

The softness of a material implies that it deforms easily when subjected to a stress. For a cell, an applied stress could arise from the cell's environment, such as the action of a wave on water-borne cells or the pressure from a crowded region in a multicellular organism. The exchange of energy with the cell's environment due to thermal fluctuations can also lead to deformations, although these may be stronger at the molecular level than the mesoscopic length scale of the cell proper. For example, Fig. 1.12 shows the fluctuations in shape of a synthetic vesicle whose membrane is a pure lipid bilayer that has low resistance to out-of-plane undulations because it is so thin. At fixed temperature, flexible systems may sample a variety of shapes, none of which need have the same energy because fixed temperature does not imply fixed energy. In this chapter, the kind of fluctuating ensembles of interest to cell mechanics are introduced in Section 2.1, followed up with a review of viscous fluids and their role in cell dynamics in Section 2.2. Many of the statistical concepts needed for describing fluctuating ensembles are then presented, using as illustrations random walks in Section 2.3 and diffusion in Section 2.4. Lastly, the subject of correlations is presented in Section 2.5, focusing on correlations within the shapes of long, sinuous filaments.

2.1 Fluctuations at the cellular scale

Among the common morphologies found among cyanobacteria (which trace their lineage back billions of years) are filamentous cells, two examples of which are displayed in Fig. 2.1. The images are shown at the same magnification, as indicated by the scale bars. The upper panel is the thin filament *Geitlerinema* PCC 7407, with a diameter of $1.5 \pm 0.2 \mu\text{m}$, while the lower panel is the much thicker filament *Oscillatoria* PCC 8973, with a diameter of $6.5 \pm 0.7 \mu\text{m}$ (Boal and Ng, 2010). The filaments have been cultured in solution, then mildly stirred before imaging; clearly, the thinner filament has a more sinuous appearance than the thicker filament when seen at the same magnification. This is as expected: the resistance to bending possessed by a uniform solid cylinder grows like the fourth power of its diameter, so the thinner filament should have much less resistance to bending and hence appear more sinuous than the thicker one.

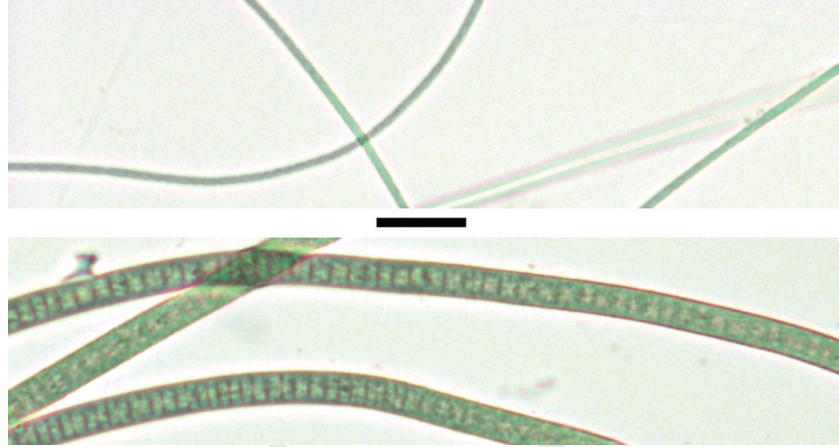


Fig. 2.1

Shape fluctuations exhibited by two species of filamentous cyanobacteria: *Geitlerinema* PCC 7407 (upper, $1.5 \pm 0.2 \mu\text{m}$) and *Oscillatoria* PCC 8973 (lower, $6.5 \pm 0.7 \mu\text{m}$), where the mean diameter of the filament is indicated in brackets. Both images are displayed at the same magnification, and the scale bar is $20 \mu\text{m}$.

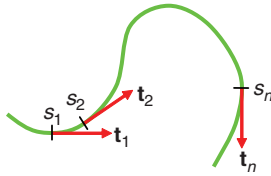


Fig. 2.2

A sinuous curve (green) can be characterized by the variation in the orientation of its tangent vectors (red: $\mathbf{t}_1, \mathbf{t}_2, \dots, \mathbf{t}_n$) at locations along the curve (s_1, s_2, \dots, s_n). The separation Δs between locations is equal to the distance along the curve, for example $\Delta s = |s_1 - s_2|$, but is not equal to the displacement between the points.

We can quantify how “sinuous” a curve is by examining the behavior of the tangent vector \mathbf{t} to the curve at different locations along it. It’s easiest to work with a unit tangent vector, which means that the length of the vector is unity according to $\mathbf{t} \cdot \mathbf{t} = 1$, where the notation $\mathbf{a} \cdot \mathbf{b}$ represents the “dot” or scalar product of the two vectors \mathbf{a} and \mathbf{b} . On Fig. 2.2 is drawn an arbitrarily shaped curve (green), along which several unit tangent vectors have been constructed (red: $\mathbf{t}_1, \mathbf{t}_2, \dots, \mathbf{t}_n$) at three locations along the curve (s_1, s_2, \dots, s_n). The separation Δs between locations is equal to the distance (or arc length) along the curve; for example, between locations s_1 and s_2 , the separation $\Delta s = |s_1 - s_2|$. Thus, the separation between points s_1 and s_n is much larger than the (vector) displacement between the points: Δs takes into account the path length from s_1 to s_n , whereas the magnitude of the displacement is the distance along a straight line drawn between the two positions.

Let’s suppose for a moment that a finite ensemble of vectors $\{\mathbf{t}_i\}$ is selected at N random locations along the curve. The magnitude of the tangent vectors \mathbf{t}_i does not change with location s_i , so that an average that is taken over the ensemble obeys

$$\langle \mathbf{t}_i \cdot \mathbf{t}_i \rangle \equiv (1/N) \sum_{i=1}^N \mathbf{t}_i \cdot \mathbf{t}_i = (1/N) \sum_{i=1}^N 1 = (1/N) \cdot N = 1, \quad (2.1)$$

because each contribution $\mathbf{t}_i \cdot \mathbf{t}_i = 1$ in the ensemble average, the latter denoted by $\langle \dots \rangle$. What happens if we take the scalar product of vectors at different locations? If the curve is a straight line, then $\mathbf{t}_i \cdot \mathbf{t}_j = 1$ even if

$i \neq j$, because all the tangent vectors to a straight line point in the same direction. However, if the tangent vectors point in different directions, then $\mathbf{t}_i \cdot \mathbf{t}_j$ can range between -1 and $+1$, so we would expect in general

$$-1 \leq \langle \mathbf{t}_i \cdot \mathbf{t}_j \rangle \leq 1, \quad (i \neq j) \quad (2.2)$$

where the equal signs hold only if all tangent vectors point in the same direction. If the set $\{\mathbf{t}_i\}$ is truly random, then the ensemble average will contain about as many cases where $\mathbf{t}_i \cdot \mathbf{t}_j$ is positive as there are examples where it is negative, in which case

$$\langle \mathbf{t}_i \cdot \mathbf{t}_j \rangle \rightarrow 0 \quad (i \neq j, \text{ random orientations}) \quad (2.3)$$

in the limit where N is large. Using calculus, it's easy enough to generalize these results to the situation where \mathbf{t} is a continuous function of s , as is done in later chapters; for the time being, all we need is the discrete case. In Section 2.5 of this chapter, we examine how $\mathbf{t}_i \cdot \mathbf{t}_j$ behaves when s_i and s_j are separated by a fixed value, rather than averaged over all values of Δs considered for Eqs. (2.2) and (2.3); we will show that $\langle \mathbf{t}_i \cdot \mathbf{t}_j \rangle_{\Delta s}$ quantitatively characterizes how sinuous the path is.

The shapes of cells in an ensemble provide another example of fluctuations of importance in cell mechanics. Figure 2.3 shows a small collection of the eukaryotic green alga *Stichococcus S*, a common alga found in freshwater ditches, ponds and similar environments; the green organelle in the cell's interior is a chloroplast. The width of these cells is fairly uniform from one cell to the next, having a mean value of $3.56 \pm 0.18 \mu\text{m}$, but the length is more variable, with a mean of $6.98 \pm 1.29 \mu\text{m}$, where the second number of each pair is the standard deviation. The large value of the standard deviation of the cell length relative to its mean value reflects the fact that the length changes by a factor of two during the division cycle.

Although the mean values of cell dimensions are obviously useful for characterizing the species, even more information can be gained from the distribution of cell shapes, as will be established in Chapter 12. For now, we simply wish to describe how to construct and utilize a continuous distribution from an ensemble using data such as the cell length and width. Knowing that *Stichococcus* grows at a fairly constant width, we choose as our geometrical observable the length to width ratio \mathcal{A} , just to make the observable dimensionless. Each cell has a particular \mathcal{A} , and from the ensemble one can determine how many cells $\Delta n_{\mathcal{A}}$ there are for a range $\Delta \mathcal{A}$ centered on a given \mathcal{A} . The total number of cells in the ensemble N is just the sum over all the cells $\Delta n_{\mathcal{A}}$ in each range of \mathcal{A} .

Now, let's convert *numbers* into *probabilities*; that is, let's determine the probability of finding a cell in a particular range of \mathcal{A} . This is straightforward: if there are $\Delta n_{\mathcal{A}}$ cells in the range, then the probability of finding a

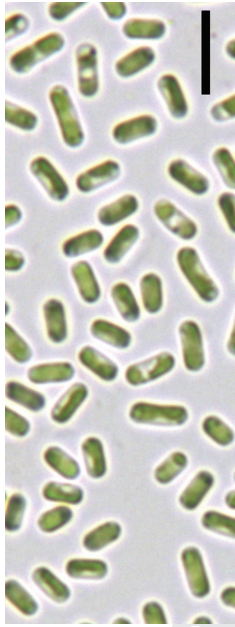


Fig. 2.3

Sample of eukaryotic green alga *Stichococcus S*; this particular strain is from a freshwater ditch in Vancouver, Canada. Scale bar is $10 \mu\text{m}$. (Forde and Boal, unpublished).

cell in this range out of the total population N is just $\Delta n_A / N$. Unfortunately, the probability as we have defined it depends on the range ΔA that we have used for collecting the individual cell measurements. We can remove this dependence on ΔA by constructing a probability density $\mathcal{P}(A)$ simply by dividing the probability for the range by the magnitude of the range itself, ΔA . Note that the probability density has units of A^{-1} because of the operation of division. Let's put these ideas into equations. Working with the finite range of ΔA , we said

$$[\text{probability of finding cell in range } \Delta A] = \Delta n_A / N, \quad (2.4)$$

and

$$\begin{aligned} [\text{probability density around } A] &= \mathcal{P}(A) \\ &= [\text{probability of finding cell in range } \Delta A] / \Delta A, \end{aligned} \quad (2.5)$$

so that

$$[\text{number of cells in range } \Delta A] = \Delta n_A = N \mathcal{P}(A) \Delta A. \quad (2.6)$$

If we now make the distribution continuous instead of grouping it into ranges of ΔA , Eq. (2.6) becomes

$$dn_A = N \mathcal{P}(A) dA. \quad (2.7)$$

By working with probability densities, we have removed the explicit dependence of the distribution on the number of cells in the sample, and at the same time have obtained an easily normalized distribution function:

$$\int \mathcal{P}(A) dA = 1, \quad (2.8)$$

from which the mean value of A is

$$\langle A \rangle = \int A \mathcal{P}(A) dA. \quad (2.9)$$

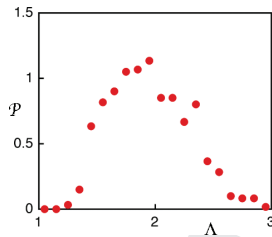


Fig. 2.4

Probability density \mathcal{P} for the length to width ratio A of the green alga *Stichococcus S*, a specimen of which is shown in Fig. 2.3 (Forde and Boal, unpublished).

