4 Transport in an Infinite Medium

In this book, Chaps. 4 and 5 are devoted to one of the most fundamental problems in physiology: the transport of solvent (water) and uncharged solute particles. Chapter 4 develops some general ideas about the movement of solutes in solution. Chapter 5 applies these ideas to movement of water and solute through a membrane.

Section 4.1 defines flux and fluence rate and derives the continuity equation. Section 4.2 shows how to calculate the solute fluence rate when the solute particles are drifting with a constant velocity, as when they are being dragged along by flowing solvent.

The next several sections are devoted to diffusion, the random motion of solute particles. Sections 4.3–4.5 describe random motion in a gas and a liquid. Section 4.6 states Fick's first law, which relates the fluence rate of diffusing particles to the gradient of their concentration. Section 4.7 relates the proportionality constant in Fick's first law to the viscous drag coefficient of the particle in the solution. Section 4.8 combines Fick's first law and the equation of continuity to give Fick's second law, the diffusion equation, that tells how the concentration $C(x, y, z, t)$ evolves with time. Section 4.9 discusses various time-independent (steady-state) solutions to the diffusion equation. Section 4.10 analyzes steady-state diffusion to or from a cell, including both diffusion through the membrane and in the surrounding medium. Section 4.11 discusses a model of steady-state diffusion of a substance that is being produced at a constant rate inside a spherical cell. Section 4.12 develops a steady-state solution when both drift and diffusion are taking place in one dimension. One technique for solving the time-dependent diffusion equation is introduced in Sect. 4.13. Section 4.14 describes a simple random-walk model for diffusion.

This chapter discusses how molecules and other objects can diffuse or drift. These physical processes occur in both living and nonliving material. However, much motion in the body arises from truly biological mechanisms (Fletcher and Theriot 2004; Hoffmann 2012). A simple example is the flagella that power the swimming of *Escherichia coli* bacteria (Berg 2003). Perhaps the best known example is the contractions caused by *myosin* and *actin* in skeletal muscle. Actin proteins form a "track," and myosin proteins "step" along the track, using energy stored in ATP. A similar molecular motor, *kinesin*, causes motion along microtubules, and is responsible for many intracellular types of motion such as chromosome migration during cell division (*mitosis*). The details about how these motors work is beyond the scope of our book, but understanding them requires knowledge from Chap. 1 (viscosity), Chap. 3 (bioenergetics), and this chapter (Brownian motion).

4.1 Flux, Fluence, and Continuity

Flow was introduced in Sect. 1.17 of Chap. 1. The *flow rate*, *volume flux*, or *volume current* i is the total volume of material transported per unit time and has units of $\mathrm{m}^3\ \mathrm{s}^{-1}$. One can also define the *mass flux* as the total mass transported per unit time or the *particle flux* as the total number of particles, and so on.

The *particle fluence* is the number of particles transported per unit area across an imaginary surface (m^{-2}). The *volume fluence* is the total volume transported across the surface per unit area and has units m^3 times m^{-2}, or m.

The *fluence rate* or *flux density* is the amount of "something" transported across an imaginary surface per unit area per unit time. It can be represented by a vector pointing in the direction the "something" moves and is denoted by $\mathbf{j}$. It has units of "something" $\mathrm{m}^{-2}\ \mathrm{s}^{-1}$. It is traditional to use a subscript to tell what is being transported: $\mathbf{j}_s$ is the solute particle fluence rate ($\mathrm{m}^{-2}\ \mathrm{s}^{-1}$), $\mathbf{j}_m$ is the mass fluence rate ($\mathrm{kg\ m}^{-2}\ \mathrm{s}^{-1}$), and $\mathbf{j}_v$ is volume flux density ($\mathrm{m}^3\ \mathrm{m}^{-2}\ \mathrm{s}^{-1}$ or $\mathrm{m\ s}^{-1}$). In a flowing fluid, $\mathbf{j}_v$ is the velocity with which the fluid moves.

Slightly different nomenclature is used in different fields. The words *flux* and *flux density* are often used interchangeably. Table 4.1 shows some of the names that are encountered. Do not spend much time memorizing it; it is provided

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Table 4.1 Units and names for j and jS in various fields

	j		jS	
	Units	Names	Units	Names
Particles	$\mathrm{m^{-2}\,s^{-1}}$	Particle fluence rate Particle current density Particle flux density Particle flux	$\mathrm{s^{-1}}$	Particle flux Particle current Particle flux
Electric charge	$\mathrm{C\,m^{-2}\,s^{-1}}$ or $\mathrm{A\,m^{-2}}$	Current density	$\mathrm{C\,s^{-1}}$ or A	Current
Mass	$\mathrm{kg\,m^{-2}\,s^{-1}}$	Mass fluence rate Mass flux density Mass flux	$\mathrm{kg\,s^{-1}}$	Mass flux Mass flow
Energy	$\mathrm{J\,m^{-2}\,s^{-1}}$ or $\mathrm{W\,m^{-2}}$	Energy fluence rate Intensity Energy flux	$\mathrm{J\,s^{-1}}$ or W	Energy flux Power

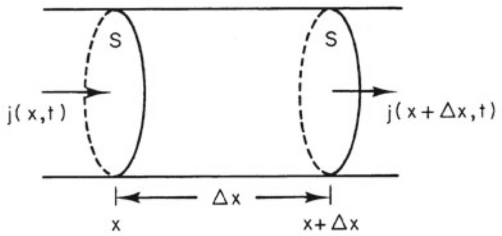

Fig. 4.1 The fluence rates used to derive the continuity equation in one dimension

to help you when you must deal with the notation in other books.

4.1.1 The Continuity Equation in One Dimension

As long as we are dealing with a substance that does not appear or disappear (as in a chemical reaction, radioactive decay, or the like), the number of particles or the mass, or in the case of an incompressible liquid, the volume, remains constant or is *conserved*. This conservation leads to a very useful equation called the *equation of continuity*. It will be derived here in terms of the number of particles.

We will first derive it in one dimension. Let the fluence rate of some species be j particles per unit area per unit time, passing a point. All motion takes place in the x direction along a tube of constant cross-sectional area S. The value of j may depend on the position in the tube and on the time: $j = j(x,t)$. The number of particles in the volume shown in Fig. 4.1 between x and $x + \Delta x$ is $N(x,t)$. At x, there may be particles moving both to the right and to the left; the net number to the right in Δt is $j(x,t)$ times the area S times the time Δt. A flux density in the $+x$ direction is called positive. The net number of particles in at x is $j(x,t)S\Delta t$. Similarly, the net number out at $x+\Delta x$ is $j(x+\Delta x,t)S\Delta t$. Combining these gives the net increase in the number of particles in the volume $S\Delta x$:

$$\Delta N = \left[j(x,t) - j(x+\Delta x,t) \right] S\,\Delta t. \tag{4.1}$$

As $\Delta x \to 0$, the quantity involving j is, by definition, related to the partial derivative of j with respect to x (Appendix N):

$$j(x,t) - j(x+\Delta x,t) = -\frac{\partial j(x,t)}{\partial x}\,\Delta x.$$

Similarly, the increase in $N(x,t)$ is

$$\Delta N(x,t) = N(x,t+\Delta t) - N(x,t) = \frac{\partial N}{\partial t}\,\Delta t.$$

These two expressions can be substituted in Eq. 4.1 to give

$$\frac{\partial}{\partial t}\,N(x,t) = -(S\Delta x)\,\frac{\partial}{\partial x}\,j(x,t).$$

This equation can be written in terms of the concentration $C(x,t)$ by dividing both sides by the volume $S\Delta x$:

$$\frac{\partial C}{\partial t} = -\frac{\partial j}{\partial x}. \tag{4.2}$$

This is the *continuity equation in one dimension*.

4.1.2 The Continuity Equation in Three Dimensions

In three dimensions $\mathbf{j}$ is a vector with components j_x, j_y, and j_z. The flux across a surface dS oriented at some arbitrary direction with the x, y, z axes is equal to the component of $\mathbf{j}$ perpendicular to the surface times dS. To see this, imagine that $\mathbf{j}$ lies in the xy plane with components j_x and j_y. If $\mathbf{j}$ makes an angle ϕ with the vertical, then $j_x = j\sin\phi$, $j_y = j\cos\phi$.

Consider the small volume shown in Fig. 4.2. If there is no buildup of particles within the volume, the flux in across the two faces parallel to the axes is equal to the flux across

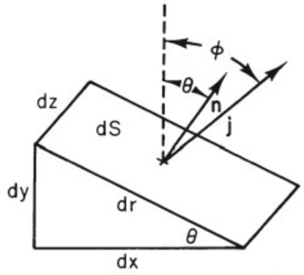

Fig. 4.2 Volume element used to relate the fluence rate across the slant face to the components of the fluence rate parallel to the x and y axes

dS. The area dS of the slant surface is $drdz$, where dz is the thickness of the volume perpendicular to the paper. The number of particles per second across the face $dydz$ is $j_x\, dydz = (j \sin\phi)(dydz)$. Since $dy = dr \sin\theta$, this may be written as $j \sin\phi \sin\theta dzdr$. Similarly, the number of particles per second in across the bottom face is $j_y\, dxdz = j \cos\phi \cos\theta dzdr$. The sum of these must be equal to the number leaving across the slant face: $j\, dzdr(\sin\phi \sin\theta + \cos\phi \cos\theta) = j\, dzdr \cos(\phi - \theta) = j\, dS \cos(\phi - \theta)$. The number of particles per unit area per second across the slant face is, therefore, $j\ \cos(\phi - \theta)$. Now $\phi - \theta$ is the angle between **j** and the unit vector $\hat{\mathbf{n}}$ perpendicular to the surface. We can write the flux density across dS as j_n (the component of **j** parallel to $\hat{\mathbf{n}}$), or $\mathbf{j} \cdot \hat{\mathbf{n}}$ (the dot product of **j** and the normal). The flux (flow per second) is sometimes written as

$$(\mathbf{j} \cdot \hat{\mathbf{n}})dS, \quad j_n dS, \quad \text{or} \quad (\mathbf{j} \cdot d\mathbf{S}). \tag{4.3}$$

These are all equivalent: vector $d\mathbf{S}$ is defined to have magnitude dS and to point along the normal to the surface that points outward from the enclosed volume. The same result is obtained (with more algebra) when **j** is not in the xy plane.

4.1.3 The Integral Form of the Continuity Equation

If we consider a closed volume as shown in Fig. 4.3, the total number of particles flowing out of the volume can be obtained by adding up the contribution from each element dS. It is

$$\begin{aligned}&(\text{total number of particles out in time } \Delta t)\\ &= \left(\iint_{\text{closed surface}} j_n dS \right) \Delta t.\end{aligned}$$

Since the total number of particles in the volume enclosed by the surface is

$$\iiint_{\text{enclosed volume}} C(x, y, z, t)\, dxdydz,$$

we can write[1]

$$\frac{\partial}{\partial t} \iiint_{\text{enclosed volume}} C\, dV = - \iint_{\substack{\text{surface enclosing}\\ \text{the volume}}} j_n\, dS. \tag{4.4}$$

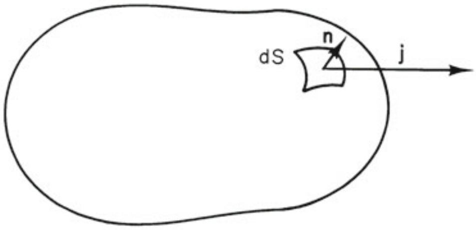

Fig. 4.3 The total number of particles per second passing through the closed surface (flux) is the sum of the contributions $j_n dS$ from all elements of the surface

The outward flux density or fluence rate of the substance integrated over a closed surface (the net flux through the surface) is equal to the rate of decrease of the amount of substance within the volume enclosed by the surface.

How to evaluate the surface integral is best shown by two examples. First consider a volume defined by a sphere of radius r. A lamp at the center of the sphere radiates light uniformly in all directions. The light leaves through the surface of the sphere. The amount of light energy in the volume defined by the sphere is not changing, so the rate of energy production by the lamp P is equal to the energy flux through the surface of the outer sphere:

$$P = \iint j_n\, dS. \tag{4.5}$$

Because of the spherical symmetry, **j** is perpendicular to the surface and is the same at all points on the sphere. Therefore,

$$P = j_n \iint dS.$$

Since the integral of dS over the surface of a sphere of radius r is $4\pi r^2$,

$$j = j_n = \frac{P}{4\pi r^2}. \tag{4.6}$$

The amount of energy per unit area per unit time crossing the surface of the sphere is the energy fluence rate or the intensity.

The second example is slightly more complicated. Suppose that **j** is parallel to the z-axis and has the same value everywhere. The net flux through any closed surface will be zero in that case, and we will verify it to show how to evaluate a surface integral. Consider the situation shown in

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[1] We can write dV as $d^3\mathbf{r}$ or $dxdydz$.

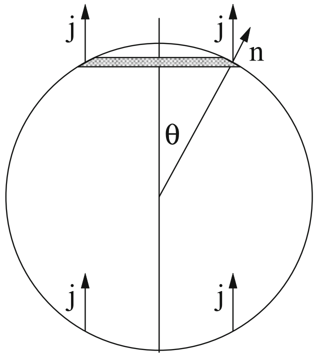

Fig. 4.4 The fluence rate is the same everywhere. The flux is $\int j_n dS$ over the entire sphere. When the normal component of the fluence rate is outward, the contribution is positive. When it is inward, the contribution is negative

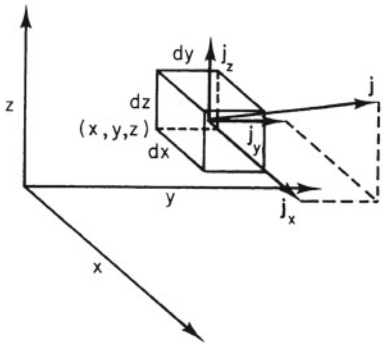

Fig. 4.5 The small volume used to derive the differential form of the continuity equation

Fig. 4.4, where j_n is integrated over the surface of the sphere. At every point in the shaded strip, $j_n = j\cos\theta$. The strip has width $r\,d\theta$ and circumference $2\pi r\sin\theta$, so its area is $2\pi r^2 \sin\theta\, d\theta$. Thus

$$\int j_n\, dS = \int_0^\pi j\cos\theta\, 2\pi r^2 \sin\theta\, d\theta$$
$$= 2\pi r^2 j \int_0^\pi \cos\theta\ \sin\theta\, d\theta = 0.$$

4.1.4 The Differential Form of the Continuity Equation

The continuity equation can be expressed in terms of derivatives instead of integrals. To derive this form, consider the increase in the number of particles in a small rectangular volume located at (x, y, z) and having sides (dx, dy, dz) as shown in Fig. 4.5. Apply Eq. 4.4 to each face of the volume. The rate at which the substance flows in through the face at x is $j_x(x)(dydz)$. At face $x + dx$, it flows out at a rate $j_x(x + dx)dydz$. There is no contribution to the flow through this face from j_y or j_z, since they are parallel to the face. The net increase in the number of particles in the volume due to the two terms is

$$-\left[j_x(x + dx) - j_x(x)\right] dydz = -\frac{\partial j_x}{\partial x}\, dxdydz.$$

Similar terms can be written for the faces perpendicular to the y and z axes. The total amount of the substance entering the volume per unit time is the rate of change of the amount within the volume, which is the rate of change of concentration times the volume $dxdydz$. Therefore,

$$\frac{\partial C}{\partial t}(dxdydz) = -\left(\frac{\partial j_x}{\partial x} + \frac{\partial j_y}{\partial y} + \frac{\partial j_z}{\partial z}\right)(dxdydz)$$

or

$$-\frac{\partial C}{\partial t} = \frac{\partial j_x}{\partial x} + \frac{\partial j_y}{\partial y} + \frac{\partial j_z}{\partial z}. \tag{4.7}$$

This is the differential form of the continuity equation. Equation 4.2 was a special case of this when **j** was parallel to the x axis.

The combination of derivatives on the right-hand side of Eq. 4.7 occurs frequently enough to warrant a special name. It is called the *divergence* of the vector **j**:[2]

$$\operatorname{div}\mathbf{j} = \nabla\cdot\mathbf{j} = \frac{\partial j_x}{\partial x} + \frac{\partial j_y}{\partial y} + \frac{\partial j_z}{\partial z}.$$

The continuity equation is therefore

$$\frac{\partial C}{\partial t} = -\operatorname{div}\mathbf{j}. \tag{4.8}$$

This differential form of the continuity equation is completely equivalent to the integral form, Eq. 4.4. It is sometimes more convenient to use Eq. 4.4 and at other times more convenient to use Eq. 4.8.

The continuity equation says that the rate of decrease of the amount of a conserved substance in a certain region expressed as $-\partial C/\partial t$ is equal to the rate at which it leaves the region expressed as the flow through the surface surrounding the region. The substance may be a certain kind of molecule, electric charge, heat, or mass. If it is electric charge, **j** is the electric current per unit area and C is the charge per unit volume. If it is mass, C is the mass per unit volume or density ρ. The continuity equation is found in many contexts; in each, it expresses the conservation of some quantity.

In the flow of a liquid, the density of the liquid ρ, the mass M, and volume V are related by $M = \rho V$. If the liquid is

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[2] The divergence is one of the concepts of vector calculus. A good review of vector calculus is Schey (2004).

incompressible, a given mass always occupies the same volume, and the density does not change. Therefore, $\partial\rho/\partial t = 0$, and the equation of continuity gives

$$\operatorname{div} \mathbf{j}_m = 0. \tag{4.9}$$

4.1.5 The Continuity Equation with a Chemical Reaction

Our derivation of the continuity equation assumed that the substance was conserved—neither created nor destroyed. If a chemical reaction is creating the substance at a rate Q particles m^{-3} s^{-1} (which may depend on position) then the continuity equation becomes

$$\frac{\partial C}{\partial t} = Q - \operatorname{div} \mathbf{j}, \tag{4.10a}$$

$$\frac{\partial}{\partial t} \underset{\text{volume}}{\iiint} C(x, y, z)\, dV \tag{4.10b}$$

$$= \underset{\text{volume}}{\iiint} Q(x, y, z)\, dV - \underset{\substack{\text{surface}\\ \text{enclosing}\\ \text{the volume}}}{\iint} j_n\, dS.$$

If particles are being consumed in the chemical reaction, then Q is negative.

