,\mu$m is

$$E = -\frac{2.2 \times 10^{-13} \times 5 \times 10^{-6}}{4\pi 80 \times 8.854 \times 10^{-12} \times 10^{3} \times 10^{-18}} = -1.2 \times 10^{5}\ \text{V/m}. \quad (7.8)$$

In fact, however, the ions are much more effective at self-screening than a relative permittivity of 80 would suggest. Indeed, in the limit of high relative permittivity, as in a conducting metal, the net charge appears as a surface charge, and the electric field inside the cell is zero.

Incidentally, the cross-sectional area of a phospholipid is about 0.25 square nm. So there are some 4 million phospholipids in a square micron of each leaflet. Phosphatidylserine (PS) carries a negative charge of $-e$, lies only on the inner leaflet of a living cell, and makes up 4 percent of the plasma membrane of a liver cell and 7 percent of that of a red-blood cell. So PS makes up about 10 percent of the cytosolic leaflet, which means that the number of PS phospholipids per square micron is 400,000. Since 1100 would be enough to make the huge electric field in the membrane, it follows that positive ions of the cytosol cancel all but 0.25 percent of the charge of the PSs. □

7.4 Potassium leak channels

The current $\boldsymbol{J}$ due to a concentration c of an ion of charge $q = ve$ in an electric field $\boldsymbol{E}$ is given by the Nernst-Planck formula (6.58)

$$\boldsymbol{J} = D\left(-\nabla c + \frac{q\boldsymbol{E}c}{kT}\right). \quad (7.9)$$

Suppose the current is in a K^+ leak channel that connects the cytosol to the outside of the cell. What voltage drop across the membrane would reduce the K^+ current through the channel to zero? Setting $\boldsymbol{J} = 0$, and taking z to be the direction normal to the membrane, we find (6.58)

$$\frac{1}{c(z)}\frac{dc(z)}{dz} = \frac{qE_z}{kT} \quad (7.10)$$

which we can integrate to

$$\ln\frac{c_e}{c_i} = -\frac{ev}{kT}\int \frac{dV(z')}{dz'}\,dz' = \frac{ev(V_i - V_e)}{kT} \quad (7.11)$$

in which v is the valence of the ion of charge $q = ve$, $e > 0$ is the proton's charge, c_e is the extracellular concentration, and c_i is the intracellular

concentration. This voltage difference

$$V_i - V_e = \frac{kT}{e} \ln \frac{c_e}{c_i} \tag{7.12}$$

is the **Nernst potential**.

Using the equilibrium condition (7.11) and the K^+ concentrations of table 7.1, we find that the voltage across the membrane needed to reduce the K^+ current in a potassium leak channel to zero is

$$V_i - V_e = \frac{kT}{e} \ln \frac{c_e}{c_i} = \frac{1}{37} \ln \frac{c_e}{c_i} = \frac{1}{37} \ln \frac{5}{140} = -0.09 \text{ V} \tag{7.13}$$

or -90 mV at 37 Celsius. The K^+ concentrations of a typical neuron listed in table 7.2 give -104 mV as the required membrane potential to stop the K^+ flow through a potassium leak channel of a neuron at body temperature. Since the resting membrane potentials usually are less than -90 mV, K^+ ions do flow through the potassium leak channels, and the Na^+–K^+ pumps must keep on pumping.

7.5 The Debye-Hückel equation

If there are several kinds of ions of charge q_i and a fixed charge distribution ρ_f, then the Poisson-Boltzmann equation (6.67) is

$$-\epsilon_m \boldsymbol{\nabla}^2 V = \rho_f + \sum_i \rho_{i,0}\, e^{-q_i V/kT}. \tag{7.14}$$

When the potential low enough and the temperature is high enough that $qV/kT \ll 1$, one can set

$$e^{-q_i V/kT} \approx 1 - \frac{q_i}{kT} V \tag{7.15}$$

and get the **linearized Poisson-Boltzmann** equation

$$-\epsilon_m \boldsymbol{\nabla}^2 V = \rho_f + \sum_i \rho_{i,0} \left(1 - \frac{q_i}{kT} V\right) \tag{7.16}$$

also known as the **Debye-Hückel** equation.

Often, the free-charge distribution ρ_f occurs on the boundary of the region of interest as a boundary condition. The charge densities $\rho_{i,0}$ often are the bulk densities which usually add to zero because cells are electrically neutral or nearly neutral. With these simplifications, the Debye-Hückel equation is

$$\boldsymbol{\nabla}^2 V = \left(\sum_i \frac{\rho_{i,0}\, q_i}{\epsilon_m\, kT}\right) V. \tag{7.17}$$

The term inside the parentheses is the inverse of the square of the **Debye length**

$$\lambda_D = \left(\frac{\epsilon_m \, kT}{\sum_i \rho_{i,0} \, q_i} \right)^{1/2} . \tag{7.18}$$

In the cytosol of a typical mammalian cell, the concentration of positive ions, mainly K^+, is 150 mM or $0.15 N_A = 9.033 \times 10^{22}$ molecules per liter, which is 9.033×10^{25} per cubic meter. The concentration of negative ions is very similar. At 37 °C, the permittivity of the cytosol is $\epsilon_c = 74.16 \, \epsilon_0 = 6.57 \times 10^{-10}$ F/m and $kT/e = 1/37.4$ V. So the Debye length of the cytosol for monovalent ions $q_i = \pm e$ is

$$\lambda_D = \left(\frac{6.57 \times 10^{-10}}{2(9.033) \times 10^{25} \, (37.4) 1.602 \times 10^{-19}} \right)^{1/2} = 7.79 \times 10^{-10} \, \text{m} \tag{7.19}$$

or about 0.8 nm.

The **Bjerrum length**

$$\ell_B = \frac{e^2}{4\pi \epsilon_c kT} \tag{7.20}$$

has a similar value at 37 °C

$$\ell_B = \frac{1.602 \times 10^{-19} \times 37.4}{4\pi \times 74.16 \times 8.854 \times 10^{-12}} = 7.26 \times 10^{-10} \, \text{m} \tag{7.21}$$

or 0.726 nm.

In one space dimension, the Debye-Hückel equation is

$$\frac{d^2 V}{dz^2} = \frac{1}{\lambda_D^2} V. \tag{7.22}$$

Example 7.3 (Field just inside a plasma membrane)**.** We can use the one-dimensional Debye-Hückel equation (7.22) to estimate the electric field due to the negative surface charge σ of the phosphatidylserine on the inner leaflet of a cell membrane. Integrating twice, we find

$$V(z) = V_0 \, e^{-z/\lambda_D} \tag{7.23}$$

in which $z > 0$ is the *distance* down into the cell, and V_0 is a constant we will determine from the boundary condition due to the surface charge σ. This boundary condition is

$$E = -\frac{dV}{dz} = \frac{\sigma}{\epsilon_c} \tag{7.24}$$

in which $\epsilon_c \approx 74 \, \epsilon_0$ is the permittivity of the cytosol. (If the cytosol and the extracellular fluid were solid dielectrics with no mobile ions, then the

boundary condition would be $E = \sigma/(\epsilon_c+\epsilon_w)$ in which ϵ_w is the permittivity of the extracellular fluid.) So we have

$$-\left.\frac{dV}{dz}\right|_{z=0} = \frac{V_0}{\lambda_D} = \frac{\sigma}{\epsilon_c} \tag{7.25}$$

or

$$V_0 = \frac{\lambda_D\,\sigma}{\epsilon_c}. \tag{7.26}$$

Thus the potential in the cytosol due to the PS on the inner leaflet is

$$V(z) = \frac{\lambda_D\,\sigma}{\epsilon_c}\,e^{-z/\lambda_D}. \tag{7.27}$$

The electric field in the cytosol falls off exponentially with the depth in units of the Debye length, z/λ_D. The huge fields we imagined in the thought experiments of example 7.2 do not exist except within about a nanometer of the inner leaflet of the membrane, within a **double layer** formed by the negative surface charge σ of the PS's and the counter ions, mainly K^+'s.

The charge density of positive ions is

$$\sigma_+ = -\epsilon_c\frac{d^2V}{dz^2} = -\frac{\sigma}{\lambda_D}e^{-z/\lambda_D}, \tag{7.28}$$

and its integral is

$$-\int_0^\infty \frac{\sigma}{2\lambda_D}e^{-z/\lambda_D}\,dz = -\sigma \tag{7.29}$$

equal and opposite to the charge density of the PSs. The cell is neutral. □

The homogeneous Debye-Hückel equation in three spatial dimensions with spherical symmetry is

$$\boldsymbol{\nabla}^2\,V = \frac{1}{r^2}\frac{d}{dr}\left(r^2\frac{dV}{dr}\right) = \frac{1}{\lambda_D^2}V \tag{7.30}$$

or more simply

$$\frac{d^2\,(r\,V)}{dr^2} = \frac{r\,V}{\lambda_D^2}. \tag{7.31}$$

Example 7.4 (Electric field about nucleus)**.** The DNA of a cell and much of its RNA is negatively charged and in the nucleus. How big is the resulting electric field? The K^+ ions and other positive ions hover about PO_4^- groups of the DNA and RNA screening most of their charges. For simplicity, however, let us imagine that the DNA lies within a sphere of radius R and charge Q, and that the K^+ and other ions lie outside this sphere. The

resulting spherical symmetry let us use the Debye-Hueckel equation (7.31) whose solution is

$$r\,V(r) = v\,e^{-r/\lambda_D}. \tag{7.32}$$

From the boundary condition

$$E(R) = -\left.\frac{dV(r)}{dr}\right|_{r=R} = \frac{Q}{4\pi\epsilon_c R^2}, \tag{7.33}$$

we determine the constant v to be

$$v = \frac{Q}{4\pi\epsilon_c}\frac{\lambda_D}{\lambda_D + R}\,e^{R/\lambda_D}. \tag{7.34}$$