Having done all of this formalism, what do the data themselves look like? Figure 2.4 shows the probability density for the length-to-width ratio of the green alga *Stichococcus S* in Fig. 2.3. The fact that \mathcal{P} is zero at small values of A just means that there are no cells in this range: $A = 1$ corresponds to a spherical cell, and *Stichococcus* is always elongated, like a cylindrical capsule. The peak in \mathcal{P} at the smaller values of A observed in the population indicates that the cell grows most slowly during this time. Once the cell begins to grow rapidly, there will be (relatively) fewer examples of it in a steady-state population, and that's what the data indicate is occurring at large values of cell length, near the end of the division cycle.

These first two examples of fluctuations at the cellular level dealt with cell shape, either fluctuations in the local orientation of a single, long bio-filament, or the fluctuations in cell length among a population under steady

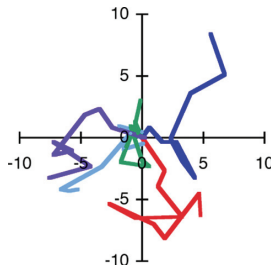


Fig. 2.5

Trajectories of five spherical polystyrene beads in pure water at room temperature, as observed under a microscope. The beads have a diameter of $1\ \mu\text{m}$, and the tracks were recorded at 5 second intervals.

state growth. As a final illustration, we examine the random motion of objects with sizes in the micron range immersed in a stationary fluid: here, the objects are plastic spheres, and in Chapter 11, they are self-propelled cells. In everyday life, we're familiar with several types of motion within a fluid, even when the fluid as a whole has no overall motion. For instance, convection is often present when there is a density gradient in the fluid, such that less dense regions rise past more dense regions: warm (less dense) air at the surface of the Earth rises through cooler air above it. But even if the fluid has a uniform density and displays no convective motion that we can see with the naked eye, there may be motion at length scales of microns or less.

Figure 2.5 shows the trajectories of small plastic (polystyrene) beads tracked at 5 s intervals as seen under a microscope; the spherical beads have a diameter of $1\ \mu\text{m}$ and they are immersed in pure water in a small chamber on a microscope slide. Several trajectories are displayed, all taken from a region within about a hundred microns. The tracks possess

- no overall drift in a particular direction that might indicate convection or fluid flow,
- no straight line behavior that would indicate motion at a constant velocity.

Rather, the trajectories change speed and direction at random, though on a time scale finer than what appears in the figure, because the time between measurements is a relatively long 5 s. This is an example of Brownian motion, which arises because of the exchange of energy and momentum between the plastic beads and their fluid environment, much like the exchange of energy and momentum among particles in a box described in Section 1.4.

An instantaneous velocity can be assigned to the beads, but it changes constantly in magnitude and direction. A plot of the position of the beads relative to their initial location when their motion began to be recorded, exhibits much scatter from bead to bead, and even the mean value of the (magnitude of the) displacement does not increase linearly with time which would be expected for constant speed. However, the mean value of the squared displacement does rise linearly with time, which is characteristic of random motion as established in Section 2.3. There aren't sufficient trajectories in Fig. 2.5 to obtain an accurate description of the motion, so we must be content with the poorly determined result $\langle r^2 \rangle = (1.1 \pm 0.3\ \mu\text{m}^2/\text{s}) t$, where r is the magnitude of the displacement from the origin, t is the time, and the ensemble average $\langle \dots \rangle$ is taken over just five trajectories. Not only can the $\langle r^2 \rangle \propto t$ behavior be explained from random motion, the proportionality constant ($1.1 \pm 0.3\ \mu\text{m}^2/\text{s}$) has its origin in the fluctuations in kinetic energy of particles moving in a viscous fluid.

In Section 1.4, we stated that the mean kinetic energy of a particle as it exchanges energy with its neighbors in an ideal system is equal to $3/2 k_B T$ in three dimensions, where T is the temperature in Kelvin and k_B is Boltzmann's constant (1.38×10^{-23} J/K). At room temperature, $3/2 k_B T = 6 \times 10^{-21}$ J. One thing to note is that the mean kinetic energy of the particles in this system is independent of their mass, meaning that lighter particles travel faster than heavier ones. For a hydrogen molecule, with a mass of 3.3×10^{-27} kg, the root mean square (rms) speed is 1930 m/s, found by equating $3k_B T/2 = m\langle v^2 \rangle/2$. The tiny plastic beads of Fig. 2.5 have a much greater mass than a diatomic molecule like H_2 , and their mean speed is thus many orders of magnitude smaller. Combining (i) the distribution of speeds in a gas at equilibrium with (ii) the drag force on an object moving in viscous medium, shows that $\langle r^2 \rangle = 6Dt$ in three dimensions, where the diffusion coefficient D is given by $D = k_B T / 6\pi\eta R$ for spheres of radius R moving in a fluid with viscosity η . We return to this expression, called the Einstein relation, in Section 2.4 and use it to interpret the measurements in Fig. 2.5 in the end-of-chapter problems.

Before undertaking any further analysis of cell motion, we review in Section 2.2 the effects of viscous drag on the movement of objects in a fluid medium. This provides a better preparation and motivation for the discussion of random walks in Section 2.3 and diffusion in Section 2.4. The formalism of correlation functions is presented in Section 2.5, but the material does not involve the properties of fluids so Sections 2.2 and 2.4 need not be read before starting Section 2.5.

2.2 Movement in a viscous fluid

A fluid is a material that can resist compression but cannot resist shear. Passing your hand through air or water demonstrates this, in that the air or water does not restore itself to its initial state once your hand has passed by – rather, there has been mixing and rearranging of the gas or liquid. Yet even if fluids have zero shear resistance, this does not mean that their deformation under shear is instantaneous: there is a characteristic time scale for a fluid to respond to an applied stress. For example, water spreads fairly rapidly when poured into a bowl, whereas salad dressing usually responds more slowly, and sugar-laced molasses slower still. What determines the response time is the strength and nature of the interactions among the fluid's molecular components. For example, the molecules could be long and entangled (as in a polymer) or they could be small, but strongly interacting (as in water or molten glass).

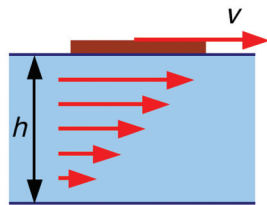


Fig. 2.6

In one measurement of viscosity, a horizontal force F is applied to a flat plate of area A in contact with a liquid, resulting in the plate moving at a velocity v . The height of the liquid in its container is h and the speed of the fluid at the lower boundary is zero.

At low speeds, the response time of a fluid to accommodating an applied stress depends on a physical property called the viscosity, η , among other factors. Unlike an elastic parameter like the compression modulus, which has the same dimensions of stress (force per unit area, or energy per unit volume in three dimensions), the dimensions of η include a reference to time. We illustrate this by considering one means of measuring η , which involves the application of a horizontal force to the surface of an otherwise stationary fluid, as illustrated in Fig. 2.6. In the figure, a flat plate of area A on one side is pulled along the surface of the fluid with a force F , giving a shear stress of F/A . If the material in the figure were a solid, it would resist this stress until it attained a deformed configuration where the applied and reaction forces were in equilibrium. But a fluid doesn't resist shear, and the floating plate continues to move at a speed v as long as the stress is applied. The magnitude of the speed depends inversely on the viscosity: the higher the viscosity the lower the speed that can be achieved with a given stress. The relationship has the form:

$$F/A = \eta (v/h), \quad (2.10)$$

where h is the height of the liquid in its container. Note that the fluid is locally stationary at its boundaries: it is at rest at the bottom of the container and moving with speed v beside the plate.

Elastic quantities such as the bulk modulus or shear modulus appear in Hooke's law expressions of the form $[stress] = [elastic\ modulus] \cdot [strain]$. Strain is a dimensionless ratio like the change in volume divided by the undeformed volume, so elastic moduli must have the dimensions of stress. Equation (2.10) is different from this, in that the ratio v/h is not dimensionless but has units of $[time]^{-1}$, so that η has dimensions of $[force/area] \cdot [time]$, or $kg/m \cdot s$ in the MKSA system. Thus, η provides the time scale for the relaxation, as expected. There are a variety of ways of measuring η ; the viscosities of some familiar fluids are given in Table 2.1. Viscosity is often quoted in units of Poise or P, which has the equivalence of $kg/m \cdot s \equiv 10\text{ P}$.

2.2.1 Translational drag

Moving through a viscous fluid, an object experiences a drag force whose magnitude depends on the speed of the object with respect to the fluid. At low speeds where the motion of the object does not induce turbulence in the fluid, the drag force rises linearly with the speed, whereas at high speeds where turbulence is present, the drag force rises like the square of the speed. The detailed relationship between the drag force F_{drag} and the speed v depends on the shape of the object among other things, so for the time being we will simply write the relationship as

Table 2.1 Viscosities of some familiar fluids measured at 20 °C. A commonly quoted unit for viscosity is the Poise; in MKSA system, 1 kg/m • s = 10 P.

Fluid	η (kg/m • s)	η (P)
Air	1.8×10^{-5}	1.8×10^{-4}
Water	1.0×10^{-3}	1.0×10^{-2}
Mercury	1.56×10^{-3}	1.56×10^{-2}
Olive oil	0.084	0.84
Glycerine	1.34	13.4
Glucose	10^{13}	10^{12}
Mixtures: blood	2.7×10^{-3}	2.7×10^{-2}

$$F_{\text{drag}} = c_1 v \quad (\text{low speeds}) \quad (2.11a)$$

$$F_{\text{drag}} = c_2 v^2, \quad (\text{high speeds}) \quad (2.11b)$$

where the constants c_1 and c_2 depend on a variety of terms. This is for linear motion through the fluid, and there are similar relations for rotational motion as will be described later in this section. Note that the power required to overcome the drag force, obtained from $[power] = Fv$, grows at least as fast as v^2 according to Eq. (2.11). Relatively speaking, viscous forces are so important in the cell that we need only be concerned with the low-speed behavior of Eq. (2.11a); the dynamic properties of systems obeying Eq. (2.11b) are treated in the problem set at the end of this chapter.

Let's now solve the motion of an object subject only to linear drag in the horizontal direction – that is, omitting gravity. The object obeys Newton's law $F = ma = m (dv/dt)$, so that the drag force from Eq. (2.11a) gives the relation

$$ma = m (dv/dt) = -c_1 v, \quad (2.12)$$

where the minus sign indicates that the force is in the opposite direction to the velocity. Equation (2.12) can be rearranged to read

$$dv/dt = -(c_1/m) v, \quad (2.13)$$

which relates a velocity to its rate of change. This equation does not yield a specific number like $v = 5$ m/s; rather, its solution gives the *form* of the function $v(t)$. It's easy to see that the solution is exponential in form, because

$$de^x/dx = e^x. \quad (2.14)$$

That is, the derivative of an exponential is itself an exponential, satisfying Eq. (2.13). One still has to take care of the factor c_1/m in Eq. (2.13), and it's easy to verify by explicit substitution that

Table 2.2 Summary of drag forces for translation and rotation of spheres and ellipsoids at low speeds. For ellipsoids, the drag force, the torque \mathcal{T} and the angular velocity ω are about the major axis; the expressions apply in the limit where the semi-major axis a is much longer than the semi-minor axis b .

	Sphere	Ellipsoid ($a \gg b$)
Translational force	$F = 6\pi\eta Rv$	$F = 4\pi\eta av \{\ln(2ab) - 1/2\}$
Rotational torque	$\mathcal{T} = 8\pi\eta R^3\omega$	$\mathcal{T} = (16/3)\pi\eta ab^2\omega$

$$v(t) = v_0 \exp(-c_1 t / m), \quad (2.15)$$

where v_0 is the speed of the object at $t = 0$.

The characteristic time scale for the velocity to decay to $1/e$ of its original value is m/c_1 . Even though the object is always moving because the velocity goes to zero only in the limit of infinite time, nevertheless, the object reaches a maximum distance mv_0/c_1 from its original location, also at infinite time. The time-dependence of the distance can be found by integrating Eq. (2.15) to yield:

$$\Delta x = (mv_0 / c_1) \cdot [1 - \exp(-c_1 t / m)], \quad (2.16)$$

where the limiting value at $t \rightarrow \infty$ is obvious.