4.2 Drift or Solvent Drag

One simple way that solute particles can move is to drift with constant velocity. They can do this in a uniform electric or gravitational field if they are also subject to viscous drag, or they can be carried along by the solvent, a process called *drift* or *solvent drag*. (The solute particles are dragged by the solvent.) The solute fluence rate is $\mathbf{j}_s$, with units of particles m^{-2} s^{-1} or just m^{-2} s^{-1}. The number of solute particles passing through a surface is the volume of solution that moves through the surface times the concentration of solute particles. Therefore,

$$\mathbf{j}_s = C\, \mathbf{j}_v. \tag{4.11}$$

This effect will be explored in greater detail in Sect. 4.12.

4.3 Brownian Motion

Table 4.2 Values of the rms velocity for various particles at body temperature

Particle	Molecular weight	Mass (kg)	v_{rms} (m s^{-1})
H_2	2	3.4×10^{-27}	1940
H_2O	18	3×10^{-26}	652
O_2	32	5.4×10^{-26}	487
Glucose	180	3×10^{-25}	200
Hemoglobin	65,000	1×10^{-22}	11
Bacteriophage	6.2×10^6	1×10^{-20}	1.1
Tobacco mosaic virus	40×10^6	6.7×10^{-20}	0.4
E. coli		2×10^{-15}	0.0025

There is also movement of solute molecules when the water is at rest. If the solution is dilute, the solute particles are far apart and hit each other only occasionally. They are struck by water molecules much more often. The result is that they are in continual helter–skelter motion. Each solute molecule is influenced by the water molecules around it, but not by other solute molecules.

In Chap. 3, it was shown that the relative probability for a particle to have energy u when it is in thermal equilibrium with a reservoir at temperature T is given by a Boltzmann factor:[3] $P \propto e^{-u/k_B T}$. In Chap. 3, the Boltzmann factor was used to show that if any energy term depends on the square of some variable, then the average value of that term is $k_B T/2$. A particle with kinetic energy of translation $m(v_x^2 + v_y^2 + v_z^2)/2$ has an average energy $k_B T/2$ for each of the three terms, or a total translational kinetic energy of $3k_B T/2$. This is true regardless of the mass of the particle. Any particle in thermal equilibrium with a reservoir (which can be the surrounding fluid) will move with a mean square velocity given by[4]

$$\overline{v^2} = \frac{3k_B T}{m}. \tag{4.12}$$

The square root of $\overline{v^2}$ is called the *root-mean-square* or *rms* velocity. It decreases with increasing mass of the particle. Table 4.2 shows values of $v_{\text{rms}} = \overline{\left(v^2\right)}^{1/2}$ for different particles at body temperature.

This movement of microscopic-sized particles, resulting from bombardment by much smaller invisible atoms, was first observed by the English botanist Robert Brown in 1827 and is called *Brownian motion*. Solute particles are also subject to this random motion. If the concentration of particles is not uniform, there will be more particles wandering from a region of high concentration to one of low concentration than vice versa. This motion is called *diffusion*.

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[3] The Boltzmann factor provided Jean Perrin with the first means to determine Avogadro's number. The density of particles in the atmosphere is proportional to $\exp(-mgy/k_B T)$, where mgy is the gravitational potential energy of the particles. Using particles for which m was known, Perrin was able to determine k_B for the first time. Since the gas constant R was already known, Avogadro's number was determined from the relationship $R = N_A k_B$. See Problem 12.

[4] The average velocity is $\bar{v}_x = 0$, since a particle with a given speed moves with equal probability to the left or right.

In the next several sections, we study random motion and diffusion, first for a gas and then for a liquid.

4.4 Motion in a Gas: Mean Free Path and Collision Time

It is possible to define a *mean free path*, which is the average distance a particle travels between successive collisions, and a *collision time*, the average length of time between collisions. Consider a collection of N_0 molecules. The number that have moved distance x without suffering a collision is $N(x)$. For short distances dx, the probability that a molecule collides with another molecule is proportional to dx: call it $(1/\lambda)dx$. Then, on the average, the number of molecules having their first collision between x and $x + dx$ is $dN = -N(x)(1/\lambda)dx$. This is the familiar equation for exponential decay. The number of molecules surviving without any collision is $N(x) = N_0 e^{-x/\lambda}$.

To compute the average distance traveled by a molecule between collisions, we multiply each possible value of x by the number of molecules that suffer their first collision between x and $x + dx$. Since $N(x)$ is the number surviving at distance x, and dx/λ is the probability that one of those will have a collision between x and $x + dx$, the mean value of x is

$$\overline{x} = \frac{1}{N_0} \int_0^\infty x N(x) \frac{1}{\lambda}\, dx.$$

With the substitutions $s = x/\lambda$ and $N(x) = N_0 e^{-s}$, this can be written as

$$\begin{aligned} \overline{x} &= \lambda \int_0^\infty e^{-s} s\, ds \qquad (4.13) \\ &= -\lambda \left[e^{-s}(s+1) \right]_0^\infty = \lambda. \end{aligned}$$

Thus λ is the mean free path.

A similar argument can be made for the length of time that each molecule survives before being hit. The probability that a molecule is hit during a short time dt is proportional to dt: call it $(1/t_c)dt$. The number of molecules surviving a time t is given by $N = N_0 e^{-t/t_c}$, and the mean time between collisions can be calculated as above. It is t_c, which is called the *collision time*. The number of collisions per second is the *collision frequency*, $1/t_c$.

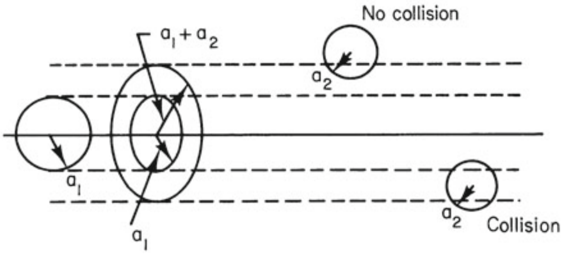

Fig. 4.6 A particle of radius a_1 moves through a gas of particles of radius a_2. A collision will occur if the center of another particle lies within a distance $a_1 + a_2$ of the trajectory of the particle under consideration

It is possible to estimate the mean-free path and the collision frequency. Consider a particle of radius a_1 moving through a dilute gas of other particles of radius a_2. For convenience, imagine that particle 1 is moving and that all the other particles are fixed in position. The path of the first particle is shown in Fig. 4.6. If the center of one of these other molecules lies within a distance $a_1 + a_2$ of the moving molecule, there will be a collision. The effect is the same as if the moving particle had radius $a_1 + a_2$ and all the other particles were points. In moving a distance x, the particle sweeps out a volume $V(x) = \pi(a_1 + a_2)^2 x$. On average, when the particle has traveled a mean-free path there is one collision. The average number of gas particles in the volume $V(\lambda) = \pi(a_1 + a_2)^2\lambda$ is therefore 1. The average number of particles per unit volume is C. Thus $1 = C\pi(a_1 + a_2)^2\lambda$, or

$$\lambda = \frac{1}{\pi(a_1 + a_2)^2 C}. \qquad (4.14)$$

The quantity $\pi(a_1 + a_2)^2$ is the area of a circle. It is called the *cross-section* for the collision of these particles. The concept of cross-section is used extensively in Chap. 15.

This estimation is somewhat crude in its assumption that only one molecule is moving. If all the molecules are of the same kind then the factor 1 in the numerator is replaced by $2^{-1/2} = 0.707$ (Reif 1965, p. 471).

For a gas at standard temperature and pressure, the volume of 1 mol is $22.4\ \mathrm{l} = 22.4 \times 10^{-3}\ \mathrm{m}^3$, so $C = 2.7 \times 10^{25}\ \mathrm{m}^{-3}$. If $a_1 = a_2 = 0.15$ nm, then Eq. 4.14 can be used to calculate the mean free path:

$$\begin{aligned} \lambda &= \frac{1}{(3.14)(.3 \times 10^{-9})^2\ \mathrm{m}^2 (2.7 \times 10^{25}\ \mathrm{m}^{-3})} \\ &= 0.13\ \mu\mathrm{m}. \end{aligned}$$

For a gas at standard temperature and pressure, the mean-free path is about 1000 times the molecular diameter, and the assumption of infrequent collisions is justified.

The collision time can be estimated by saying that

$$t_c = \frac{\lambda}{\overline{v}},$$

where $\overline{v}$ is the average speed of the molecules. Using the rms velocity for $\overline{v}$, we can use Eq. 4.12 to write

$$t_c \approx \lambda \left(\frac{m}{3k_B T} \right)^{1/2}. \qquad (4.15)$$

The important feature of this is the dependence on $m^{1/2}$ and on λ. For air at room temperature, $t_c = 2 \times 10^{-10}$ s.

4.5 Motion in a Liquid

The assumptions of the previous section do not hold in a liquid, in which the particle is being continually bombarded by neighbors. Blindly applying Eq. 4.14 to water, we can use the fact that 1 mol is 18 g and occupies 18 cm^3, to obtain $\lambda = 0.1$ nm, so that $a/\lambda \approx 1$, and the assumptions behind the derivation break down. Estimating the collision time with Eq. 4.15 gives a value that is a factor of 1000 less than for the gas, or 10^{-13} s.

Although these estimates of the mean-free path and the collision time are undoubtedly wrong, the concepts appear to be valid. Computer simulations of molecular collisions show that the distribution of free paths is exponential even though the mean-free path is only a fraction of a molecular diameter. In Sect. 4.12, we will regard diffusion as a random walk of the diffusing particles and relate the diffusion constant to the mean-free path and collision time. Equations 4.14 and 4.15 can then be used to show that the diffusion constant should be inversely proportional to the square of the particle radius. This has been verified experimentally for the diffusion of certain liquids. Evidence for the validity of this random-walk model for diffusion in liquids has been summarized by Hildebrand et al. (1970, pp. 36–39).

A particle in a liquid is subject to a fluctuating force $\mathbf{F}(t)$, which is random in magnitude and direction. The particle begins to move in response to this force. However, once it has begun to move, it suffers more collisions in front than behind, so the force slows it down. As the particle can neither stay at rest nor continue to move in the same direction, it undergoes a random, zig-zag motion with average translational kinetic energy $3k_BT/2$. The mean square velocity is not zero, but the mean vector velocity is zero.

For each particle, Newton's second law is $m(d\mathbf{v}/dt) = \mathbf{F}(t)$. This is not very useful as it stands. To make it more tractable, consider a particle with average velocity $\overline{\mathbf{v}}$. (The average means that an ensemble of identically prepared particles is examined.) The particle has more collisions on the front that slow it down. We therefore break up $\mathbf{F}(t)$ into two parts: an average drag force, which will be the same for all the particles in the ensemble, and a rapidly fluctuating part $\mathbf{g}(t)$, which will vary with time and from particle to particle. Newton's second law is then $m(d\mathbf{v}/dt) = (\text{drag force}) + \mathbf{g}(t)$, where $\mathbf{g}(t)$ is random in direction. The drag force will be zero when $\overline{\mathbf{v}}$ is zero. For average velocities that are not too large, it can be approximated by a linear term:

$$(\text{drag force}) = -\beta\,\overline{\mathbf{v}}.$$

With this approximation, Newton's second law is known as the *Langevin equation:*

$$m\frac{d\mathbf{v}}{dt} = -\beta\,\overline{\mathbf{v}} + \mathbf{g}(t). \tag{4.16}$$

(If the liquid is moving, the drag force will be zero when the particle has the same average velocity as the liquid. So $\overline{\mathbf{v}}$ can be interpreted as the relative velocity of the particle with respect to the liquid.) This equation often has another term in it, which does not average to zero and which represents some external force such as gravity that acts on all the particles. This approximate equation can be solved in some cases, though with difficulty, and has formed the basis for some treatments of the motion of large particles in fluids. With suitable interpretation, it can describe motion of the fluid molecules themselves.[5] In particular, when dealing with molecular motion it is necessary to consider the fact that the molecules do not move independently of one another.

For a Newtonian fluid (Eq. 1.33) with viscosity η, one can show (although it requires some detailed calculation,[6] see Problem 46 in Chap. 1) that the drag force on a spherical particle of radius a is given by

$$\mathbf{F}_{\text{drag}} = -\beta\overline{\mathbf{v}} = -6\pi\eta a\overline{\mathbf{v}}. \tag{4.17}$$

This equation is valid when the sphere is so large that there are many collisions of fluid molecules with it and when the velocity is low enough so that Reynolds number is small. This result is called *Stokes' law.*

If the sphere is not moving in an infinite medium but is confined within a cylinder, then a correction must be applied.[7] In that case, the viscous drag depends on the velocity of the spherical particle through the fluid, the average velocity of the fluid through the cylinder, and the distance of the particle from the axis of the cylinder.[8]

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[5] See, for example, Pryde (1966, p. 161).

[6] This is an approximate equation. See Barr (1931, p. 171).

[7] An early correction for particles on the axis of a cylinder is found in Barr (1931, p. 183). More recent work is by Levitt (1975), by Bean (1972), and by Paine and Scherr (1975).

[8] Stokes' law is valid for a particle in a gas if the mean free path is much less than the particle radius a, so that many collisions with neighboring molecules occur. At the other extreme, a mean free path much greater than the particle radius, the drag force turns out to be $F_{\text{drag}} = \alpha\eta a(a/\lambda)\overline{v}$. Although this will not be directly useful to us in considering biological systems, it is mentioned here to show how important it is to understand the conditions under which an equation is valid. Although the dimensions of this new equation are unchanged (we have introduced a factor a/λ, which is dimensionless), the drag force depends on a^2 instead of on a. The reason for the difference is that collisions are now infrequent and that the probability of a collision that imparts some average momentum change is proportional to the projected cross-sectional area of the sphere, πa^2. In the regime of interest to us, in which there are many collisions, we would not expect the force

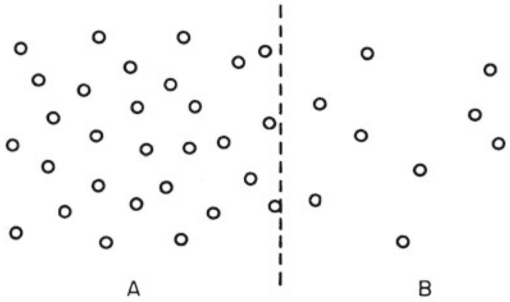

Fig. 4.7 An example of diffusion. Each molecule at A or B can wander with equal probability to the left or right. There are more molecules at A to wander to the right than there are at B to wander to the left. There is a net flow of molecules from A to B

4.6 Diffusion: Fick's First Law

Diffusion is the random movement of particles from a region of higher concentration to a region of lower concentration. The diffusing particles move independently of one another; they may collide frequently with the molecules of the fluid in which they are immersed, but they rarely collide with one another. The surrounding fluid may be at rest, in which case diffusion is the only mechanism for transport of the solute, or it may be flowing, in which case it carries the solute along with it (solvent drag). Both effects can occur together.

We first consider diffusion from a macroscopic point of view and write down an approximate differential equation to describe it. We then obtain a second equation describing diffusion by combining this with the continuity equation. After discussing some solutions to these equations, we look at the problem from a microscopic point of view, considering the random motion of the particles, and show that we get the same results.

Suppose that the surrounding solvent does not move. If the solute concentration is completely uniform, there is no net flow. As many particles wander to the left as to the right, and the concentration remains the same. There will be local fluctuations in concentration, analogous to those we have seen in the preceding chapter for fluctuations in the concentration of a gas, but that is all.

However, if the concentration is higher in region A than in region B to the right of it, there are more particles to wander to the right from A to B than there are to wander to the left from B to A (Fig. 4.7). If the problem is one-dimensional, there is no net flow if $\partial C/\partial x = 0$, but there is flow if $\partial C/\partial x \neq 0$. If the concentration difference is small, then the flux density j is linearly proportional to the concentration gradient $\partial C/\partial x$. The equation is

$$j_x = -D\frac{\partial C}{\partial x}. \tag{4.18a}$$

Constant D is called the *diffusion constant*. The units of D are m^2 s^{-1}, as may be seen by noting that the units of j are (something) m^{-2} s^{-1} and the units of $\partial C/\partial x$ are (something) m^{-4}. This relationship is called *Fick's first law of diffusion*, after Adolf Fick, a German physiologist in the last half of the nineteenth century. The minus sign shows that the flow is in the direction from higher concentration to lower concentration: if $\partial C/\partial x$ is positive, the flow is in the $-x$ direction.

If the actual process is not linear, this can be thought of as the first term of a Taylor's series expansion (Appendix D).

Fick's first law is one of many forms of the transport equation. Other forms are shown in Table 4.3. The units of the constant are different for the last three entries in the table because the quantity that appears on the right has different units than the quantity on the left. In each case, however, a fluence rate or flux density (of particles, mass, energy, electric charge, or momentum) is related to a rate of change of some other quantity with position. This rate of change is called the *gradient* of the quantity. The gradient is often called the *driving force*. The concentration gradient or driving force causes the diffusion of particles; the temperature gradient "causes" the heat flow; the electric voltage gradient "causes" the current flow; the velocity gradient "causes" the momentum flow.

