

**Friction factor**

The friction factor is a parameter that relates the size and shape of a molecule to the drag (the resistance to movement) it generates in a fluid.

depends upon molecular parameters, such as size and shape, and also the characteristics of the solution through which molecules move, particularly its viscosity.

Experimental determinations of diffusion constants show that, as one expects, larger molecules move more slowly than smaller ones. But the dependence of  $D$  on molecular weight is not linear. In order to understand what the relationship is we need to consider the effects of friction on molecular movement.

The resistance to motion in a fluid is due to the need to move the fluid out of the path of the moving object. This results in a friction force that is dependent on the size and shape of the object, and on the velocity of motion and the characteristics of the solvent. An object moving rapidly meets more resistance than one moving slowly. The friction force,  $F_{\text{friction}}$ , depends on the velocity,  $v$ , as follows:

$$F_{\text{friction}} = -f v \quad (17.29)$$

The proportionality constant,  $f$ , is called the **friction factor**, and it incorporates the size, shape and solvent contributions. The negative sign on the right hand side reflects the fact that the friction force resists motion and hence its direction is opposite to that of the velocity. Given Equation 17.29 and the units for force ( $\text{g}\cdot\text{cm}\cdot\text{sec}^{-2}$ ) and velocity ( $\text{cm}\cdot\text{sec}^{-1}$ ), the friction factor must have the nonintuitive units of  $\text{g}\cdot\text{sec}^{-1}$ .

Under an applied force, such as gravity, an object will accelerate according to Newton's law ( $F = ma$ ) until the friction force equals the applied force, at which point the object reaches a **terminal velocity**. The frictional force exactly cancels that causing acceleration when the terminal velocity is reached.

The dependence of frictional force on the shape of an object is well known in skydiving, an acrobatic feat in which the friction factor has a major practical role (Figure 17.20). A skydiver in free fall in a typical 'spread eagle' position reaches a terminal velocity of about 120 mph, while if the arms and legs are pulled in tightly the velocity goes up to about 200 mph—the difference coming just from the change in friction factor due to shape. When the skydiver opens a parachute the cross-section moving through the air increases enormously, and hence so does the friction factor—this slows the fall to a speed of about 12 mph, slow enough to make a safe landing.

### 17.16 The diffusion constant is inversely related to the friction factor

Albert Einstein deduced that the random movement of very small particles in liquids can be understood in terms of frictionally damped motion. Such motion was first described for pollen granules by Robert Brown (and became known as Brownian motion). Einstein recognized that the motion of the molecules must be related to the driving force for diffusion.

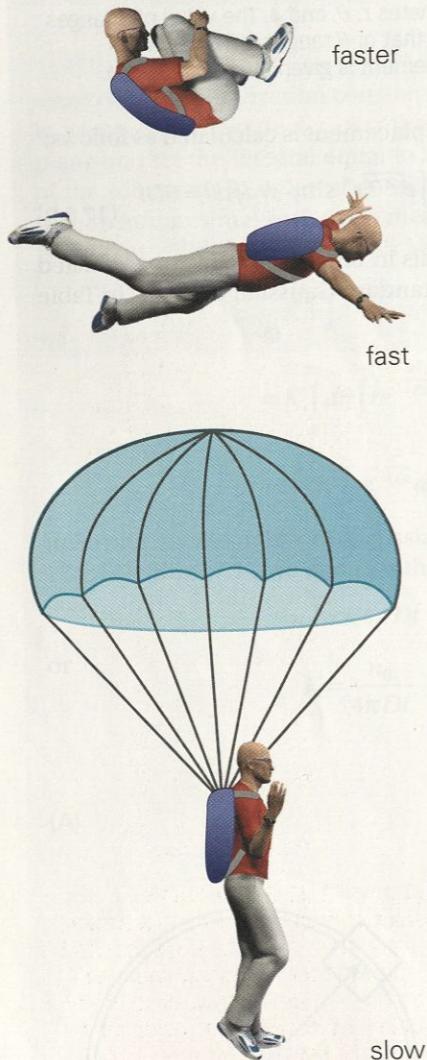
In Equation 17.14 we defined  $D$  as the proportionality constant between the flux of molecules through a plane, and the concentration gradient. To connect this with molecular properties we can think about the same principle in terms of motion of individual molecules. Again considering an imaginary plane passing through a sample, the flux of molecules through the plane will depend on the average velocity  $v$  with which particles are moving, and on the number of particles near the plane, that is their concentration.

$$J(x) = v \times c(x) \quad (17.30)$$

Now we connect with the idea that molecules moving under a driving force,  $F_{\text{drive}}$ , reach a terminal velocity,  $v_{\text{terminal}}$ , when the driving force is balanced by the frictional force:

$$F_{\text{friction}} = -v_{\text{terminal}} f = -F_{\text{drive}} \quad (17.31)$$