The strength of the drag force depends not only on the viscosity at low speeds, but also on the cross-sectional shape that is presented to the fluid by the object in its direction of motion. A cigar, for instance, will experience less drag when moving parallel to its long axis than when moving with that axis perpendicular to the direction of motion. Analytical expressions are available for the drag force at low speeds, two examples of which are given in Table 2.2. The most commonly quoted one is Stokes' law for a sphere of radius R :

$$F = 6\pi\eta Rv. \quad (2.17)$$

This expression will be used momentarily in an example. A sphere is a special case of an ellipsoid of revolution where the semi-major axis a and the semi-minor axis b are both equal: $a = b = R$. When $a \gg b$, the drag force becomes

$$F = 4\pi\eta av \{\ln(2ab) - 1/2\}, \quad (2.18)$$

for motion at low speed parallel to the long axis of the ellipsoid. In this expression, note that if b is fixed, then the drag force increases with the length of the ellipsoid as $a/\ln a$.

At higher speeds when turbulence is present, the drag force for translational motion not only depends on the square of the speed, but it also has a different dependence on the shape of the object:

$$F = (\rho/2)AC_D v^2, \quad (2.19)$$

where ρ is the density of the fluid and A is the cross-sectional area of the object in its direction of motion (πR^2 for a sphere). The dimensionless drag coefficient C_D is often about 0.5 for many shapes of interest, and somewhat less than this for sports cars (0.3). Note that the drag force in Eq. (2.19) depends on the density of the fluid, rather than its viscosity η in Eq. (2.18). Also, note the dependence on the square of the transverse dimension in Eq. (2.19), compared to the linear dependence in Eq. (2.18).

Example 2.1. Consider an idealized bacterium swimming in water, assuming:

- the bacterium is a sphere of radius $R = 1 \mu\text{m}$,
- the fluid medium is water with $\eta = 10^{-3} \text{ kg / m} \cdot \text{s}$,
- the density of the cell is that of water, $\rho = 1.0 \times 10^3 \text{ kg/m}^3$,
- the speed of the bacterium is $v = 2 \times 10^{-5} \text{ m/s}$.

What is the drag force experienced by the cell? If the cell's propulsion system were turned off, over what distance would it come to a stop (ignoring thermal contributions to the cell's kinetic energy from the its environment)?

First, we calculate the prefactor c_1 in Eq. (2.11a)

$$c_1 = 6\pi\eta R = 6\pi \cdot 10^{-3} \cdot 1 \times 10^{-6} = 1.9 \times 10^{-8} \text{ kg/s},$$

so that the drag force on the cell can then be obtained from Stoke's law:

$$F_{\text{drag}} = c_1 v = 1.9 \times 10^{-8} \cdot 2 \times 10^{-5} = 0.4 \text{ pN} \quad (\text{pN} = 10^{-12} \text{ N}).$$

To determine the maximum distance that the cell can drift without propulsion, we first calculate the mass of the cell m ,

$$m = \rho \cdot 4\pi R^3 / 3 = 10^3 \cdot 4\pi (1 \times 10^{-6})^3 / 3 = 4.2 \times 10^{-15} \text{ kg},$$

from which the stopping distance becomes, using Eq. (2.16)

$$\begin{aligned} x &= mv_0 / c_1 = 4.2 \times 10^{-15} \cdot 2 \times 10^{-5} / 1.9 \times 10^{-8} \\ &= 4.4 \times 10^{-12} \text{ m} = 0.04 \text{ \AA}. \end{aligned}$$

2.2.2 Rotational drag

The stress experienced by the surface of an object moving through a viscous fluid can retard the rotational motion of the object, as well as its translational motion. The effect of rotational drag is to produce a torque \mathcal{T} that reduces the object's angular speed ω with respect to the fluid. At low angular speed, the torque from drag is linearly proportional to ω , just as the linear relation Eq. (2.11a) governs translational drag:

$$\mathcal{T} = -\chi\omega. \quad (2.20)$$

where the minus sign indicates \mathcal{T} acts to reduce the angular speed. Here, we adopt the usual convention that counter-clockwise rotation corresponds to positive ω . For a sphere of radius R , the drag parameter χ is

$$\chi = 8\pi\eta R^3, \quad (2.21)$$

where η is the viscosity of the medium. The expression for χ for an ellipsoid of revolution is given in Table 2.2. Similar to the expressions for force, the power required to overcome the torque from viscous drag is given by $[power] = \mathcal{T}\omega$, which grows as ω^2 for Eq. (2.20). Confusion can sometimes arise between frequency (revolutions per second) and angular speed (radians per second): ω is equal to 2π times the frequency of rotation. Both quantities have units of $[time]^{-1}$ because radians are dimensionless.

It's straightforward to set up the dynamical equations for rotational motion under drag, and to solve for the functional form $\omega(t)$ of the angular speed and $\theta(t)$ of the angle swept out by the object. For instance, if the rotation is about the longest or shortest symmetry axis of the object, then the torque produces an angular acceleration α that determines $\omega(t)$ via

$$\mathcal{T} = I\alpha = I(d\omega/dt) = -\chi\omega, \quad (2.22)$$

where I is the moment of inertia about the axis of rotation. For a sphere of radius R , the moment of inertia about all axes through the center of the sphere is $I = mR^2/2$. As in our discussion of translational motion, Eq. (2.22) determines the functional form of $\omega(t)$:

$$\omega(t) = \omega_0 \exp(-\chi t / I), \quad (2.23)$$

where ω_0 is the initial value of ω . Equation (2.23) can be integrated to yield the angle traversed during the slowdown, but this is left as an example in the problem set.

Example 2.2. Consider an idealized bacterium swimming in water, assuming:

- the bacterium is a sphere of radius $R = 1 \mu\text{m}$,
- the fluid medium is water with $\eta = 10^{-3} \text{ kg / m} \cdot \text{s}$,
- the bacterium rotates at a frequency of 10 revolutions per second.

Find the retarding torque from drag experienced by the cell.

First, the frequency of 10 revolutions per second corresponds to an angular frequency of $\omega = 20\pi \text{ s}^{-1}$. Next, the prefactor χ in Eq. (2.21) is

$$\chi = 8\pi\eta R^3 = 8\pi \cdot 10^{-3} \cdot (1 \times 10^{-6})^3 = 8\pi \times 10^{-21} \text{ kg-m}^2/\text{s},$$

so that the magnitude of the drag torque on the cell can then be obtained from:

$$\mathcal{T}'_{\text{drag}} = \chi\omega = 8\pi \times 10^{-21} \cdot 20\pi = 1.6 \times 10^{-18} \text{ N-m}.$$

As a final caveat, most readers with a physics background are aware that the kinematic quantities ω , α , and \mathcal{T}' are vectors and I is a tensor. Thus, the situations we have described are specific to rotations about a particular set of axes through an object. When ω and \mathcal{T}' have arbitrary orientations with respect to the symmetry axes, the motion is more complex than what has been described here.

2.2.3 Reynolds number

In Example 2.1 for translational motion, the drag force is so important that it causes a moving cell to stop in less than an atomic diameter once a cell's propulsion unit is turned off. In the problem set, it is shown that rotational motion also ceases abruptly under similar circumstances. (Note that both of these conclusions ignore any contribution to the kinetic energy from thermal fluctuations.) Put another way, the effect of drag easily overwhelms the cell's inertial movement at constant velocity that follows Newton's First Law of mechanics.

In fluid dynamics, a benchmark exists for estimating the importance of the inertial force compared to the drag force. This is the Reynolds number, a dimensionless quantity given by

$$\mathbf{R} = \rho v \lambda / \eta, \quad (2.24)$$

where v and λ are the speed and length of the object, and ρ and η are the density and viscosity of the medium, all respectively. We won't provide a derivation of \mathbf{R} from the ratio of the inertia to drag forces experienced an object (see Nelson, 2003) as \mathbf{R} will not be used elsewhere in this text. The crossover between drag-dominated motion at small \mathbf{R} and inertia-dominated motion at large \mathbf{R} is in the range $\mathbf{R} \sim 10\text{--}100$.

Let's collect the terms on the right-hand side of Eq. (2.24) into properties of the fluid (ρ/η) and those of the object ($v\lambda$); for water at room temperature, ρ/η is 10^6 s/m². Common objects like fish and boats, with lengths and speeds of meters and meters per second, respectively, have $v\lambda$ in the range of 1–1000 m²/s. Thus, \mathbf{R} for everyday objects moving in water is 10^6 or more, and such motion is dominated by inertia, even though viscous effects are present. This conclusion also applies for cars and planes as they travel through air, where ρ/η is 0.5×10^5 s/m² under standard conditions. However, for the motion of a cell, the product $v\lambda$ is far smaller: even if $\lambda = 4$ μm and $v = 20$ $\mu\text{m/s}$, then $v\lambda = 8 \times 10^{-11}$ m²/s, such that \mathbf{R} is less than 10^{-4} . Clearly, this value is well below unity so the motion of a typical cell is dominated by viscous drag. In the context of the Reynolds number, the reason for this is the very small size and speed of cells compared to everyday objects.

2.3 Random walks

The motion of microscopic plastic spheres as they interact with their fluid environment was displayed in Fig. 2.5. As shown, the trajectories are just a coarse representation of the motion, in that the positions of the spheres were sampled every five seconds, so that the fine details of the motion were not captured. However, the behavior of each trajectory over long times is correctly represented, permitting the calculation of the ensemble average $\langle r^2 \rangle$ over the suite of positions $\{\mathbf{r}_k\}$ as a function of the elapsed time t , where the index k is a particle label. In discussing Fig. 2.5, it was pointed out that $\langle r^2 \rangle$ does not increase like t^2 , as it would for motion at constant velocity; rather, $\langle r^2 \rangle \propto t$, which we now interpret in terms of the behavior of random walks.

Each step of a walk, random or otherwise, can be represented by a vector \mathbf{b}_i , where the index i runs over the N steps of the walk. The contour length of the path L is just the scalar sum over the lengths of the individual steps:

$$L = \sum_{i=1, N} b_i. \quad (2.25)$$

There is no direction dependence to Eq. (2.25) so that no matter how the path twists and turns, the contour length is always the same so long as the average step size is the same. In contrast, the displacement of the path \mathbf{r}_{ee} from one end to the other is a vector sum:

$$\mathbf{r}_{ee} = \sum_{i=1, N} \mathbf{b}_i. \quad (2.26)$$

The situation is illustrated in Fig. 2.7 for four arbitrary walks of fixed step length, where the magnitude of \mathbf{r}_{ee} for each walk is obviously less than the contour length L .

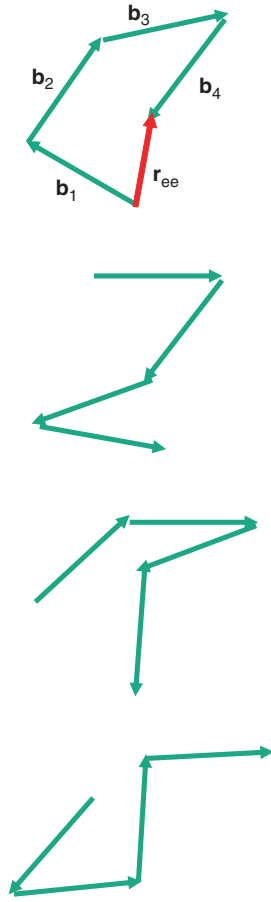


Fig. 2.7

A walk with four steps represented by the vectors $\mathbf{b}_1 \dots \mathbf{b}_4$ has a contour length $L = b_1 + b_2 + b_3 + b_4$ (scalar sum) and an end-to-end displacement $\mathbf{r}_{ee} = \mathbf{b}_1 + \mathbf{b}_2 + \mathbf{b}_3 + \mathbf{b}_4$ (vector sum). Several walks are shown, each with the same L in this example, but different \mathbf{r}_{ee} .