The diffusive fluence rate can be related to the gradient of the chemical potential of the solute. With the notation $C_1 = C_s$ and $C_2 - C_1 = \Delta C_s$, Eq. 3.48 can be rewritten as

$$\begin{aligned}\Delta\mu_s &= k_B T \ln(C_2/C_1) = k_B T \ln(1 + \Delta C_s/C_s) \\ &\approx k_B T \Delta C_s/C_s,\end{aligned}$$

from which $\Delta C_s \approx C_s \Delta\mu_s / k_B T$, so

$$\frac{\partial C_s}{\partial x} = \frac{C_s}{k_B T}\frac{\partial \mu_s}{\partial x}$$

and

$$j_{sx} = -\frac{D C_s}{k_B T}\frac{\partial \mu_s}{\partial x}. \tag{4.18b}$$

The solute flux density is proportional to the diffusion constant, the solute concentration, and the gradient in the chemical potential per solute particle.

In three dimensions, the flow of particles can point in any direction and have components j_x, j_y, and j_z. An equation can be written for each component that is analogous to Eq. 4.18a or 4.18b. We can write one vector equation instead

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to depend on λ. We hope that this will convince you of the danger in using someone else's equation without understanding it.

Table 4.3 Various forms of the transport equation

Substance flowing	Equation	Units of j	Units of the constant
Particles	$j_s = -D \dfrac{\partial C}{\partial x}$	$\mathrm{m^{-2}\ s^{-1}}$	$\mathrm{m^2\ s^{-1}}$
Mass	$j_m = -D \dfrac{\partial \rho}{\partial x}$	$\mathrm{kg\ m^{-2}\ s^{-1}}$	$\mathrm{m^2\ s^{-1}}$
Heat	$j_H = -\kappa \dfrac{\partial T}{\partial x}$	$\mathrm{J\ m^{-2}\ s^{-1}}$ or $\mathrm{kg\ s^{-3}}$	$\mathrm{J\ K^{-1}\ m^{-1}\ s^{-1}}$
Electric charge	$j_e = -\sigma \dfrac{\partial V}{\partial x}$	$\mathrm{C\ m^{-2}\ s^{-1}}$	$\mathrm{C\ m^{-1}\ s^{-1}\ V^{-1}}$ or $\Omega^{-1}\ \mathrm{m^{-1}}$
Viscosity (y component of momentum transported in the x direction)	$j_p = -\eta \dfrac{\partial v_y}{\partial x}$	$\mathrm{N\ m^{-2}}$ or $\mathrm{kg\ m^{-1}\ s^{-2}}$	$\mathrm{kg\ m^{-1}\ s^{-1}}$ or Pa s

of three equations for the three components by defining $\hat{\mathbf{x}}$, $\hat{\mathbf{y}}$, and $\hat{\mathbf{z}}$ to be unit vectors along the axes. Then

$$\begin{aligned} &j_x\hat{\mathbf{x}} + j_y\hat{\mathbf{y}} + j_z\hat{\mathbf{z}} \\ &= -D\left(\frac{\partial C}{\partial x}\hat{\mathbf{x}} + \frac{\partial C}{\partial y}\hat{\mathbf{y}} + \frac{\partial C}{\partial z}\hat{\mathbf{z}}\right). \end{aligned}$$

We have created a vector that depends on $C(x, y, z, t)$ by performing the indicated differentiations on C and multiplying the results by the appropriate unit vectors. This vector function is the gradient of C in three dimensions:

$$\operatorname{grad} C = \nabla C = \frac{\partial C}{\partial x}\hat{\mathbf{x}} + \frac{\partial C}{\partial y}\hat{\mathbf{y}} + \frac{\partial C}{\partial z}\hat{\mathbf{z}}. \qquad (4.19)$$

Fick's first law with this notation is

$$\mathbf{j} = -D \operatorname{grad} C = -D\,\nabla C. \qquad (4.20)$$

Remember that this is simply shorthand for three equations like Eq. 4.18a. If you feel a need to review vector calculus, which deals with the divergence and gradient, an excellent text is the one by Schey (2004).

4.7 The Einstein Relationship Between Diffusion and Viscosity

Before we can apply Fick's first law to real problems, we must determine the value of the diffusion constant D. The experimental determination of D is often based on Fick's second law of diffusion, which combines the first law with the equation of continuity and is discussed in the next section. It is closely related to the viscosity, as was first pointed out by Albert Einstein. This is not surprising, since diffusion is caused by the random motion of the particles under the bombardment of neighboring atoms, and viscous drag is also caused by the bombardment by neighboring atoms. What is remarkable is that a general relationship between them can be deduced quite easily by imagining just the right sort of experiment.

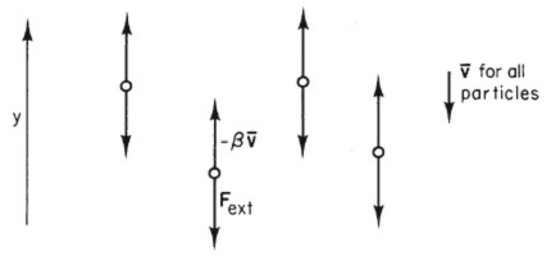

Fig. 4.8 Particles drifting under the influence of a downward force $\mathbf{F}_{\text{ext}}$

Consider a collection of particles uniformly suspended in a fluid at rest. Imagine that each particle is suddenly subjected to an external force $\mathbf{F}_{\text{ext}}$ (such as gravity) that acts in the $-y$ direction, as shown in Fig. 4.8. The particles will all begin to drift downward, speeding up until the upward viscous force on them balances the external force: $\mathbf{F}_{\text{ext}} - \beta\,\bar{\mathbf{v}} = 0$. In terms of magnitudes, $F_{\text{ext}} = \beta v$.

Because these particles are all moving downward, there is a downward flux density. With reference to Fig. 4.9, the number of particles crossing area S in time Δt will be those within the cylinder of height $\overline{v}\Delta t$. That number is the concentration times the volume $(S\overline{v}\Delta t)$. Dividing by S and Δt gives

$$\mathbf{j}_{\text{drift}} = -\overline{v}C(y)\hat{\mathbf{y}}.$$

As the particles move down, they deplete the upper region of the fluid and cause a concentration gradient. This concentration gradient causes an upward diffusion of particles, with a flux density given by

$$\mathbf{j}_{\text{diff}} = -D\,\frac{\partial C}{\partial y}\hat{\mathbf{y}}.$$

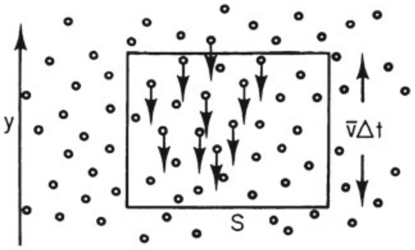

Fig. 4.9 Calculating the fluence rate of particles drifting downward

Equilibrium will be established when these two flux densities are equal in magnitude: $|\mathbf{j}_{\text{drift}}| = |\mathbf{j}_{\text{diff}}|$,

$$|\overline{v}C(y)| = \left| D\frac{\partial C}{\partial y} \right|. \tag{4.21}$$

But equilibrium means that the particles have a Boltzmann distribution in y, because their potential energy increases with y (work is required to lift them in opposition to $\mathbf{F}_{\text{ext}}$). For a constant $\mathbf{F}_{\text{ext}}$ independent of y, the energy is $u(y) = F_{\text{ext}}y$, where F_{ext} is the magnitude of the force. The concentration is

$$C(y) = C(0)e^{-F_{\text{ext}}y/k_BT}.$$

Therefore

$$\frac{\partial C}{\partial y} = -\frac{F_{\text{ext}}}{k_BT}C(y).$$

Inserting this in Eq. 4.21 gives $\overline{v} = DF_{\text{ext}}/k_BT$ or $D = \overline{v}k_BT/F_{\text{ext}}$. In equilibrium, the magnitude of F_{ext} is equal to the magnitude of the viscous force $\mathbf{f}$. Therefore $D = k_BT\overline{v}/f$. Since the viscous force is proportional to the velocity, $|f| = |\beta\overline{v}|$,

$$D = \frac{k_BT}{\beta}. \tag{4.22}$$

The derivation of this equation required only that the velocities be small enough so that the linear approximations for Fick's first law and the viscous force are valid. It is independent of the nature of the particle or its size. If in addition the diffusing particles are large enough so that Stokes' law is valid, then $\beta = 6\pi\eta a$ and

$$D = \frac{k_BT}{6\pi\eta a}. \tag{4.23}$$

The diffusion constant is inversely proportional to the fluid viscosity and the radius of the particle.

Combining Eqs. 4.18b and 4.22 shows that in terms of the chemical potential,

$$j_{sx} = -\frac{C_s}{\beta}\frac{\partial \mu_s}{\partial x}.$$

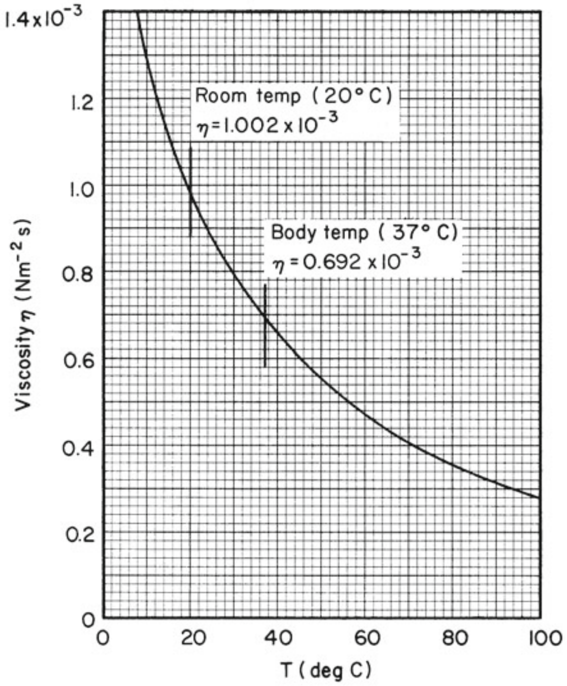

Fig. 4.10 Viscosity of water at various temperatures. (Data are from Weast 1972, p. F-36)

Sometimes minus the gradient of the chemical potential is called the driving force. To see why, note that for solvent drag, $j_s = C_s\overline{v}$, so $\beta\overline{v} = -\partial\mu_s/\partial x$ is the driving force.

The viscosity of water varies rapidly with temperature, as shown in Fig. 4.10. These values of viscosity and Eq. 4.23 have been used to calculate the solid lines for D vs a shown in Fig. 4.11. Various experimental values are also shown. The diffusion constant increases rapidly with temperature, so that care must be taken to specify the temperature at which the data are obtained. Since not all the molecules are spherical, there is some uncertainty in the value of the particle radius a.

Figure 4.12 is a plot of D for particles diffusing in water at 20 °C (293 K) vs. molecular weight M. Although the solid line provides a rough estimate of D if M is known, scatter is considerable because of varying particle shape. DNA lies a factor of 10 below the curve, presumably because it is partially uncoiled and presents a larger size than other molecules of comparable molecular weight.

It is possible to measure the *self-diffusion* of water in water by using a few water molecules in which one hydrogen atom is radioactive and measuring how they diffuse. Water has an unusually large self-diffusion constant.[9]

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[9] For self-diffusion (such as radioactively tagged water in water), a hydrodynamic calculation shows that $\beta = 4\pi\eta a$ instead of $6\pi\eta a$ (Bird et al. 1960, p. 514ff.).

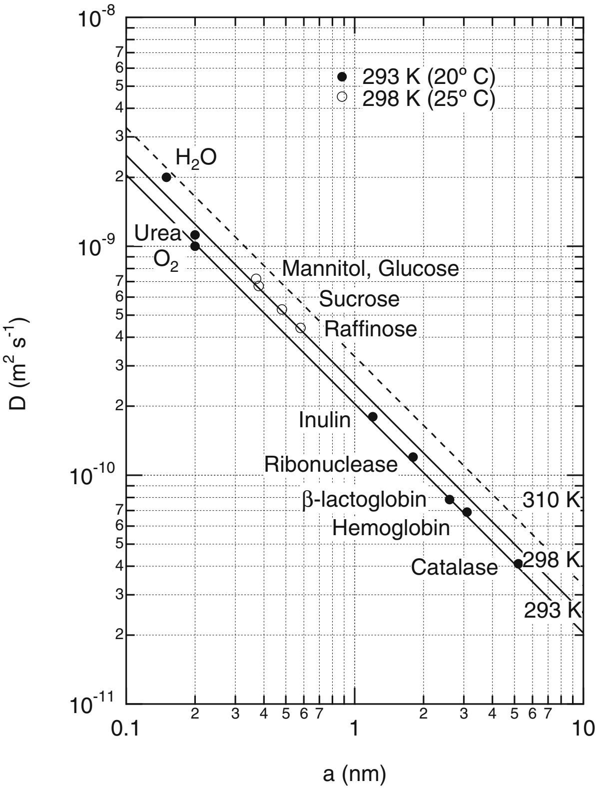

Fig. 4.11 Diffusion constant versus sphere radius a for diffusion in water at three different temperatures. Experimental data at 20 °C (293 K) are from Benedek and Villars (2000, Vol. 2, p. 122). Data at 25 °C (298 K) are from Weast (1972, p. F-47)

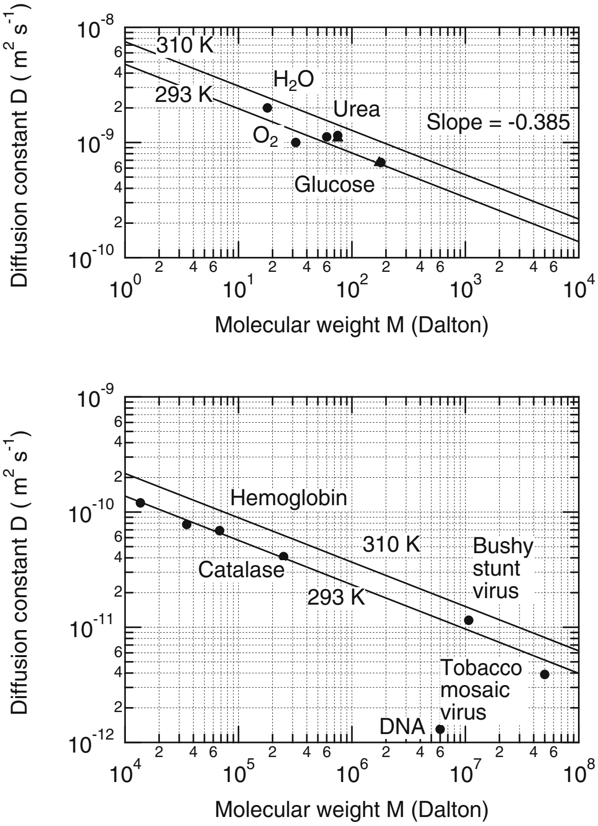

Fig. 4.12 Diffusion constant versus molecular weight in daltons. (One dalton is the mass of one hydrogen atom.) Data at 293 K are from Benedek and Villars (2000, Vol. 2, p. 122). The 293-K solid line was drawn by eye through the data; the line at 310 K was drawn parallel to it using the temperature change in Eq. 4.23. Data scatter around the line by about 30%, with occasional larger departures

If all of the molecules shown had the same density, then their radius would depend on $M^{1/3}$ and the line would have a slope of $-\frac{1}{3}$. The slope is steeper than this, suggesting that the molecules are larger for large M than constant density would predict. This increase in size may be partially attributable to water of hydration. The precise values of diffusion constants depend on many details of the particle structure; however, the lines in Fig. 4.12 provide an order-of-magnitude estimate.

The assumption that the flux depends linearly on the concentration gradient was an approximation. The diffusion constant is found, as a result, to be somewhat concentration dependent.

4.8 Fick's Second Law of Diffusion

Fick's first law of diffusion, Eq. 4.18a, is the observation that for small concentration gradients, the diffusive flux density is proportional to the concentration gradient: $j_x = -D\,\partial C/\partial x$. If this is differentiated, one obtains $\partial j_x/\partial x = -D\,\partial^2 C/\partial x^2$. Similar equations hold for the y and z directions. The equation of continuity, Eq. 4.2, is

$$-\frac{\partial C}{\partial t} = \frac{\partial j_x}{\partial x} + \frac{\partial j_y}{\partial y} + \frac{\partial j_z}{\partial z}.$$

If we combine these two equations, we get *Fick's second law of diffusion,* also known as the *diffusion equation*:

$$\frac{\partial C}{\partial t} = D\left(\frac{\partial^2 C}{\partial x^2} + \frac{\partial^2 C}{\partial y^2} + \frac{\partial^2 C}{\partial z^2}\right). \tag{4.24}$$

The first law relates the flux of particles to the concentration gradient. The second law tells how the concentration at a point changes with time. It combines the first law and the equation of continuity. The function on the right-hand side of Eq. 4.24,

$$\frac{\partial^2 C}{\partial x^2} + \frac{\partial^2 C}{\partial y^2} + \frac{\partial^2 C}{\partial z^2},$$

is called the *Laplacian* of C. It is often abbreviated as $\nabla^2 C$ (read "del squared C") in American textbooks or ΔC in

European books. It is given in other coordinate systems in Appendix L.

In principle, if $C(x, y, z)$ is known at $t = 0$, Eq. 4.24 can be solved for $C(x, y, z, t)$ at all later times. (We develop a general, and sometimes useful, equation for doing this below.) We may also look at this equation as a local equation, telling how C changes with time at some point if we know how the concentration changes with position in the neighborhood of that point. The change of concentration with position determines the flux **j**. The changes in flux with position determine how the concentration changes with time.

There is extensive literature on how to solve the diffusion equation (or the heat-flow equation, which is the same thing).[10] Instead of discussing a large number of techniques, we show by substitution that a Gaussian or normal distribution function, spreading in a certain way with time, is one solution to Eq. 4.24. In Sect. 4.14, we independently derive the same solution from a random-walk model of diffusion. An important feature of the Gaussian solution is that the center of the distribution of concentration does not move.