So the potential is

$$V(r) = \frac{Q}{4\pi\epsilon_c}\frac{\lambda_D}{\lambda_D + R}\,\frac{e^{-(r-R)/\lambda_D}}{r}. \tag{7.35}$$

The electric field at $r > R$ then is

$$E(r) = \frac{Q}{4\pi\epsilon_c}\frac{\lambda_D + r}{\lambda_D + R}\,\frac{e^{-(r-R)/\lambda_D}}{r^2}. \tag{7.36}$$

How big is this electric field? The human genome contains 3.2×10^9 base pairs. So its charge is $-6.4 \times 10^9\,e = -10^{-9}$ C or -1 nC. So at the edge of a nucleus, at $R = 4\mu$m, the electric field (7.36) is 5.6×10^{11} V/m which is enough to ionize atoms. This is a gross overestimate because we ignored the K^+ counterions inside the nucleus. Our formula (7.36) becomes much more reasonable for $r > R$. Since the Debye length (7.19) in the cytosol at 37 °C is $\lambda_D = 0.8$ nm, at $r = 4.02\,\mu$m, for instance, the exponential factor in the electric field (7.36) is

$$e^{-(r-R)/\lambda_D} = e^{-2\times10^{-8}/(8\times10^{-10})} = 10^{-11}, \tag{7.37}$$

and so the field is negligible at more than 20 nm from the nucleus. □

7.6 The Poisson-Boltzmann equation in one dimension

If there are several kinds of ions of charge q_i and no fixed charge distribution, then the Poisson-Boltzmann equation (6.67) is

$$-\epsilon\,\boldsymbol{\nabla}^2 V = \sum_i \rho_{i,0}\,e^{-q_i V/kT}. \tag{7.38}$$

Gouy and Chapman solved this equation (Gouy, 1910; Chapman, 1913) in one dimension

$$-\epsilon \frac{d^2 V}{dz^2} = \sum_i \rho_{i,0}\, e^{-q_i V/kT}. \tag{7.39}$$

Let's consider a fluid that contains ions and counterions of charge $\pm e$ whose charge densities in the bulk are equal, $\rho_{+,0} = -\rho_{-,0} = \rho_0$. Then the one-dimensional Gouy-Chapman equation (7.39) for monovalent ions is

$$-\epsilon \frac{d^2 V}{dz^2} = \rho_0 \left(e^{-eV/kT} - e^{eV/kT} \right) \tag{7.40}$$

in which $z > 0$ is the distance away from the surface charge density σ. One may verify (exercise 7.1) that the second derivative of the potential

$$V(z) = \frac{2kT}{e} \ln \left[\frac{1 + e^{-(z+z_0)/\lambda_D}}{1 - e^{-(z+z_0)/\lambda_D}} \right] \tag{7.41}$$

multiplied by $-\epsilon$ is

$$-\epsilon \frac{d^2 V}{dz^2} = -\frac{4\epsilon kT}{e\lambda_D^2} \frac{e^{-(z+z_0)/\lambda_D} + e^{-3(z+z_0)/\lambda_D}}{\left(1 - e^{-2(z+z_0)/\lambda_D}\right)^2}, \tag{7.42}$$

and that it is equal to the other side of the Gouy-Chapman equation (7.40) because of the definition (7.18) of the Debye length (exercise 7.2). One may adjust the parameter z_0 to satisfy the boundary condition (7.25)

$$e^{-z_0/\lambda_D} = \frac{2kT\epsilon_c}{e\lambda_D \sigma} \left[\sqrt{1 + \left(\frac{e\lambda_D \sigma}{2kT\epsilon_c} \right)^2} - 1 \right] \tag{7.43}$$

(exercise 7.3). The solution then at $z \gg \lambda_D$ approaches the solution (7.27) to the Debye-Hückel equation (7.22) (exercise 7.4).

7.7 Neurons

Transporters, mainly sodium-potassium pumps, water channels, and gated ion channels, and channels, mainly the potassium leak channel, control the osmotic pressure of a cell and maintain the concentrations of sodium, potassium, and chloride at about 14, 140, and 14 mM inside the cell while the extracellular fluid has Na^+, K^+, and Cl^- concentrations of 140, 3, and 146 mM as listed in table 7.2. The resulting resting voltage across the membrane about $V_0 = -70$ mV, and the electric field points into the neuron.

The voltage drop across the membrane $\Delta V = V_c - V_e$ is the same for all

Ion	Intracellular concentration (mM)	Extracellular concentration (mM)	Relative chord conductance g_s/g_0
K^+	140	3	0.649
Na^+	14	140	0.026
Cl^-	14	146	0.325
Ca^{2+}	10^{-4}	1.5	0

Table 7.2 *Intracellular and extracellular concentrations (mM) of some ions in and near a typical neuron (Hammond, 2015, chap. 3).*

three species Na^+, K^+, and Cl^-. For each kind of ion, this voltage is the sum of the IR voltage and the Nernst potential (7.12)

$$\begin{aligned}\Delta V = V_c - V_e &= I_{Na^+} R_{Na^+} + V_{N,Na^+} = I_{K^+} R_{K^+} + V_{N,K^+} \\ &= I_{Cl^-} R_{Cl^-} + V_{N,Cl^-}\end{aligned} \tag{7.44}$$

where the Nernst potential for each species is

$$V_{N,s} = V_{N,s,c} - V_{N,s,e} = -\frac{kT}{z_s e} \ln \frac{c_{s,c}}{c_{s,e}} \tag{7.45}$$

in which z_s is the valence, which is unity for the principal ions Na^+, K^+, and Cl^-. While the neuron is quiet with no signal running along the axon, the total current through the membrane vanishes. And so if g_s is the conductance of species s, then the sum of the currents $j_s = (V_0 - V_{N,s})\, g_s$ over the species is zero Na^+, K^+, and Cl^-

$$0 = \sum_s (V_0 - V_{N,s})\, g_s. \tag{7.46}$$

The total conductance is

$$g_0 = \sum_s g_s. \tag{7.47}$$

In terms of it the resting voltage V_0 is

$$V_0 = \sum_s \frac{g_s}{g_0} V_{N,s} \tag{7.48}$$

which is the **chord conductance formula**.

Further reading

The book *Molecular Biology of the Cell* may be the best textbook ever written. Chapters 22 and 23 of the excellent book *Molecular Driving Forces* by Ken Dill and Sarina Bromberg discuss the Poisson-Boltzmann and Debye-Hückel equations. Philip Nelson's fine book *Biological Physics* discusses the Gouy-Chapman equation.

Exercises

7.1 Show that the second derivative of the Gouy-Chapman potential (7.41) is given by (7.42).

7.2 Show that the second derivative (7.42) of the Gouy-Chapman potential (7.41) is equal to the other side of the Gouy-Chapman equation (7.40).

7.3 Show that the formula (7.43) for z_0 satisfies the boundary condition (7.25).

7.4 Take the limit $z \to \infty$ of the Gouy-Chapman solution (7.41) and show that it is the solution (7.27) to the Debye-Hückel equation (7.22).

8

Polymers

8.1 Freely jointed polymers

A **freely jointed polymer** is a linear chain of segments of the same length a joined together with no constraints on the orientations $\boldsymbol{a}$ of successive segments. If tail of the first segment is at the origin, then the nose of the Nth segment is at

$$\boldsymbol{a}_N = \sum_{i=1}^{N} \boldsymbol{a}_i. \tag{8.1}$$

The mean value of the square of the displacement of the whole polymer is

$$\langle \boldsymbol{a}_N \cdot \boldsymbol{a}_N \rangle = \langle \sum_{i=1}^{N} \boldsymbol{a}_i \cdot \sum_{j=1}^{N} \boldsymbol{a}_j \rangle = \sum_{i,j=1}^{N} \langle \boldsymbol{a}_i \cdot \boldsymbol{a}_j \rangle. \tag{8.2}$$

Since successive segments rotate freely, the mean value of the dot product of segment i with segment j vanishes unless $i = j$

$$\langle \boldsymbol{a}_i \cdot \boldsymbol{a}_j \rangle = a^2 \, \delta_{ij}. \tag{8.3}$$

Thus the mean value $\langle \boldsymbol{a}_N \cdot \boldsymbol{a}_N \rangle$ is

$$\langle \boldsymbol{a}_N \cdot \boldsymbol{a}_N \rangle = \sum_{i,j=1}^{N} \langle \boldsymbol{a}_i \cdot \boldsymbol{a}_j \rangle = \sum_{i,j=1}^{N} a^2 \, \delta_{ij} = N a^2. \tag{8.4}$$

The apparent length of a freely jointed polymer therefore increases as the square-root of the number of segments

$$\sqrt{\langle \boldsymbol{a}_N \cdot \boldsymbol{a}_N \rangle} = a \sqrt{N}. \tag{8.5}$$

8.2 Entropic force

In section 4.6, we found that Gauss's limit (4.56) of the binomial probability distribution (4.48) for n wins in N tries is

$$P_{BG}(n,p,N) = \frac{1}{\sqrt{2\pi pqN}} \exp\left(-\frac{(n-pN)^2}{2pqN}\right) \tag{8.6}$$

in which p is the probability of success on each try and $q = 1-p$. If $p = 1/2$, this distribution applies to a random walk in one dimension.

$$P_{rw}(n,N) = \sqrt{\frac{2}{\pi N}} \exp\left(-\frac{2(n-N/2)^2}{N}\right) \tag{8.7}$$