Even though \mathbf{r}_{ee}^2 may be different for each path, it is easy to calculate the average value of \mathbf{r}_{ee}^2 when taken over many configurations. For now, each step is assumed to have the same length b , even though the directions are different from step to step. From Eq. (2.26), the general form of the dot product of \mathbf{r}_{ee} with itself for a particular walk is

$$\begin{aligned} \mathbf{r}_{ee} \cdot \mathbf{r}_{ee} &= (\sum_{i=1,N} \mathbf{b}_i) \cdot (\sum_{j=1,N} \mathbf{b}_j) \\ &= (\mathbf{b}_1 + \mathbf{b}_2 + \mathbf{b}_3 + \dots) \cdot (\mathbf{b}_1 + \mathbf{b}_2 + \mathbf{b}_3 + \dots) \\ &= b_1^2 + b_2^2 + b_3^2 \dots + 2\mathbf{b}_1 \cdot \mathbf{b}_2 + 2\mathbf{b}_1 \cdot \mathbf{b}_3 + \dots + 2\mathbf{b}_2 \cdot \mathbf{b}_3, \dots \end{aligned} \quad (2.27)$$

In this sum, there are N terms of the form \mathbf{b}_i^2 , each of which is just b^2 if all steps have the same length. Thus, for a given walk

$$\mathbf{r}_{ee}^2 = Nb^2 + 2\mathbf{b}_1 \cdot \mathbf{b}_2 + 2\mathbf{b}_1 \cdot \mathbf{b}_3 + 2\mathbf{b}_1 \cdot \mathbf{b}_4 + \dots + 2\mathbf{b}_2 \cdot \mathbf{b}_3, \dots \quad (2.28)$$

But there may be many walks of N steps starting from the same origin, again as illustrated in Fig. 2.7. The average value $\langle \mathbf{r}_{ee}^2 \rangle$ is obtained by summing over all these paths

$$\langle \mathbf{r}_{ee}^2 \rangle = Nb^2 + 2\langle \mathbf{b}_1 \cdot \mathbf{b}_2 \rangle + 2\langle \mathbf{b}_1 \cdot \mathbf{b}_3 \rangle + 2\langle \mathbf{b}_1 \cdot \mathbf{b}_4 \rangle + \dots + 2\langle \mathbf{b}_2 \cdot \mathbf{b}_3 \rangle, \dots \quad (2.29)$$

Each dot product $\mathbf{b}_i \cdot \mathbf{b}_j$ ($i \neq j$) may have a value between $-b^2$ and $+b^2$. In a large ensemble of random walks, for every configuration with a particular scalar value $\mathbf{b}_i \cdot \mathbf{b}_j = b_{ij}$, there is another configuration with $\mathbf{b}_i \cdot \mathbf{b}_j = -b_{ij}$, so that the average over all available configurations becomes

$$\langle \mathbf{b}_i \cdot \mathbf{b}_j \rangle \rightarrow 0. \quad (2.30)$$

Combining Eqs. (2.29) and (2.30) yields the elegant result

$$\langle \mathbf{r}_{ee}^2 \rangle = Nb^2. \quad \text{random walk} \quad (2.31)$$

Example 2.3. Each amino acid in a protein contributes 0.36 nm to its contour length. For example, the protein actin, a major part of our muscles, is 375 amino acids long, giving an overall length of about 135 nm. But the amino acid backbone of a protein does not behave like a stiff rod; rather, it wiggles and sticks to itself at various locations. The random walk gives an approximate value for its size:

$$\langle \mathbf{r}_{ee}^2 \rangle = Nb^2 = 375 (0.36)^2$$

or

$$r_{ee,av} \sim \sqrt{375 \times 0.36} = 7.0 \text{ nm.}$$

In other words, the radius of a random ball of actin (<10 nm) is *much* less than its length when fully stretched (135 nm).

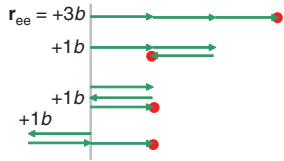


Fig. 2.8

Configurations for a one-dimensional walk with three segments of equal length b ; the red dot indicates the end of the path. Only half of the allowed configurations are shown, namely those with displacement $r_{ee} > 0$.

Random walks were introduced in this section as a description of the thermal motion of microscopic spheres. If each movement of a sphere in a given time step has a fixed length, then Eq. (2.31) establishes that $\langle r_{ee}^2 \rangle$ should grow linearly with time (i.e. linearly with the number of steps). It will be shown in Chapter 3 that even when the assumption of fixed step size is dropped, $\langle r_{ee}^2 \rangle$ still rises linearly with time. Yet random walks have greater applicability than just the description of thermal motion. Example 2.3 illustrates the conceptual importance of random walks in understanding the sizes of flexible macromolecules. We now probe the characteristics of random walks more deeply by examining the distribution in r_{ee}^2 within an ensemble of walks, in an effort to understand the distribution of polymer sizes and, in Chapter 3, the importance of entropy in polymer elasticity.

Consider the set of one-dimensional walks with three steps shown in Fig. 2.8: each walk starts off at the origin, and each step can point to the right or the left. Given that each step has 2 possible orientations, there are a total of $2^3 = 8$ possible configurations for the walk as a whole. Using $C(r_{ee})$ to denote the number of configurations with a particular end-to-end displacement r_{ee} , the eight configurations are distributed according to:

$$C(+3b) = 1 \quad C(+1b) = 3 \quad C(-1b) = 3 \quad C(-3b) = 1. \quad (2.32)$$

The reader will recognize that these values of $C(r_{ee})$ are equal to the binomial coefficients in the expansion of $(p + q)^3$; i.e. the values are the same as the coefficients $N! / i! j!$ in the expansion

$$(p + q)^N = \sum_{i=0, N} \{N! / i! j!\} p^i q^j, \quad (2.33)$$

where $j = N - i$. Is this fortuitous? Not at all; the different configurations in Fig. 2.8 just reflect the number of ways that the left- and right-pointing vectors can be arranged. So, if there are i vectors pointing left, and j pointing right, such that $N = i + j$, then the total number of ways in which they can be arranged is just the binomial coefficient

$$C(i, j) = N! / i! j!. \quad (2.34)$$

One can think of the configurations in Fig. 2.8 as random walks in which each step (or link) along the walk occurs with probability $1/2$. Thus, the probability $P(i, j)$ for there to be a configuration with (i, j) steps to the (left, right) is equal to the product of the total number of configurations ($C(i, j)$ from Eq. (2.34)) with the probability of an individual configuration, which is $(1/2)^i (1/2)^j$:

$$P(i, j) = \{N! / i! j!\} (1/2)^i (1/2)^j. \quad (2.35)$$

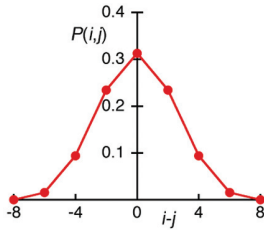


Fig. 2.9

Probability distribution from Eq. (2.35) for a one-dimensional walk with six segments.

Note that the probability in Eq. (2.35) is appropriately normalized to unity, as can be seen by setting $p = q = 1/2$ in Eq. (2.33):

$$\sum_{i=0,N} P(i, j) = \sum_{i=0,N} \{N! / i! j!\} (1/2)^i (1/2)^j = (1/2 + 1/2)^N = 1. \quad (2.36)$$

What happens to the probability distribution as the number of steps increases and the distribution consequently appears more continuous? The probability distribution for a one-dimensional walk with $N = 6$ is shown in Fig. 2.9, where we note that the end-to-end displacement $\mathbf{r}_{ee} = (j - i) = (2j - N)$ changes by 2 for every unit change in i or j . The distribution is peaked at $\mathbf{r}_{ee} = 0$, as one would expect, and then falls off towards zero at large values of $|\mathbf{r}_{ee}|$ where $i = 0$ or N . As becomes ever more obvious for large N , the shape of the curve in Fig. 2.9 resembles a Gaussian distribution, which has the form

$$\mathcal{P}(x) = (2\pi\sigma^2)^{-1/2} \exp[-(x-\mu)^2 / 2\sigma^2]. \quad (2.37)$$

Normalized to unity, this expression is a probability density (i.e. a probability per unit value of x) such that the probability of finding a state between x and $x + dx$ is $\mathcal{P}(x)dx$. The mean value μ of the distribution can be obtained from

$$\mu = \langle x \rangle = \int x \mathcal{P}(x) dx, \quad (2.38)$$

and its variance σ^2 is

$$\sigma^2 = \langle (x - \mu)^2 \rangle = \langle x^2 \rangle - \mu^2, \quad (2.39)$$

as expected.

Equation (2.37) is the general form of the Gaussian distribution, but the values of μ and σ are specific to the system of interest. As a trivial example, consider a random walk along the x -axis starting from the origin. First, $\mu = 0$ because the vectors \mathbf{r}_{ee} are equally distributed to the left and right about the origin, whence their mean displacement must be zero. Next, $\langle x^2 \rangle = Nb^2$ according to Eq. (2.31), so Eq. (2.39) implies $\sigma^2 = Nb^2$ when $\mu = 0$. Proofs of the equivalence of the Gaussian and binomial distributions at large N can be found in most statistics textbooks. However, the Gaussian distribution provides a surprisingly accurate approximation to the binomial distribution even for modest values of N , as can be seen from Fig. 2.9.

There is more to random or constrained walks and their relation to the properties of polymers than what we have established in this brief introduction. Other topics include the effects of unequal step size or constraints between successive steps, such as the restricted bond angles in a polymeric chain. In addition, the scaling behavior $\langle r_{ee}^2 \rangle \sim N$ may be modified in the presence of attractive interactions between different elements of the walk, useful when the walk is viewed as a polymer chain. These and other properties will be treated in Chapter 3.

2.4 Diffusion

The random walk introduced in Section 2.3 can be applied to a variety of problems and phenomena in physics and biology. In some cases, the trajectory of an object is precisely the linear motion with random forces that we have described in obtaining the generic properties of random walks. The analogous problem of rotational motion with random torques also is a random walk, but in the azimuthal angle of the object about a rotational axis. In other cases, the conformations of a system such as a polymer may be viewed as random walks even though there is no motion of the polymer itself; Example 2.3 illustrates this behavior for the protein actin. In this section of Chapter 2, we apply the properties of random walks to diffusive systems from two different perspectives:

- (i) as the translational and rotational motion of a single object in contact with its environment,
- (ii) as the collective motion of objects at sufficiently high number density that they can be described by continuous variables such as concentrations.

For the second situation, we will establish how the time evolution of the concentration obeys a relationship like Fick's Law. The inverse problem of the capture of a randomly moving object is treated in Chapter 11.

The trajectory of an individual molecule diffusing through a medium has the form of a random walk, which we characterize by the displacement vector \mathbf{r}_{ee} from the origin of the walk to its end-point. Suppose that the diffusing molecule travels a distance λ before it collides with some other component of the system. Then the random walk tells us that the average end-to-end displacement of the molecule's motion is

$$\langle \mathbf{r}_{ee}^2 \rangle = \lambda^2 N, \quad (2.40)$$

where $\langle \dots \rangle$ indicates an average and where N is the number of steps. How big is λ ? As illustrated in Fig. 2.10, λ might be very large for a gas molecule traveling fast in a dilute environment, but λ is rather small for a protein moving in a crowded cell. If there is one step per unit time, then $N = t$ and

$$\langle \mathbf{r}_{ee}^2 \rangle = \lambda^2 t. \quad (2.41)$$

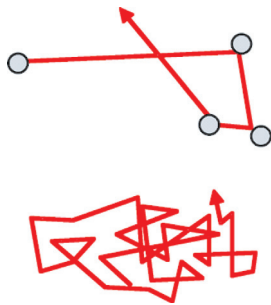


Fig. 2.10

Examples of single-particle diffusion at low (upper panel) and high (lower panel) densities.

Now, the units of Eq. (2.41) aren't quite correct, in that the left-hand side has units of $[length^2]$ while the right-hand side has $[length^2] \cdot [time]$. We accommodate this by writing the displacement as

$$\langle \mathbf{r}_{ee}^2 \rangle \equiv 6Dt, \quad \text{diffusion in three dimensions} \quad (2.42)$$

where D is defined as the diffusion coefficient. A molecule diffusing in a liquid of like objects has a diffusion coefficient D in the range 10^{-14} to 10^{-10} m²/s, depending on the size of the molecule.