We need to know what  $F_{\text{drive}}$  is. From basic physics we know that forces correspond to the derivatives of potentials. The electrical forces on a charged particle,



**Figure 17.20** Skydiving, an example of friction relating to speed. The rate of the skydiver falling is greatly decreased by the parachute opening. This occurs because the open parachute creates a large amount of friction by requiring that a larger volume air be moved around it.

for example, arise from differences in electrical potential between two points in space, as discussed in Section 9.12. For diffusion the force arises from the difference in **chemical potential** at different points in space, due to a concentration difference.

The chemical potential was developed from the concept of free energy, and was discussed in detail in Chapter 10. For the present discussion we shall define the chemical potential on a per molecule basis rather than the per mole basis used in Chapter 10. This simply means that we need to switch from  $R$  to  $k_B$  in front of the logarithm of the concentration term in the equation for the chemical potential:

$$\mu = \mu^0 + k_B T \ln\left(\frac{c}{1}\right) \quad (17.32)$$

In Equation 17.32,  $\mu^0$  is the chemical potential of the standard state (1 M solution). If we consider a gradient in just the  $x$  direction then the driving force for diffusion,  $F_{\text{drive}}$ , will be:

$$F_{\text{drive}} = \frac{-d\mu}{dx} = -k_B T \frac{d}{dx} \ln[c(x)] = -k_B T \frac{1}{c(x)} \frac{dc(x)}{dx} \quad (17.33)$$

We now combine Equation 17.33 with Fick's first law (Equation 17.27) and with Equation 17.32 to give:

$$J(x) = \frac{F_{\text{drive}}}{f} c(x) = \frac{-k_B T}{f} \frac{dc(x)}{dx} \quad (17.34)$$

The key is now to compare two equations that describe the flux of molecules (Equation 17.14 and 17.34):

$$J(x) = -D \frac{dc(x)}{dx} \quad \text{and} \quad J(x) = \frac{-k_B T}{f} \frac{dc(x)}{dx} \quad (17.35)$$

By comparing these two different descriptions of flux, which must correspond to the same thing and hence be equal, we obtain a relationship between the diffusion constant and the friction factor,  $f$ :

$$D = \frac{k_B T}{f} \quad (17.36)$$

While this equation shows that the rate of diffusion and the friction factor,  $f$ , are inversely related, it does not provide any insight into the relationship of either to molecular parameters. To take this next set step we need to consider the characteristics of the solution and examine how it interacts with a moving molecule.

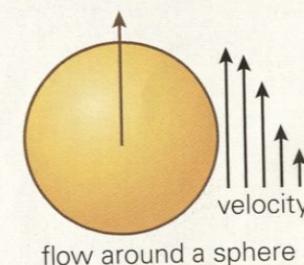
### 17.17 Viscosity is a measure of the resistance to flow

To understand the behavior of solutions we need to understand how the motion of a moving particle is coupled to that of the solvent around it. A few solvent molecules will stick to the surface of the particle, and will be carried along with it. On the other hand, at a large distance away from the particle the solvent molecules will not be affected by the movement of the particle.

The dragging of solvent with the particle corresponds to transfer of momentum from the particle to the solvent. Recall from basic physics that the momentum,  $p$ , is the product of mass,  $m$ , and velocity,  $v$ :  $p = mv$ . When one part of a fluid is moving faster than another a gradient in momentum is created, as illustrated in Figure 17.21. The flux in momentum,  $J_{p_x}$ , is the momentum transferred along the  $x$  direction per unit area per unit time. The **viscosity** of the solvent (given the symbol  $\eta$ ) is the proportionality constant between the momentum flux and the velocity gradient along a direction  $z$  orthogonal to  $x$ :

$$J_{p_x} = -\eta \frac{dv_x}{dz} \quad (17.37)$$

A 'sticky' solvent will transfer momentum over long distances, which corresponds to high viscosity. A 'thin' solvent will only transfer momentum over short distances, and has a low viscosity.



**Figure 17.21** Gradients in momentum. Flow around a sphere and in a tube are shown with vectors indicating the velocity of the flow at different positions relative to the boundary between the object and the fluid (solvent). For flow around a particle, the object is moving and the solvent is not, except near the particle, where interactions occur. For flow in a tube, the walls of the tube are fixed, while the fluid is moving. In both cases, the behavior is governed by the same rules and the same fundamental parameter—the viscosity of the solvent.