After n wins or steps forward by a and $N-n$ steps backwards by a, the walker is at

$$x = na - (N-n)a = 2a(n-N/2). \tag{8.8}$$

So the probability of being at x, that is between $x - a/2$ and $x + a/2$, is

$$P_{rw}(x,N) = \sqrt{\frac{2}{\pi N}} \exp\left(-\frac{x^2}{2Na^2}\right). \tag{8.9}$$

In three dimensions, there are only $N/3$ tries in each direction, and so the probability of being at $\boldsymbol{r}$ is

$$P_{rw}(\boldsymbol{r},N) = \left(\frac{6}{\pi N}\right)^{3/2} \exp\left(-\frac{3\boldsymbol{r}^2}{2Na^2}\right). \tag{8.10}$$

Let's now apply this calculation to the problem of a polymer made up of monomers of length a that are joined so that successive monomers either make right angles with each other or are parallel or antiparallel. We fix one end of the polymer at the origin. Then the random-walk distribution (8.10) gives the probability that the other end of the polymer made of N monomers of length a is at $\boldsymbol{r}$. The classical entropy (5.24) of a system of such noninteracting polymers is proportional to the logarithm of the number of configurations $S_c = k \ln N$. The probability that the end of a polymer is at $\boldsymbol{r}$ also is proportional to the number of polymer configurations that go from the origin to $\boldsymbol{r}$. So the classical entropy of the system of polymers that get to $\boldsymbol{r}$ is

$$S_c = k \ln P_{rw}(\boldsymbol{r},N) = S_0 - \frac{3k\boldsymbol{r}^2}{2Na^2}. \tag{8.11}$$

The Helmholtz free energy of this system is

$$F = E - TS = E + \frac{3kT\boldsymbol{r}^2}{2Na^2}. \tag{8.12}$$

This harmonic-oscillator potential is an instance of Hooke's law.

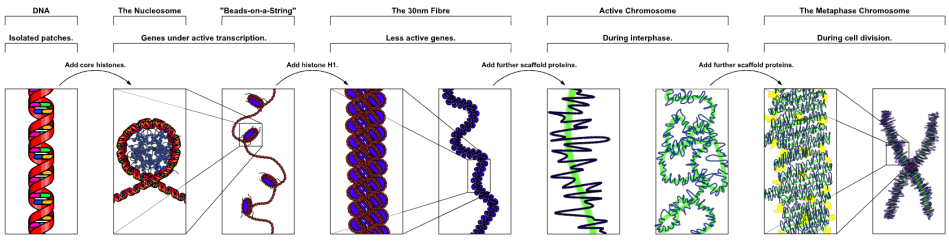

Figure 8.1 Successive stages of the organized compactification of DNA in eukaryotic cells. (Courtesy of Wilipedia)

9

Some Experimental Methods

The wavelength of visible photons is between 390 and 700 nm or half the length of a bacterium. Most globular proteins have radii of between 1 and 5 nm. Over such a small distance, the phase $\exp(i\boldsymbol{k}\cdot\boldsymbol{r})$ of an optical photon changes by less than 1 part in 100. So quantum-mechanical amplitudes in a macromolecule often add constructively.

9.1 Time-dependent perturbation theory

Particle physicists describe electrodynamics as the exchange of photons between charged particles. But the language of non-relativistic quantum mechanics is more appropriate for the absorption and emission of light by macromolecules.

Most books on quantum mechanics discuss time-dependent perturbation theory. Here are the basic ideas: We split the hamiltonian H into a simple hamiltonian H_0 whose eigenstates $|n\rangle$ we know

$$H_0|n\rangle = E_n^0|n\rangle \tag{9.1}$$

and a remainder V

$$H = H_0 + V. \tag{9.2}$$

In Dirac's interaction picture, operators have the simple time dependence of the free hamiltonian

$$A_i(t) = e^{iH_0t/\hbar}Ae^{-iH_0t/\hbar}. \tag{9.3}$$

To recover the full time dependence of operators

$$A(t) = e^{iHt/\hbar}Ae^{-iHt/\hbar}, \tag{9.4}$$

we require the states to evolve according to a unitary operator $U(t)$

$$\begin{aligned}\langle\phi|A(t)|\psi\rangle &= \langle\phi|e^{iHt/\hbar}Ae^{-iHt/\hbar}|\psi\rangle \\ &= \langle\phi|e^{iHt/\hbar}e^{-iH_0t/\hbar}A_i(t)e^{iH_0t/\hbar}e^{-iHt/\hbar}|\psi\rangle \\ &= \langle\phi|\,U^\dagger(t)\,A_i(t)\,U(t)\,|\psi\rangle \end{aligned} \tag{9.5}$$

given by

$$U(t) = e^{iH_0t/\hbar}e^{-iHt/\hbar} \tag{9.6}$$

This time-evolution operator $U(t)$ obeys the differential equation

$$\begin{aligned} i\,\hbar\,\frac{dU(t)}{dt} &= e^{iH_0t/\hbar}\,(H - H_0)\,e^{-iHt/\hbar} = e^{iH_0t/\hbar}\,V\,e^{-iHt/\hbar} \\ &= e^{iH_0t/\hbar}\,V\,e^{-iH_0t/\hbar}e^{iH_0t/\hbar}\,e^{-iHt/\hbar} \\ &= V_i(t)\,U(t) \end{aligned} \tag{9.7}$$

in which

$$V_i(t) = e^{iH_0t/\hbar}\,V\,e^{-iH_0t/\hbar} \tag{9.8}$$

is V in the interaction picture. The solution to U's differential equation (9.7) is the time-ordered exponential

$$U(t) = \mathcal{T}\left\{\exp\left[-\frac{i}{\hbar}\int_0^t V_i(t')\,dt'\right]\right\} \tag{9.9}$$

which satisfies the boundary condition $U(0) = 1$ implied by its definition (9.6). The time ordering indicated by the symbol $\mathcal{T}$ means that in any expansion of (9.9)

$$\begin{aligned} U(t) = 1 &- \frac{i}{\hbar}\int_0^t V_i(t)\,dt + \left(-\frac{i}{\hbar}\right)^2\int_0^t V_i(t_1)\,dt_1\int_0^{t_1} V_i(t_2)\,dt_2 \\ &+ \left(-\frac{i}{\hbar}\right)^3\int_0^t V_i(t_1)\,dt_1\int_0^{t_1} V_i(t_2)\,dt_2\int_0^{t_2} V_i(t_3)\,dt_3 + \ldots \end{aligned} \tag{9.10}$$

$V_i(t')$ stands to the left of $V_i(t'')$ when $t' > t''$. The time derivative of this expansion is

$$\begin{aligned} i\,\hbar\,\frac{dU(t)}{dt} &= V_i(t) - \frac{i}{\hbar}\,V_i(t)\int_0^t V_i(t)\,dt \\ &\quad + \left(-\frac{i}{\hbar}\right)^2 V_i(t)\int_0^t V_i(t_1)\,dt_1\int_0^{t_1} V_i(t_2)\,dt_2 + \ldots \\ &= V_i(t)\,U(t). \end{aligned} \tag{9.11}$$

So the definition (9.9) of $U(t)$ as a time-ordered exponential solves its differential equation (9.7).

9.2 FRET

Fluorochrome resonant energy transfer (FRET) or Föster resonant energy transfer is the transfer of energy from one excited fluorochrome to another by the interaction of their electric dipoles. The transfer is rapid at resonance, that is, when the excitation energies of the two fluorochromes are nearly the same. Like any dipole-dipole interaction, the transfer falls as the sixth power of the distance between the two fluorochromes. It is efficient when the fluorochromes are separated by less than 6 nm.

The hamiltonian for the interaction of two fluorochromes is

$$H = H_d + H_a + V \tag{9.12}$$

in which H_d is the hamiltonian of the donor fluorochrome, H_a is that of the acceptor fluorochrome, and V is the coulombic interaction of the electrons of the two fluorochromes. We let

$$H_0 = H_d + H_a \tag{9.13}$$

be the free hamiltonian for FRET. We will use only the first excited state of the donor fluorochrome and the ground state of the acceptor fluorochrome

$$H_0|10\rangle = E_d|10\rangle, \tag{9.14}$$

the first excited state of the acceptor fluorochrome and the ground state of the donor fluorochrome

$$H_0|01\rangle = E_a|01\rangle, \tag{9.15}$$

and the state of both fluorochromes in their ground states

$$H_0|00\rangle = 0 \tag{9.16}$$

which we take to have energy zero.

A photon strikes the donor fluorochrome and takes the system to the state $|10\rangle$ in which the donor fluorochrome is in an excited state (1) and the acceptor fluorochrome is in its ground state (0). The amplitude for this state to become the state $|01\rangle$ in which the donor fluorochrome is in its ground state and the acceptor fluorochrome is in the excited state (1) in time t is

$$\langle 01|e^{-iHt/\hbar}|10\rangle = \langle 01|e^{-iH_0t/\hbar}\,U(t)|10\rangle. \tag{9.17}$$

Since the initial and final states $|10\rangle$ and $|01\rangle$ are eigenstates (9.14 & 9.15) of the free hamiltonian H_0, this amplitude is

$$\langle 01|e^{-iHt/\hbar}|10\rangle = e^{-iE_a t/\hbar}\langle 01|\,U(t)|10\rangle, \tag{9.18}$$

and the second factor is to first order in V

$$\begin{aligned}\langle 01|U(t)|10\rangle &= -\frac{i}{\hbar}\langle 01|\int_0^t V_i(t')\,dt'\,|10\rangle \\ &= -\frac{i}{\hbar}\langle 01|\int_0^t e^{iH_0t'/\hbar}\,V\,e^{-iH_0t'/\hbar}\,dt'\,|10\rangle \\ &= -\frac{i}{\hbar}\langle 01|\int_0^t e^{i(E_a-E_d)t'/\hbar}\,V\,dt'\,|10\rangle \\ &= \frac{1-e^{i(E_a-E_d)t/\hbar}}{E_a-E_d}\,\langle 01|\,V\,|10\rangle. \end{aligned}\tag{9.19}$$

The probability of an energy transfer is proportional to the square of the modulus of this amplitude

$$\frac{4\,|\langle 01|\,V\,|10\rangle|^2}{|E_a-E_d|^2}\,\sin^2\left[\frac{(E_a-E_d)\,t}{2\hbar}\right] \tag{9.20}$$

and is unaffected by the phase $\exp(-iE_at/\hbar)$ that multiplies it in equation (9.18). The factor $1/|E_a-E_d|^2$ means that the transfer of energy is fast when the energies are nearly the same, that is, at resonance $E_a \approx E_d$.