For simplicity, consider the one-dimensional case. Take the distribution to be centered at the origin and find those conditions under which[11]

$$C(x,t) = \frac{N}{\sqrt{2\pi}\sigma(t)} e^{-x^2/2\sigma^2(t)}. \tag{4.25}$$

We can view the one-dimensional case in either of two ways. If it represents diffusion along a pipe, then $C(x, t)$ is the number of particles per unit length in a slice between x and $x + dx$, and N is the total number of particles. If it represents a three-dimensional problem with concentration changing only in the x direction, then $C(x, t)$ is the number of particles per unit volume and N is the number of particles per unit area.

Eq. 4.25 is a solution to the one-dimensional version of Eq. 4.24:

$$\frac{\partial C}{\partial t} = D \frac{\partial^2 C}{\partial x^2}. \tag{4.26}$$

To check this, we will need various derivatives of Eq. 4.25. They can be evaluated using the chain rule:

$$\begin{aligned}
\frac{\partial C}{\partial t} &= \frac{N}{\sqrt{2\pi}} \left(-\frac{1}{\sigma^2} e^{-x^2/2\sigma^2} + \frac{x^2}{\sigma^4} e^{-x^2/2\sigma^2} \right) \frac{d\sigma}{dt}, \\
\frac{\partial C}{\partial x} &= -\frac{N}{\sqrt{2\pi}} e^{-x^2/2\sigma^2} \frac{x}{\sigma^3}, \\
\frac{\partial^2 C}{\partial x^2} &= \frac{N}{\sqrt{2\pi}} \left(-\frac{1}{\sigma^3} e^{-x^2/2\sigma^2} + \frac{x}{\sigma^3} e^{-x^2/2\sigma^2} \frac{x}{\sigma^2} \right).
\end{aligned}$$

When these are substituted in Eq. 4.26, the result is

$$\begin{aligned}
&\frac{N}{\sqrt{2\pi}\sigma^2} e^{-x^2/2\sigma^2} \left(-1 + \frac{x^2}{\sigma^2} \right) \frac{d\sigma}{dt} \\
&= D \frac{N}{\sqrt{2\pi}\sigma^3} e^{-x^2/2\sigma^2} \left(-1 + \frac{x^2}{\sigma^2} \right).
\end{aligned}$$

We can divide both sides of this equation by

$$\frac{N}{\sqrt{2\pi}\sigma^2} e^{-x^2/2\sigma^2}$$

because this factor is never zero. The result is

$$\left(\frac{x^2}{\sigma^2} - 1 \right) \frac{d\sigma}{dt} = \frac{D}{\sigma} \left(\frac{x^2}{\sigma^2} - 1 \right).$$

We can divide by $\left(x^2/\sigma^2 - 1\right)$ for all values of x except $x = \pm\sigma$. These values of x are where the second derivative of C vanishes; at these points, $\partial C/\partial t = 0$ for any value of σ. At all other points, the solution will satisfy the equation only if

$$\sigma \frac{d\sigma}{dt} = D.$$

This can be integrated to give

$$\int \sigma \, d\sigma = \int D \, dt$$

or

$$\frac{1}{2}\sigma^2(t) = Dt + \text{const.}$$

Multiply through by 2 and observe that $\sigma^2(0) = 2\text{const}$, so that

$$\sigma^2(t) = 2Dt + \sigma^2(0). \tag{4.27}$$

If the concentration is initially Gaussian with variance $\sigma^2(0)$, after time t it will still be Gaussian, centered on the same point, with a larger variance given by Eq. 4.27. Figure 4.13 shows this spreading in a typical case. At still earlier times, the concentration would have been even more narrowly peaked. In the limit when $\sigma(t)$ is zero, all the particles are at the origin, giving an infinite concentration. This is, of course, impossible. However, all the particles could be very close to the origin, giving a very tall, narrow curve for $C(x)$.

The width of the curve, determined by σ, increases as the square root of the time. A square-root increase is less rapid than a linear increase, reflecting the fact that as the particles spread out, the concentration does not change as rapidly with distance, so that the flux and the rate of spread decrease.

Note that the rate of change of concentration with time depends on the second derivative of the concentration with distance. This is because the rate of buildup is the flux into a region at some surface minus the flux out through a nearby

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[10] See, for example, Crank (1975) or Carslaw and Jaeger (1959).

[11] The properties of the Gaussian function, Eq. 4.25, are discussed in Appendix I.

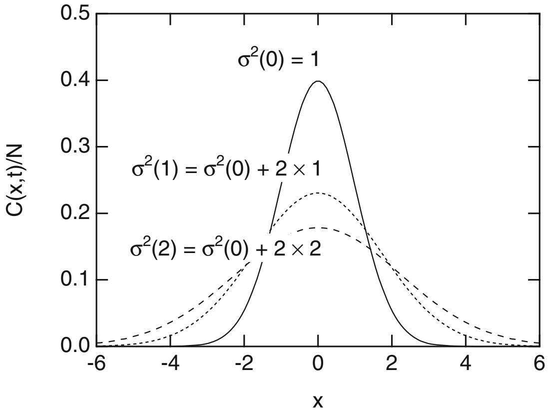

Fig. 4.13 Spreading of particles by diffusion assuming $D = 1$

surface; each flux is proportional to the gradient of the concentration, so the buildup is proportional to the difference in gradients or the second derivative.

In the problems at the end of this chapter, you will discover that diffusion of small particles through water for a distance of 1 μm takes about 1 ms, and diffusion through 100 μm takes 100^2 times as long, or 10 s. The times are even longer for larger particles. Thus, diffusion is an effective mode of transport for distances comparable to the size of a cell, but it is too slow for larger distances. This is why multicelled organisms evolve circulatory systems.

4.9 Time-Independent Solutions

In this section, we develop general solutions for diffusion and solvent drag when particles are conserved and the concentration and fluence rate are not changing with time. The system is in the steady state. The continuity equation, Eq. 4.8, then becomes div $\mathbf{j} = 0$. We consider the solutions for C and $\mathbf{j}$ in one, two, and three dimensions when the symmetry is such that $\mathbf{j}$ depends on only one position coordinate, x or r. These solutions are sometimes appropriate models for limited regions of space. There is always some other region of space, serving as a source or sink for the particles that are diffusing, where the model does not apply.

The behavior of $\mathbf{j}$ can be deduced from the continuity equation. In one dimension, such as flow in a pipe or between two infinite planes, the continuity equation is

$$\frac{dj_x}{dx} = 0, \tag{4.28}$$

which has a solution $j_x = b_1$ where b_1 is a constant. (The subscript denotes the constant for the one-dimensional case.) The total flux or current i is constant, so

$$j_x = \frac{i}{S}, \tag{4.29}$$

where S is the area perpendicular to the flow.

In two dimensions, we consider a problem with cylindrical symmetry and consider only flow radially away from or toward the z-axis. In that case, the equation in Table L.1 for the divergence becomes

$$\frac{1}{r}\frac{d}{dr}(rj_r) = 0, \tag{4.30}$$

from which

$$\frac{d}{dr}(rj_r) = 0. \tag{4.31}$$

This means that (rj_r) is constant, or

$$j_r = \frac{b_2}{r}. \tag{4.32}$$

This is valid everywhere except along the z-axis, where there is a source of particles and the divergence is not zero. The total current i leaving a region of length L parallel to the z axis is also constant,

$$j_r = \frac{i}{2\pi Lr}. \tag{4.33}$$

In three dimensions with spherical symmetry, the radial component of the divergence is

$$\frac{1}{r^2}\frac{d}{dr}(r^2 j_r) = 0,$$

from which

$$\frac{d}{dr}(r^2 j_r) = 0, \tag{4.34}$$

so that

$$j_r = \frac{b_3}{r^2} \tag{4.35}$$

or

$$j_r = \frac{i}{4\pi r^2}. \tag{4.36}$$

This is valid everywhere except at the origin, where there is a source of particles.

These results depend only on continuity, time independence, and the assumed symmetry. They are true for diffusion, solvent drag, or any other process. Note the progression in going to higher dimensions: in n dimensions $r^{n-1}j_r$ is constant.

Now consider how the concentration varies in the two limiting cases of pure solvent drag and pure diffusion. (Sect. 4.12 discusses what happens when both transport modes are important.)

For solvent drag, the velocity of the solvent is the volume flux density $\mathbf{j}_v$, which also satisfies the continuity equation. In one dimension $j_v = i_v/S$. In two dimensions $j_v = i_v/2\pi Lr$, and in three dimensions $j_v = i_v/4\pi r^2$. In each case

$$C_s = \frac{j_s}{j_v} = \frac{i_s}{i_v}. \tag{4.37}$$

Since C_s is constant, there is no diffusion.

For the case of diffusion, $\mathbf{j} = -D\nabla C$. In one dimension this becomes

$$\frac{dC}{dx} = -\frac{i}{SD},$$

which is integrated to give

$$C = -\frac{i}{SD}x + b_1,$$

where b_1 is the constant of integration. The concentration varies linearly in the one-dimensional case. If i is positive (flow in the $+x$ direction), C decreases as x increases. Often the concentration is known at x_1 and x_2, and one wants to know the current. We can write

$$C_1 = -\frac{i}{SD}x_1 + b_1,$$
$$C_2 = -\frac{i}{SD}x_2 + b_1,$$

and solve for i:

$$i = \frac{(C_1 - C_2)}{(x_2 - x_1)}SD. \tag{4.38a}$$

In two dimensions

$$\frac{dC}{dr} = -\frac{i}{2\pi LD}\frac{1}{r},$$

and the solution is

$$C(r) = -\frac{i}{2\pi LD}\ln r + b_2.$$

We can again solve for the current when the concentrations are known at two different radii:

$$i = \frac{2\pi LD(C_1 - C_2)}{\ln(r_2/r_1)} = \frac{2\pi LD(C_2 - C_1)}{\ln(r_1/r_2)}. \tag{4.38b}$$

Diffusion in two dimensions with cylindrical symmetry has been used to model the concentration of substances in the region between two capillaries.

In three dimensions, the diffusion equation is

$$\frac{dC}{dr} = -\frac{i}{4\pi Dr^2},$$

which has a solution

$$C(r) = \frac{i}{4\pi Dr} + b_3.$$

The current in terms of the concentration is

$$i = \frac{4\pi D\,[C(r_1) - C(r_2)]}{1/r_1 - 1/r_2}. \tag{4.38c}$$

The three-dimensional case is worth further discussion, because it can help us to understand the diffusion of nutrients to a single spherical cell or the diffusion of metabolic waste products away from the cell. Consider the case in which the cell has radius $r_1 = R$, the concentration at the cell surface is C_0, and the concentration at infinity is zero. Then

$$i = 4\pi D\,C_0 R, \tag{4.39a}$$

$$C(r) = \frac{C_0 R}{r}, \tag{4.39b}$$

$$j_r = \frac{C_0 DR}{r^2}. \tag{4.39c}$$

The particle current depends on the radius of the cell, R, not on R^2. This very important result is not what we might naively expect. Diffusion-limited flow of solute in or out of the cell is proportional not to the cell surface area, but to the cell radius. The reason is that the particle movement is limited by diffusion in the region around the cell, and as the cell radius increases, the concentration gradient decreases. (It is possible for the rate of particle migration into the cell to be proportional to the surface area of the cell if some other process, such as transport through the cell membrane, is the rate-limiting step.)

If diffusion is toward the cell, the concentration is C_0 infinitely far away. At the cell surface, every diffusing molecule that arrives is assumed to be captured, and the concentration is zero. The solutions are then

$$i = -4\pi DC_0 R, \tag{4.40a}$$

$$C(r) = C_0\,(1 - R/r)\,, \tag{4.40b}$$

$$j_r(r) = -\frac{C_0 DR}{r^2}. \tag{4.40c}$$

4.10 Example: Steady-State Diffusion to a Spherical Cell and End Effects

In the preceding section, we considered diffusion from infinitely far away to the surface of a spherical cell where the concentration was zero. We now add the effect of steady-state diffusion through a series of pores or channels in the cell membrane. This will lead to a very important result: it does not require very many pores per unit area in the cell membrane to "keep up with" the rate of diffusion of chemicals toward or away from the cell. The result is important for understanding how cells acquire nutrients, how bacteria move in response to chemical stimulation (chemotaxis), and how the leaves of plants function.

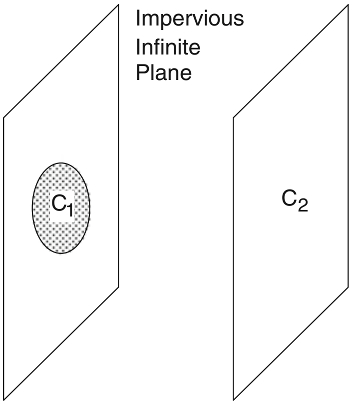

Fig. 4.14 The diffusion flux from the disk of radius a and concentration C_1 to the infinite sheet where the concentration is C_2 is given by $i = 4Da(C_1 - C_2)$

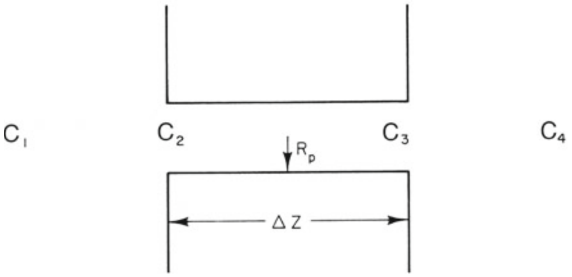

Fig. 4.15 End effects in diffusion through a pore

To develop the model we need one more result: the current due to diffusion from a disk of radius a where the concentration is C_1 to a plane far away where the concentration is C_2. The disk is embedded in the surface of an impervious plane as shown in Fig. 4.14, so particles cannot cross to the region behind the disk. The current is (Eq. 6.97)

$$i = 4Da\,(C_1 - C_2). \tag{4.41}$$

It is proportional to the radius of the disk, not its surface area. (Obtaining this result requires solving the diffusion equation in three dimensions. See Carslaw and Jaeger (1959), p. 215.)

Consider diffusion through a pore of radius R_p which pierces a membrane of thickness ΔZ, including diffusion in the medium on either side of the membrane (Fig. 4.15). If the material on either side were well stirred, there would be a uniform concentration C_1 on the left and C_4 on the right. Because it is not stirred, there is diffusion in the exterior fluid. Let C_1 and C_4 be measured far away, and call the concentrations at the ends of the pore C_2 on the left and C_3 on the right.

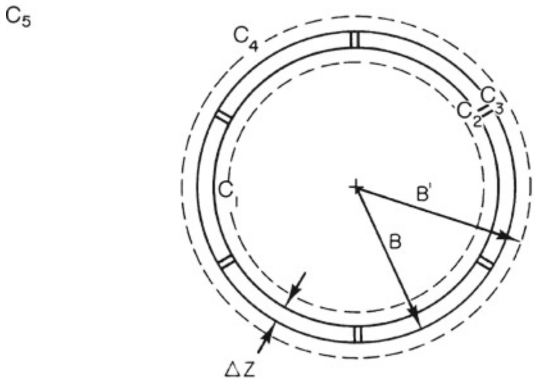

Fig. 4.16 Diffusive end effects for a spherical cell pierced by pores

Equation 4.38a gives the diffusion flux within the pore

$$i = \frac{\pi R_p^2 D\,(C_2 - C_3)}{\Delta Z}. \tag{4.42}$$

Diffusion from C_1 to C_2 is given by Eq. 4.41. It is

$$i = 4D\,R_p(C_1 - C_2), \tag{4.43}$$

while from C_3 to C_4, it is

$$i = 4D\,R_p(C_3 - C_4). \tag{4.44}$$

In the steady state, there is no buildup of particles and i is the same in each region. We can solve Eqs. 4.42–4.44 simultaneously to relate i to concentrations C_1 and C_4:

$$i = \frac{\pi R_p^2\,D}{\Delta Z + 2\pi R_p/4}(C_1 - C_4). \tag{4.45}$$

This has the same form as Eq. 4.42, except that the membrane thickness has been replaced by an effective thickness

$$\Delta Z' = \Delta Z + 2\frac{\pi R_p}{4}. \tag{4.46}$$

An extra length $\pi R_p/4$ has been added at each end to correct for diffusion in the unstirred layer on each side of the pore. This correction is important when the pore length is less than two or three times the pore radius.

Now consider diffusion in or out of the spherical cell shown in Fig. 4.16. The radius of the cell is B. The membrane has thickness ΔZ and is pierced by a total of N pores, each of radius R_p. Within the cell, we do not know the details of the concentration distribution, since they depend on what sort of chemical reactions are taking place and where. But we will assume that at the radius where diffusion to the pores becomes important, the concentration is C_1. At the inner face of each pore it is C_2, at the outer face it is C_3, and over an approximately spherical surface of radius B' it is C_4. Far away, the concentration is C_5. As a result, there are four separate regions in which we must consider diffusion. The first is from C_1 to the opening of each pore; the second is through the pore; third, there is diffusion from the outer face of each pore to C_4; and, finally, there is diffusion from the spherical object of radius B' to the surrounding medium.

