

# CHAPTER 17

## Diffusion and Transport

This trajectory ends up after two steps to the right of the origin—that is, it has traveled a distance of two units from the origin ( $\Delta x = 2$ ).

If steps to the right and to the left are equally likely, then we expect that, on aver-

**T**hroughout every cell the movement of molecules from one region to another is important to meet the demands of the processes that sustain life. A small molecule, such as ATP (the energy currency of cells), is synthesized by enzymes at the membranes of mitochondria, but is then needed in remote parts of the cell, where it is used for reactions such as powering chaperones for protein folding. Proteins themselves are synthesized by ribosomes in the cytoplasm, but may need to function elsewhere in the cell, such as by binding to DNA in the nucleus.

Much of the movement of molecules in cells is passive, requiring no energy source, and occurs in random directions. The random motions of molecules arise from constant collisions with water and other molecules. Such collisions cause transient accelerations in random directions and also cause the molecules to rotate. The resulting motions are maintained for only a very short time before further collisions change both the direction and the speed of the motion. Over time, these random motions cause molecules to move significant distances in a process referred to as **diffusion**. The same effects occur with larger particles, resulting in **Brownian motion** (in Brownian motion, the diffusing particles are large enough to see with a microscope). **Passive transport**, which occurs through diffusion alone, can be too slow to meet all of the needs of a cell. As a consequence, **active transport**, which requires an energy source, is also important. Some of the concepts that we shall develop in this chapter to describe diffusion are also useful for understanding aspects of active transport.

In this chapter, we describe the quantitative relationships between molecular properties, such as mass and shape, and the rates of diffusion and other processes related to it. These relationships make it possible to deduce information about the molecular properties from measurements of rates of movement, and also to predict what processes in cells would be too slow if they occurred only through diffusion. Understanding diffusion also helps us to understand the maximum rate with which a chemical reaction can occur.

### A. RANDOM WALKS

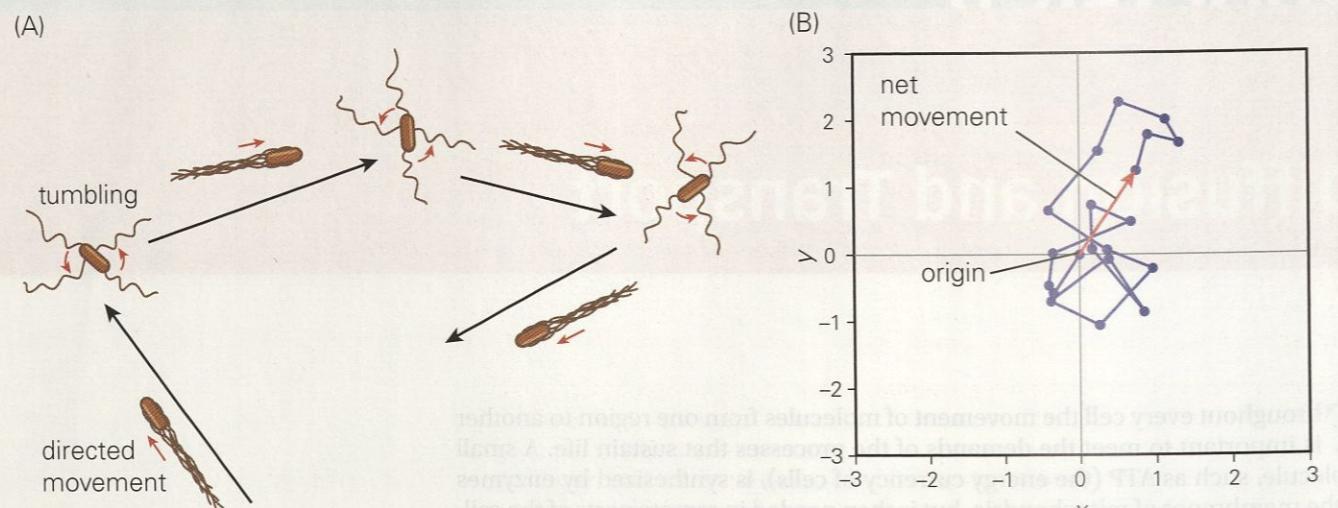
#### 17.1 Microscopic motion is well described by trajectories called random walks

To begin to understand the net movement of molecules undergoing random motions, let us first look at a slightly larger scale system, that of bacteria “swimming.” The movement of many kinds of bacteria occurs as a series of discrete steps of directed movement, interspersed by tumbling that randomizes the direction for the subsequent step. The alternation of tumbling and directed motion makes the movement of bacteria similar to that of molecules, which move in a series of very many small steps in which the direction of movement changes randomly at each step.