For times long compared to $\hbar/(E_a-E_d) \sim 10^{-15}\,\mathrm{s}$, we can use Dirac's delta function

$$\lim_{t\to\infty}\frac{1}{|E_a-E_d|^2}\,\sin^2\left[\frac{(E_a-E_d)\,t}{2\hbar}\right] = \frac{\pi\,t}{2\,\hbar}\,\delta(E_a-E_d) \tag{9.21}$$

to get as the probability of a FRET transition to a given excited state of the acceptor fluorochrome

$$P(t) = \frac{2\pi\,t}{\hbar}\,|\langle 01|\,V\,|10\rangle|^2\delta(E_a-E_d). \tag{9.22}$$

The transition rate then is

$$\Gamma = \frac{dP(t)}{dt} = \frac{2\pi}{\hbar}\,|\langle 01|\,V\,|10\rangle|^2\delta(E_a-E_d). \tag{9.23}$$

We now integrate over the density $dN_a(E_a)/dE_a$ of energy eigenstates of the acceptor fluorochrome and so get as the FRET rate

$$\begin{aligned}\Gamma &= \frac{\pi}{2\,\hbar}\int dE_a\,\frac{dN_a(E_a)}{dE_a}\,4\,|\langle 01|\,V\,|10\rangle|^2\delta(E_a-E_d) \\ &= \frac{2\pi}{\hbar}\,\frac{dN_a(E_d)}{dE_a}\,|\langle 01|\,V\,|10\rangle|^2. \end{aligned}\tag{9.24}$$

If the acceptor atom has only a single state or a few states at the energy E_d of the donor atom, then the density of states $dN_a(E_d)/dE_a$ becomes ambiguous unless we allow these states to have finite widths. In such a case, we let γ be the average width of the two states and use the estimate

$$\frac{dN_a(E_d)}{dE_a} = \frac{1}{\gamma}. \tag{9.25}$$

Our estimate for the rate then is

$$\Gamma = \frac{2\pi}{\hbar\,\gamma}\,|\langle 01|\,V\,|10\rangle|^2. \tag{9.26}$$

Thus the key to FRET is the matrix element $\langle 01|\,V\,|10\rangle$. The potential V is the electrostatic energy of the electrons of the donor fluorochrome due to the electrons and nuclei of the acceptor fluorochrome and the energy of the electrons of the acceptor fluorochrome due to the electrons and nuclei of the donor fluorochrome as well as the coulombic energy of the nuclei of charge Z_{am} of the acceptor fluorochrome interacting with those of the donor fluorochrome of charge Z_{dn}. If the centers of the two fluorochromes are at $\boldsymbol{r}_d$ and $\boldsymbol{r}_a$, then the electrons and nuclei of the donor fluorochrome are at $\boldsymbol{r}_d+\boldsymbol{x}_j$ and $\boldsymbol{r}_d+\boldsymbol{x}_n$, while those of the acceptor fluorochrome are at $\boldsymbol{r}_a+\boldsymbol{y}_k$ and $\boldsymbol{r}_a+\boldsymbol{y}_m$. The interaction V is then

$$V = \frac{e^2}{4\pi\epsilon_0}\left[\sum_{j,k}\frac{1}{|\boldsymbol{r}_a+\boldsymbol{y}_k-\boldsymbol{r}_d-\boldsymbol{x}_j|}+\sum_{m,n}\frac{Z_{am}\,Z_{dn}}{|\boldsymbol{r}_a+\boldsymbol{y}_m-\boldsymbol{r}_d-\boldsymbol{x}_n|}\right.$$
$$\left.-\sum_{k,n}\frac{Z_{dn}}{|\boldsymbol{r}_a+\boldsymbol{y}_k-\boldsymbol{r}_d-\boldsymbol{x}_n|}-\sum_{j,m}\frac{Z_{am}}{|\boldsymbol{r}_a+\boldsymbol{y}_m-\boldsymbol{r}_d-\boldsymbol{x}_j|}\right]. \tag{9.27}$$

The distance $R=|\boldsymbol{r}_a-\boldsymbol{r}_d|$ between the centers of the fluorochromes is longer than the distances $|\boldsymbol{x}|$ and $|\boldsymbol{y}|$ of the electrons and nuclei of a fluorochrome from its center. So we can expand all the denominators in inverse powers of R. For instance, the first term is

$$\begin{aligned}\frac{1}{|\boldsymbol{r}_a+\boldsymbol{y}_k-\boldsymbol{r}_d-\boldsymbol{x}_j|} &= \frac{1}{\sqrt{(\boldsymbol{r}_a-\boldsymbol{r}_d)^2+2(\boldsymbol{r}_a-\boldsymbol{r}_d)\cdot(\boldsymbol{y}_k-\boldsymbol{x}_j)+(\boldsymbol{y}_k-\boldsymbol{x}_j)^2}}\\ &= \frac{1}{R\sqrt{1+2(\boldsymbol{r}_a-\boldsymbol{r}_d)\cdot(\boldsymbol{y}_k-\boldsymbol{x}_j)/R^2+(\boldsymbol{y}_k-\boldsymbol{x}_j)^2/R^2}}\\ &\approx \frac{1}{R}\left[1-(\boldsymbol{r}_a-\boldsymbol{r}_d)\cdot(\boldsymbol{y}_k-\boldsymbol{x}_j)/R^2-\frac{1}{2}(\boldsymbol{y}_k-\boldsymbol{x}_j)^2/R^2\right.\\ &\quad\left.+\frac{3}{2}[(\boldsymbol{r}_a-\boldsymbol{r}_d)\cdot(\boldsymbol{y}_k-\boldsymbol{x}_j)/R^2]^2\right].\end{aligned} \tag{9.28}$$

When all four terms of (9.28) are combined, the $1/R$ terms cancel because the fluorochromes are neutral.

In evaluating the remaining terms, it is convenient to sum over electrons and protons rather than electrons and nuclei of various charges. We then see that the $1/R^2$ terms cancel, since

$$\begin{aligned} &-(\boldsymbol{r}_a-\boldsymbol{r}_d)\cdot(\boldsymbol{y}_k-\boldsymbol{x}_j)/R^3-(\boldsymbol{r}_a-\boldsymbol{r}_d)\cdot(\boldsymbol{y}_m-\boldsymbol{x}_n)/R^3 \\ &+(\boldsymbol{r}_a-\boldsymbol{r}_d)\cdot(\boldsymbol{y}_k-\boldsymbol{x}_n)/R^3+(\boldsymbol{r}_a-\boldsymbol{r}_d)\cdot(\boldsymbol{y}_m-\boldsymbol{x}_j)/R^3 \\ &\qquad=\frac{(\boldsymbol{r}_a-\boldsymbol{r}_d)}{R^3}\cdot[-\boldsymbol{y}_k+\boldsymbol{x}_j-\boldsymbol{y}_m+\boldsymbol{x}_n+\boldsymbol{y}_k-\boldsymbol{x}_n+\boldsymbol{y}_m-\boldsymbol{x}_j]=0. \end{aligned} \tag{9.29}$$

The remaining terms are of order $1/R^3$, so the interaction energy is approximately

$$\begin{aligned} V=\frac{e^2}{4\pi\epsilon_0 R^3}\Bigg[&\frac{1}{2}\sum\Big(-(\boldsymbol{y}_k-\boldsymbol{x}_j)^2-(\boldsymbol{y}_m-\boldsymbol{x}_n)^2+(\boldsymbol{y}_k-\boldsymbol{x}_n)^2+(\boldsymbol{y}_m-\boldsymbol{x}_j)^2\Big) \\ &+\frac{3}{2R^2}\sum\Big([(\boldsymbol{r}_a-\boldsymbol{r}_d)\cdot(\boldsymbol{y}_k-\boldsymbol{x}_j)]^2+[(\boldsymbol{r}_a-\boldsymbol{r}_d)\cdot(\boldsymbol{y}_m-\boldsymbol{x}_n)]^2 \\ &-[(\boldsymbol{r}_a-\boldsymbol{r}_d)\cdot(\boldsymbol{y}_k-\boldsymbol{x}_n)]^2-[(\boldsymbol{r}_a-\boldsymbol{r}_d)\cdot(\boldsymbol{y}_m-\boldsymbol{x}_j)]^2\Big)\Bigg]. \end{aligned} \tag{9.30}$$