4.10.1 Diffusion Through a Collection of Pores, Corrected

The first three processes are taken into account by applying the end correction to each end of the pores. The flow through one pore is, using Eq. 4.45,

$$i_{\text{pore}} = \frac{\pi R_p^2 D}{\Delta Z'}(C_1 - C_4), \tag{4.47}$$

where $\Delta Z'$ is given by Eq. 4.46. Since there are N pores in all, the total flow through the cell membrane is

$$i_{\text{cell}} = N i_{\text{pore}} = \frac{N\pi R_p^2 D}{\Delta Z'}(C_1 - C_4). \tag{4.48}$$

The diffusion from C_4 to infinity is given by Eq. 4.38c.

$$i_{\text{cell}} = 4\pi D\, B'(C_4 - C_5), \tag{4.49}$$

where B' is the effective radius for diffusion to the surrounding medium. It is slightly larger than B. If we equate Eqs. 4.48 and 4.49, solve for C_4 and substitute this result back in Eq. 4.49, we get

$$i_{\text{cell}} = \frac{4\pi D B' N R_p^2}{N R_p^2 + 4B'\Delta Z'}(C_1 - C_5). \tag{4.50}$$

This can be rewritten as

$$i_{\text{cell}} = \frac{N\pi R_p^2 D}{\Delta Z_{\text{eff}}}(C_1 - C_5), \tag{4.51}$$

where

$$\Delta Z_{\text{eff}} = \Delta Z + 2\frac{\pi R_p}{4} + N\frac{R_p^2}{4B'}. \tag{4.52}$$

The first term in ΔZ_{eff} is the membrane thickness. The second term corrects for diffusion from the end of each pore to the surrounding fluid; the last corrects for diffusion away from the cell into the surrounding medium. The third term can be expressed as

$$\frac{N R_p^2}{4B'} = \frac{B}{B'} B f,$$

where

$$f = \frac{N\pi R_p^2}{4\pi B^2} \tag{4.53}$$

is the fraction of the cell surface occupied by pores.

We now assume that $B = B'$. (Problem 33 shows that the difference is usually very small.) The effective pore length is then

$$\Delta Z_{\text{eff}} = \Delta Z + 2\left(\frac{\pi R_p}{4}\right) + Bf. \tag{4.54}$$

Equations 4.51–4.54 treat the problem as diffusion through a collection of N pores, corrected for diffusion outside the pore by increasing the length of the pore.

4.10.2 Diffusion from a Sphere, Corrected

It is also useful to write these results as the equation for diffusion to or from a sphere, Eqs. 4.39, corrected for the diffusion through the cell membrane. Writing it in this form gives us insight into how much of the cell membrane must be occupied by pores for efficient particle transfer. Solve Eq. 4.53 for $N R_p^2$ and substitute the result in Eq. 4.50. The result is

$$\begin{aligned} i_{\text{cell}} &= \frac{4\pi D\, B' B^2\, f\, (C_1 C_5)}{B^2 f + B'\Delta Z'} \\ &= 4\pi B D\,(C_1 - C_5)\left(\frac{B'}{B}\right)\frac{f}{f + (B'/B)(\Delta Z'/B)}. \end{aligned} \tag{4.55}$$

This has the form of diffusion to the sphere multiplied by a correction factor. With B'/B again approximated by unity, the correction factor is

$$\frac{f}{f + \Delta Z'/B}.$$

The correction factor is zero when f is zero and becomes nearly unity when the entire cell surface is covered by pores.

4.10.3 How Many Pores Are Needed?

We now ask what fraction of the cell's surface area must be occupied by pores. The cell will receive half the maximum possible diffusive flow when the fraction $f = \Delta Z'/B$. For a typical cell with $B = 5$ μm and $\Delta Z = 5$ nm, $f = 0.001$. This is a surprisingly small number, but it means that there is plenty of room on the cell surface for different kinds of pores. There are two ways to understand why this number is so small. First, we can regard the ratio of concentration difference to flow as a resistance, analogous to electrical resistance. The total resistance from the inside of the cell to infinity is made up of the resistance from the outside of the cell to infinity plus the resistance of the parallel combination of N pores. Once the resistance of this parallel combination is equal to the resistance from the cell to infinity, adding more pores in parallel does not change the overall resistance very much. The second way to look at it is in terms of the random walks of the diffusing solute molecules. Once a solute molecule has diffused into the neighborhood of the cell, it undergoes many random walks. When it strikes the cell membrane, it wanders away again, to return shortly and strike the cell membrane someplace else. If the first contact is not at a pore, there are more opportunities to strike a pore on a subsequent contact with the surface.

4.10.4 Other Applications of the Model

The same sort of analysis that we have made here can be applied to a plane surface area, such as the underside of a leaf (Meidner and Mansfield 1968) and to a cylindrical geometry, such as a capillary wall.

The analysis can also be applied to the problem of bacterial chemotaxis—the movement of bacteria along concentration gradients. This problem has been discussed in detail by Berg and Purcell (1977).[12] The cell detects a chemical through some sort of chemical reaction between the chemical and the cell. Suppose that the reaction takes place between the chemical and a binding site of radius R_p on the surface of the cell. We want to know what fraction of the surface area of the cell must be covered by binding sites. This is similar to the diffusion problem of Eq. 4.55, except that if the binding site is on the surface of the cell, there is no diffusion through a pore of length ΔZ. The effective pore length $\Delta Z'$ is just the end correction for one end of the pore, $\pi R_p/4$. Half of the maximum possible flow to the binding site occurs when

$$f = \pi R_p / 4B.$$

A typical bacterium might have a radius $B = 1$ µm; the binding site might have a radius of a few atoms or 1 nm. With these values $f = 7.9 \times 10^{-4}$. The number of sites would be $f 4\pi B^2/\pi R_p^2 = \pi B/R_p = 3000$. There is plenty of room on the cell surface for many different binding sites, each specific for a particular chemical.

An *E. coli* cell typically travels 10–20 body lengths per second. It detects concentration gradients as changes with time. Because of this, Berg and Purcell concluded that a uniform distribution of chemoreceptors over the surface of the cell would be optimum. It would give the highest probability of capture of a chemical molecule that wandered near the cell. However, studies of *E. coli* have shown that the receptors are located near the poles of the cell [Maddock and Shapiro (1993); see also the comment by Parkinson and Blair (1993), who point out that the reduced efficiency of sensors could make sense if "eating" or transport into the cell is more important than "smelling."]

The Berg–Purcell model has been extended to provide a time-dependent solution and allow the receptors not to be perfectly absorbing (Zwanzig and Szabo 1991) and also to have a process in which the molecules attach to the membrane and then diffuse in the two-dimensional membrane surface (Wang et al. 1992; Axelrod and Wang 1994).

4.11 Example: A Spherical Cell Producing a Substance

Here is a simple model that extends the arguments of Sect. 4.9 to develop a steady-state solution for a spherical cell excreting metabolic products. The cell has radius R. The concentration of some substance inside the cell is $C(r)$, independent of time t and the spherical coordinate angles θ and ϕ. (Spherical coordinates are described in Appendix L.) The substance is produced at a constant rate Q particles per unit volume per second throughout the cell and leaves through the surface of the cell at a constant fluence rate $j(R)$, independent of t, θ, and ϕ. Assume that all transport is by pure diffusion and the diffusion constant for this substance is D everywhere inside and outside the cell. The material inside the cell is not well stirred. (For this model we assume that the cell membrane does not affect the transport process. We could make the model more complicated by introducing the features described in Sect. 4.10.) With these assumptions, the cell can be modeled as an infinite homogeneous medium with diffusion constant D that contains a spherical region producing material at rate Q per unit volume per second.

We first find the concentration $C(r)$ inside and outside the cell by using a technique that only works because of the spherical symmetry. We use the continuity equation in the form Eq. 4.10b. Because the concentration is not changing with time, the total amount of material flowing through a spherical surface of radius r is equal to the amount produced within that sphere. For $r < R$

$$4\pi r^2 j(r) = 4\pi r^3 Q/3,$$
$$j(r) = Qr/3.$$

For $r > R$

$$4\pi r^2 j(r) = 4\pi R^3 Q/3,$$
$$j(r) = QR^3/3r^2.$$

Using the fact that $j(r) = -D dC/dr$, we obtain for $r < R$

$$\frac{dC}{dr} = -\frac{Q}{3D} r,$$
$$C(r) = -\frac{Qr^2}{6D} + b_1,$$

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[12] See also Berg (1975, 1983) and Purcell (1977).

where b_1 is the constant of integration. For $r > R$,

$$\frac{dC}{dr} = -\frac{QR^3}{3Dr^2},$$
$$C(r) = \frac{QR^3}{3Dr} + b_2.$$

The fact that the concentration must be zero far from the cell means that $b_2 = 0$. Matching the two expressions at $r = R$ gives

$$-QR^2/6D + b_1 = QR^2/3D,$$
$$b_1 = QR^2/2D,$$

so that

$$C(r) = \begin{cases} \dfrac{Q}{6D}(3R^2 - r^2), & r \le R \\ \dfrac{QR^3}{3Dr}, & r \ge R. \end{cases}$$

The other method is more general and can be extended to problems that do not have spherical symmetry. We find solutions to Fick's second law, modified to include the production term Q and with the concentration not changing with time:

$$0 = \frac{\partial C}{\partial t} = D\,\nabla^2 C + Q,$$
$$\nabla^2 C = -\frac{Q}{D}.$$

In spherical coordinates (Appendix L; Schey 2004) this is

$$\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial C}{\partial r}\right) + \frac{1}{r^2\sin\theta}\frac{\partial}{\partial\theta}\left(\sin\theta\frac{\partial C}{\partial\theta}\right) + \frac{1}{r^2\sin^2\theta}\left(\frac{\partial^2 C}{\partial\phi^2}\right) = -\frac{Q}{D}.$$

Since there is no angular dependence, we have separate equations for each domain:

$$\frac{1}{r^2}\frac{d}{dr}\left(r^2\frac{dC}{dr}\right) = \begin{cases} -\dfrac{Q}{D}, & r < R \\ 0, & r > R. \end{cases}$$

It is necessary to solve each equation in its domain, and then at the boundary require that C be continuous and also that j and therefore dC/dr be continuous. For $r < R$ we get the following (b_1 and b_2 are constants of integration):

$$r^2\frac{dC}{dr} = -\frac{Qr^3}{3D} + b_1,$$
$$\frac{dC}{dr} = -\frac{Qr}{3D} + \frac{b_1}{r^2},$$
$$C(r) = -\frac{Qr^2}{6D} - \frac{b_1}{r} + b_2.$$

Since the concentration is finite at the origin, $b_1 = 0$:

$$C(r) = b_2 - \frac{Qr^2}{6D}, \qquad r < R.$$

For $r > R$, we can use the general solution with $Q = 0$ and different constants:

$$C(r) = -\frac{b_1'}{r} + b_2'.$$

Far away, the concentration is zero, so $b_2' = 0$. Matching dC/dr at the boundary gives

$$-\frac{QR}{3D} = \frac{b_1'}{R^2}, \quad b_1' = -Q\frac{R^3}{3D}.$$

Matching $C(r)$ at the boundary gives

$$-\frac{QR^2}{6D} + b_2 = -\frac{b_1'}{R}.$$

Putting all of this together gives the same expression for the concentration we had earlier. This technique is a bit more cumbersome, but there are many mathematical tools to extend this technique to cases where there is not spherical symmetry and where Q is a function of position. These advanced techniques can also be used when C is changing with time.

4.12 Drift and Diffusion in One Dimension

The particle fluence rate due to diffusion in one dimension is $j_{\text{diff}} = -D\,(\partial C/\partial x)$. That of particles drifting with velocity v is $j_{\text{drift}} = vC$. The total flux density or fluence rate is the sum of both terms:

$$j_s = -D\frac{\partial C}{\partial x} + vC. \tag{4.56}$$

The homogeneous ($j_s = 0$) solution was discussed in Sect. 4.7, where cancellation of these two terms in equilibrium was used to derive the relationship between the diffusion constant and viscosity. Using the techniques of Appendix F, we can write the homogeneous solution as

$$C(x) = Ae^{(v/D)x}. \tag{4.57}$$

This can be used to solve the problem of $j_s = \text{const}$ when the concentration is C_0 at $x = 0$ and C_0' at $x = x_1$. $C(x)$ must vary in such a way that the total flux density, the sum of the diffusive and drift terms, is constant. Suppose both terms give flow from left to right. If the concentration is high, then the drift flux density is large and the concentration gradient must be small. If the concentration is small, the diffusive flux, and hence the gradient, must be large. To develop a formal solution, write Eq. 4.56 as

$$\frac{dC}{dx} - \frac{1}{\lambda}C = -\frac{j_s}{D}, \tag{4.58}$$

where $\lambda = D/v$ has the dimensions of length and can be interpreted as the distance over which diffusion is important. If the velocity is zero, diffusion is important everywhere and $\lambda = \infty$. If the velocity is very large, $\lambda \rightarrow 0$. Since v can be either positive or negative, so can λ. A particular solution to Eq. 4.58 is

$$C(x) = \frac{\lambda j_s}{D} = \frac{j_s}{v}.$$

The general solution is the sum of the particular solution and the homogeneous solution, Eq. 4.57:

$$C(x) = Ae^{x/\lambda} + j_s/v. \tag{4.59}$$

The situation is slightly different than what we encountered in Chap. 2. We must determine two constants, A and j_s, given the two concentrations C_0 and C_0'. Writing Eq. 4.59 for $x = 0$ and for $x = x_1$, we obtain

$$\begin{aligned} C_0 &= A + \frac{j_s}{v}, \\ C_0' &= Ae^{x_1/\lambda} + \frac{j_s}{v}. \end{aligned} \tag{4.60}$$

Subtracting these gives

$$\begin{aligned} C_0' - C_0 &= A(e^{x_1/\lambda} - 1), \\ A &= (C_0' - C_0)/(e^{x_1/\lambda} - 1). \end{aligned} \tag{4.61}$$

This can be combined with either of Eqs. 4.60 to give

$$j_s = \frac{C_0 e^{x_1/\lambda} - C_0'}{e^{x_1/\lambda} - 1} v. \tag{4.62}$$

We can also substitute Eqs. 4.61 and 4.62 in 4.59 to obtain an expression for $C(x)$. The result is

$$C(x) = \frac{C_0(e^{x_1/\lambda} - e^{x/\lambda}) + C_0'(e^{x/\lambda} - 1)}{e^{x_1/\lambda} - 1}. \tag{4.63}$$

We will discuss the implications of this equation below.

Let us first determine the average concentration between $x = 0$ and $x = x_1$. The average concentration is defined by

$$\overline{C} = \frac{1}{x_1}\int_0^{x_1} C(x)\,dx. \tag{4.64}$$

While one could integrate this directly, it is much easier to integrate Eq. 4.56 from 0 to x_1:

$$-D\int_0^{x_1}\left(\frac{dC}{dx}\right)dx + v\int_0^{x_1} C(x)\,dx = +j_s\int_0^{x_1} dx.$$

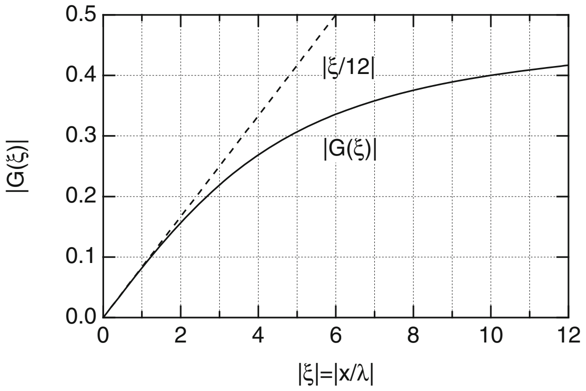

Fig. 4.17 The correction factor $G(\xi)$ used in Eq. 4.68. The dashed line is the approximation $G(\xi) = \xi/12$, which is valid for small ξ and is used in Eq. 4.67

The first term is $-D(C_0' - C_0)$. The second is $vx_1\overline{C}$. The third is $j_s x_1$. The equation can therefore be rewritten as

$$v\overline{C} = \frac{D\,(C_0' - C_0)}{x_1} + j_s. \tag{4.65}$$

Substituting Eq. 4.62 for j_s gives the average concentration

$$\overline{C} = \frac{C_0 e^{x_1/\lambda} - C_0'}{e^{x_1/\lambda} - 1} - \frac{\lambda}{x_1}(C_0 - C_0'). \tag{4.66}$$

The exponentials can be expanded to give an approximate expression for small values of x_1/λ[13]

$$\overline{C} = \frac{(C_0 + C_0')}{2} + \frac{x_1}{\lambda}\frac{1}{12}(C_0 - C_0'). \tag{4.67}$$

For larger values of x_1/λ, the mean can be written

$$\overline{C} = \frac{(C_0 + C_0')}{2} + (C_0 - C_0')\,G\left(\frac{x_1}{\lambda}\right). \tag{4.68}$$

The correction factor $G(x_1/\lambda) = G(\xi)$, given by

$$G(\xi) = \frac{1}{2}\frac{e^{\xi} + 1}{e^{\xi} - 1} - \frac{1}{\xi}, \tag{4.69}$$

is plotted in Fig. 4.17. The function is odd, and only values for $\xi \geq 0$ are shown. For $\xi = 0$ ($\lambda = \infty$, pure diffusion), the average concentration is $(C_0 + C_0')/2$.

Figure 4.18 shows the concentration profile calculated from Eq. 4.63. The concentration is 5 times larger on the left, so diffusion is from left to right. When $x_1/\lambda = x_1 v/D = 0.8$, drift is also from left to right. As the concentration falls, the magnitude of the gradient rises, so that the sum of the diffusive and drift fluxes remains the same. When $x_1/\lambda = -0.8$,

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[13] See Levitt (1975, p. 537). For $x_1/\lambda = 1.5$, this approximation is within 1%. For $x_1/\lambda = 2.5$, the error is about 6 %.