**Viscosity**

The viscosity of a solvent describes the coupling between movement of solute molecules and the solvent. In solvents with high viscosity, the movement of a solute disturbs the movement of the solvent over greater distances than for a solvent with lower viscosity. The higher the viscosity, the more the solvent resists the movement of the solute.

To understand the effect of viscosity on molecular movement note that if the viscosity is high then the layer of solvent molecules near the solute molecule affects other solvent molecules over a longer distance than when the viscosity is low. More solvent is dragged along with the solute molecule as it moves, making it more difficult for the solute molecule to move. Viscosity also determines the rate of flow of the solution as a whole. For example, if a solution is moving in a narrow tube the layer of molecules at the inner surface of the tube may tend to stick to the surface (see Figure 17.21). If the viscosity is high then the resistance to movement persists over a long distance, making flow of the solvent through the tube slow. If the viscosity is low then the effect of the layer at the wall does not propagate very far, and the center part will move with little resistance.

To determine the units of the viscosity,  $\eta$ , we look at the components of Equation 17.37. The momentum flux (momentum per unit area per unit time) will have units  $(\text{g} \cdot \text{cm} \cdot \text{sec}^{-1}) (\text{cm}^{-2}) (\text{sec}^{-1}) = \text{g} \cdot \text{cm}^{-1} \cdot \text{sec}^{-2}$ . The velocity gradient has units  $(\text{cm} \cdot \text{sec}^{-1} \cdot \text{cm}^{-1}) = (\text{sec}^{-1})$ , and hence the viscosity must have units of  $\text{g} \cdot \text{cm}^{-1} \cdot \text{sec}^{-1}$  (the units of parameters such as this are not intuitively obvious, but can easily be determined from the defining equation, such as 17.36 in this case). The standard unit for viscosity is the **poise** ( $1 \text{ P} = \text{g} \cdot \text{cm}^{-1} \cdot \text{sec}^{-1}$ ), but units of **centipoise** ( $1 \text{ cP} = 10^{-2} \text{ P} = 10^{-2} \text{ g} \cdot \text{cm}^{-1} \cdot \text{sec}^{-1}$ ) are most commonly used for biological systems because the viscosity of water is approximately 1 cP.

### 17.18 Liquids with strong interactions between molecules have high viscosity

A large part of the value of the viscosity comes from the molecular characteristics of the solvent. Solvents with weak interactions between molecules (such as acetone, which is the principal component of nail polish remover) have low viscosity and they flow very easily. Acetone has a viscosity of 0.31 cP at 25°C. In water, the molecules form hydrogen bonds with other water molecules. This facilitates the transfer of momentum over longer distances, and so water has substantially higher viscosity than acetone, with a value of ~1 cP at 25°C. Glycerol ( $\text{HOCH}_2\text{CH}(\text{OH})\text{CH}_2\text{OH}$ ) has more extensive hydrogen bonding between molecules than does water, and a much higher viscosity, ~900 cP. Concentrated solutions of sugars have even higher viscosity. The viscosity of maple syrup, for example, is ~3200 cP.

Solutions of macromolecules have substantially higher viscosity than water. The fluid inside cells, the cytosol, is a rather concentrated solution of molecules and ions, in which proteins comprise 20–40% of the mass. Experimental measurements show that the viscosity of the cytosol in cells is approximately 20 to 50 times that of water. As we shall see in the next section, the diffusion constant is inversely proportional to the viscosity. As a consequence, proteins move much slower in the cytoplasm than they do in water.

### 17.19 The Stokes-Einstein equation allows us to calculate the diffusion coefficients of molecules

A complicated set of differential equations, known as the Navier-Stokes equations, must be solved in order to describe fluid flow around an object as it moves. These equations include terms arising from the conservation of mass, energy, momentum, and angular momentum. For an object with an arbitrary shape, these equations cannot be solved analytically (that is, the solution cannot be written as an equation). Fortunately, as for the diffusion equation, the Navier-Stokes equations can be solved numerically on a computer for any case of interest.

For objects with very small masses, the forces arising from viscosity dominate the flow around the object (this is always the case for very small particles like individual molecules). In this limit the equations can be solved analytically for simple shapes, like a sphere. For a sphere, the friction factor for moving through liquid is:

$$f_{\text{sphere}} = 6\pi\eta r \quad (17.38)$$

in which  $\eta$  is the viscosity of the fluid and  $r$  is the radius of the sphere. George Gabriel Stokes derived this relationship, and hence it is known as **Stokes' law**. This can then be combined with the relationship that Einstein derived, Equation 17.36, to give the **Stokes-Einstein equation**:

$$D_{\text{sphere}} = \frac{k_B T}{6\pi\eta r} \quad (17.39)$$

A good estimate of the rate of diffusion of nearly spherical molecules in solution can be made using the Stokes-Einstein equation, based just on the size of the molecule and the solvent viscosity. Note the inverse relationship between the diffusion constant and the viscosity, as expected from the discussion in the last section. High viscosity means high resistance to motion and hence slow diffusion.