Some of these terms also cancel:

$$\begin{aligned} &-(\boldsymbol{y}_k-\boldsymbol{x}_j)^2-(\boldsymbol{y}_m-\boldsymbol{x}_n)^2+(\boldsymbol{y}_k-\boldsymbol{x}_n)^2+(\boldsymbol{y}_m-\boldsymbol{x}_j)^2 \\ &\qquad=2(\boldsymbol{y}_k-\boldsymbol{y}_m)\cdot(\boldsymbol{x}_j-\boldsymbol{x}_n), \end{aligned} \tag{9.31}$$

and

$$\begin{aligned} &[(\boldsymbol{r}_a-\boldsymbol{r}_d)\cdot(\boldsymbol{y}_k-\boldsymbol{x}_j)]^2+[(\boldsymbol{r}_a-\boldsymbol{r}_d)\cdot(\boldsymbol{y}_m-\boldsymbol{x}_n)]^2 \\ &-[(\boldsymbol{r}_a-\boldsymbol{r}_d)\cdot(\boldsymbol{y}_k-\boldsymbol{x}_n)]^2-[(\boldsymbol{r}_a-\boldsymbol{r}_d)\cdot(\boldsymbol{y}_m-\boldsymbol{x}_j)]^2 \\ &\qquad=-2(\boldsymbol{r}_a-\boldsymbol{r}_d)\cdot(\boldsymbol{y}_k-\boldsymbol{y}_m)\,(\boldsymbol{r}_a-\boldsymbol{r}_d)\cdot(\boldsymbol{x}_j-\boldsymbol{x}_n). \end{aligned} \tag{9.32}$$

So to order $1/R^3$, the dipole approximation V_3 to the interaction V is

$$\begin{aligned} V_3=\frac{e^2}{4\pi\epsilon_0 R^3}\Bigg[&\sum(\boldsymbol{y}_k-\boldsymbol{y}_m)\cdot(\boldsymbol{x}_j-\boldsymbol{x}_n) \\ &-\frac{3}{R^2}\sum(\boldsymbol{r}_a-\boldsymbol{r}_d)\cdot(\boldsymbol{y}_k-\boldsymbol{y}_m)\,(\boldsymbol{r}_a-\boldsymbol{r}_d)\cdot(\boldsymbol{x}_j-\boldsymbol{x}_n)\Bigg]. \end{aligned} \tag{9.33}$$

The dipole operators of the donor and acceptor fluorochromes are the sums over electrons and protons

$$\begin{aligned} \boldsymbol{D}_d&=\sum\boldsymbol{x}_n-\boldsymbol{x}_j \\ \boldsymbol{D}_a&=\sum\boldsymbol{y}_m-\boldsymbol{y}_k. \end{aligned} \tag{9.34}$$

The unit vector

$$\hat{\boldsymbol{r}} = (\boldsymbol{r}_a - \boldsymbol{r}_d)/R \tag{9.35}$$

points from the center of the donor fluorochrome to the center of the acceptor fluorochrome. In these terms, the interaction is

$$V_3 = \frac{e^2}{4\pi\epsilon_0 R^3} \left(\boldsymbol{D}_d \cdot \boldsymbol{D}_a - 3\,\hat{\boldsymbol{r}} \cdot \boldsymbol{D}_d\; \hat{\boldsymbol{r}} \cdot \boldsymbol{D}_a\right). \tag{9.36}$$

Our formula (9.24) now gives the FRET rate in the dipole approximation as

$$\Gamma = \frac{2\pi}{\hbar} \frac{dN_a(E_d)}{dE_a} \left|\langle 01|\, V\, |10\rangle\right|^2 \tag{9.37}$$

$$\approx \frac{2\pi}{\hbar} \frac{dN_a(E_d)}{dE_a} \left(\frac{e^2}{4\pi\epsilon_0 R^3}\right)^2 \left|\langle 01\,|\, \boldsymbol{D}_d \cdot \boldsymbol{D}_a - 3\,\hat{\boldsymbol{r}} \cdot \boldsymbol{D}_d\; \hat{\boldsymbol{r}} \cdot \boldsymbol{D}_a\,|\, 10\rangle\right|^2 \tag{9.38}$$

which falls off with the distance R between the fluorochromes as $1/R^6$. The fine-structure constant is

$$\alpha = \frac{e^2}{4\pi\epsilon_0 \hbar c} \approx \frac{1}{137}. \tag{9.39}$$

In terms of it, the FRET rate for $R \gg 2$ nm is

$$\Gamma \approx \frac{2\pi\hbar c^2 \alpha^2}{R^6} \frac{dN_a(E_d)}{dE_a} \left|\langle 01\,|(\boldsymbol{D}_d \cdot \boldsymbol{D}_a - 3\,\hat{\boldsymbol{r}} \cdot \boldsymbol{D}_d\; \hat{\boldsymbol{r}} \cdot \boldsymbol{D}_a)|\, 10\rangle\right|^2 \tag{9.40}$$

in which $dN_a(E_d)/dE_a$ is the number of acceptor states per unit energy.

The dipole approximation separates the donor coordinates $\boldsymbol{x}_j$ and $\boldsymbol{x}_n$ from the acceptor coordinates $\boldsymbol{y}_k$ and $\boldsymbol{y}_m$. So in the dipole approximation we may write the matrix element that determines the rate (9.40) more simply as

$$\begin{aligned} \langle 01\,|(\boldsymbol{D}_d \cdot \boldsymbol{D}_a - 3\,\hat{\boldsymbol{r}} \cdot \boldsymbol{D}_d\; \hat{\boldsymbol{r}} \cdot \boldsymbol{D}_a)|\, 10\rangle = {} & \langle 0\,|\boldsymbol{D}_d|\, 1\rangle \cdot \langle 1\,|\boldsymbol{D}_a|\, 0\rangle \\ & - 3\,\hat{\boldsymbol{r}} \cdot \langle 0\,|\boldsymbol{D}_d|\, 1\rangle\; \hat{\boldsymbol{r}} \cdot \langle 1\,|\boldsymbol{D}_a|\, 0\rangle \end{aligned} \tag{9.41}$$

which shows that the FRET transition rate is fastest when the two dipoles $\boldsymbol{D}_d$ and $\boldsymbol{D}_a$ and the displacement $\hat{\boldsymbol{r}}$ are parallel or antiparallel.

We can find the mean value of the square of the modulus of this expression by choosing the phases of the states and a coordinate system such that

$$\begin{aligned} \langle 0|\boldsymbol{D}_d|1\rangle &= d_d\,(0, 0, 1) \\ \langle 1|\boldsymbol{D}_a|0\rangle &= d_a\,(e^{i\beta} \sin\psi, 0, \cos\psi) \\ \hat{r} &= (\sin\theta\cos\phi, \sin\theta\sin\phi, \cos\theta) \end{aligned} \tag{9.42}$$

with d_d and d_a real. The mean value is the integral

$$\int |\langle 0|\boldsymbol{D}_d|1\rangle \cdot \langle 1|\boldsymbol{D}_a|0\rangle - 3\hat{\boldsymbol{r}} \cdot \langle 0|\boldsymbol{D}_d|1\rangle\, \hat{\boldsymbol{r}} \cdot \langle 1|\boldsymbol{D}_a|0\rangle|^2 \; \frac{d\cos\psi d\cos\theta d\phi}{8\pi} \tag{9.43}$$

over the 4π orientations of the unit vectors $\hat{r}$ and over the angle ψ between the dipoles. Apart from the factor $d_d^2 d_a^2/8\pi$ the integral is

$$\begin{aligned} A = & \int |\cos\psi - 3\cos\theta(e^{i\beta}\sin\psi\sin\theta\cos\phi + \cos\psi\cos\theta)|^2 \, d\cos\psi d\cos\theta d\phi \\ = & \int \big\{[\cos\psi - 3\cos\theta(\cos\beta\sin\psi\sin\theta\cos\phi + \cos\psi\cos\theta)]^2 \\ & +[3\cos\theta\sin\beta\sin\psi\sin\theta\cos\phi]^2\big\} \; d\cos\psi d\cos\theta d\phi \\ = & \int \big[\cos^2\psi - 6\cos\beta\cos\psi\sin\psi\cos\theta\sin\theta\cos\phi - 6\cos^2\psi\cos^2\theta \\ & + 9\sin^2\psi\cos^2\theta\sin^2\theta\cos^2\phi + 18\cos\beta\cos\psi\sin\psi\cos^3\theta\sin\theta\cos\phi \\ & +9\cos^2\psi\cos^4\theta\big] \; d\cos\psi d\cos\theta d\phi. \end{aligned} \tag{9.44}$$

The integral A is the sum of several terms:

$$\begin{aligned} T_1 = & \int \cos^2\psi \, d\cos\psi d\cos\theta d\phi = 4\pi \int_{-1}^{1} x^2 \, dx = \frac{8\pi}{3} \\ T_2 = & -6\cos\beta \int \cos\psi\sin\psi\cos\theta\sin\theta\cos\phi \, d\cos\psi d\cos\theta d\phi = 0 \\ T_3 = & -6\int \cos^2\psi\cos^2\theta \, d\cos\psi d\cos\theta d\phi = -\frac{16\pi}{3} \\ T_4 = & \, 9\int \sin^2\psi\cos^2\theta\sin^2\theta\cos^2\phi \, d\cos\psi d\cos\theta d\phi \\ = & \, 9\pi\int_{-1}^{1}(1-x^2)dx \int y^2(1-y^2)dy = 9\pi\frac{4}{3}\frac{4}{15} = \frac{16\pi}{5} \\ T_5 = & \, 18\cos\beta \int \cos\psi\sin\psi\cos^3\theta\sin\theta\cos\phi \, d\cos\psi d\cos\theta d\phi = 0 \\ T_6 = & \, 9\int \cos^2\psi\cos^4\theta \, d\cos\psi d\cos\theta d\phi = 18\pi \int x^2 y^4 \, dxdy = \frac{24\pi}{5}. \end{aligned} \tag{9.45}$$

So the square of the modulus of the factorized matrix element (9.41) averaged over orientations is 2/3.

The FRET rate (9.40) averaged over relative orientations then is

$$\overline{\Gamma} = \frac{4\pi\hbar c^2\alpha^2 \, d_a^2 d_d^2}{3R^6} \frac{dN_a(E_d)}{dE_a} \tag{9.46}$$

in which d_d and d_a are the effective lengths of the donor and acceptor dipoles.