Recall from the discussion of bacterial chemotaxis in Chapter 14 that many bacteria that undergo active movement have fibers, known as flagella, that extend from

#### Passive transport

Passive transport is the movement of molecules through the process of diffusion. In contrast, the active transport of molecules in cells is driven by chemical energy—usually the hydrolysis of ATP or other nucleoside triphosphates.



**Figure 17.1** Bacterial chemotaxis can be described as a random walk. (A) In the absence of a chemical attractant or repellent, the bacteria alternate between straight swimming and tumbling (Figure 17.1A). During straight swimming, the counterclockwise rotation of the flagella causes them to form a bundle and work together like a miniature propeller. Tumbling occurs when the flagella rotate in a clockwise fashion, which causes them to separate and the directed movement to stop.

Each straight swim constitutes a step in a **random walk**, because the period of tumbling that follows the straight step causes the next straight step to occur in a random direction (Figure 17.1B). When bacteria are living in a thin film of water on top of a plate of agar in a Petri dish, as they commonly would be in a laboratory culture, their motion is basically constrained to two dimensions. If we start with a large number of bacteria in a single small spot on a plate, how far they will spread with time? By treating the movement of bacteria as a random walk, we can predict how quickly the clump of bacteria will spread out.

## 17.2 The analysis of bacterial movement is simplified by considering one-dimensional random walks with uniform step lengths and time intervals

To begin a quantitative analysis of the random motion of bacteria, we shall make a simplifying assumption. We will assume that each step has a uniform length and occurs over a fixed period of time. As we saw in the last section, this is not how bacteria actually move. Nevertheless, it turns out that after many steps, both the average size of the step and the average number of steps per unit time become precisely defined. As a consequence, the movement of bacteria over long times is well predicted by using this simpler approach.

We can simplify the process even further and consider just movement in one dimension, with each step going either to the left or to the right. We can then obtain information about movement in two or three dimensions by combining two or three one-dimensional random walks in orthogonal directions, as we discuss later.

The average displacement,  $\delta$ , from the original position after a total number of random steps,  $N_{\text{total}}$ , is given by the difference between the number of steps to the right,  $N_R$ , and the number of steps to the left,  $N_L$ :

$$\text{displacement, } \delta = (N_R - N_L) \quad (17.1)$$

We have assumed in Equation 17.1 that each step is of unit length. If the steps are not of unit length, then the actual displacement is obtained by multiplying the

value of  $\delta$  by the length of each step,  $l_{\text{step}}$ . Note that in Equation 17.1  $\delta$  refers to the distance between the initial point and the end point, and not to the summed length of all the steps, which is simply  $N_{\text{total}}$ .