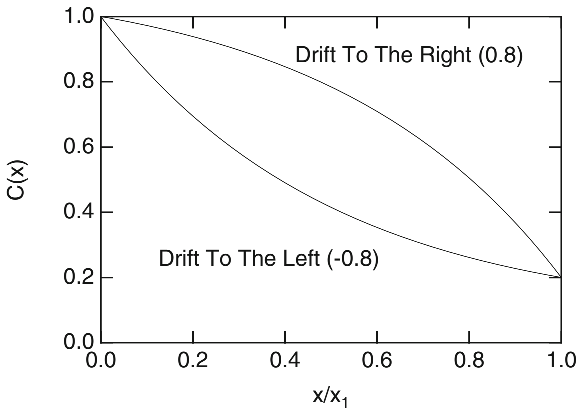


Fig. 4.18 Concentration profile for combined drift and diffusion. The concentration is 1.0 on the left and 0.2 on the right. For $x_1/\lambda = x_1 v/D = 0.8$, drift and diffusion are both to the right. As the concentration falls, the magnitude of the gradient increases. For $x_1/\lambda = x_1 v/D = -0.8$ drift opposes diffusion. As the concentration falls, so does the magnitude of the gradient

drift is opposite to diffusion. Therefore, both the concentration and the magnitude of the gradient must rise and fall together to keep total flux density constant.

Equation 4.65 can be rewritten as

$$j_s = \frac{-D\,(C_0' - C_0)}{x_1} + v\overline{C}. \tag{4.70}$$

This can be interpreted as meaning that the fluence rate is given by the sum of a diffusion term with the average concentration gradient and a drift term with the average concentration. However, the discussion in the preceding paragraph showed that there is actually a continuous change of the relative size of the diffusion and drift terms for different values of x.

4.13 A General Solution for the Particle Concentration as a Function of Time

If $C(x,0)$ is known for $t = 0$, it is possible to use the result of Sect. 4.8 to determine $C(x,t)$ at any later time. The key to doing this is that if $C(x,t)\,dx$ is the number of particles in the region between x and $x + dx$ at time t, it may be be interpreted as the probability of finding a particle in the interval (x, dx) multiplied by the total number of particles. (Recall the discussion on p. 96 about the interpretation of $C(x,t)$.) The spreading Gaussian then represents the spread of probability that a particle is between x and $x + dx$.

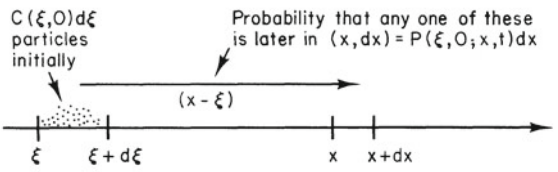


Fig. 4.19 Diffusion from ξ to x

If a particle is definitely at $x = \xi$ at $t = 0$, then $\sigma^2(0) = 0$. The particle cannot remain there because of equipartition of energy: collisions cause it to acquire a mean square velocity $3k_BT/m$ and move. Some time later

$$\sigma(t) = (2Dt)^{1/2}. \tag{4.71}$$

Define $P(\xi, 0; x, t)\,dx$ to be the probability that a particle has diffused to a location between x and $x + dx$ at time t, if it was at $x = \xi$ when $t = 0$. This probability is given by Eq. 4.25, except that the distance it has diffused is now $x - \xi$ instead of x. The variance $\sigma^2(t)$ is given by Eq. 4.71. The result is

$$P(\xi, 0; x, t)\,dx = \frac{1}{\sqrt{4\pi Dt}} e^{-(x-\xi)^2/4Dt}\,dx. \tag{4.72}$$

The number of particles initially between $x = \xi$ and $x = \xi + d\xi$ is the concentration per unit length times the length of the interval $N = C(\xi,0)d\xi$, as shown in Fig. 4.19.

The particles can diffuse in either direction. At a later time t, the average number between x and $x + dx$ that came originally from between $x = \xi$ and $x = \xi + d\xi$ is the original number in $(\xi, d\xi)$ times the probability that each one got from there to x. This number is a differential of a differential, $d\,[C(x,t)dx]$, because it is only that portion of the particles in dx that came from the interval $d\xi$:

$$d\,[C(x,t)\,dx] = C(\xi,0)\,d\xi \frac{1}{\sqrt{4\pi Dt}} e^{-(x-\xi)^2/4Dt}\,dx.$$

To get $C(x,t)dx$, it is necessary to integrate over all possible values of ξ:

$$C(x,t)\,dx = \frac{1}{\sqrt{4\pi Dt}} \left[\int_{-\infty}^{\infty} C(\xi,0) e^{-(x-\xi)^2/4Dt}\,d\xi \right] dx. \tag{4.73}$$

This equation can be used to find $C(x,t)$ at any time, provided that $C(x,t)$ was known at some earlier time. The factor that multiplies $C(\xi,0)$ in the integrand is called the *influence function* or *Green's function* for the diffusion problem; it gives the relative weighting of $C(\xi,0)$ in contributing to the later value $C(x,t)$.

As an example of using this integral, consider a situation in which the initial concentration has a constant value C_0 from $\xi = -\infty$ to $\xi = 0$ and zero for all positive ξ, as shown

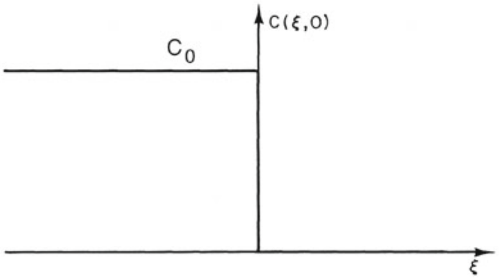


Fig. 4.20 The initial concentration is constant to the left of the origin and zero to the right of the origin

in Fig. 4.20. At $t = 0$ the diffusion starts. The concentration at later times is given by

$$C(x,t) = \frac{C_0}{\sqrt{4\pi Dt}} \int_{-\infty}^{0} e^{-(x-\xi)^2/4Dt}\, d\xi.$$

Such integrals are most easily evaluated by using the *error function*, defined by

$$\mathrm{erf}(z) = \frac{2}{\sqrt{\pi}} \int_0^z e^{-t^2} dt. \tag{4.74}$$

The error function is plotted in Fig. 4.21. One must be careful in using tables, which may be for related functions that differ in normalization constants or the limits of integration.

To use the error function in evaluating the integral in Eq. 4.73, make the substitution $s = (x - \xi)/(4Dt)^{1/2}$. The integral becomes

$$C(x,t) = \frac{-C_0}{\sqrt{4\pi Dt}} \int_{\infty}^{x/\sqrt{4Dt}} e^{-s^2} \sqrt{4Dt}\, ds.$$

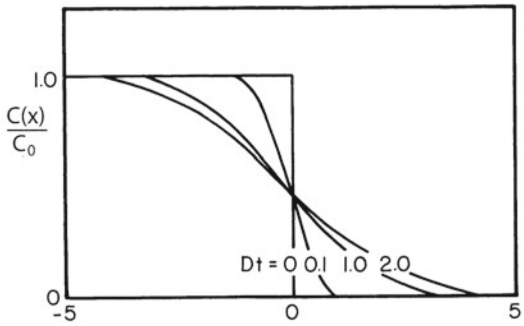


Fig. 4.22 The spread of an initially sharp boundary due to diffusion

Since $\int_A^B f(x)\,dx = \int_0^B f(x)\,dx + \int_A^0 f(x)\,dx = \int_0^B f(x)\,dx - \int_0^A f(x)\,dx$, this can be written as

$$\begin{aligned} C(x,t) &= \frac{-C_0}{\sqrt{\pi}} \left(\int_0^{x/\sqrt{4Dt}} e^{-s^2} ds - \int_0^{\infty} e^{-s^2} ds \right) \\ &= \frac{C_0}{2} \left[1 - \mathrm{erf}(x/\sqrt{4Dt}) \right]. \end{aligned} \tag{4.75}$$

The plot in Fig. 4.22 shows how the initially sharp concentration step becomes more diffuse with passing time. Quantitative measurements of the concentration can be used to determine D. Benedek and Villars (2000, pp. 126–136) discuss some experiments to verify the solution we have obtained above and to determine D.

Many other solutions to the diffusion equation and techniques for solving it are known. See Crank (1975) or Carslaw and Jaeger (1959).

4.14 Diffusion as a Random Walk

The spreading solution to the one-dimensional diffusion equation that we verified can also be obtained by treating the

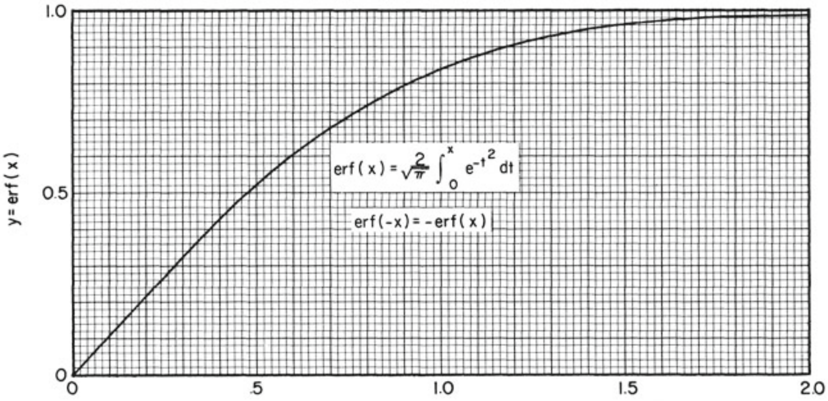


Fig. 4.21 Plot of the error function erf(x)

motion of a molecule as a series of independent steps either to the right or to the left along the x axis. (The same treatment can be extended to three dimensions, but we will not do so.) The derivation gives us a somewhat simplified molecular picture of diffusion. The derivation also provides an opportunity to see how the Gaussian distribution approximates the binomial distribution. This section is not necessary to understand the rest of Chaps. 4 and 5, and you should tackle it only if you are familiar with the binomial and Gaussian probability distributions (Appendices H and I). The model is more restrictive than the diffusion equation derived above, since the latter is the linear approximation to the transport problem.

We use a simplified model in which the diffusing particle always moves in steps of length λ (the mean free path), either in the $+x$ or $-x$ direction. Let the total number of steps taken by the particle be N, of which n are to the right and n' are to the left: $N = n + n'$. Also let $m = n - n'$. The particle's net displacement in the $+x$ direction is then

$$n\lambda - n'\lambda = m\lambda.$$

Since the steps are independent and a step to the left or right is equally likely ($p = 1/2$), the probability of having a displacement $m\lambda$ is given by the binomial probability $P(n; N)$:

$$P(n; N) = \frac{N!}{(n!)(N-n)!}\left(\frac{1}{2}\right)^{n}\left(\frac{1}{2}\right)^{n'}. \tag{4.76}$$

Since this problem is analogous to a coin being tossed, and we know that on the average we get the same number of heads (steps to the left) as tails (steps to the right), we know that the distribution is centered at $n = n'$ or $m = 0$. We also know [Eq. G.4] that the variance in n is given by $\overline{n^2} - \overline{n}^2 = Npq = N/4$. Since $\overline{n} = N/2$, this says that $\overline{n^2} = N/4 + N^2/4$. However, we need the variance in m, $\overline{m^2} - \overline{m}^2$. To obtain it, we write $m = 2n - N$ and $m^2 = 4n^2 + N^2 - 4nN$. Therefore,

$$\overline{m^2} = 4\overline{n^2} + N^2 - 4N\overline{n} = N.$$

The variance of the distribution of displacement x is equal to the step length λ times the variance in the number of steps:

$$\sigma^2 = \overline{x^2} = \lambda^2\overline{m^2} = \lambda^2 N.$$

The number of steps is the elapsed time divided by the collision time $N = t/t_c$. Therefore,

$$\sigma^2 = \frac{\lambda^2 t}{t_c}.$$

Comparing this with Eq. 4.71, we identify $D = \lambda^2/2t_c$, so that

$$\sigma^2 = 2Dt. \tag{4.77}$$

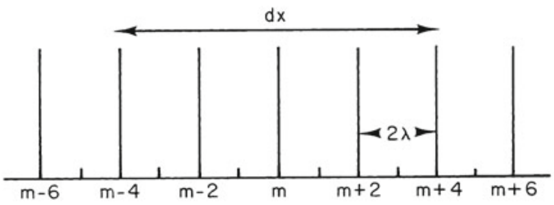


Fig. 4.23 Relationship between the values of x and the allowed values of m. Every other value of m is missing

We have shown that this simple model gives a distribution with fixed mean which spreads with a variance proportional to t. We now must show that the shape is Gaussian. Appendix I shows that the Gaussian is an approximation to the binomial distribution in the limit of large N. Since $\sigma_n^2 = N/4$ and $\overline{n} = N/2$, Eq. G.4 can be used to write

$$P(n) = \left(\frac{2\pi N}{4}\right)^{-1/2} e^{-(n-N/2)^2/(2N/4)}.$$

This can be rewritten in terms of the net number of steps to the right, since $m = n - n' = 2n - N$:

$$P(m) = \left(\frac{2}{\pi N}\right)^{1/2} e^{-m^2/2N}.$$

Note that only every other value of m is allowed. Since $m = 2n - N$, m goes in steps of 2 from $-N$ to N as n goes from 0 to N.

To write the probability distribution in terms of x and t, refer to Fig. 4.23. The spacing between each allowed value of x is 2, so that the number of allowed values of m in interval $(x, x + dx)$ is $dx/2\lambda$. Therefore, $P(x)\,dx = P(m)(dx/2\lambda)$,

$$P(x) = \sqrt{\frac{2}{\pi N 4\lambda^2}}\, e^{-m^2/2N}.$$

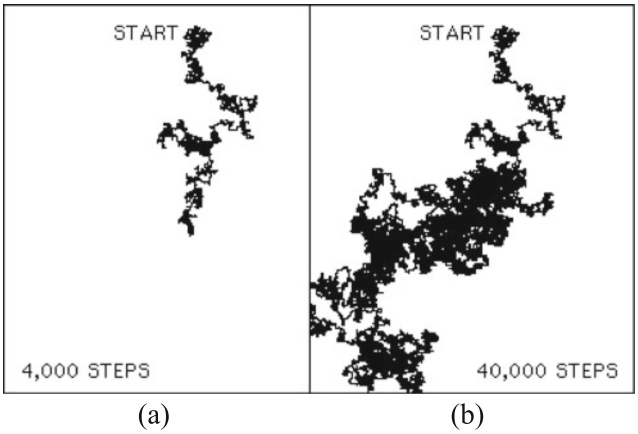
With the substitutions $m = x/\lambda$ and $N = t/t_c$, this becomes

$$P(x, t) = \sqrt{\frac{t_c}{2\pi\lambda^2 t}}\, e^{-x^2(t_c/2\lambda^2 t)}.$$

With the substitutions $D = \lambda^2/2t_c$ and $C(x, t) = C(0)P(x, t)$, we obtain Eq. 4.25.

The result of Eq. 4.71 is easily extended to two dimensions. Imagine that a total of N steps are taken, half in the x direction and half in the y direction. Then $\sigma_x^2 = \sigma_y^2 = \lambda^2(N/2)$. If $r^2 = x^2 + y^2$, $\sigma_r^2 = \sigma_x^2 + \sigma_y^2 = \lambda^2 N$. We still define D in any direction as $\lambda^2/2t_c$, where t_c is the time between steps in that direction. After a total time t, N steps have been taken, but only half of them were in, say, the x direction. Therefore $t_c = 2t/N$. Therefore

$$\sigma_r^2 = \sigma_x^2 + \sigma_y^2 = 4Dt \quad \text{(two dimensions)}. \tag{4.78}$$



(a) (b)

Fig. 4.24 **a** Trail of a particle for 4000 steps. **b** Trail for additional steps to total 40,000

A similar argument in three dimensions gives

$$\sigma_r^2 = \sigma_x^2 + \sigma_y^2 + \sigma_z^2 = 6Dt \quad \text{(three dimensions)}. \tag{4.79}$$

Figure 4.24 shows the result of a computer simulation of a two-dimensional random walk. A random number is selected to determine whether to step one pixel to the left, up, right, or down—each with the same probability. The trail for 4000 steps is shown in Fig. 4.24a. The results of continuing for 40,000 steps are shown in Fig. 4.24b. Note how the particle wanders around one region of space and then takes a number of steps in the same direction to move someplace else. The particle trajectory is “thready.” It does not cover space uniformly. A uniform coverage would be very nonrandom. It is only when many particles are considered that a Gaussian distribution of particle concentration results.

Both results in Fig. 4.24 were for the same sequence of random numbers. A computer simulation with 328 runs of 10,000 steps each gave $\overline{x} = -3.3$, $\sigma_x^2 = 5142$, $\overline{y} = 8.2$, $\sigma_y^2 = 4773$, and $\overline{x^2 + y^2} = 10,027$. The expected values are, respectively, 0, 5000, 0, 5000, and 10,000.