The factor of 6 in Eq. (2.42) is dimension-dependent: for each Cartesian axis, the mean squared displacement is equal to $2Dt$. That is, if an object diffuses in one dimension only (for example, a molecule moves randomly along a track) then

$$\langle \mathbf{r}_{ee}^2 \rangle = 2Dt \quad \text{diffusion in one dimension} \quad (2.43)$$

and if it is confined to a plane, such as a protein moving in the lipid bilayer of the cell's plasma membrane, then

$$\begin{aligned} \langle \mathbf{r}_{ee}^2 \rangle &= \langle \mathbf{r}_{ee,x}^2 \rangle + \langle \mathbf{r}_{ee,y}^2 \rangle && \text{diffusion in two dimensions} \\ &= 2Dt + 2Dt = 4Dt. && (2.44) \end{aligned}$$

In all of these cases, D has units of $[length]^2 / [time]$.

Example 2.4. How long does it take for a randomly moving protein to travel the distance of a cell diameter, say 10 μm, if its diffusion coefficient is 10⁻¹² m²/s?

Inverting Eq. (2.42) yields

$$t = \langle \mathbf{r}_{ee}^2 \rangle / 6D,$$

so that

$$t = (10^{-5})^2 / 6 \cdot 10^{-12} = 16 \text{ s.}$$

Thus, it takes a protein less than a minute to diffuse across a cell at this diffusion coefficient; it would take much longer if the protein were large and $D \sim 10^{-14}$ m²/s.

The diffusion coefficient can be determined analytically for a few specific situations. One case is the random motion of a sphere of radius R subject to Stokes' Law for drag, Eq. (2.17): $F = 6\pi\eta Rv$, where v is the speed of the sphere and η is the viscosity of the fluid. The so-called Einstein relation that governs the diffusion coefficient reads

$$D = k_B T / 6\pi\eta R, \quad \text{Einstein relation} \quad (2.45)$$

where k_B is Boltzmann's constant. Now, $k_B T$ is close to the mean kinetic energy of a particle in a thermal environment, so the Einstein equation tells us that:

- the higher the temperature, the greater is an object's kinetic energy and the faster it diffuses,

Table 2.3 Examples of diffusion coefficients, showing the range of values from dilute gases to proteins in water. All measurements are at 25 °C, except xenon gas at 20 °C.

System	D (m ² /s)
Xenon	5760×10^{-9}
Water	2.1×10^{-9}
Sucrose in water	0.52×10^{-9}
Serum albumin in water	0.059×10^{-9}

- the larger an object's size, or the more viscous its environment, the slower it diffuses.

Equation (2.45) permits us to interpret the data presented at the beginning of this chapter for plastic spheres diffusing in water; the calculation is performed in the end-of-chapter problems. Lastly, Table 2.3 provides representative values for the diffusion coefficient for various combinations of solute and solvent. Note that D depends on both of these quantities, as can be seen in Eq. (2.45) where the solute dependence enters through its molecular radius R and the solvent enters through its viscosity η .

Example 2.5. A biological cell contains internal compartments with radii in the range 0.3 to 0.5 μm . Estimate their diffusion coefficient.

Suppose a cellular object like a vesicle has a radius of 0.3 μm and moves in a medium with viscosity $\eta = 2 \times 10^{-3} \text{ kg / m} \cdot \text{s}$. At room temperature, the Einstein relation predicts

$$D = 4 \times 10^{-21} / (6\pi \cdot 2 \times 10^{-3} \cdot 3 \times 10^{-7}) = 4 \times 10^{-13} \text{ m}^2/\text{s},$$

which has the order of magnitude that we expect.

Although the *translational* motion of an object is the most common example of diffusion, it's not the only one. For example, a molecule like a protein can rotate around its axis at the same time as it travels. Although this rotation could be driven by an external force with a particular angular speed ω , it could also just be random, such that ω changes in both magnitude and direction continuously and randomly. When we talk about a protein docking onto a substrate or receiving site, it may be undergoing rotational diffusion before the optimal orientation is achieved. A random "walk" in angle θ as an object rotates around its axis can be written as

$$\langle \theta^2 \rangle = 2D_r t, \quad (2.46)$$

where D_r is the rotational diffusion coefficient. Once again, the mean change in θ from its original value at $t = 0$ grows like the square root of the elapsed time.

For a sphere rotating in a viscous medium, there is an expression for D_r , just like the translational diffusion of Eq. (2.45), namely

$$D_r = k_B T / 8\pi\eta R^3. \quad \text{rotational diffusion} \quad (2.47)$$

Note, the units of D_r are $[time^{-1}]$, whereas D is $[length^2]/[time]$; hence, there is an extra factor of R^2 in the denominator of Eq. (2.47) compared to Eq. (2.45).

2.4.1 Densities and fluxes

We have approached the phenomenon of diffusion at the microscopic level by considering the trajectories of individual particles, from which ensemble averages can be constructed. This tells us the average behavior of particles moving in a fluid. An alternate approach involves the behavior of macroscopic quantities such as concentrations and fluxes, that themselves represent ensemble averages over the locations of individual particles. Within this description based on local averages, quantities such as the temperature and concentration of the system's components need not be spatially uniform, and their time evolution can be understood using a mathematical formalism that we now develop.

To introduce the concepts behind the mathematics, consider the situation in Fig. 2.11, where a small amount of deep red dye has been placed in a uniform layer at the bottom of a fluid-filled container. The figure shows the appearance of the dye at three different times, starting just after the dye has been introduced (on the left) to after it has diffused through the medium to produce a largely homogenous solution (on the right). We will assume that the concentration of the dye depends only on height (which we will define as the x -direction) and is the same at all locations with the same height at any given time. The concentration $c(x,t)$ then depends on two variables: the location x above the bottom of the container, and the time t from when the dye was introduced. At the microscopic level, we know that dye molecules are moving through the solvent at speeds dictated by the temperature (through $k_B T$), colliding with solvent molecules and slowly moving up through the fluid. At the macroscopic level, we say that the concentration of dye molecules evolves like the schematic representation in Fig. 2.12: at small t , $c(x,t)$ falls rapidly with x while at large times $c(x,t)$ is asymptotically independent of x .

The change in concentration with time is accompanied by a net migration of solute molecules, which is characterized macroscopically by a flux $j(x,t)$. From our microscopic picture, we know that solute molecules are moving in all directions, but that, on average, more of them are moving

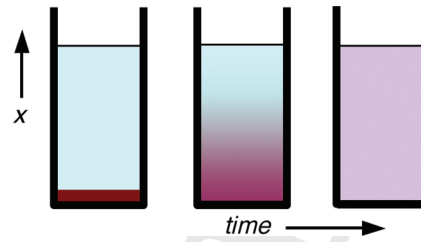


Fig. 2.11

Diffusion of a deep red dye in a light blue solvent. Examples are shown at early, intermediate and late times, from left to right respectively; the x -axis is drawn vertically in this diagram, so the concentration of dye, $c(x,t)$ falls with increasing x . The concentration is uniform in the horizontal plane.

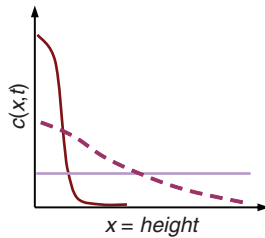


Fig. 2.12

Concentration profiles corresponding to the diffusion of a dye shown in Fig. 2.11.

upward in Fig. 2.11 than are moving downward, giving a net upward drift of solute. The flux is the net number of molecules, per unit area per unit time, crossing an imaginary plane in the yz directions at location x . That is, if the plane has area A and Δn is the net number of molecules crossing it in time Δt , then the flux is $A^{-1} \Delta n / \Delta t$, where the infinitesimal limit $A^{-1} dn/dt$ is clear. At early times, when the concentration gradient dc/dx is the largest, the flux will also be large. At late times, when the system is almost uniform so that the concentration gradient is very small, the flux is also small. In other words, what drives the flux is the concentration gradient, not the concentration itself: at long times in Fig. 2.11, the concentration may still be large, but the gradient is tiny because the system has become uniform.

Now let's express the previous paragraph in mathematical terms by saying that the flux is proportional to the (negative) gradient of the concentration, as

$$j \propto -dc/dx. \quad (2.48)$$

The minus sign is required in Eq. (2.48) because the flux is positive when the gradient is negative: otherwise, molecules would spontaneously move from regions of low concentration to regions of high concentration, completely counter to our expectations from entropy. The proportionality sign can be removed by introducing the diffusion coefficient D ,

$$j = -D dc/dx, \quad \text{Fick's Law} \quad (2.49)$$

an expression known as Fick's First Law of diffusion. At this point, we have not established that D in Eq. (2.49) is the same as the diffusion coefficient appearing in Eqs. (2.42)–(2.44), but we will do so shortly.

Fick's first law is almost the only result for diffusion that appears in the remainder of this book. Nevertheless there are two other important results about diffusion that are easily obtained, and so we present them here. The first is the equation of continuity, which is a conservation law applicable to a variety of situations involving fluids. We consider the diffusion of fluid particles in a cylindrical region of constant cross-sectional

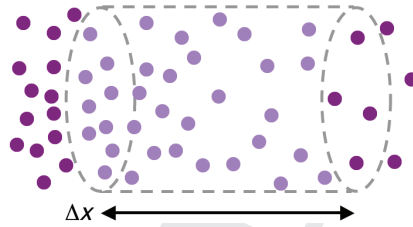


Fig. 2.13

Diffusion of particles along a concentration gradient. The uniform cylinder with cross-sectional area A and length Δx is a strictly mathematical surface: we allow particles to enter and leave this surface only longitudinally through its ends, not laterally through its sides.

area A , as shown in Fig. 2.13. The cylinder is not meant to be a physical object, just a mathematical surface with a defined shape, such that the net motion of particles is along the x -axis. At the left-hand end of the cylinder at $x = 0$, there is a flow of particles into the cylindrical region if $j > 0$, and at the right-hand end at $x = \Delta x$ there is a flow out, again if $j > 0$. If the fluxes at the two ends are not the same, then the number of fluid particles in the cylinder must increase or decrease, where we have imposed the condition that there is no net lateral flow. The total increase in the number of particles ΔN in an elapsed time Δt is then

$$\Delta N = \{[\text{flux at } x = 0] - [\text{flux at } x = \Delta x]\} \cdot [\text{cross-sectional area of cylinder}] \cdot [\text{elapsed time}].$$

In symbols, this is

$$\Delta N = \{j(0) - j(\Delta x)\} A \Delta t. \quad (2.50)$$

The change in the concentration Δc of particles in the cylinder arising from diffusion is $\Delta N / (A \Delta x)$, where $A \Delta x$ is the volume of the cylinder. Thus, after some rearrangement

$$\Delta c / \Delta t = \{j(0) - j(\Delta x)\} / \Delta x. \quad (2.51)$$

By definition, the change in the flux across the cylinder Δj has the opposite sign to the flux difference in Eq. (2.51): $\Delta j = j(\Delta x) - j(0)$. Thus, rewriting Eq. (2.51) in its infinitesimal limit,

$$dc/dt = -dj / dx, \quad \text{continuity equation} \quad (2.52)$$

which is the continuity equation. Note that in Eqs. (2.50)–(2.52), some of the functional dependence of c and j has been suppressed for notational simplicity.

Lastly, we substitute Eq. (2.49) into the right-hand side of Eq. (2.52) to obtain Fick's second law of diffusion (also known as the diffusion equation), namely

$$\partial c / \partial t = D \partial^2 c / \partial x^2, \quad \text{diffusion equation} \quad (2.53)$$

where we have assumed D does not depend on x . We've had to be slightly less cavalier with our calculus by writing the derivatives as partial derivatives like $\partial/\partial x$, in recognition that c depends on both x and t , so that a derivative with respect to x is taken with t fixed, and vice versa. We can now return to the equivalence of the diffusion coefficient in Eqs. (2.29) and (2.43).