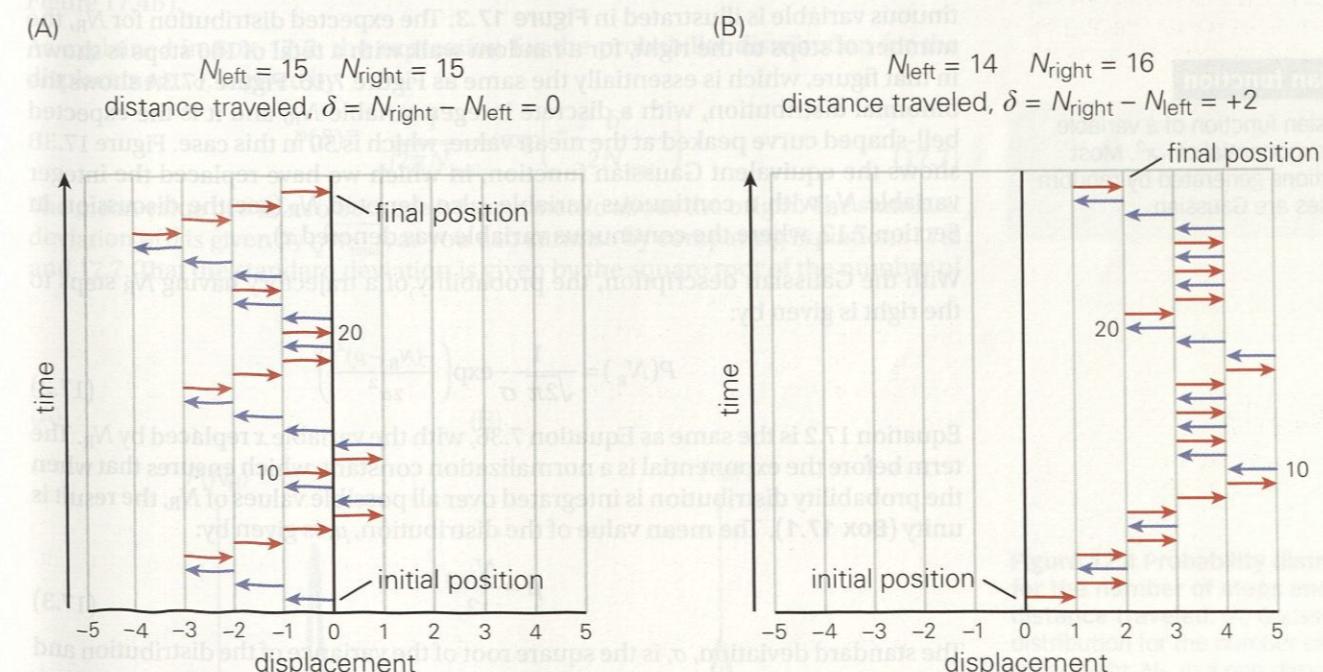
Two one-dimensional random-walk trajectories of 30 steps each are illustrated in Figure 17.2, with each step separated vertically in time in the diagram. Both trajectories have uniform step lengths and start at the same point. One trajectory (shown in Figure 17.2A) consists of 15 steps to the left with 15 steps to the right mixed in randomly, and so the trajectory ends up where it began (the value of  $\delta$  is zero). The second trajectory consists of 14 steps to the left and 16 steps to the right. This trajectory ends up at two steps to the right of the origin—that is, it has traveled a distance of two units from the origin ( $\delta = +2$ ).

If steps to the right and to the left are equally likely, then we expect that, on average, the distance traveled will be zero. But, as shown in Figure 17.1B, trajectories with nonzero displacements are also possible. A trajectory would have maximum displacement if all of the steps went in one direction only, which is very unlikely, but not impossible.

## 17.3 The probability distribution for the number of moves in one direction is given by a Gaussian function

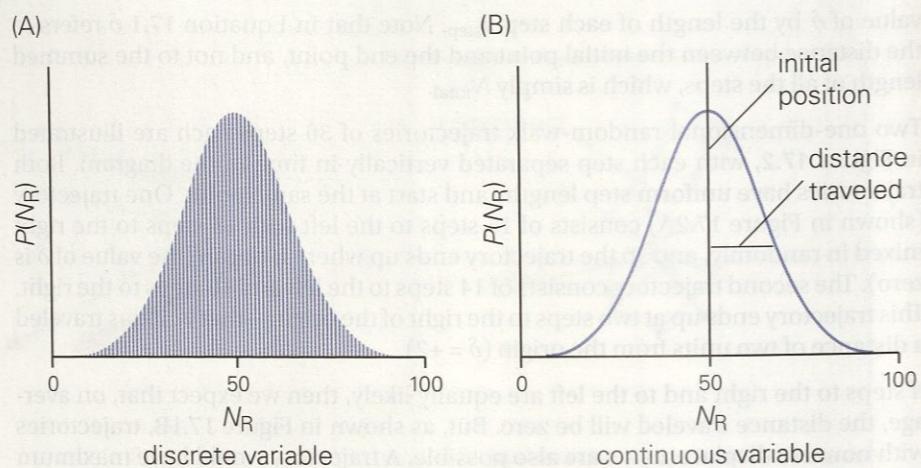
A one-dimensional random walk with uniform step size is analogous to a series of coin flips. In particular, we might consider a step to the right to correspond to a coin flip that comes up “heads” and a step to the left to one that comes up “tails.” Any particular trajectory then corresponds to a series of coin tosses, with one particular pattern of heads and tails.

Recall, from the discussion of entropy in Chapter 7, that any particular sequence of heads and tails is equally likely (see Section 7.1). For example, the two trajectories shown in Figure 17.2 are equally likely. But, when we consider the probability of moving a certain distance from the origin (or obtaining a specified number of



**Figure 17.2** One-dimensional random walks. Two independent trajectories are shown, each with 20 uniform steps. Whether each step is to the left or the right is random and uncorrelated with the directions of other steps. Both trajectories start at the origin (0), but then propagate randomly. (A) The trajectory consists of 15 steps to the right and 15 steps to left, ending up at zero. (B) The trajectory consists of 16 steps to the right and 14 steps to the left, ending up at +2. In this illustration the steps are assumed to have unit length, and so the distance traveled is simply given by the difference between the number of steps to the right and to the left.