To make things as simple as possible, let's consider the case in which of two hydrogen atoms in which a photon has raised the donor atom to a $2p$ state. Then the length d_d is 0.0394 nm. The only possible acceptor state is also a $2p$ state with $d_a = 0.0394$ nm. The estimate (9.26) of the rate in terms of the average width γ of the donor and acceptor states, the time-energy uncertainty relation $\tau\,\gamma \gtrsim \hbar$, and the lifetime (9.77) of the $2p \to 1s$ transition $\tau = 1.60 \times 10^{-9}$ s now give

$$\frac{dN_a(E_d)}{dE_a} \approx \frac{1}{\gamma} \approx \frac{\tau}{\hbar} = \frac{1.60 \times 10^{-9}\,\mathrm{s}}{6.58 \times 10^{-16}\,\mathrm{eV\,s}} = \frac{2.43 \times 10^7}{\mathrm{eV}}. \tag{9.47}$$

We then have

$$\overline{\Gamma} = \frac{4\pi\hbar c^2\alpha^2\, d_a^2 d_d^2}{3R^6}\,\frac{1}{\gamma} = \frac{4\pi\hbar c^2\alpha^2\,(0.0394\,\mathrm{nm})^4}{3R^6}\,\frac{2.43 \times 10^7}{\mathrm{eV}}. \tag{9.48}$$

Since $\hbar c = 197$ eV nm, $\alpha = 1/137$, and $c = 3 \times 10^{17}$ nm/s, we find

$$\overline{\Gamma} = \frac{4\pi\,197\,\mathrm{eV\,nm}\,3 \times 10^{17}\mathrm{nm}\,(0.0394\,\mathrm{nm})^4\,2.43 \times 10^7}{3\,(137)^2\,R^6\,\mathrm{eV\,s}} \tag{9.49}$$

$$= \frac{3.92 \times 10^{15}}{(R/\mathrm{nm})^6}\,\mathrm{s}^{-1}. \tag{9.50}$$

This very high rate is due to the sharpness of the $2\,p$ state of hydrogen for which $\gamma \approx 4.2 \times 10^{-8}$ eV. The various fluorescent proteins emit light with widths of 50–100 nm. Setting $\lambda = 475$ nm, we find that their widths are about $\gamma \approx 0.41$ eV. So a more realistic rate would be

$$\overline{\Gamma} \approx \frac{4 \times 10^8}{(R/\mathrm{nm})^6}\,\mathrm{s}^{-1}. \tag{9.51}$$

Let's estimate the FRET rate Γ by assuming plausible values for the effective lengths d_d and d_a of the donor and acceptor dipoles and for the density dN_a/dE_a of acceptor states. The electric dipole moments of fluorochromes often are quoted in Debye units. One Debye or D is 3.33564×10^{-30} C m or 0.020819434 e nm in which e is the charge of the proton. Values of a few D are common. We set $d_d = d_a \approx 0.06$ nm. We estimate the density dN_a/dE_a of acceptor states as $1/\gamma$ where $\gamma \approx 0.41$ eV is the full width of the emission spectrum at half maximum. The average FRET rate then is

$$\overline{\Gamma} \approx \frac{4\pi\hbar c^2\alpha^2\, d_a^2 d_d^2}{3R^6\,\gamma} \approx \frac{4.2 \times 10^{11}}{(R/\mathrm{nm})^6}\,\mathrm{s}^{-1} = \frac{5.7 \times 10^8}{(R/3\mathrm{nm})^6}\,\mathrm{s}^{-1}. \tag{9.52}$$

The lifetime is about 1.7 nanoseconds when the chromophores are 3 nm apart.

For very short distances, one should use the full formula (9.24) and the exact potential (9.27).

9.3 Fluorescence

Let's compare FRET with fluorescence, that is, the emission of a photon by an excited atom or molecule. The initial state is an excited state of the (donor) molecule $|1,0\rangle$ and no photons. The final state is the ground state of the (donor) molecule $|0,\boldsymbol{k}\rangle$ and a photon of momentum $\hbar\boldsymbol{k}$. The hamiltonian is

$$H = H_d + H_0 + V \tag{9.53}$$

in which H_0 is the hamiltonian of the photons

$$H_0 = \sum_{\boldsymbol{k}} \hbar\omega_k \, a^\dagger(\boldsymbol{k}, s) a(\boldsymbol{k}, s) \tag{9.54}$$

which counts the photons of each momentum $\hbar\boldsymbol{k}$ (and polarization s) and assigns energy $h\nu_k = \hbar\omega_k = \hbar c|\boldsymbol{k}| = \hbar c k$ to each one. The (nonrelativistic) interaction V between the electrons of the molecule and the electromagnetic field $\boldsymbol{A}$ is

$$V = -\sum_j \frac{e}{m} \, \boldsymbol{p}_j \cdot \boldsymbol{A}(\boldsymbol{x}_j) \tag{9.55}$$

to lowest order in the Coulomb gauge $\boldsymbol{\nabla \cdot A = 0}$.

The basic commutation relation $[x_{ji}, p_{j'i'}] = i\hbar\,\delta_{jj'}\,\delta_{ii'}$ implies that the commutator of $\boldsymbol{x}_j$ with the donor hamiltonian is

$$[\boldsymbol{x}_j, H_d] = \sum_{j'} \left[\boldsymbol{x}_j, \frac{\boldsymbol{p}_{j'}^2}{2m} \right] = \left[\boldsymbol{x}_j, \frac{\boldsymbol{p}_j^2}{2m} \right] = i\hbar \, \frac{\boldsymbol{p}_j}{m}. \tag{9.56}$$

So we can rewrite the interaction (9.55) as

$$V = -\sum_j \frac{e}{m} \, \boldsymbol{p}_j \cdot \boldsymbol{A}(\boldsymbol{x}_j) = \sum_j \frac{ie}{\hbar} \, [\boldsymbol{x}_j \cdot \boldsymbol{A}(\boldsymbol{x}_j), H_d]. \tag{9.57}$$

In Dirac's interaction picture (9.12– **??**), the amplitude for a transition from the state $|1,0\rangle$ to the state $|0,\boldsymbol{k},s\rangle$ in time t is

$$\langle 0,\boldsymbol{k},s|e^{-iHt/\hbar}|1,0\rangle = -\frac{i}{\hbar} e^{-i\omega_k t} \langle 0,\boldsymbol{k},s| \int_0^t V_i(t')\,dt' \,|1,0\rangle. \tag{9.58}$$

The interaction $V(t')$ evolves with the time dependence of the "free" hamiltonian $H_d + H_0$ of the donor molecule and of the electromagnetic field

$$V_i(t') = e^{i(H_d+H_0)t'/\hbar}\, V\, e^{-i(H_d+H_0)t'/\hbar}. \tag{9.59}$$

So the amplitude is

$$\begin{aligned}\langle 0, \boldsymbol{k}, s|e^{-iHt/\hbar}|1,0\rangle &= \frac{-i}{\hbar}e^{-i\omega_k t}\langle 0,\boldsymbol{k},s|\int_0^t e^{i\frac{(H_d+H_0)t'}{\hbar}} V e^{-i\frac{(H_d+H_0)t'}{\hbar}} dt'|1,0\rangle \\ &= -\frac{i}{\hbar}e^{-i\omega_k t}\,\langle 0,\boldsymbol{k},s|\int_0^t e^{i\omega_k t'}\, V\, e^{-iE_d t'/\hbar}\, dt'\,|1,0\rangle \\ &= e^{-i\omega_k t}\,\frac{1-e^{i(\omega_k - E_d/\hbar)t}}{\hbar\omega_k - E_d}\,\langle 0,\boldsymbol{k},s|\,V\,|1,0\rangle. \end{aligned} \tag{9.60}$$

Since $H_d|1,0\rangle = E_d|1,0\rangle$ and $H_d|0,\boldsymbol{k},s\rangle = 0$, our formula (9.57) for the interaction V implies that

$$\begin{aligned}\langle 0,\boldsymbol{k},s|\,V\,|1,0\rangle &= \langle 0,\boldsymbol{k},s|\sum_j \frac{ie}{\hbar}\,[\boldsymbol{x}_j\cdot\boldsymbol{A}(\boldsymbol{x}_j), H_d]\,|1,0\rangle \\ &= \frac{ieE_d}{\hbar}\,\langle 0,\boldsymbol{k},s|\sum_j \boldsymbol{x}_j\cdot\boldsymbol{A}(\boldsymbol{x}_j)\,|1,0\rangle. \end{aligned} \tag{9.61}$$

In the Coulomb gauge, the electromagnetic field (at time $t = 0$) is a sum over the two polarizations s and over all momenta $\hbar\boldsymbol{k}$

$$\boldsymbol{A}(\boldsymbol{x}) = \sum_{\boldsymbol{k},s}\sqrt{\frac{\hbar}{2V\epsilon_0\,\omega_k}}\boldsymbol{\epsilon}(\boldsymbol{k},s)\,\left[a(\boldsymbol{k},s)\,e^{i\boldsymbol{k}\cdot\boldsymbol{x}} + a^\dagger(\boldsymbol{k},s)\,e^{-i\boldsymbol{k}\cdot\boldsymbol{x}}\right] \tag{9.62}$$

in which the operator $a^\dagger(\boldsymbol{k},s)$ creates a photon of momentum $\hbar\boldsymbol{k}$ and polarization s from the state of no photons $a^\dagger(\boldsymbol{k},s)|1,0\rangle = |1,\boldsymbol{k}\rangle$. The photon operators obey the rule

$$[a(\boldsymbol{k},s), a^\dagger(\boldsymbol{k}',s')] = \delta_{\boldsymbol{k},\boldsymbol{k}'}\,\delta_{s,s'}. \tag{9.63}$$