The profiles in Fig. 2.12 schematically represent how the concentration $c(x,t)$ of a layer of dye evolves with time. Equation (2.53) provides us with the means of identifying the appropriate functional form for $c(x,t)$ from an initial configuration. One such solution for a solute initially concentrated at the coordinate origin is

$$c(x,t) = c_0 (4\pi Dt)^{-1/2} \exp(-x^2 / 4Dt), \quad (2.54)$$

where c_0 is a parameter. The proof is left as an exercise in the end-of-chapter problems. To characterize how the concentration profile changes with time, we evaluate the mean square displacement of the solute particles from the origin using Eq. (2.54). Applying the usual rules for the construction of ensemble averages, we find

$$\begin{aligned} \langle x^2 \rangle &= \int x^2 c(x,t) dx / \int c(x,t) dx \\ &= \int_0^\infty x^2 \exp(-x^2 / 4Dt) dx / \int_0^\infty \exp(-x^2 / 4Dt) dx. \end{aligned} \quad (2.55)$$

This equation contains definite integrals, whose values are given in the end-of-chapter problems. Substituting,

$$\langle x^2 \rangle = (4Dt) \cdot (\sqrt{\pi} / 4) / (\sqrt{\pi} / 2) = 2Dt. \quad (2.56)$$

This is nothing more than Eq. (2.43), and it shows that we have been using the symbol for the diffusion coefficient correctly.

2.5 Fluctuations and correlations

In the simplest random walk (see Section 2.3), the direction of each step in the walk is completely uncorrelated with its neighbors, and this characteristic gives rise to a particularly simple form for the mean squared end-to-end displacement, $\langle \mathbf{r}_{ee}^2 \rangle = Nb^2$, where each walk in the ensemble has N steps of identically the same length b . That neighboring steps are uncorrelated has the mathematical consequence that the mean value of the scalar product of neighboring bond vectors vanishes when the number of walks in the ensemble is large, $\langle \mathbf{b}_i \cdot \mathbf{b}_{i+1} \rangle \rightarrow 0$, where the average is performed at the same step i on all walks in the ensemble. For the same reason, it is also true that when steps i and j are far from each other on a given walk, $\langle \mathbf{b}_i \cdot \mathbf{b}_j \rangle \rightarrow 0$.

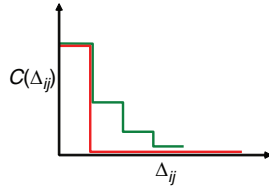


Fig. 2.14

Correlation function $C(\Delta_{ij})$ for the scalar product of bond vectors $\mathbf{b}_i \cdot \mathbf{b}_j$, separated by Δ_{ij} steps on a random walk: the green curve is a schematic representation of a restricted walk while the red curve is for an unrestricted walk.

Suppose now that the directions of neighboring steps are correlated; for instance, suppose that neighboring bond vectors cannot change direction by more than 90° . In terms of scalar products, this implies $0 \leq \mathbf{b}_i \cdot \mathbf{b}_{i+1} \leq b^2$, still assuming that all steps have the same length. For bonds pointing in three dimensions, it is straightforward to show that $\langle \mathbf{b}_i \cdot \mathbf{b}_{i+1} \rangle = b^2/2$, which is left as an exercise for the interested reader. Going to second-nearest neighbors gives a non-vanishing result for $\langle \mathbf{b}_i \cdot \mathbf{b}_{i+2} \rangle$, which is smaller than $b^2/2$, but still larger than zero applicable when the steps are uncorrelated. As the distance along the contour of the walk increases, the mean value $\langle \mathbf{b}_i \cdot \mathbf{b}_j \rangle$ gradually vanishes towards the same limit as walks with uncorrelated steps, as shown schematically in Fig. 2.14. This means that $\langle \mathbf{r}_{cc}^2 \rangle$ of the walk with correlated steps still is still proportional to N for long walks, $\langle \mathbf{r}_{cc}^2 \rangle \propto N$, but the proportionality constant for correlated walks is no longer b^2 ; for the particular correlated walk that we have just described, $\langle \mathbf{r}_{cc}^2 \rangle > Nb^2$ and the effective “size” of the walk is larger than it is for its uncorrelated cousin.

In describing the behavior of random walks, the quantity $\langle \mathbf{b}_i \cdot \mathbf{b}_j \rangle$ may play the role of a correlation function, a quantity that portrays the magnitude of the correlations in a system as a function of an independent variable, which in the case of random walks or polymers could be the separation $\Delta_{ij} = |i-j|$ along the contour. To illustrate the general behavior of correlation functions, let's start by defining

$$C(\Delta_{ij}) \equiv \langle \mathbf{b}_i \cdot \mathbf{b}_j \rangle_{\Delta_{ij}} / b^2. \quad (2.57)$$

Here, Δ_{ij} may be as small as zero, in which case $C(0) = 1$ because the numerator of the right-hand side of Eq. (2.57) is just the mean squared length of the steps on the walk, b^2 by construction. On the other hand, both types of walks we have discussed above (unrestricted step-to-step bond directions and partly restricted bond directions) display $\langle \mathbf{b}_i \cdot \mathbf{b}_j \rangle_{\Delta_{ij}} \rightarrow 0$ at large separations. This behavior for $C(\Delta_{ij})$ is plotted schematically in Fig. 2.14: the red curve is the unrestricted walk where the only non-vanishing value of the correlation function is $C(0) = 1$, while the green curve is the restricted walk, where $C(0) = 1$, $C(\Delta_{ij} = 1) = 1/2$, etc. In the language of correlation functions, it is often conventional to define a quantity to be correlated when $C = 1$ and uncorrelated when C vanishes, and we see that this normalization applies to the orientations of the bond directions as expressed in $\langle \mathbf{b}_i \cdot \mathbf{b}_j \rangle$.

The decay of the correlation function provides a quantitative measure of the range of Δ_{ij} where strong correlations are present. In the unrestricted walk, $C(\Delta_{ij})$ falls to zero at $\Delta_{ij} = 1$, whereas in the restricted case, the fall-off is slower because correlations exist to larger values of Δ_{ij} as expected. We will establish in Chapter 3 that $C(x)$ for random walks should decay exponentially with x as

$$C(x) \propto \exp(-x/\xi), \quad (2.58)$$

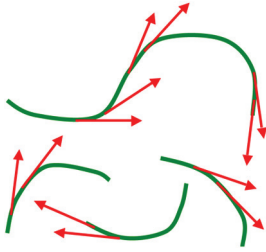


Fig. 2.15

Two approaches of obtaining a tangent-tangent correlation function at modest values of the separation Δs along the curve. In the top panel, a long curve is sampled at many different pairs of locations, each separated by the same Δs . In the bottom panel, a larger number of short paths are sampled to determine the correlation function with the same accuracy, but at only modest values of Δs .

where ξ is a characteristic of the system. For walks and polymers, ξ is the correlation length, while in other situations, ξ could be a correlation time or some other variable. The correlation length is also manifested in the physical “size” of the walk, in that $\langle r_{ee}^2 \rangle$ is linearly proportional to ξ : from Chapter 3, $\langle r_{ee}^2 \rangle = 2\xi L$, where $L = Nb$ is the contour length. For the unrestricted random walk, $\xi = b/2$.

In this text, much of the experimental interest in correlation lengths includes not just random walks and rotations, but also physical systems such as macromolecules and filamentous cells whose size and sinuous shape obey the same mathematical expressions as the random walk. In such cases, it is not always possible to obtain long polymers or filaments that would provide good statistical accuracy for the correlation function at separations large compared to the correlation length. That is, it may not be possible to follow $C(x)$ out to large enough x to see it fall below $1/e$ of its initial value, as in the top panel of Fig. 2.15. When this occurs, an alternate strategy is to measure $C(x)$ accurately at modest values of x by sampling a much larger number of configurations, as in the bottom panel of Fig. 2.15. For this strategy to work, however, the sample must be sufficiently large to yield very accurate values of the correlation function, because the range in x over which $C(x)$ is to be fitted by the exponential function is not large.

Correlation functions describing the orientation of objects, as expressed through tangents to curves or normal vectors to undulating surfaces, have widespread application and appear in many chapters of this text, starting in Chapter 3. However, correlations in time, rather than orientation, are also important, as we illustrate by considering the process of cell division. Consider a species that is capable of forming a robust filament starting from a single cell. After the first doubling time has elapsed, two daughter cells remain attached and form the beginning of a filament. Because the cleavage plane during division is very close to the center of the cell, the daughter cells have almost equal length. These two cells will then grow and divide to create a short filament, with four almost-identical cells. Over an interval of several doubling times, all cells in the filament have very similar lengths, although the average cell length increases continuously throughout the division cycle, as one would expect.

Not only are there are small variations in the length of the daughter cells, there are variations in the growth rates of the cells such that their division times gradually lose synchronization. Thus, as the filament lengthens, there will be regions of 2^4 or 2^5 cells all of which have grown in synchrony, adjoining other regions of where the cell lengths are slightly different. The greatest variation will occur when the cells are near their division point, where a string of very long cells that have grown at the same rate lie beside a string of short cells whose parent cell divided a little earlier than its neighbors. Some sample data are shown in Fig. 2.16 from the rod-shaped alga

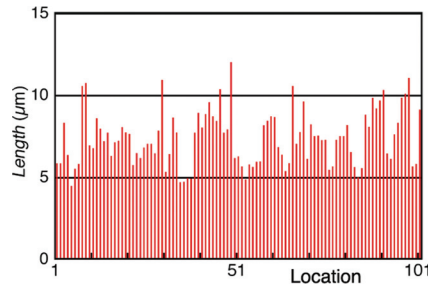


Fig. 2.16

Cell lengths (in μm) for 100 sequential cells as a function of position on a linear filament of the green alga *Stichococcus Y*.

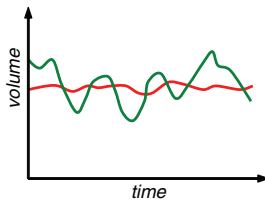


Fig. 2.17

Schematic representation of the fluctuations in volume at fixed temperature for a system with a large (red) and small (green) compression resistance. The fluctuations are recorded as a function of time.

Stichococcus; the plot shows the length of each cell as a function of its position in the linear filament. The cell lengths are locally correlated: domains of high correlation in length between neighboring cells have grown in synchrony from their common parent.

Before closing this chapter, we make a slightly more mathematical pass through a concept introduced in Chapter 1 when discussing the shape fluctuations of soft filaments in thermal equilibrium. Fluctuations arise in the energy of a system owing to the interaction with its environment at fixed temperature. As we described in Chapter 1, the stiffer a filament is, the smaller will be the variations in its shape arising from thermal fluctuations. This is illustrated in Fig. 2.17 for two systems with the same mean volume V_{av} but differing compression resistance. The red curve represents a stiff system with a large compression resistance: as time passes, the volume of the system stays fairly close to its mean value. In contrast, the green curve has low compression resistance, which reflects its ability to explore a larger range of configurations without a large change in its energy.

Put mathematically, the statistical variance of a quantity x about its mean value x_{av} , namely $\langle (x - x_{\text{av}})^2 \rangle$, is inversely proportional to a system's resistance to change of that quantity. That is, the variance of the volume of a system is inversely proportional to its compression modulus; similarly, the variance in the energy of a system at fixed temperature is inversely proportional to its heat capacity. Let's now make this exact. The compression modulus of a material is defined as

$$K_V^{-1} = -V^{-1} (\partial V / \partial P)_T, \quad (2.59)$$

where the subscript “T” means that the partial derivative is performed at constant temperature. This definition implies that the larger the volume change (ΔV) in response to a pressure change (ΔP), the *smaller* the compression modulus: a large value for K_V means that the system has a large resistance to change. The minus sign is needed on the right-hand side of the equation because the volume decreases as the pressure increases. Note that K_V has the units of pressure, or energy per unit volume.