To illustrate the utility of the Stokes-Einstein equation, we shall use it to calculate the diffusion constant in water for the protein myoglobin, familiar to us from Chapters 4 and 5 (see Figure 4.1). Myoglobin has a radius of ~20 Å, and is roughly spherical in shape. By convention, the diffusion constant has units of  $\text{cm}^2 \cdot \text{sec}^{-1}$ , and so the radius of the myoglobin,  $r$ , must be expressed in centimeters for the dimensions to balance in Equation 17.39. Also, because the units of the viscosity,  $\eta$ , are  $\text{g} \cdot \text{cm}^{-1} \cdot \text{sec}^{-1}$ , we must express the Boltzmann constant ( $k_B$ ) in consistent units. To begin with, we write down the values of each of the terms in Equation 17.39.

$$\begin{aligned} k_B &= 1.381 \times 10^{-23} \text{ m}^2 \cdot \text{kg} \cdot \text{sec}^{-2} \cdot \text{K}^{-1} \\ &= 1.381 \times 10^{-16} \text{ cm}^2 \cdot \text{g} \cdot \text{sec}^{-2} \cdot \text{K}^{-1} \end{aligned} \quad (17.40)$$

Assuming that the temperature is 300 K (approximately room temperature), we obtain the following value for  $k_B T$ :

$$k_B T = (1.381 \times 10^{-16})(300) = 4.14 \times 10^{-14} \text{ cm}^2 \cdot \text{g} \cdot \text{sec}^{-2} \quad (17.41)$$

The values of the radius of myoglobin and the viscosity of water at room temperature are:

$$\begin{aligned} r &= 20 \times 10^{-8} \text{ cm} \\ \eta &= 1 \text{ cP} = 0.01 \text{ g} \cdot \text{cm}^{-1} \cdot \text{sec}^{-1} \end{aligned} \quad (17.42)$$

Substituting all of these values into the Stokes-Einstein equation, we get:

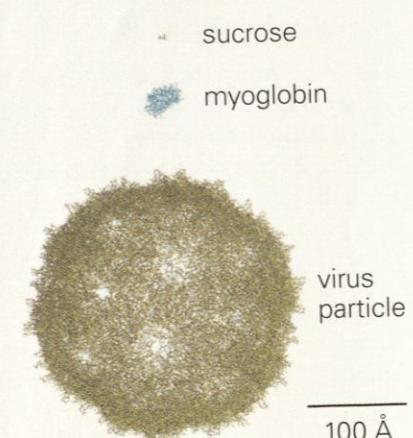
$$D(\text{myoglobin}, 300\text{K}) = 1.1 \times 10^{-6} \text{ cm}^2 \cdot \text{sec}^{-1} \quad (17.43)$$

It turns out that this value for the diffusion constant is very close to the value measured experimentally for myoglobin in water. We can now use this value of  $D$  to calculate the r.m.s. displacement of myoglobin molecules after 1 second of three-dimensional diffusion, by using Equation 17.28:

$$\text{r.m.s. displacement} = \sqrt{6Dt} = 2.6 \times 10^{-3} \text{ cm} = 26 \mu\text{m} \quad (17.44)$$

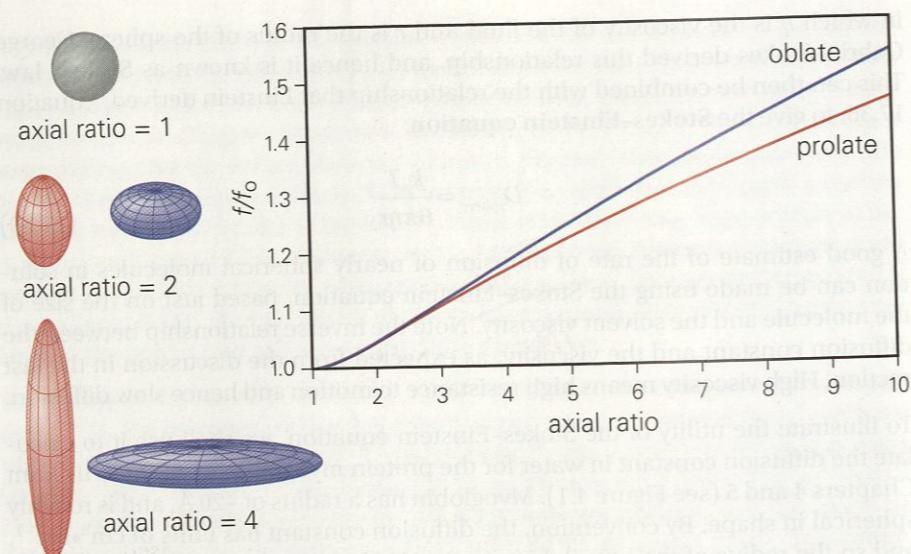
Thus, the typical distance that a myoglobin molecule will have moved from its starting point after 1 second of diffusion in water is about 26 μm. We can compare this rate of movement with that of a small metabolite molecule, such as sucrose (Figure 17.22). If we assume that the radius of sucrose is ~4 Å (that is, five times smaller than that of myoglobin), then the value of  $D$  is five times larger than for myoglobin ( $5.5 \times 10^{-6} \text{ cm}^2 \cdot \text{sec}^{-1}$ ). The time taken to travel a certain distance is inversely related to the diffusion constant, and so a sucrose molecule travels about five times faster than myoglobin. A small virus particle with a radius of ~140 Å, such as the one shown in Figure 17.22, travels about seven times slower than myoglobin.