Using these commutation relations, you can show that the matrix element in the amplitude (9.61) is

$$\begin{aligned}\langle 0,\boldsymbol{k},s|\sum_j \boldsymbol{x}_j\cdot\boldsymbol{A}(\boldsymbol{x}_j)\,|1,0\rangle &= \langle 0,0|a(\boldsymbol{k},s)\sum_j \boldsymbol{x}_j\cdot\boldsymbol{A}(\boldsymbol{x}_j)\,|1,0\rangle \\ &= \sqrt{\frac{\hbar}{2V\epsilon_0\,\omega_k}}\langle 0,0|\sum_j \boldsymbol{x}_j\cdot\boldsymbol{\epsilon}(\boldsymbol{k},s)e^{-i\boldsymbol{k}\cdot\boldsymbol{x}_j}\,|1,0\rangle. \end{aligned} \tag{9.64}$$

The wavelength of visible photons is between 390 and 700 nm, and most

molecules are less than 1 nm in length. So the argument $|\boldsymbol{k}\cdot\boldsymbol{x}_j|$ of the exponential is

$$|\boldsymbol{k}\cdot\boldsymbol{x}_j| \lesssim 2\pi/390 \approx 0.016 \tag{9.65}$$

which is small enough to neglect. In this dipole approximation, the matrix element $\langle 0,\boldsymbol{k},s|\,V\,|1,0\rangle$ is proportional to the dipole transition moment of the molecule

$$\begin{aligned}\langle 0,\boldsymbol{k},s|\,V\,|1,0\rangle &= \frac{ieE_d}{\hbar}\sqrt{\frac{\hbar}{2V\epsilon_0\,\omega_k}}\;\boldsymbol{\epsilon}(\boldsymbol{k},s)\cdot\langle 0,0|\sum_j \boldsymbol{x}_j\,|1,0\rangle \\ &= \frac{ieE_d}{\sqrt{2V\epsilon_0\,\hbar\omega_k}}\;\boldsymbol{\epsilon}(\boldsymbol{k},s)\cdot\langle 0,0|\,\boldsymbol{D}\,|1,0\rangle. \end{aligned}\tag{9.66}$$

So the amplitude (9.60) is

$$\begin{aligned}\langle 0,\boldsymbol{k},s|e^{-iHt/\hbar}|1,0\rangle &= e^{-i\omega_k t}\,\frac{1-e^{i(\omega_k-E_d/\hbar)t}}{\hbar\omega_k-E_d}\,\langle 0,\boldsymbol{k},s|\,V\,|1,0\rangle \\ &= \frac{ieE_d\,e^{-i\omega_k t}}{\sqrt{2V\epsilon_0\,\hbar\omega_k}}\;\frac{1-e^{i(\omega_k-E_d/\hbar)t}}{\hbar\omega_k-E_d}\;\boldsymbol{\epsilon}(\boldsymbol{k},s)\cdot\langle 0,0|\,\boldsymbol{D}\,|1,0\rangle. \end{aligned}\tag{9.67}$$

The probability of emitting the photon is the square of the modulus of this amplitude (9.67) as in the formula (9.20):

$$P(t) = \frac{4\,e^2E_d^2\;\left|\epsilon(\boldsymbol{k},s)\cdot\langle 0,0|\,\boldsymbol{D}\,|1,0\rangle\right|^2}{2V\epsilon_0\,\hbar\omega_k\,|\hbar\omega_k-E_d|^2}\,\sin^2\left[\frac{(\hbar\omega_k-E_d)\,t}{2\hbar}\right]. \tag{9.68}$$

For times long compared to $\hbar/(\hbar\omega_k-E_d)$, we can use Dirac's delta function

$$\lim_{t\to\infty}\frac{1}{|\hbar\omega_k-E_d|^2}\,\sin^2\left[\frac{(\hbar\omega_k-E_d)\,t}{2\hbar}\right] = \frac{\pi\,t}{2\,\hbar}\,\delta(\hbar\omega_k-E_d) \tag{9.69}$$

to write the probability as

$$P(t) = \frac{\pi e^2E_d^2\,t\;\left|\boldsymbol{\epsilon}(\boldsymbol{k},s)\cdot\langle 0,0|\,\boldsymbol{D}\,|1,0\rangle\right|^2}{V\epsilon_0\,\hbar^2\omega_k}\,\delta(\hbar\omega_k-E_d). \tag{9.70}$$

The rate of emission is the time derivative of this probability integrated over final states. In a box of volume $V=L^3$, there are this many states

$$dN = \frac{V\,d^3p}{h^3} = \frac{V\,d^3k}{(2\pi)^3} = \frac{V\,k^2dkd\Omega}{(2\pi)^3} = \frac{V\,\omega^2d(\hbar\omega)d\Omega}{(2\pi)^3\hbar\,c^3}. \tag{9.71}$$

So the emission rate into solid angle $d\Omega$ is

$$\begin{aligned}\Gamma &= \int \frac{dP(t)}{dt}\, dN \\ &= \int \frac{\pi e^2 E_d^2 \,|\epsilon(\boldsymbol{k},s)\cdot\langle 0,0|\,\boldsymbol{D}\,|1,0\rangle|^2}{V\epsilon_0\,\hbar^2\omega_k}\,\delta(\hbar\omega_k - E_d)\,\frac{V\,\omega^2 d(\hbar\omega)d\Omega}{(2\pi)^3\hbar\,c^3} \\ &= \frac{e^2\omega_k^3\,|\epsilon(\boldsymbol{k},s)\cdot\langle 0,0|\,\boldsymbol{D}\,|1,0\rangle|^2}{4\pi\epsilon_0\,\hbar c\,2\pi c^2}\,d\Omega \\ &= \frac{\alpha\omega_k^3\,|\epsilon(\boldsymbol{k},s)\cdot\langle 0,0|\,\boldsymbol{D}\,|1,0\rangle|^2}{2\pi c^2}\,d\Omega \end{aligned} \tag{9.72}$$

in which $\alpha = e^2/(4\pi\epsilon_0\hbar c) = 1/137.036$ is the fine-structure constant.

Usually, we don't measure the polarization of the emitted photon or the orientation of the dipole vector $\boldsymbol{D}$ of the molecule, so we should sum over the polarizations. In Coulomb's gauge, the polarization vectors $\epsilon(\boldsymbol{k},s)$ are unit vectors perpendicular to $\boldsymbol{k}$. So if $\boldsymbol{k}$ is in the $\hat{3}$ direction, then $\epsilon(\boldsymbol{k},s)$ are the unit vectors $\hat{1}$ and $\hat{2}$, and the sum is

$$\begin{aligned}\sum_s |\boldsymbol{\epsilon}(\boldsymbol{k},s)\cdot\langle 0,0|\,\boldsymbol{D}\,|1,0\rangle|^2 &= |\langle 0,0|\boldsymbol{D}_1|1,0\rangle|^2 + |\langle 0,0|\boldsymbol{D}_2|1,0\rangle|^2 \\ &= |\langle 0,0|\boldsymbol{D}|1,0\rangle|^2\left(1-\cos^2\theta\right)\end{aligned} \tag{9.73}$$

in which the angle θ is defined by

$$\cos^2\theta\,|\langle 0,0|\,\boldsymbol{D}\,|1,0\rangle|^2 = \left|\hat{\boldsymbol{k}}\cdot\langle 0,0|\,\boldsymbol{D}\,|1,0\rangle\right|^2. \tag{9.74}$$

Summing over the polarizations and integrating over angles $d\Omega = 2\pi d\cos\theta$, we find for the emission rate

$$\begin{aligned}\Gamma &= \frac{\alpha\omega_k^3\,|\langle 0,0|\,\boldsymbol{D}\,|1,0\rangle|^2}{2\pi c^2}\int_{-1}^{1}\left(1-\cos^2\theta\right)\,2\pi\,d\cos\theta \\ &= \frac{4\alpha\omega_k^3\,|\langle 0,0|\,\boldsymbol{D}\,|1,0\rangle|^2}{3c^2}.\end{aligned} \tag{9.75}$$

Using $\hbar c = 197.33$ eV nm and $\hbar = 6.582\times10^{-16}$ eV s, we can estimate this rate for a green photon of energy $\hbar\omega = 2.33$ eV and a dipole moment of $|\langle 0,0|\,\boldsymbol{D}\,|1,0\rangle| = 0.06$ nm (or $e|\langle 0,0|\,\boldsymbol{D}\,|1,0\rangle| \approx 3\,\boldsymbol{D}$) as

$$\begin{aligned}\Gamma &= \frac{4\alpha(\hbar\omega)^3|\langle 0,0|\,\boldsymbol{D}\,|1,0\rangle|^2}{3(\hbar c)^2\hbar} \\ &= \frac{4(2.33\,\text{eV})^3(0.06\,\text{nm})^2}{3(137)(197.3\,\text{eV nm})^2\,6.582\times10^{-16}\,\text{eV s}} = 1.73\times10^7\,\text{s}^{-1}\end{aligned} \tag{9.76}$$

or a lifetime of $\tau = 5.78\times10^{-8}$ s.

The dipole moment of the $2p \to 1s$ transition in atomic hydrogen is $|\langle 1s|\boldsymbol{r}|2p\rangle| = 0.744\, a_0$ in which the Bohr radius is $a_0 = \hbar^2/me^2 = 0.0529177$ nm. So $|\langle 1s|\boldsymbol{r}|2p\rangle| = 0.0394$ nm. So the rate for the $2p \to 1s$ transition is

$$\Gamma(2p \to 1s) = 1.73 \times 10^7 \left(\frac{10.2}{2.33}\right)^3 \left(\frac{0.0394}{0.06}\right)^2 = 6.261 \times 10^8\, \mathrm{s}^{-1}, \quad (9.77)$$

and its life time $\tau = 1/\Gamma(2p \to 1s) = 1.60 \times 10^{-9}$ s.