Establishing the link between K_V and the variance of V takes a few more concepts from statistical mechanics than we have at our fingertips right now, so the proof is relegated to Appendix D. The relation is

$$K_V^{-1} = \langle (V - V_0)^2 \rangle / (k_B T V_0), \quad (2.60)$$

where V_0 is the mean value of the volume at the fixed temperature and pressure of interest. As required, this equation provides K_V with units of energy (through $k_B T$) per unit volume and it demonstrates the inverse relation between K_V and the variance of the volume. Similar expressions can be obtained for other elastic moduli such as the shear modulus and Young's modulus.

Summary

The softness of the cell's mechanical components means that their shapes may fluctuate as the component exchanges energy with its thermal environment. This is particularly true at the molecular level, but may also be seen at larger length scales for biofilaments like actin or membranes like the lipid bilayer. In this chapter, we provide some of the mathematical formalism needed for the description of fluctuating systems, and apply this formalism to linear polymers and diffusion in a viscous medium.

The distribution of values of an observable A is described by the probability density $\mathcal{P}(A)$, which is obtained from the number of times dn_A that the observable is found in the range A to $A + dA$, in a sample of N trials; namely, $\mathcal{P}(A) dA = dn_A / N$. Having units of A^{-1} , $\mathcal{P}(A)$ is normalized to unity via $\int \mathcal{P}(A) dA = 1$, permitting the calculation of ensemble averages via expressions such as $\langle A^n \rangle \equiv \int A^n \mathcal{P}(A) dA$. Although the mean value of an observable $\langle A \rangle$ is useful for characterizing the properties of a system, it is often important to understand the behavior of the underlying distribution $\mathcal{P}(A)$ itself. As an example, the probability of a random walk in one dimension, consisting of i steps to the left and j steps to the right, is $P(i, j) = \{N! / i! j!\} (1/2)^i (1/2)^j$, where the probability of stepping in either direction is equal to $1/2$ and the total number of steps is N . When N is large, the end-to-end distance of the walk satisfies $\langle r_{ee}^2 \rangle = Nb^2$, where each step in the walk has identically the same length b . The important feature of this result is that the mean value of r_{ee}^2 is proportional to N , rather than N^2 ; equivalently, $\langle r_{ee}^2 \rangle$ is proportional to the contour length $L = Nb$, rather than the square of the contour length as it would be for a straight line. As N becomes large, the probability distribution $P(i, j)$ looks increasingly like a smooth Gaussian distribution, with a probability density of the form $\mathcal{P}(x) = (2\pi\sigma^2)^{-1/2} \exp[-(x-\mu)^2 / 2\sigma^2]$, where the parameters are given by $\mu = \langle x \rangle$ and $\sigma^2 = \langle x^2 \rangle - \mu^2$.

By means of the fluctuation-dissipation theorem, probability distributions such as $\mathcal{P}(A)$ permit one to determine material characteristics such as elastic moduli or the specific heat. In thermal equilibrium, the energy and other characteristics of a system fluctuate about some mean value, say A_0 . The variance of the fluctuations of this characteristic, $\langle (A - A_0)^2 \rangle$, is inversely proportional to the system's resistance to change of that quantity. For example, the compression modulus K_V at constant temperature is related to the change in volume V with pressure via $K_V^{-1} = -V^{-1}(\partial V / \partial P)_T$: the more rapidly the volume changes with pressure, the lower the compression modulus. In terms of fluctuations, the compression modulus is given by $K_V^{-1} = \langle (V - V_0)^2 \rangle / (k_B T V_0)$, where V_0 is the equilibrium value of the volume at fixed T and P .

Probability distributions $\mathcal{P}(A)$ are functions of a single variable, A . Yet within a sequence of measurements, there may be correlations among the values of A as measured at different locations within the system or at the same location but at different times. An example is the local orientation of a unit tangent vector $\mathbf{t}(s)$ measured at location s along a wiggling biofilament. The mean value of \mathbf{t} measured over all locations at the same time, or a specific location as a function of time, vanishes if the filament executes random motion: $\langle \mathbf{t} \cdot \mathbf{t}_0 \rangle = 0$, where \mathbf{t}_0 is a fixed reference direction, although $\langle t^2 \rangle = 1$ because the vector has unit length. However, the directions of \mathbf{t} at nearby locations s_i and s_j may be correlated such that $\langle \mathbf{t}_i \cdot \mathbf{t}_j \rangle \neq 0$ when averaged over all pairs of locations separated by the same $\Delta s = |s_i - s_j|$. If the local orientations of the filament are uncorrelated at large separations, then $\langle \mathbf{t}_i \cdot \mathbf{t}_j \rangle \rightarrow 0$ as $\Delta s \rightarrow \infty$. This suggests that a correlation length ξ characterizes the decay of the correlations with increasing distance. For many systems, the decay is exponential, and the correlation function $C(\Delta s) \equiv \langle \mathbf{t}_i \cdot \mathbf{t}_j \rangle_{\Delta s}$ can be parametrized as $C(\Delta s) = \exp(-\Delta s / \xi)$. As will be established later, the mean square end-to-end displacement of a random walk can be written as $\langle r_{ee}^2 \rangle = 2\xi L$, where L is the contour length of the walk as defined above.

The diffusion of the cell's molecular components, and perhaps the random motion of the cell itself in a fluid environment, are formally similar to random walks. In a viscous environment, the motion of an object is affected by the presence of drag forces that depend upon the instantaneous speed of the object: the higher the speed, the larger the force. For slowly moving objects, viscous drag exerts a force $F \propto -v$ for linear motion and a torque of $\mathcal{T} \propto -\omega$ for rotational motion, where ω is the angular speed and the minus sign indicates that drag opposes the motion of the object. Given that force is proportional to the rate of change of velocity according to Newton's Second Law of mechanics, the speed of an object initially moving at low speeds in a viscous environment obeys $dv/dt \propto -v$, which means that $v(t)$ must decay exponentially with time (similarly for torque and the rate of change of the angular velocity). The form of the drag force

is known analytically for a few simple shapes like a sphere of radius R : $F = -6\pi\eta Rv$ (Stokes' Law) and $T' = -8\pi\eta R^3\omega$, where η is the viscosity of the medium. In fluid mechanics, a useful benchmark for assessing the importance of drag is provided by a dimensionless quantity called the Reynolds number $\mathbf{R} \equiv \rho v \lambda / \eta$, where ρ is the density of the fluid and λ is the length of the object along the direction of motion. When \mathbf{R} is large, the motion is dominated by inertia, while at small values of \mathbf{R} , the motion is dominated by drag; the transition between these two domains occurs for \mathbf{R} around 10–100. A bacterium swimming in water has $\mathbf{R} < 10^{-4}$, meaning that its motion is overwhelmingly dominated by drag.

Strong as the drag forces on a cell may be, this does not mean that cells or their molecular components are motionless unless they have some means of generating movement. The energy provided through the interaction of the cell with its thermal environment causes the cell to move randomly, even if slowly. This is an example of diffusive motion, which is formally equivalent to a random walk in that the end-to-end displacement of the trajectory of a diffusing particle obeys $\langle r_{ee}^2 \rangle = 2Dt$, $4Dt$ or $6Dt$ in one, two or three dimensions, respectively, where D is called the diffusion coefficient; in these expressions, the elapsed time t takes the place of the number of steps N in a random walk. Einstein analyzed the diffusion of a sphere in a thermal environment, and was able to establish that $D = k_B T / 6\pi\eta R$, where η is the viscosity of the medium, as usual. Objects can also rotate diffusively, with their angular change obeying $\langle \theta^2 \rangle = 2D_r t$, where the rotational diffusion coefficient of a sphere has the form $D_r = k_B T / 8\pi\eta R^3$.

We have introduced diffusion in terms of the motion of a single object or particle, both its translational motion through its environment or its rotational motion about an axis. Another approach to diffusion involves quantities that represent averages over many objects, assumed to have high enough numerical density that the averages apply to a local region of the system. That is, we assume that the concentration of particles, $c(x, t)$ can be determined within a sufficiently small volume that $c(x, t)$ can be assigned a meaningful and accurate value for each location x and time t . For our purposes, we take the concentration to vary only along the x -axis of the system. Changes in the concentration with time usually result from a flux $j(x, t)$, which is the net number of particles per unit area per unit time crossing an imaginary plane in the yz directions at a location x . Fick's first law relates the flux to the gradient of the concentration through $j = -D dc/dx$, where D is the diffusion coefficient introduced previously. As particles diffuse through the system, the concentration at a specific location changes with time according to the equation of continuity $dc/dt = -dj/dx$. These two equations for flux can be combined to yield the diffusion equation $\partial c / \partial t = D \partial^2 c / \partial x^2$, where partial derivatives are required because $c(x, t)$ depends on both x and t .

Having made a first pass through the mathematical machinery for describing fluctuating systems, the next two chapters deal with the properties of flexible polymers in greater detail. If much of the material in the current chapter is new to the reader, it is probably advisable to solve a selection of the problems in the next section to build a working knowledge of applying the formalism to physical systems.

Problems

Applications

- 2.1. In a series of experiments, a parameter A is found to have values between 0 and 1 (A is measured in fictitious units we will call dils) according to the following distribution.

Range of A (dils)	Number
0.0 – 0.2	15
0.2 – 0.4	65
0.4 – 0.6	55
0.6 – 0.8	30
0.8 – 1.0	10

Determine the probability density $\mathcal{P}(A)$ for the distribution (including units), and evaluate $\langle A \rangle$ and $\langle A^2 \rangle$.

- 2.2. Calculate the mass of a plastic bead with a diameter of $1 \mu\text{m}$ and a density of $1.0 \times 10^3 \text{ kg/m}^3$. Find its root mean square speed at room temperature if its mean kinetic energy is equal to $3k_{\text{B}}T/2$.
- 2.3. The magnitude of the viscous drag force exerted by a stationary fluid on a spherical object of radius R is $F = 6\pi\eta Rv$ at low speeds and $F = (\rho/2)AC_{\text{D}}v^2$ at high speeds. Apply this to a spherical cell $1 \mu\text{m}$ in radius, moving in water with $\eta = 10^{-3} \text{ kg/m} \cdot \text{s}$ and $\rho = 10^3 \text{ kg/m}^3$. Take the cell to have the same density as water, and let its drag coefficient C_{D} be 0.5.
- Plot the two forms of the drag force as a function of cell speed up to $100 \mu\text{m/s}$.
 - Find the speed at which the linear and quadratic drag terms are the same.
- 2.4. What is the drag force that a molecular motor must overcome to transport a vesicle in a cell? Assume that the vesicle has a radius of

- 100 nm and travels at 0.5 $\mu\text{m/s}$. Take the viscosity of the cytoplasm to be one hundred times that of water. What power must the motor generate as it transports the vesicle?
- 2.5. Some bacteria have the approximate shapes of spherocylinders – a uniform cylinder (length L , radius R) which is capped at each end by hemispheres. Take *E. coli* to have such a shape, with a diameter of 1 μm and an overall length of 4 μm . Find the drag force experienced by a cell of this shape if the drag force is in the turbulent regime where $F_{\text{drag}} \sim v^2$. Take the density of the fluid medium to be 10^3 kg/m^3 , the drag coefficient to be 0.5 and the cell to be traveling at 20 $\mu\text{m/s}$.
- (a) Evaluate the force for two different orientations of the cell – motion along its symmetry axis and motion transverse to its axis. Quote your answer in pN.
- (b) Show that the ratio of the drag forces in these orientations (transverse:longitudinal) is equal to $1 + 12/\pi$.
- 2.6. Calculate the power required to maintain a spherical bacterium (diameter of 1 μm) rotating at a frequency of 10 Hz when it is immersed in a fluid of viscosity $10^{-3} \text{ kg/m}\cdot\text{s}$. If the energy released per ATP hydrolysis is $8 \times 10^{-20} \text{ J}$, how many ATP molecules must be hydrolyzed per second to support this motion?
- 2.7. The Reynolds number for the motion of cells in water is in the 10^{-5} range. To put this number into everyday context, consider a person swimming in a fluid of viscosity η . Making reasonable assumptions for the length and speed of the swimmer, what value of η corresponds to a Reynolds number of 10^{-5} ? Compare your result with the fluids in Table 2.1.
- 2.8. The sources of household dust include dead skin cells, which we will model as cubes 5 μm to the side having a density of 10^3 kg/m^3 .
- (a) What is the root mean square speed of this hypothetical dust particle at $T = 20 \text{ }^\circ\text{C}$ due to thermal motion alone?
- (b) To what height h above the ground could this particle rise at room temperature before its thermal energy is lost to gravitational potential energy? Assume that the gravitational acceleration g is 10 m/s^2 .
- 2.9 (a) A particular insect flies at a constant speed of 1 m/s, and randomly changes direction every 3 s. How long would it take for the end-to-end displacement of its random motion to equal 10 m on average?
- (b) Suppose the insect emitted a scent that was detectable by another of its species even at very low concentrations. The molecule of the scent travels at 300 m/s, but changes direction through collisions