Many eukaryotic cells are 10–50 μm across, and so our estimates of the speed of diffusion suggest that metabolites and small proteins can traverse the cell within a second. The actual movement of molecules inside a cell is much slower because, as we mentioned earlier, the viscosity of the cytoplasm is higher than that of water,



**Figure 17.22 Relative sizes of biological molecules.** Three rather different molecules are shown here. At the top, and barely visible, is sucrose (8 Å in diameter). In the middle is myoglobin (diameter of ~45 Å) and at the bottom is a virus known as MS2 (280 Å in diameter). The virus diffuses about 35 times more slowly in water than does sucrose.

**Figure 17.23 Ratios of the friction factor for prolate and oblate shapes.** A sphere and prolate (red) and oblate (blue) shaped objects with axial ratios of 2 and 4 (all of which occupy the same volume of space—that is, correspond to the same molecular weight) are shown. At the right, a graph of the ratio of the friction factor to that for a sphere is shown for axial ratios between 1 and 10. Friction factors for the 2:1 ratio only differ from that of a sphere ( $f_0$ ) by about 5%. The friction factors are generated by solving Navier-Stokes equations.



leading to diffusion constants for proteins the size of myoglobin that are in the range of  $10^{-7}$  to  $10^{-8} \text{ cm}^2 \cdot \text{sec}^{-1}$ , compared to  $10^{-6}$  in water. The apparent diffusion constants of proteins and other macromolecules can also be much slower than expected even after accounting for the viscosity of the cytoplasm. This is because macromolecules often interact with structural elements in the cell, instead of diffusing freely. As a consequence, cells often require active transport processes that consume energy to move certain molecules around at the speed that is required for essential processes (see Section 17.25).

All proteins are comprised of the same amino acids, which are all made from similar chemical groups, and so the density of a protein,  $\rho_p$ , is quite constant from one protein to another. Comparing spherical proteins, the mass (and hence the molecular weight,  $M$ ) will be related to the volume of the protein:

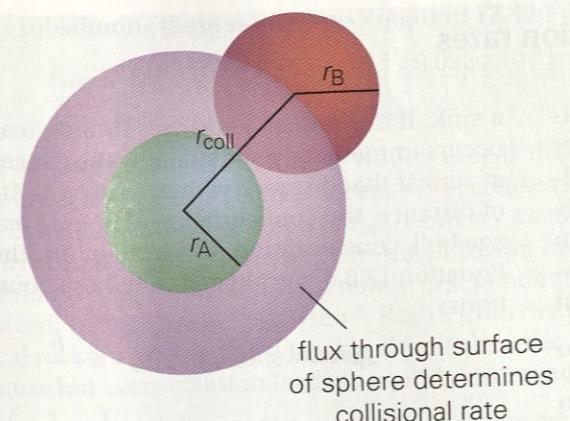
$$M = \rho_p \frac{4}{3} \pi r^3 \quad \text{and} \quad r \propto \sqrt[3]{M} \quad (17.45)$$

Thus, for spherical molecules, the diffusion constant depends inversely on the cube root of the molecular weight.