Atomic physicists call the **dimensionless** quantity

$$f_{ni} = \frac{2m\omega_{ni}}{\hbar} \left|\langle n \left|\boldsymbol{D}\right| i\rangle\right|^2 \quad (9.78)$$

the **oscillator strength** between levels i and n.

9.4 Some mathematics

The number N of living things supplied with ample food and no predation grows with the time t as

$$\frac{dN(t)}{dt} = rN(t) \quad (9.79)$$

in the simplest models. We solve this equation by writing it as

$$\frac{dN}{N} = r\, dt \quad (9.80)$$

and integrating

$$\ln N(t) - \ln N(0) = r\, t \quad (9.81)$$

in which $N(0)$ is the number of cells or rabbits at time $t = 0$. Taking the exponential of both sides, we get

$$N(t) = N(0)\, e^{rt} = N(0)\, (e^{\ln 2})^{rt/\ln 2} = N(0)\, 2^{rt/\ln 2} = N(0)\, 2^{t/\tau} \quad (9.82)$$

in which $\tau = 2/\ln 2$ is the doubling time.

When food is scarce or predators are near, the simplest model is changed to the **logistic** equation

$$\frac{dN(t)}{dt} = rN(t) \left(1 - \frac{N}{K}\right) \quad (9.83)$$

in which K will turn out to be the number of living things as $t \to \infty$.

To simplify the notation, we divide both sides of the differential equation (9.83) by K and set $n = N/K$:

$$\frac{dn}{dt} = rn\,(1 - n)\,. \quad (9.84)$$

Proceeding as we did in the simplest model, we get

$$\frac{dn}{n\,(1-n)} = \frac{dn}{n} + \frac{dn}{1-n} = r\,dt \tag{9.85}$$

which we integrate to

$$\ln n - \ln(1-n) - \ln c = \ln\left(\frac{n}{c(1-n)}\right) = r(t-t_0). \tag{9.86}$$

(In class, I left out the constant term $\ln c$; it is simpler to keep it and drop t_0.) Exponentiating both sides, we get

$$\frac{n}{c(1-n)} = e^{rt}. \tag{9.87}$$

Rearranging terms and recalling that $n = N/K$, we find

$$\frac{N}{K} = \frac{ce^{rt}}{1+ce^{rt}}. \tag{9.88}$$

If $N_0 = N(0)$ is the number of animals at $t = 0$, then the relation

$$\frac{N_0}{K} = \frac{c}{1+c} \tag{9.89}$$

gives us the constant c as

$$c = \frac{N_0}{K-N_0}. \tag{9.90}$$

Substituting this expression for c into our formula (9.88) for N/K, we get

$$N = \frac{N_0 K e^{rt}}{K + N_0(e^{rt}-1)} \tag{9.91}$$

which is equation (3.9) of PBoC and which goes to K for huge t.

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Index

acyl, 8
adenine, 9
adenine triphosphate, 10
aldehyde group, 6
aldose, 6
alpha carbon, 15
amide groups, 17
amino acids, 15–17
amino group, 15
atoms and molecules, 1–18
  adenine, 9
  adenine triphosphate, 10
  aldehyde group, 6
  aldose, 6
  alpha carbon, 15
  amide groups, 17
  amino acids, 15–17
  amino group, 15
  bases, 9
  carbonyl group, 6
  carboxylic group, 7
  carboxylic-acid group, 15
  cellulose, 7
  charged amino acids, 16
  codons, 13, 16
  condensation reaction, 7
  covalent bonds, 4
  cytosine, 9
  deoxyribonucleotides, 9
  dihydroxyacetone, 6
  disaccharide, 7
  disulfide bond, 17
  DNA, 12
  DNA error rate, 14
  DNA polymerase, 14
  electrolytes, 15
  ester linkages, 9
  eucaryotic cell, 10
  exercises, 18
  fats, 7–9
  fatty acid, 8
fatty acids, 7–9
Gauss's law, 10
genetic code, 16
glucose, 6
glyceraldehyde, 6
glycerol, 8
glycogen, 7
glycolipids, 7
glycoproteins, 7
glycosaminoglycans, 7
glycosidic bond, 7
guanine, 9
guanine triphosphate, 10
hybrid potential, 4
hydrocarbons, 7–9
hydrophobic amino acids, 16
hydroxyl group, 6
inorganic phosphate, 10
isomers, 7
ketone group, 6
ketose, 6
kinases, 17
Lennard-Jones potential, 5
messenger RNA, 12
micro RNA, 14
mitochondrion, 10
monophosphate nucleotides, 10
monosaccharides, 6
nonpolar, 16
nonpolar amino acids, 16
nucleotides, 9–14
oligosaccharide, 7
oxidation, 17
pH, 15
phosphodiester bond, 11
phosphoric acid, 12
physiological conditions, 15
polar, 16
polar amino acids, 16
polysaccharide, 7
principal molecules in cells, 1

proteins, 17–18
purines, 9
pyrimidines, 9
reduction, 17
ribonucleotides, 9
ribose, 6
ribosomal RNA, 13
ribosomes, 13, 14
RNA, 10
RNA polymerase II, 14
saturated hydrocarbons, 7
small nuclear RNAs, 14
sugars, 5–7
synthetases, 13
thiol groups, 17
thymine, 9
transfer RNA, 13
triacylglycerides, 9
triglycerides, 9
unsaturated hydrocarbons, 7
uracil, 9
Avogadro's number, 2

bases, 9
binomial distribution, 27–30
Boltzmann distribution, 47
bonds between atoms, 1–5
brownian motion, 57–60

carbonyl group, 6
carboxylic group, 7
carboxylic-acid group, 15
cell structure, 66–79
exercises, 79
cellulose, 7
central limit theorem, 39–41
characteristic functions, 38–39
charged amino acids, 16
codons, 13, 16
condensation reaction, 7
counting fluorescent molecules, 29–30
covalent bond, 4
cytosine, 9

Debye-Hückel equation, 73–77
deoxyribonucleotides, 9
dielectrics, 70
diffusion, 31–32, 55–66
Fick's law, 56
dihydroxyacetone, 6
disaccharide, 7
disulfide bond, 17
DNA, 12
DNA error rate, 14
DNA polymerase, 14

Einstein-Nernst relation, 60–62
electric constant, 1, 63, 70
electric susceptibility, 70
electrolytes, 15
electron Volt, 2
electrostatics
dielectrics, 70–79
entropy, 47–48
Equilibrium, 44–47
error function, 35–36
ester linkages, 9
eucaryotic cell, 10
Euler's equation, 66

Faraday's law, 70
fats, 7–9
fatty acid, 8
fatty acids, 7–9
Fluid mechanics, 66
forces between atoms, 1–5
hydrogen bonds, 2
ionic bonds, 1
van der Waals bonds, 3
free energy, 51–53
freely jointed polymers, 79–80

Gauss's distribution, 33–35
Gauss's law, 10, 62, 70
genetic code, 16
Gibbs free energy, 52–53
glucose, 6
glyceraldehyde, 6
glycerol, 8
glycogen, 7
glycolipids, 7
glycoproteins, 7
glycosaminoglycans, 7
glycosidic bond, 7
Gouy-Chapman, 76–77
guanine, 9
guanine triphosphate, 10

Helmholtz free energy, 51–52
hybrid potential, 4
hydrocarbons, 7–9
hydrogen bonds, 2
hydrophobic amino acids, 16
hydroxyl group, 6

inorganic phosphate, 10
ionic bonds, 1
isomers, 7

ketone group, 6
ketose, 6
kilocalorie, 2
kinases, 17

Lennard-Jones potential, 5
liquids, 54–66

Maxwell-Boltzmann distribution, 36–41
mean and variance, 26–27
membranes, 66–79
messenger RNA, 12
micro RNA, 14
mitochondria, 68
mitochondrion, 10

mol, 2
molecular devices, 22–25
monophosphate nucleotides, 10
monosaccharides, 6

Navier-Stokes equation, 66
neurons, 77–78
nonpolar, 16
nonpolar amino acids, 16
nucleotides, 9–15

oligosaccharide, 7
oscillator strength, 96
oxidation, 17
oxoacid, 8

partition function, 49–51
permittivity, 2, 63, 70
pH, 15
phosphatidylserine, 72
phosphodiester bond, 11
phosphoric acid, 12
physiological conditions, 15
Poisson distribution, 32–33
Poisson-Boltzmann equation, 62–63
polar, 16
polar amino acids, 16
polymers, 79–82
polysaccharide, 7
potassium leak channels, 72–73
probability and statistics, 25–43
  Bernoulli's distribution, 28
  brownian motion
    Einstein-Nernst relation, 60–62
  characteristic functions, 38–39
  convergence in probability, 41
  diffusion constant, 60
  Einstein's relation, 60
  Einstein-Nernst relation, 60–62
  ensemble average, 58
  exercises, 41–43
  normal distribution, 35
  viscous-friction coefficient, 60
proteins, 17–18
purines, 9
pyrimidines, 9

random walks, 30–31
reduction, 17
relative permittivity, 70
Reynolds number, 63–66
ribonucleotides, 9
ribose, 6
ribosomal RNA, 13
ribosomes, 13, 14
RNA, 10
RNA polymerase II, 14

saturated hydrocarbons, 7
small nuclear RNAs, 14
Statistical Mechanics, 43–54
statistical mechanics
  exercises, 53–54
sugars, 5–7
synthetases, 13

temperature, 48–49
thiol groups, 17
thymine, 9
transfer RNA, 13
triacylglycerides, 9
triglycerides, 9

unsaturated hydrocarbons, 7
uracil, 9

van der Waals bonds, 3
van der Waals's gas law, 51