- every 10^{-11} s. Once the molecule has been released by the insect, how long would it take for the end-to-end displacement of its trajectory to equal 10 m on average?
- (c) From your results in parts (a) and (b), what is the better strategy for an insect looking for a mate, which it can detect through an emitted pheromone: (i) be motionless and wait for a scent, or (ii) actively search for a mate by flying?
- 2.10. An experiment was described in Section 2.1 in which the two-dimensional trajectories of plastic beads in water were found to obey $\langle r_{ee}^2 \rangle = (1.1 \pm 0.3 \mu\text{m}^2/\text{s})t$. What diffusion coefficient D describes these data? Using the Einstein relation, calculate D expected for spheres of diameter $1 \mu\text{m}$ moving in water, and compare with the measured value.
- 2.11. A spherical bacterium with a radius of $1 \mu\text{m}$ moves freely in water at 20°C .
- (a) What is its rotational diffusion coefficient?
- (b) What is the root mean square change in angle around a rotational axis over an interval of 1 minute arising from thermal motion?

Be sure to quote your units for parts (a) and (b).

- 2.12. The plasma membrane plays a pivotal role in maintaining and controlling the cell's contents, as can be seen in the following simplified example. Suppose that the number density of a particular small molecule, which we'll call molly, is 10^{25} m^{-3} higher in the cytoplasm than the medium surrounding the cell. Let molly have a diffusion coefficient in the cytoplasm of $5 \times 10^{-10} \text{ m}^2/\text{s}$.
- (a) If the drop in concentration of molly from the inside to the outside of the cell occurred over a distance of 5 nm, the thickness of the lipid bilayer, with what flux would molly pass out of the cell?
- (b) If the cells in question are spherical with a diameter of $4 \mu\text{m}$, how many copies of molly are there per cell?
- (c) If molly continued to diffuse out of the cell at the rate found in (a), ignoring the drop in the internal concentration of molly with time, how long would it take for the concentration of molly to be the same on both sides of the membrane?
- 2.13. Consider three different power-law forms of the drag force with magnitudes:

$$F_{1/2} = a v^{1/2} \quad (\text{square root})$$

$$F_1 = b v^1 \quad (\text{linear})$$

$$F_{3/2} = c v^{3/2} \quad (3/2 \text{ power}).$$

Traveling horizontally from an initial speed v_0 , an object experiencing one of these drag forces would come to rest at

$$x_{\max} = (2m/3a)v_0^{3/2} \quad (\text{square root})$$

$$x_{\max} = mv_0/b \quad (\text{linear})$$

$$x_{\max} = 2m v_0^{1/2}/c \quad (3/2 \text{ power}).$$

- (a) Determine the coefficients a , b and c (quote your units) for a cell of mass 1×10^{-14} kg whose drag force is measured to be 5 pN when traveling at $10 \mu\text{m/s}$.
- (b) Find the maximum displacement that the cell could reach for each force if $v_0 = 1 \mu\text{m/s}$.
- 2.14. In a particularly mountainous, and imaginary, region of the world, the only way to get from A to B is by one of several meandering roads. A group of unsuspecting tourists set out from town A one morning with enough gas in each of their cars to travel 100 km, which is 10 km more than the displacement from A to B. They take different routes, but each car runs out of gas before the reaching the destination, at displacements of 60, 64, 75 and 83 km from town A as the proverbial crow flies. Treating them as an ensemble, what is the persistence length of the roads?
- 2.15. The persistence length of DNA is measured to be 53 nm.
- (a) Over what distance along the contour has its tangent correlation function dropped to $1/10$?
- (b) Using the result from Chapter 3 that $\langle r_{ee}^2 \rangle = 2\xi_p L$, find the root mean square end-to-end length of a strand of DNA from *E. coli* with a contour length of 1.6 mm. Quote your answer in microns.

Formal development and extensions

Some of the following problems require definite integrals for their solution.

$$\int_0^{\infty} \exp(-x^2) dx = \sqrt{\pi}/2 \quad \int_0^{\infty} x^2 \exp(-x^2) dx = \sqrt{\pi}/4$$

$$\int_0^{\infty} x^3 \exp(-x^2) dx = 1/2 \quad \int_0^{\infty} x^4 \exp(-x^2) dx = 3\sqrt{\pi}/8$$

- 2.16. The probability density for a particular distribution has the form $\mathcal{P}(A) = AA^n$, where n is a parameter and A has a range $0 \leq A \leq 1$.

Determine the normalization constant A for this power-law function and calculate $\langle A \rangle$ and $\langle A^2 \rangle$.

2.17. At a temperature T , the distribution of speeds v for an ideal gas of particles has the form $\mathcal{P}(v) = Av^2 \exp(-mv^2/2k_B T)$, where m is the mass of each particle.

- Determine A such that $\int_0^\infty \mathcal{P}(v) dv = 1$.
- Show that the mean kinetic energy is $\langle K \rangle = (3/2)k_B T$.
- Show that the most probable kinetic energy of the particles is $k_B T$.

2.18. (a) In Section 2.2, we stated that the position $x(t)$ of an object of mass m , subject to the drag force $F = c_1 v$, is described by

$$x(t) = (mv_0/c_1) \cdot [1 - \exp(-c_1 t/m)].$$

Differentiate this to establish that the corresponding velocity is

$$v(t) = v_0 \exp(-t/t_{\text{visc}}),$$

with a characteristic time $t_{\text{visc}} = m/c_1$.

(b) The quadratic drag force is parametrized by $F = c_2 v^2$, resulting in

$$x(t) = (v_0/k) \cdot \ln(1 + kt),$$

where

$$k = c_2 v_0/m.$$

Establish that the corresponding velocity is

$$v(t) = v_0 / (1 + c_2 v_0 t/m).$$

Does x reach a limiting value for quadratic drag?

2.19. Calculate the ratio of the drag force at low speeds for an ellipsoid compared to a sphere; the direction of motion is along the semi-major axis of the ellipsoid. Take the semi-minor axis of the ellipsoid to be R , and plot your results as a function of $\alpha \equiv a/R$ for $2 \leq \alpha \leq 5$. Comment on how fast the drag force rises with the length of the ellipsoid.

2.20. Consider a power-law form of the drag force with magnitude:

$$F_{1/2} = a v^{1/2} \quad (\text{square root}).$$

Establish that an object traveling horizontally from an initial speed v_0 , would come to rest at $x_{\text{max}} = (2m/3a)v_0^{3/2}$ for such a force.

2.21. Consider a power-law form of the drag force with magnitude:

$$F_{3/2} = c v^{3/2} \quad (3/2 \text{ power}).$$

Establish that an object traveling horizontally from an initial speed v_0 , would come to rest at $x_{\max} = 2m v_0^{1/2}/c$ for this force.

- 2.22. Consider a rotational drag torque of the form $\mathcal{T} = -\chi\omega$, where $\chi = 8\pi\eta R^3$.
- Find $\omega(t)$ and $\theta(t)$ for an object rotating at an initial angular frequency ω_0 , experiencing no force other than drag. Take the initial angle to be zero.
 - Show that the characteristic time scale for the decay of the angular speed is I/χ , where I is the moment of inertia about the axis of rotation. Show that this time scale is $m / (20\pi\eta R)$ for a sphere of mass m and radius R .
 - Find the value of θ as $t \rightarrow \infty$ if the initial frequency is 10 revolutions per second; assume $R = 1 \mu\text{m}$, $\eta = 10^{-3} \text{ kg/m}\cdot\text{s}$, and the mass of the object is $4 \times 10^{-15} \text{ kg}$.
- 2.23. It is established in Problem 2.22 that the time scale for the decay of rotational speed of a sphere subject to rotational drag is $m/(20\pi\eta R)$ where m and R are the mass and radius of the sphere.
- For a cell with mass $4 \times 10^{-15} \text{ kg}$ and radius $1 \mu\text{m}$, calculate the time scales for the decay of translational and rotational motion when the cell is immersed in a fluid of viscosity $10^{-3} \text{ kg/m}\cdot\text{s}$.
 - Show analytically that the ratio of the times (rotational: translational) is 3/10.
- 2.24. Consider a one-dimensional random walk centered on $x = 0$, where the probabilities of stepping to the left or to the right are both equal to 1/2. Find the probability $P(i, j)$ of the discrete walk at $x = 0$ for walks with $N = 4, 8$ and 12 steps. Compare this result with the continuous probability density $\mathcal{P}(x)\Delta x$. [Hint: you must determine what value of Δx corresponds to the change in end-to-end length of the walk when i and j change by one unit each at fixed N .] For simplicity, make the step length b equal unity.
- 2.25. By explicit substitution, show that the following expression for the concentration satisfies Fick's second law of diffusion:
- $$c(x,t) = c_0 (4\pi Dt)^{-1/2} \exp(-x^2/4Dt).$$
- 2.26. In three dimensions, the concentration of a mobile species spreading from a point at the coordinate origin is given by
- $$c(\mathbf{r},t) = c_0 (4\pi Dt)^{-3/2} \exp(-r^2/4Dt).$$

For this profile, calculate the time dependence of $\langle r^2 \rangle$, just as we calculated $\langle x^2 \rangle$ in Section 2.4. Comment on the factor of 6 in your result. As a three-dimensional average, the volume element in $\langle \dots \rangle$ in

polar coordinates is $d\varphi \sin\theta d\theta r^2 dr$, where $0 \leq \theta \leq \pi$ and $0 \leq \varphi \leq 2\pi$ as usual.

- 2.27. Consider a restricted random walk in which neighboring bond vectors, each with length b , have directions that are different by 90° at the most.
- Show that $\langle \mathbf{b}_i \cdot \mathbf{b}_{i+1} \rangle / b^2 = 1/2$ for walks in three dimensions.
 - Find $\langle \mathbf{b}_i \cdot \mathbf{b}_{i+1} \rangle / b^2$ for walks in two dimensions. Explain in words why $\langle \mathbf{b}_i \cdot \mathbf{b}_{i+1} \rangle$ in two dimensions should be larger or smaller than in three dimensions.
 - What is the minimum value of $\mathbf{b}_i \cdot \mathbf{b}_{i+2} / b^2$?
- 2.28. A variable x fluctuates around its mean value x_{av} . For an ensemble of measurements, show that $\langle \Delta x^2 \rangle = \langle x^2 \rangle - x_{\text{av}}^2$, where $\Delta x = x - x_{\text{av}}$.
- 2.29. The exponential is not the only function that decays smoothly to zero with time: there are other algebraic forms that might appear as correlation functions. Suppose that the correlation function $C(x)$ has the form $1/(1 + x/a)$. Equate the derivative of $C(x)$ with that of the exponential $\exp(-x/\xi)$ at small values of x in order to relate the parameter a to the persistence length ξ . With this identification, calculate the ratio of the two functions at $x = \xi$.
- 2.30. In the NPT ensemble, the temperature T , pressure P and number of particles N are all fixed, but the volume V fluctuates about a mean value determined by the choice of NPT . Consider an ideal gas obeying $PV = Nk_B T$ (where V is really the mean value of V).
- Show that the compression modulus K_V is equal to the pressure.
 - Find how the volume fluctuations $\Delta V^2 / V_{\text{av}}^2$ depends on N , where $\Delta V = V - V_{\text{av}}$.