### 17.20 The diffusion constants for nonspherical molecules are only slightly different from those calculated from the spherical approximation

For nonspherical molecules, the friction force is larger than for a spherical molecule with the same molecular weight. Although general equations cannot be written for the friction factors for arbitrary shapes, as noted above the values of the friction factors can be calculated with computers. By analyzing the results of such calculations we find that the values of the friction factor are only moderately sensitive to shape. For prolate spheroid shapes (like an American football), characterized by a long axis length  $a$  and short axis length  $b$ , a ratio of  $a/b = 2$  gives  $f = 1.044 \times f_{\text{sphere}}$ , where  $f$  and  $f_{\text{sphere}}$  are the friction factors for the two different shapes. A very asymmetric shape with  $a/b = 10$  gives  $f = 1.54 \times f_{\text{sphere}}$ . For oblate, ellipsoidal shapes (that is, disk-like),  $a/b = 0.5$  gives  $f = 1.042 \times f_{\text{sphere}}$  and  $a/b = 0.1$  gives  $f = 1.46 \times f_{\text{sphere}}$ . A graph showing the  $f/f_{\text{sphere}}$  value versus axial ratio is shown in Figure 17.23.

The increased friction, particularly for the prolate shape, seems counterintuitive because we might think that motion along the direction of the long axis would be facilitated, because of the narrower cross-section along this direction. While this is true, the direction of motion is actually random, and the molecule also frequently



**Figure 17.24 Calculation of the diffusional collision rate.** Two spherical molecules, A and B, are shown here. The rate of collisions between them is obtained by calculating the flux of B molecules through the surface of a sphere around A, as explained in Box 17.6. The radius of this sphere,  $r_{\text{coll}}$ , is the sum of the radii of the two types of atoms.

moves in the directions of the short axes. The observed friction factors reflect an appropriately weighted average over motion in all directions. The viscous drag on molecules is larger than their momentum, and so they do not move continuously in the direction of least resistance the way macroscopic objects do.

### 17.21 Diffusion-limited reaction rate constants can be calculated from the diffusion constants of molecules

The idea that a rate constant cannot exceed the rate of collisions of the reactant molecules was discussed in Section 15.25. Reactions that occur at the rate of collisions are called **diffusion limited**, because the rate of collisions is determined by the rate of diffusion. The rate of collisions through diffusion can be calculated using Fick's laws. This is done by considering a sphere of radius  $r_{\text{coll}}$  around a molecule, chosen such that, if the intermolecular distance reaches  $r_{\text{coll}}$ , then a collision occurs (Figure 17.24). For spherical molecules, this corresponds just to the sum of the radii of the molecules. The rate of collisions is obtained by calculating the flux of molecules that would go through the surface of this sphere.

The details of the rate calculations were worked out by Marian Smoluchowski and are explained in Box 17.6. The result is that the rate at which the A and B molecules collide with each other is given by:

$$\text{collision rate} = 4\pi r_{\text{coll}} (D_A + D_B) \bar{c}_A \bar{c}_B \quad (17.46)$$

Here,  $D_A$  and  $D_B$  are the diffusion constants for the A and B molecules. The variables  $\bar{c}_A$  and  $\bar{c}_B$  are the bulk concentrations of the A and B molecules, expressed as number of molecules per  $\text{cm}^3$ . The diffusion constants are in units of  $\text{cm}^2 \cdot \text{sec}^{-1}$  and, if the radius is expressed in units of cm, then the rate in Equation 17.46 is in units of  $\text{molecules} \cdot \text{sec}^{-1}$ . In Section 15.8, we described the more familiar rate equation in which concentrations are expressed in molar units:

$$\frac{d[\text{AB}]}{dt} = k_{\text{coll}} [\text{A}][\text{B}] \quad (17.47)$$

As explained in Box 17.6, the **collision rate constant**,  $k_{\text{coll}}$ , in Equation 17.47 is related to the diffusion constants of A and B in the following way:

$$k_{\text{coll}} = 4\pi r_{\text{coll}} (D_A + D_B) (6.022 \times 10^{20}) \quad (17.48)$$

The last term in Equation 17.48 is a conversion factor that has units of  $\text{M}^{-1} \cdot \text{cm}^{-3}$ , which ensures that the units of  $k$  are  $\text{M}^{-1} \cdot \text{sec}^{-1}$ .

Let us now use Equation 17.48 to calculate what the collision rate constant is for sucrose molecules colliding with each other in water. In Section 17.19 we said that the radius of sucrose is  $\sim 4 \text{ \AA}$ , and so the value of  $r_{\text{coll}}$  is  $8 \text{ \AA}$  ( $8 \times 10^{-8} \text{ cm}$ ). We calculated the diffusion constant for sucrose in water to be  $5.5 \times 10^{-6} \text{ cm}^2 \cdot \text{sec}^{-1}$  (that is, five times greater than that of myoglobin). The collision rate constant for sucrose