Symbols Used in Chap. 4

Symbol	Use	Units	First used page
a, a_1, a_2	Particle radius	m	90
b_1, b_2, b_3	Constants		97
f	Fraction of cell surface area		100
g	Gravitational acceleration	m s^{-2}	89
$\mathbf{g}$	Force	N	91
i	Particle current	s^{-1}	85
$j, \mathbf{j}, j_s$	Solute fluence rate	m^{-2} s^{-1}	85
$j_{\text{drift}}, j_{\text{diff}}$	Solute fluence rate due to drift velocity, diffusion	m^{-2} s^{-1}	93
$\mathbf{j}_m$	Mass fluence rate	kg m^{-2} s^{-1}	85
j_n	Component of **j** normal to a surface	m^{-2} s^{-1}	87
j_p	Momentum fluence rate	N m^{-2}	93
$\mathbf{j}_v$	Volume fluence rate	m s^{-1}	85
j_x, j_y, j_z	Components of **j**	m^{-2} s^{-1}	87
k_B	Boltzmann’s constant	J K^{-1}	89
l	Linear separation of pores on cell surface	m	112
m	Mass	kg	89
m	$n - n'$		106
$\hat{\mathbf{n}}$	Unit vector normal to a surface		87
n, n'	Number of steps to right, left		106
p, q	Probabilities		106
r	Distance, radius	m	87
s	Dummy variable		90
t	Time	s	85
t_c	Collision time	s	90
u	Energy of a particle	J	89
$v, \mathbf{v}$	Velocity	m s^{-1}	89
x, y, z	Cartesian coordinates	m	85
A	Constant		103
B, B'	Cell radius	m	99
C, C_s	Concentration	m^{-3}	85
D	Diffusion constant	m^2 s^{-1}	92
$F, \mathbf{F}, \mathbf{F}_{\text{ext}}$	Force	N	91
G	Correction factor for average concentration		103
K	Thermal conductivity	J K^{-1} m^{-1} s^{-1}	93
L	Length	m	97
M	Mass	kg	88
M	Molecular weight		94
N, N_0	Number of molecules		86
N	Number of pores on cell surface		100
N	Number of steps in a random walk		106
P	Rate of energy production (power)	W	87
P	Probability		89
Q	Rate of creating a substance per unit volume	m^{-3} s^{-1}	89
R	Gas constant	J K^{-1} mol^{-1}	103
R	Radius of a sphere	m	98
R_p	Radius of a pore	m	99
S	Surface area	m^2	86
$d\mathbf{S}$	Vector surface element pointing in the direction of the normal	m^2	87
T	Absolute temperature	K	89
V	Volume	m^3	88
ΔZ	Cell membrane thickness	m	99
α	Proportionality constant		91
β	Proportionality constant between force and velocity	N s m^{-1}	91
λ	Mean free path	m	90
λ	Ratio of D/v	m	103
θ, ϕ	Angles		86
η	Coefficient of viscosity	Pa s	93
σ	Standard deviation		96
σ	Electrical conductivity	Ω^{-1} m^{-1}	93
ξ	Position	m	104
ξ	Dimensionless variable		103
ρ	Mass density	kg m^{-3}	88
μ_s	Chemical potential of solute	J molecule^{-1}	92

Problems

Section 4.1

Problem 1. A cylindrical pipe with a cross-sectional area $S = 1$ cm^2 and length 0.1 cm has $j_s(0)S = 200$ s^{-1} and $j_s(0.1)S = 150$ s^{-1}.

(a) What is the total rate of buildup of particles in the pipe?
(b) What is the average rate of change of concentration in the section of pipe?

Problem 2. Write the continuity equation in cylindrical coordinates if $j_\phi = 0$ but j_r and j_z can be nonzero.

Problem 3. Consider two concentric spheres of radii r and $r + dr$. If the particle fluence rate points radially and depends only on r, and the number of particles between r and $r + dr$ is not changing, show that $d(r^2 j)/dr = 0$.

Problem 4. Integrate Eq. 4.8 over a volume and subtract the result from Eq. 4.4. The resulting relationship is called the *divergence theorem*.

Section 4.2

Problem 5. Suppose that the total blood flow through a region is F (m^3 s^{-1}). A chemically inert substance is carried into the region in the blood. The total number of molecules of the substance in the region is N. The amount of blood in the region is not changing. Show that $dN/dt = (C_A - C_V)F$, where C_A and C_V are the concentrations of substance in the arterial and venous blood. This is known as the Fick principle or the Fick tracer method. It is often used with radioactive tracers.

Section 4.3

Problem 6. Allen et al. (1982) report seeing regular movement of particles in the axoplasm of a squid axon. At a temperature of 21 °C, the following mean drift speeds were observed:

Particle size (μm)	Typical speed (μm s^{-1})
0.8 – 5.0	0.8
0.2 – 0.6	2

How do these values compare to thermal speeds? (Make a reasonable assumption about the density of particles and assume that they are spherical.)

Problem 7. This problem looks at the original observations of Robert Brown that established Brownian motion.

(a) Combine Eqs. 4.23 and 4.71 to determine an expression for the average distance a particle of radius a will diffuse through a fluid of viscosity η in time t.
(b) Assume you observe a pollen grain with a radius of 50 microns in water at room temperature, and that your visual perception is particularly sensitive to motions occurring over a time of about one second. What is the average distance you observe the grain to move?
(c) Now assume your eye cannot see movements that occur over angles of less than 1 min of arc, or 3×10^{-4} radians (In Chap. 14, we estimate 3 min of arc, but use 1 min here to be conservative). Most eyes cannot focus on objects closer than 25 cm. Determine the smallest displacement you can observe with the naked eye.
(d) Robert Brown had a microscope that could magnify objects by a factor of about 370. What is the smallest displacement he could observe with his microscope? Is this larger or smaller than the displacement of a pollen grain in one second?

In fact, Brown did not observe the motion of entire pollen grains. He observed fat and starch particles about 2 μm in diameter that are released by pollen. For more on Brown's original observations, see Pearle et al. (2010).

Section 4.4

Problem 8. (a) Use the ideal gas law, $pV = Nk_BT = nRT$ to compute the volume of 1 mole of gas at $T = 30\,°\mathrm{C}$ and $p = 1\,\mathrm{atm}$. Express your answer in liters. Show that this is equivalent to a concentration of 2.4×10^{25} molecule m^{-3}.
(b) Find the concentration of liquid water molecules at room temperature.

Problem 9. Using the information on the mean free path in the atmosphere and assuming that all molecules have a molecular weight of 30, find the height at which the mean free path is 1 cm. Assume the atmosphere has a constant temperature.

Section 4.6

Problem 10. Suppose $C(x,t) = \left(N/\sqrt{4\pi Dt}\right) e^{-x^2/4Dt}$. Find an expression for $j_s(x,t)$.

Problem 11. Show that the momentum flux density, j_p, in Table 4.3 has the same units as force per unit area. Compare the equation to Eq. 1.33 and interpret η physically.

Problem 12. Jean Perrin measured the distribution of gamboge particles in water as a function of height, to determine Avagadro's number (Perrin 1910). The radius of the spherical particles was 0.212 μm, the density of water was 1 g cm^{-3}, the density of the particles was 1.207 g cm^{-3}, and the temperature was 20 °C. He counted 13,000 particles, and found their relative number, N, as a function of height, z, to be (data normalized so N is 100 at $z = 5$ μm)

z (μm)	N
5	100
35	47
65	22.6
95	12

(a) Fit these data to a Boltzmann distribution, and determine a value for Boltzmann's constant. Include the effect of buoyancy in your calculation. Fitting techniques are discussed in Chap. 11.

(b) In Perrin's time, the gas constant was known approximately: $R = 8.32$ J K^{-1} mol^{-1}. Use this value and your result from part (a) to calculate Avogadro's number.

Section 4.7

Problem 13. If all macromolecules have the same density, derive the expression for D versus the molecular weight that was used to draw the line in Fig. 4.12.

Problem 14. For diagnostic studies of the lung, it would be convenient to have radioactive particles that tag the air and that are small enough to penetrate all the way to the alveoli. It is possible to make the isotope ^{99m}Tc into a "pseudogas" by burning a flammable aerosol containing it. The resulting particles have a radius of about 60 nm (Burch et al. 1984). Estimate the mean free path for these particles. If it is small compared to the molecular diameter, then Stokes' law applies, and you can use Eq. 4.23 to obtain the diffusion constant. (The viscosity of air at body temperature is about 1.8×10^{-5} Pa s.)

Problem 15. Figure 4.12 shows that D for O_2 in water at 298 K is 1.2×10^{-9} m^2 s^{-1} and that the molecular radius of O_2 is 0.2 nm. The diffusion constant of a dilute gas (where the mean free path is larger than the molecular diameter) is $D = \lambda^2/2t_c$, where the collision time is given by Eq. 4.15.

(a) Find a numeric value for the diffusion constant for O_2 in O_2 at 1 atm and 298 K and its ratio to D for O_2 in water. The molecular weight of oxygen is 32.

(b) Assuming that this equation for a dilute gas is valid in water, estimate the mean free path of an oxygen molecule in water.

Section 4.8

Problem 16. (a) The three-dimensional normalized analog of Eq. 4.25 is

$$C(x,y,z,t) = \frac{N}{\left[2\pi\sigma^2(t)\right]^{3/2}} \exp\left(-\frac{x^2+y^2+z^2}{2\sigma^2(t)}\right).$$

Find the three-dimensional analog of Eq. 4.27.

(b) Show that $\sigma^2 = \overline{x^2} + \overline{y^2} + \overline{z^2} = 6Dt$.

Problem 17. A crude approximation to the Gaussian probability distribution is a rectangle of height P_0 and width $2L$. It gives a constant probability for a distance L either side of the mean.

(a) Determine the value of P_0 and L so that the distribution has the same value of σ as a Gaussian.

(b) Plot $P(x,t)$ if σ is given by Eq. 4.27 and the mean remains centered at the origin for times of 1, 5, 50, 100, and 500 ms. Use D for oxygen diffusing in water at body temperature.

(c) How long does it take for the oxygen to have a reasonable probability of diffusing a distance of 8 μm, the diameter of a capillary?

(d) For $t = 100$ ms, plot both the accurate Gaussian and the rectangular approximation.

Problem 18. Write an equation for Fick's second law in three-dimensional Cartesian coordinates when the diffusion constant depends on position: $D = D(x,y,z)$.

Problem 19. The heat-flow equation in one dimension is

$$j_H = -\kappa\left(\frac{\partial T}{\partial x}\right),$$

where κ is the thermal conductivity in W m^{-1} K^{-1}. One often finds an equation for the "diffusion" of energy by heat flow:

$$\frac{\partial T}{\partial t} = D_H\left(\frac{\partial^2 T}{\partial x^2}\right).$$

The units of j_H are J m^{-2} s^{-1}. The internal energy per unit volume is given by $u = \rho c T$, where c is the heat capacity per unit mass and ρ is the density of the material. Derive the second equation from the first and show how D_H depends on κ, c, and ρ.

Problem 20. The dimensionless *Lewis number* is defined as the ratio of the diffusion constant for molecules and the diffusion constant for heat flow (see Problem 19). If the Lewis number is large, molecular diffusion occurs much more rapidly than the diffusion of energy by heat flow. If the Lewis number is small, energy diffuses more rapidly than molecules. Use the following parameters:

	Air	Water
D (m^2 s^{-1})	2×10^{-5}	2×10^{-9}
κ (W m^{-1} K^{-1})	0.03	0.6
c (J kg^{-1} K^{-1})	1000	4000
ρ (kg m^{-3})	1.2	1000.

(a) Calculate the Lewis number for oxygen in air and in water.

(b) Is it possible using either air or water to design a system in which oxygen is transported by diffusion with almost no transfer of heat?

Problem 21. A sheet of labeled water molecules starts at the origin in a one-dimensional problem and diffuses in the x direction.

(a) Plot σ vs t for diffusion of water in water.
(b) Deduce a "velocity" versus time.
(c) How long does it take for the water to have a reasonable chance of traveling 1 μm? 10 μm? 100 μm? 1 mm? 1 cm? 10 cm?

Problem 22. In three dimensions the root-mean-square diffusion distance is $\sigma = \sqrt{6Dt}$, where t is the diffusion time. Consider the diffusion of oxygen from air to the blood in the lungs. The terminal air sacs in the lungs, the alveoli, have a radius of about 100 μm. The radius of a capillary is about 4 μm. Estimate the time for an oxygen molecule to diffuse from the center to the edge of an alveolus, and the time to diffuse from the edge to the center of a capillary. Which is greater? From the data in Table 1.4 estimate how long blood remains in a capillary. Is it long enough for diffusion of oxygen to occur? Assume the diffusion constant of oxygen in air is 2×10^{-5} m^2 s^{-1} and in water is 2×10^{-9} m^2 s^{-1}.

Problem 23. Why breathe? Estimate the time required for oxygen to diffuse from our nose to our lungs. Assume the diffusion constant of oxygen in air is 2×10^{-5} m^2 s^{-1}.

Problem 24. At a nerve-muscle junction, the signal from the nerve is transmitted to the muscle by a chemical junction or synapse. Molecules of acetylcholine (ACh) must diffuse from the end of the nerve cell across an extracellular gap about 20 nm wide, to the muscle cell in order to activate the muscle. Assuming one-dimensional diffusion, estimate the signal delay caused by the time needed for ACh to diffuse. The delay of the signal at the nerve-muscle junction is about 0.5 ms. How does this compare to the diffusion time? Use a diffusion constant of 5×10^{-10} m^2 s^{-1}.

Problem 25. A substance has diffusion constant D, and its concentration is distributed in space according to $C(x,t) = A(t)\sin(2\pi x/L)$, where L is the wavelength and $A(t)$ is the amplitude of the distribution. Use the one-dimensional diffusion equation, Eq. 4.26, to show that the concentration decays exponentially with time, $A(t) \propto e^{-t/\tau}$. Determine an expression for the time constant τ in terms of L and D. Which decays faster: a long-wavelength (diffuse) distribution, or a short-wavelength (localized) distribution? This result can be used with the Fourier methods developed in Chap. 11 to derive very general solutions to the diffusion equation.

Problem 26. Some tissues, such as skeletal muscle, are anisotropic: the rate of diffusion depends on direction. In these tissues, Fick's first law in two dimensions has the form

$$\begin{pmatrix} j_x \\ j_y \end{pmatrix} = -\begin{pmatrix} D_{xx} & D_{xy} \\ D_{yx} & D_{yy} \end{pmatrix} \begin{pmatrix} \partial C/\partial x \\ \partial C/\partial y \end{pmatrix}.$$

The 2×2 matrix is called the *diffusion tensor*. It is always symmetric, so $D_{xy} = D_{yx}$.

(a) Derive the two-dimensional diffusion equation for anisotropic tissue. Assume the diffusion tensor depends on direction but not on position.
(b) If the coordinate system is rotated from (x, y) to (x', y') by

$$\begin{pmatrix} x' \\ y' \end{pmatrix} = \begin{pmatrix} \cos\theta & \sin\theta \\ -\sin\theta & \cos\theta \end{pmatrix} \begin{pmatrix} x \\ y \end{pmatrix},$$

the diffusion tensor changes by

$$\begin{pmatrix} D_{x'x'} & D_{x'y'} \\ D_{x'y'} & D_{y'y'} \end{pmatrix} = \begin{pmatrix} \cos\theta & \sin\theta \\ -\sin\theta & \cos\theta \end{pmatrix} \begin{pmatrix} D_{xx} & D_{xy} \\ D_{xy} & D_{yy} \end{pmatrix} \begin{pmatrix} \cos\theta & -\sin\theta \\ \sin\theta & \cos\theta \end{pmatrix}.$$

Find the angle θ such that the tensor is diagonal ($D_{x'y'} = 0$). Typically, this direction is parallel to a special direction in the tissue, such as the direction of fibers in a muscle.
(c) Show that the *trace* of the diffusion tensor (the sum of the diagonal terms) is the same in any coordinate system ($D_{xx} + D_{yy} = D_{x'x'} + D_{y'y'}$ for any θ). Basser et al. (1994) invented a way to measure the diffusion tensor using Magnetic Resonance Imaging (Chap. 18). From the diffusion tensor, they can image the direction of the fiber tracts. When they want images that are independent of the fiber direction, they use the trace.

Problem 27. Calcium ions diffuse inside cells. Their concentration is also controlled by a *buffer*:

$$\mathrm{Ca} + \mathrm{B} \iff \mathrm{CaB}.$$

The concentrations of free calcium, unbound buffer, and bound buffer ([Ca], [B], and [CaB]) are governed, assuming the buffer is immobile, by the differential equations

$$\begin{aligned} \frac{\partial[\mathrm{Ca}]}{\partial t} &= D\nabla^2[\mathrm{Ca}] - k^+[\mathrm{Ca}][\mathrm{B}] + k^-[\mathrm{CaB}], \\ \frac{\partial[\mathrm{B}]}{\partial t} &= -k^+[\mathrm{Ca}][\mathrm{B}] + k^-[\mathrm{CaB}], \\ \frac{\partial[\mathrm{CaB}]}{\partial t} &= k^+[\mathrm{Ca}][\mathrm{B}] - k^-[\mathrm{CaB}]. \end{aligned}$$

(a) What are the dimensions (units) of k^+ and k^- if the concentrations are measured in mol l^{-1} and time in s?
(b) Derive differential equations governing the total calcium and buffer concentrations, $[\mathrm{Ca}]_T = [\mathrm{Ca}] + [\mathrm{CaB}]$ and $[\mathrm{B}]_T = [\mathrm{B}] + [\mathrm{CaB}]$. Show that $[\mathrm{B}]_T$ is independent of time.
(c) Assume calcium and buffer interact so rapidly that they are always in equilibrium:

$$\frac{[\mathrm{Ca}][\mathrm{B}]}{[\mathrm{CaB}]} = K,$$

where $K = k^-/k^+$. Write $[\mathrm{Ca}]_T$ in terms of [Ca], $[\mathrm{B}]_T$, and K (eliminate [B] and [CaB]).

(d) Differentiate your expression in (c) with respect to time and use it in the differential equation for $[\mathrm{Ca}]_T$ found in (b). Show that [Ca] obeys a diffusion equation with an "effective" diffusion constant that depends on [Ca]:

$$D_{\mathrm{eff}} = \frac{D}{1 + \frac{K[\mathrm{B}]_T}{(K+[\mathrm{Ca}])^2}}.$$

(e) If $[\mathrm{Ca}] \ll K$ and $[\mathrm{B}]_T = 100K$ (typical for the endoplasmic reticulum), determine D_{eff}/D.

For more about diffusion with buffers, see Wagner and Keizer (1994).

Problem 28. Inside cells, calcium is stored in compartments, such as the sarcoplasmic reticulum. In some cells, a rise in calcium concentration, C, triggers the release of this stored calcium. A model of such *calcium-induced calcium release* is

$$\frac{dC}{dt} = -\frac{k}{C_0^2} C\,(4C - C_0)\,(C - C_0) \tag{1}$$

(a) Plot the rate of calcium release (the right-hand side of Eq. 1) vs C. Identify points for which the calcium release is zero (steady-state solutions to Eq. 1). By qualitative reasoning, determine which of these points are stable and which are unstable. (Will a small change in C from the steady-state value cause C to return to the steady-state value or move farther away from it?)