### Box 17.6 Calculating diffusion-limited collision rates

The first step toward calculating the collision rate in solution, with molecules diffusing randomly, is to consider the coordinate system used for the calculation. For calculating the rate at which collisions occur, what matters is the just distance between the centers of the collision partners. The problem has inherent spherical symmetry. We initially discussed a concentration gradient along a single axis, so the derivative  $\frac{\partial c}{\partial x}$  was sufficient to

describe the position dependence of concentration. In a general case, the gradient is a vector quantity (that is, it has a direction) and is written in a more general form using the gradient operator ( $\text{grad} = \nabla$ ) in Cartesian coordinates with unit vectors  $\hat{x}, \hat{y}, \hat{z}$ :

$$\nabla c(x, y, z) = \left( \frac{\partial}{\partial x} \hat{x} + \frac{\partial}{\partial y} \hat{y} + \frac{\partial}{\partial z} \hat{z} \right) c(x, y, z) \quad (17.6.1)$$

This can be rewritten in polar coordinates. The second derivative, used for Fick's second law, looks more formidable in polar form, but is easier to use in cases of spherical symmetry:

$$\nabla^2 c(r, \theta, \phi) = \left[ \frac{\partial^2}{\partial r^2} + \frac{2}{r} \frac{\partial}{\partial r} + \frac{1}{r^2} \left( \frac{1}{\sin^2 \theta} \frac{\partial^2}{\partial \theta^2} + \frac{1}{\sin \theta} \frac{\partial}{\partial \theta} \sin \theta \frac{\partial}{\partial \theta} \right) \right] c(r, \theta, \phi) \quad (17.6.2)$$

To obtain the rate at which diffusive collisions occur, we set one atom (for example, A) at the origin, and then calculate the flux of B molecules that would come through a spherical surface surrounding it. The size of the sphere is chosen such that, when the center of a B atom crosses the surface of this sphere, a collision occurs. If the radii of A and B are  $r_A$  and  $r_B$ , then the radius of the sphere is  $r_{\text{coll}} = r_A + r_B$ .

For a uniform, mixed solution in which a reaction is occurring, there is no concentration gradient, and so there is no time dependence of concentration from diffusion. Writing Fick's second law using the grad operator with this assumption then gives:

$$D \nabla^2 c_B = \frac{\partial c_B}{\partial t} = 0 \quad (17.6.3)$$

In polar form, using the fact that changes in angles  $\theta$  and  $\phi$  do not change distance and hence cannot cause collisions, the derivatives with them can be eliminated, giving:

$$\frac{\partial^2 c_B}{\partial r^2} + \frac{2}{r} \frac{\partial c_B}{\partial r} = 0 \quad (17.6.4)$$

A key step in then being able to calculate the actual collision rate (an approach originally used by Smoluchowski in 1917) is to consider that at any given instant it is very unlikely that a collision will actually be occurring, so the concentration of B at a distance  $r_{\text{coll}}$  can be set to 0. This is equivalent to saying that the boundary at  $r_{\text{coll}}$  acts as

a sink. If a B molecule reaches it, then reaction with A occurs immediately, maintaining the concentration of B at zero at that distance with respect to A. At large values of distance, the concentration of B must reach the average bulk concentration,  $\bar{c}_B$ , in solution. The solution to Equation 17.6.4 is evaluated with these boundary conditions:

$$\text{general solution: } c(r) = a + \frac{b}{r}$$

$$\text{specific case: } c(r) = \left( 1 - \frac{r_{\text{coll}}}{r} \right) \bar{c} \quad (17.6.5)$$

In this approach, although there is not a macroscopic gradient, the assumption in the initial condition that no collision is occurring means that there is a gradient of collision partners as a function of distance from the molecule at the origin. The flux through the imaginary collision threshold sphere of radius  $r_{\text{coll}}$  is calculated using Fick's first law:

$$J(r_{\text{coll}}) = D \left[ \frac{\partial c_B(r)}{\partial r} \right]_{r=r_{\text{coll}}} \quad (17.6.6)$$

For the concentration as a function of distance calculated in Equation 17.6.5, this gives:

$$\frac{\partial c_B(r)}{\partial r} = \frac{r_{\text{coll}} \bar{c}_B}{r^2} \Big|_{r=r_{\text{coll}}} = \frac{\bar{c}_B}{r_{\text{coll}}}$$

and so:

$$J(r_{\text{coll}}) = \frac{D \bar{c}_B}{r_{\text{coll}}} \quad (17.6.7)$$

Remember that the flux is defined as molecules crossing a unit area per unit time. To calculate the rate of collisions, then, the flux must be multiplied by the area of the surface,  $A_{\text{sphere}} = 4\pi r_{\text{coll}}^2$ , so:

$$\text{collision rate} = J(r_{\text{coll}})(\text{area}) = \frac{D \bar{c}_B}{r_{\text{coll}}} 4\pi r_{\text{coll}}^2 = 4\pi r_{\text{coll}} D \bar{c}_B \quad (17.6.8)$$

Comparing this with the chemical kinetic version, rate =  $k \bar{c}$ , then gives:

$$k = 4\pi D r_{\text{coll}} \quad (17.6.9)$$

One further note is that  $D$  is the diffusion constant describing the *relative motion* of the colliding molecules. We have taken one molecule at the origin and then considered the motion of the other one. This means that the effective diffusion constant,  $D$ , in the equations above, is really the sum of the diffusion constants of the two colliding molecules. We initially designated them A and B for considering the distance at which a collision occurs,  $r_{\text{coll}} = r_A + r_B$ . Using the same kind of notation,  $D = D_A + D_B$ .

is then given by substituting these values into Equation 17.48:

$$\begin{aligned} k_{\text{coll}} &= 4\pi (8 \times 10^{-8})(2)(5.5 \times 10^{-6})(6.022 \times 10^{20}) \\ &= 6659 \times 10^6 \approx 1 \times 10^{10} \text{ M}^{-1} \cdot \text{sec}^{-1} \end{aligned} \quad (17.49)$$

At first glance, looking at Equation 17.48, it would appear that the rate of collisions would be lower for larger molecules because  $D$  decreases with the size of the molecule (see Equation 17.39). The value of  $r_{\text{coll}}$ , however, *increases* with the size of the molecule, which offsets the decrease in the diffusion constant and leaves the diffusion-limited rate of collisions essentially independent of the size of the molecule involved, with  $k_{\text{coll}} \approx 10^{10} \text{ M}^{-1} \cdot \text{sec}^{-1}$ . Recall from Section 15.26 that the fastest chemical reactions occur considerably slower than the rate of diffusional collisions because not every collision leads to a productive reaction.

Equations 17.46 and 17.48 emphasize the relationship between the collision rate constant and the diffusion constants. Alternatively, we can express  $k_{\text{coll}}$  in terms of the viscosity by substituting Equation 17.39 (the Stokes-Einstein equation) into Equation 17.48. For the case where there is only one kind of molecule colliding with itself:

$$\begin{aligned} k_{\text{coll}} &= 4\pi (2r)(2D)(6.022 \times 10^{20}) \\ &= 4\pi (2r)(2) \left( \frac{k_B T}{6\pi \eta r} \right) (6.022 \times 10^{20}) \\ &= \left( \frac{8}{3} \right) \left( \frac{k_B T}{\eta} \right) (6.022 \times 10^{20}) \end{aligned} \quad (17.50)$$

We have to be careful about units here. If we express  $k_B T$  in units of  $\text{J}(\text{kg} \cdot \text{m}^2 \cdot \text{sec}^{-2})$ , then we have to multiply by  $10^7$  in order to match the units of the viscosity ( $\text{g} \cdot \text{cm}^{-1} \cdot \text{sec}^{-1}$ ).

The expression for  $k_{\text{coll}}$  then becomes:

$$\begin{aligned} k_{\text{coll}} &= \left( \frac{8}{3} \right) \left( \frac{k_B T}{\eta} \right) (6.022 \times 10^{20})(10^7) \\ &= \frac{8RT}{3\eta} \times 10^4 \end{aligned} \quad (17.51)$$

where  $R$  is the gas constant in units of  $\text{J} \cdot \text{K}^{-1}$ ,  $T$  is the absolute temperature, and  $\eta$  is the viscosity in units of poise ( $\text{g} \cdot \text{cm}^{-1} \cdot \text{sec}^{-1}$ ).

### 17.22 One-dimensional searches on DNA increase the rate at which transcription factors find their targets

In introducing random walks, we used the example of bacteria swimming in two dimensions—that is, on a surface. When considering the diffusion of biological macromolecules, we naturally think about their movement in three-dimensional space within the cell. There are circumstances, however, in which restricted diffusion (that is, in less than three dimensions) plays an important role in biology. One such example is provided by the binding of transcription factors to specific sites on DNA. To bind a particular target sequence, a protein must come into contact with that specific site (typically 10–20 base pairs in length) among all of the other genomic DNA that is present ( $10^6$  to  $10^{10}$  base pairs or more, depending on the organism).

A bacterial transcription factor known as lactose repressor (*lac*) binds to a specific sequence on DNA known as the operator (see Sections 13.8 and 13.9 for a discussion of how the lactose repressor recognizes specific sites on DNA). The rate constant for the bimolecular reaction of the repressor binding to its operator is  $\sim 1 \times 10^{10} \text{ M}^{-1} \cdot \text{sec}^{-1}$ . This is essentially the same as the rate of diffusional collisions between two small molecules that we calculated in the last section, and it is very