(b) If $C \ll C_0/4$, what does Eq. 1 become, and what is its solution?

(c) Eq. 1 is difficult to solve analytically. To find a numerical solution, approximate it as

$$\frac{C(t+\Delta t) - C(t)}{\Delta t} = -\frac{k}{C_0^2} C(t)\,[4C(t) - C_0]\,[C(t) - C_0]\,. \tag{2}$$

Write a computer program to determine $C(t)$ at times $t = n\Delta t$, $n = 1, 2, 3, \ldots, 100$, using $\Delta t = 0.1$ s, $k = 1\,\mathrm{s}^{-1}$, $C_0 = 1$ µM, and $C(t = 0) = C'$. Find the threshold value of C', below which $C(t)$ goes to zero, and above which $C(t)$ goes to C_0.

(d) If we include diffusion of calcium in one dimension, Eq. 1 becomes

$$\frac{\partial C}{\partial t} = D\frac{\partial^2 C}{\partial x^2} - \frac{k}{C_0^2} C\,(4C - C_0)\,(C - C_0)\,. \tag{3}$$

This is a type of *reaction–diffusion equation*. To solve Eq. 3 numerically, divide the distance along the cell into discrete points, $x = m\Delta x$, $m = 0, 1, 2, \ldots, M$. Approximate Eq. 3 as

$$\begin{aligned}\frac{C(x, t+\Delta t) - C(x,t)}{\Delta t} &\qquad\qquad (4)\\ = D\frac{C(x+\Delta x,t) - 2C(x,t) + C(x-\Delta x,t)}{(\Delta x)^2}&\\ - \frac{k}{C_0^2} C(x,t)\,(4C(x,t) - C_0)\,(C(x,t) - C_0)&\end{aligned}$$

Assume the ends of the cell are sealed, so $C(0,t) = C(\Delta x,t)$ at one end and $C(M\Delta x,t) = C((M-1)\Delta x,t)$ at the other. Start with the cell at $C(x,0) = 0$ for all points except at one end, where $C(0,0) = C_0$. Calculate $C(x,t)$ using $\Delta x = 5$ µm, $\Delta t = 0.1$ s, $D = 200\,\mu\mathrm{m}^2\,\mathrm{s}^{-1}$, and $C_0 = 1$ µM. You should get a wave of calcium propagating down the cell. What is its speed?

Calcium waves play an important role in many cells. This simple model does not include a mechanism to return the calcium concentration to its originally low value after the wave has passed (a process called recovery). For a more realistic model, see Tang and Othmer (1994). For more information about numerical methods, see Press et al. (1992).

Problem 29. The numerical approximation for the diffusion equation, derived as part of Problem 28, has a key limitation: it is unstable if the time step is too large. This problem can be avoided using the Crank–Nicolson method. Replace the first time derivative in the diffusion equation with a finite difference, as was done in Problem 28. Next, replace the second space derivative with the finite difference approximation from Problem 28, but instead of evaluating the second derivative at time t, use the average of the second derivative evaluated at times t and $t + \Delta t$.

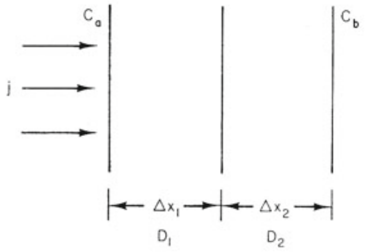
(a) Write down this numerical approximation to the diffusion equation, analogous to Eq. 4 in Problem 28.

(b) Explain why this expression is more difficult to compute than the expression given in the first two lines of Eq. 4. Hint: consider how you determine $C(t + \Delta t)$ once you know $C(t)$. The difficulty you discover in part (b) is offset by the advantage that the Crank–Nicolson method is stable for any time step. For more information about the Crank–Nicolson method, stability, and other numerical issues, see Press et al. (1992).

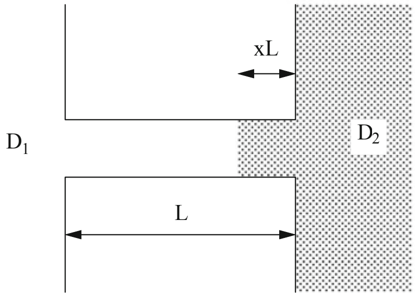
Section 4.9

Problem 30. Consider steady-state diffusion through two plane layers as shown in the figure. Show that the diffusion is the same as through a single plane layer of thickness $\Delta x_1 + \Delta x_2$, with diffusion constant

$$D = \frac{D_1 D_2}{\frac{\Delta x_1}{\Delta x_1 + \Delta x_2} D_2 + \frac{\Delta x_2}{\Delta x_1 + \Delta x_2} D_1}.$$



Problem 31. A fluid on the right of a membrane has different properties than the fluid on the left. Let the diffusion constants on left and right be D_1 and D_2, respectively, and let the pores in the membrane be filled by the fluid on the right a distance xL, where L is the thickness of the membrane.



(a) Use the results of Problem 30 to determine the effective diffusion constant D for a membrane of thickness L when $D_2 = yD_1$, $\Delta x_1 = (1-x)L$, and $\Delta x_2 = xL$. Neglect end effects.

(b) In the case that oxygen is diffusing in air and water at 310 K, the diffusion constants are $D_1 = 2.2 \times 10^{-5}$ m^2 s^{-1}, $D_2 = 1.6 \times 10^{-9}$ m^2 s^{-1}. Plot D/D_1 vs x.

Section 4.10

Problem 32.

(a) Derive Eq. 4.45.

(b) Derive Eqs. 4.51 and 4.52 from Eqs. 4.48 and 4.49.

Problem 33. We can estimate B/B' of Eqs. 4.49–4.55 by noting that B' must be larger than B because of two effects. First, it is larger by $\pi R_p/4$ because of end effects. Second, the concentration varies near the pores and smooths out further away, so B' must also be larger by an amount roughly equal to l, the spacing of the pores. There are $N/4\pi B^2$ pores per m^2, so $l \approx R_p(\pi/f)^{1/2}$. Use the example in the text: $B = 5$ μm, $\Delta Z = 5$ nm, $f = 0.001$, to estimate these two corrections. Assume that the pore radius, R_p, is smaller than ΔZ. Are these corrections important?

Problem 34. Consider an impervious plane at $z = 0$ containing a circular disk of radius a having a concentration C_0. The concentration at large z goes to zero. Carslaw and Jaeger (1959) show that the steady-state solution to the diffusion equation is

$$C(r,z) = \frac{2C_0}{\pi}\sin^{-1}\left[\frac{2a}{\sqrt{(r-a)^2+z^2}+\sqrt{(r+a)^2+z^2}}\right].$$

(a) (optional) Verify that $C(r,z)$ satisfies $\nabla^2 C = 0$. The calculation is quite involved, and you may wish to use a computer algebra program such as Mathematica or Maple.

(b) Show that for $z = 0$, $C = C_0$ if $r < a$.

(c) Show that for $z = 0$, $dC/dz = 0$ if $r > a$.

(d) Integrate j_z over the disk ($z = 0$, $0 < r < a$) and show that $i = 4DaC_0$.

Problem 35. Apply the analysis of Sect. 4.10 to determine how the current i_{vessel} depends on the fraction of surface area covered by pores, for a cylindrical vessel of radius B. Assume that the concentration reaches a value C_5 at some large finite radius R.

Section 4.11

Problem 36. The processes of heat conduction and diffusion are similar: the concentration and temperature both obey the diffusion equation (Problem 19). Consider a spherical cow of radius R having a specific metabolic rate Q W kg^{-1}. Assume the temperature of the outer surface of the cow is the same as the surroundings, T_{sur}. Assume that heat transfer within the cow is by heat conduction.

(a) Calculate the steady state temperature distribution inside the animal and find the core temperature at the center of the sphere.

(b) Consider a smaller (but still spherical) animal such as a rabbit. What is its core temperature?

(c) Calculate the temperature distribution and core temperature in a rabbit covered with fur of thickness d.

Assume the bodies of the cow and rabbit have the thermal properties of water and that the fur has the thermal properties of air. Let $d = 0.03$ m and $T_{\text{sur}} = 20\,°$C .

	Water	Air
κ (W m^{-1} K^{-1})	0.6	0.03
c (J kg^{-1} K^{-1})	4000	1000
ρ (kg m^{-3})	1000	1.2
	Cow	Rabbit
R (m)	0.3	0.05
Q (W kg^{-1})	0.6	1.6

Problem 37. The goal of this problem is to estimate how large a cell living in an oxygenated medium can be before it is limited by oxygen transport. Assume the extracellular space is well stirred with uniform oxygen concentration C_0.

The cell is a sphere of radius R. Inside the cell oxygen is consumed at a rate Q molecule m^{-3} s^{-1}.The diffusion constant for oxygen in the cell is D.

(a) Calculate the concentration of oxygen in the cell in the steady state.
(b) Assume that if the cell is to survive the oxygen concentration at the center of the cell cannot become negative. Use this constraint to estimate the maximum size of the cell.
(c) Calculate the maximum size of a cell for $C_0 = 8$ mol m^{-3}, $D = 2 \times 10^{-9}$ m^2 s^{-1}, $Q = 0.1$ mol m^{-3} s^{-1}. (This value of Q is typical of protozoa; the value of C_0 is for air and is roughly the same as the oxygen concentration in blood.)

Problem 38. A diffusing substance is being consumed by a chemical reaction at a rate Q per unit volume per second. The reaction rate is limited by the concentration of some enzyme, so Q is independent of the concentration of the diffusing substance. For a slab of tissue of thickness b with concentration C_0 at both $x = 0$ and $x = b$, solve the equation to find $C(x)$ in the steady state. This is known as the *Warburg equation* (Warburg 1923). It is a one-dimensional model for the consumption of oxygen in tissue: points $x = 0$ and $x = b$ correspond to the walls of two capillaries side by side.

Problem 39. Suppose that a diffusing substance disappears in a chemical reaction and that the rate at which it disappears is proportional to the concentration $-kC$. Write down the Fick's second law in this case. Show what the equation becomes if one makes the substitution $C(x, y, z, t) = C'(x, y, z, t)e^{-kt}$.

Problem 40. A spherical cell has radius R. The flux density through the surface is given by $j_s = -D \,\mathrm{grad}\, C$. Suppose that the substance in question has concentration $C(t)$ inside the cell and zero outside. The material outside is removed fast enough so that the concentration remains zero. Using spherical coordinates, find a differential equation for $C(t)$ inside the cell. The thickness of the cell membrane is $\Delta r \ll R$.

Problem 41. The cornea of the eye must be transparent, so it can contain no blood vessels. (Blood absorbs light.) Oxygen needed by the cornea must diffuse from the surface into the corneal tissue. Model the cornea as a plane sheet of thickness $L = 500\,\mu\text{m}$. The oxygen concentration, C, is governed by a one-dimensional steady-state diffusion equation

$$D\frac{d^2C}{dx^2} = Q.$$

Assume the cornea is consuming oxygen at a rate $Q = 4 \times 10^{22}$ molecule m^{-3} s^{-1} and has a diffusion constant $D = 3 \times 10^{-9}$ m^2 s^{-1}. The rear surface of the cornea is in contact with the aqueous humor, which has a uniform oxygen concentration $C_2 = 1.8 \times 10^{24}$ molecule m^{-3}. Consider three cases for the front surface:

(a) Solve the diffusion equation for $C(x)$ when the front surface is in contact with air, which has an oxygen concentration $C_1 = 5 \times 10^{24}$ m^{-3}.
(b) The eye is closed, but a layer of tears maintains the concentration at the front surface that is the same as the aqueous humor: $C_1 = 1.8 \times 10^{24}$ m^{-3}. Plot $C(x)$.
(c) The eye is covered by an oxygen-impermeable contact lens, so that at the front surface $dC/dx = 0$. Solve the diffusion equation and plot $C(x)$.

Supplying oxygen to the cornea is a major concern for people who wear contact lenses. Often a tear layer between the contact and cornea, replenished by blinking, is sufficient to keep the cornea oxygenated. If you sleep wearing a contact lens, this tear layer may not be replenished, and the cornea will be deprived of oxygen. For a similar but somewhat more realistic model, see Fatt and Bieber (1968).

Problem 42. The distance L that oxygen can diffuse in the steady-state is approximately $L = \sqrt{CD/Q}$,where C is the oxygen concentration, D is the diffusion constant, and Q is the rate per unit volume that oxygen is used for metabolism.

(a) Show that L has dimensions of length.
(b) The diffusion of oxygen in air is about 10,000 times larger than the diffusion of oxygen in water (Denny 1993). By how much will the diffusion distance L change if oxygen diffuses through air instead of water, all other things being equal?

Insects deliver oxygen to their flight muscles by diffusion down air-filled tubes instead of by blood vessels, thereby taking advantage of the large diffusion constant of oxygen in air (Weiss-Fogh 1964).

Section 4.12

Problem 43. Dimensionless numbers, like the Reynolds number of Chap. 1, are often useful for understanding physical phenomena. The *Péclet number* is the ratio of transport by drift to transport by diffusion. When the Péclet number is large, drift dominates. The solute fluence rate from drift is Cv, where C is the concentration and v the solvent speed. The solute fluence rate from diffusion is D times the concentration gradient (roughly C/L, where L is some characteristic distance over which the concentration varies).

(a) Determine an expression for the Péclet number in terms of C, L, v, and D.
(b) Verify that the Péclet number is dimensionless.
(c) Which parameter in Sect. 4.12 is equivalent to the Péclet number?
(d) Estimate the Péclet number for oxygen for a person walking.

(e) Estimate the Péclet number for a swimming bacterium. For more about the Péclet number, see Denny (1993) and Purcell (1977).

The Péclet number is sometimes known as the *Sherwood number*.

Problem 44. Extend Fick's second law in one dimension $\partial C/\partial t = D\,(\partial^2 C/\partial x^2)$ to include solvent drag.

Problem 45. Use Eqs. 4.63 and 4.64 to derive Eq. 4.66.

Problem 46. Expand $e^x = 1 + x + x^2/2! + x^3/3!$ to derive Eq. 4.67 from Eq. 4.66.

Problem 47. Use a Taylor's series expansion to show that $G(\xi)$in Eq. 4.69 is equal to $\xi/12$ for small ξ.

Problem 48. Consider Eq. 4.63 with $C_0 = 0$ and $C_0' = 1$.

(a) If $v > 0$, write an equation for $C(x)$. Plot $C(x)$ for $0 < x/x_1 < 1$ for two cases: $x_1 \ll \lambda$ and $x_1 \gg \lambda$. Interpret these results physically.

(b) Repeat the analysis for $v < 0$.

Section 4.14

Problem 49. We can use the microscopic model of a random walk to derive important information about diffusion without ever using the binomial probability distribution. Let $x_i(n)$ be the position of the ith particle after n steps of a random walk. Then

$$x_i(n) = x_i(n) \pm \lambda,$$

where half the time you take the $+$ sign and half the time the $-$ sign. Then $\overline{x}(n)$, the value of x averaged over N particles, is

$$\overline{x}(n) = \frac{1}{N}\sum_{i=1}^{N} x_i(n).$$

(a) Show that $\overline{x}(n) = \overline{x}(n-1)$ so that on average the particles go nowhere.

(b) Show that $\overline{x^2}(n) = \overline{x^2}(n-1) + \lambda^2$. Use this result to show that $\overline{x^2}(n) = n\lambda^2$.

For a detailed discussion of this approach, see Denny (1993).

Problem 50. We can write the diffusion constant, D, and the thermal speed, v_{rms}, in terms of the step size, λ, and the collision time, t_c, as

$$D = \frac{\lambda^2}{2t_c},$$

$$v_{\mathrm{rms}} = \frac{\lambda}{t_c}.$$

Solve for λ and t_c in terms of D and v_{rms}.

Problem 51. Using the definitions in Prob. 50, write the diffusion constant in terms of λ and v_{rms}. By how much do you expect the diffusion constant for *heavy water* (water in which the two hydrogen atoms are deuterium, ^{2}H) to differ from the diffusion constant for water? Assume the mean free path is independent of mass.

Problem 52. Write a computer program to model a two-dimensional random walk. Make several repetitions of a random walk of 3600 steps and plot histograms of the displacements in the x and y directions and mean square displacement.

Problem 53. Write a program to display the motion of 100 particles in two dimensions.

Problem 54. Particles are released from a point between two perfectly absorbing plates located at $x = 0$ and $x = 1$. The particles random walk in one dimension until they strike a plate. Find the probability of being captured by the right-hand plate as a function of the position of release, x. (Hint: The probability is related to the diffusive fluence rate to the right-hand plate if the concentration is C_0 at x and is 0 at $x = 0$ and $x = 1$.)

Problem 55. The text considered a one-dimensional random-walk problem. Suppose that in two dimensions the walk can occur with equal probability along $+x$, $+y$, $-x$, or $-y$. The total number of steps is $N = N_x + N_y$, where the number of steps along each axis is not always equal to $N/2$.

(a) What is the probability that N_x of the N steps are parallel to the x axis?

(b) What is the probability that the net displacement along the x axis is $m_x\lambda$?

(c) Show that the probability of a particle being at $(m_x\lambda, m_y\lambda)$ after N steps is

$$P'(m_x, m_y) = \sum_{N_x}\left(\frac{N!}{N_x!\,(N-N_x)!}\right)\left(\frac{1}{2}\right)^N P(m_x, N_x)\,P(m_y, N-N_x),$$

where $P(m, N)$ on the right-hand side of this equation is given by Eq. 4.76.

(d) The factor $N!/N_x!(N-N_x)!$ is proportional to a binomial probability. What probability? Where does this factor peak when N is large?

(e) Using the above result, show that $P'(m_x, m_y) = P(m_x, N/2)\,P(m_y, N/2)$.

(f) Write a Gaussian approximation for two-dimensional diffusion.

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