**Figure 17.3 Probability distributions for a one-dimensional random walk.** (A) Binomial distribution for the probability of observing different numbers of right-hand steps in a random walk with 100 steps. The number of steps to the right,  $N_R$ , is an integer and takes on values between 0 and 100. When averaged over many trajectories, the mean value of  $N_R$  is 50. (B) If we assume that the number of steps to the right is a continuous variable, then the probability distribution is given by a Gaussian function. This is an accurate description of the probability distribution when the number of steps is very large (see Figure 7.16).



heads in a series of coin tosses), then the probability is given by the binomial distribution, and chance favors trajectories that do not move very far from the origin (that is, an even distribution of heads and tails is more likely; see Section 7.7).

The distance between the initial point and the end point in a random-walk trajectory is given by the difference between the number of steps to the right and to the left, as given by Equation 17.1 and illustrated in Figure 17.2. Different trajectories travel different distances from the origin, and the distribution of distances travelled has exactly the same form as the binomial distribution for the outcomes of coin flips. When the number of steps is large, the distribution is well described by a **Gaussian function** (see Section 7.12).

The conversion of a discrete binomial distribution to a Gaussian function of a continuous variable is illustrated in Figure 17.3. The expected distribution for  $N_R$ , the number of steps to the right, for a random walk with a total of 100 steps is shown in that figure, which is essentially the same as Figure 7.16. Figure 17.3A shows the binomial distribution, with a discrete integer variable  $N_R$ , and it is the expected bell-shaped curve peaked at the mean value, which is 50 in this case. Figure 17.3B shows the equivalent Gaussian function, in which we have replaced the integer variable  $N_R$  with a continuous variable, also denoted  $N_R$  (see the discussion in Section 7.12, where the continuous variable was denoted  $x$ ).

With the Gaussian description, the probability of a trajectory having  $N_R$  steps to the right is given by:

$$P(N_R) = \frac{1}{\sqrt{2\pi}\sigma} \exp\left(-\frac{(N_R - \mu)^2}{2\sigma^2}\right) \quad (17.2)$$

Equation 17.2 is the same as Equation 7.36, with the variable  $x$  replaced by  $N_R$ . The term before the exponential is a normalization constant, which ensures that when the probability distribution is integrated over all possible values of  $N_R$ , the result is unity (Box 17.1). The mean value of the distribution,  $\mu$ , is given by:

$$\mu = \frac{N_{\text{total}}}{2} \quad (17.3)$$

The standard deviation,  $\sigma$ , is the square root of the variance of the distribution and is given by:

$$\sigma = \sqrt{\frac{N_{\text{total}}}{2}} \quad (17.4)$$

The standard deviation is the **root mean square displacement** (r.m.s. displacement) of the values in the distribution from the mean value (see Box 17.1).

Figure 17.1 Bacterial movement can be described as a random walk. (A) In the absence of a chemical attractant or repellent, bacteria explore their environment by switching between random movements in opposite directions. (B) In the presence of a chemical attractant, the random walk becomes biased toward the source.

### Gaussian function

A Gaussian function of a variable  $x$  is an exponential of  $-x^2$ . Most distributions generated by random processes are Gaussian.

Substituting these expressions for  $\mu$  and  $\sigma$  into Equation 17.2, we get an expression for the probability distribution that depends only on the total number of steps,  $N_{\text{total}}$ :

$$P(N_R) = \frac{2}{\sqrt{2\pi N_{\text{total}}}} \exp\left[\frac{-\left(N_R - \frac{N_{\text{total}}}{2}\right)^2}{\frac{N_{\text{total}}}{2}}\right] \quad (17.5)$$

### 17.4 The probability of moving a certain distance in a one-dimensional random walk is also given by a Gaussian function

In the preceding sections we have discussed the probability that a random walk trajectory has a certain number of steps in one direction (for example,  $N_R$ ). We are usually more interested, however, in the probability that a trajectory ends up at a certain displacement,  $\delta$ , from the starting position. The value of  $\delta$  is related to the number of steps in one direction (for example,  $N_R$ ) in the following way:

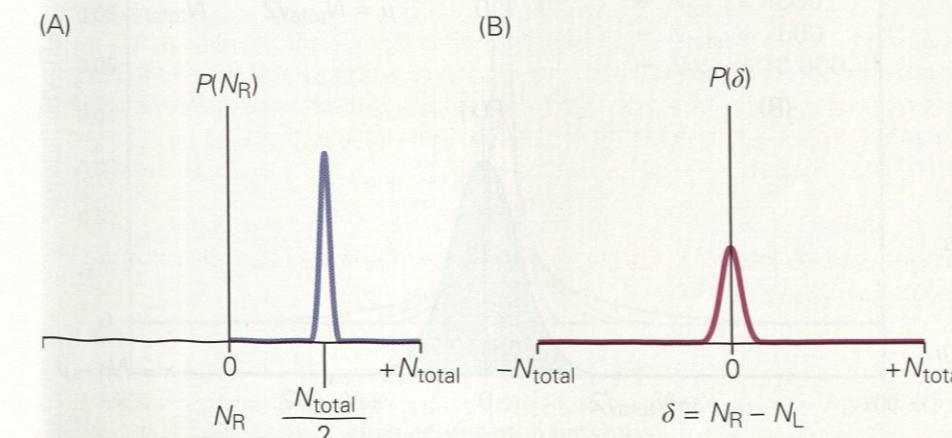
$$\begin{aligned} \delta &= N_R - N_L = N_R - (N_{\text{total}} - N_R) \\ &= 2N_R - N_{\text{total}} = 2(N_R - \mu) \end{aligned} \quad (17.6)$$

How do we convert the known probability distribution for  $N_R$  (Equation 17.5) into a probability distribution for  $\delta$ ? Recognize that  $\delta$  is defined by the value of  $N_R$ . The probability that the displacement is  $\delta$  is given by the probability that there are  $N_R$  steps to the right (that is, if the trajectory consists of  $N_R$  steps to the right, then according to Equation 17.6, the displacement from the origin must be  $\delta$ ). There is one subtlety, however, which is that the probability distribution for  $\delta$ ,  $P(\delta)$ , will have a different normalization constant than does  $P(N_R)$ . This is because, as shown in Figure 17.4A,  $N_R$  has a range from 0 to  $N_{\text{total}}$ , the total number of steps. The range of  $\delta$ , in contrast, is twice as large, and extends from  $-N_{\text{total}}$ , when all of the moves are to the left, to  $+N_{\text{total}}$ , when all of the moves are to the right (see Figure 17.4B).

As explained in Box 17.2, the expression for the probability distribution for the displacement,  $\delta$ , is given by:

$$P(\delta) = \frac{1}{\sqrt{2\pi N_{\text{total}}}} \exp\left(-\frac{\delta^2}{2N_{\text{total}}}\right) \quad (17.7)$$

The mean value of  $\delta$  is zero because it is symmetric about the origin. The standard deviation of  $\delta$  is given by  $\sqrt{N_{\text{total}}}$ , as you can surmise by comparing Equations 17.2 and 17.7. That the standard deviation is given by the square root of the number of



**Figure 17.4 Probability distributions for the number of steps and the distance traveled.** (A) Gaussian distribution for the number of steps to the right,  $N_R$ , in a one-dimensional random walk with  $N_{\text{total}}$  steps. (B) Distribution of net displacements from the origin,  $\delta$ , in the same random walk. The distribution is also described by a Gaussian function, with larger width.

### Box 17.1 Gaussian distributions

Here we review a few properties of Gaussian functions that are useful for the discussion in the main text.

#### Normalizing a Gaussian probability distribution

The first property of Gaussian functions is that the probability distribution must be normalized, which means that the integral of the probability distribution over the range of values is 1.0. This is because the total probability of obtaining *any* value of  $N_R$  has to be unity:

$$\int_0^{N_{\text{total}}} P(N_R) dN_R = \frac{1}{\sqrt{2\pi}\sigma} \int_0^{N_{\text{total}}} \exp\left[-\frac{(N_R - \mu)^2}{2\sigma^2}\right] dN_R = 1 \quad (17.1.1)$$

It is instructive to verify that the probability distribution is indeed normalized, by evaluating the integral in Equation 17.1.1. To do this, we define a variable,  $x$ , such that  $x = N_R - \mu$ . This corresponds to simply shifting the function so that the mean value is zero, as shown in Figure 17.1.1. It follows from this definition that the differential elements of  $x$  and  $N_R$  are equal—that is,  $dx = dN_R$ . While the range of  $N_R$  is from 0 to  $N_{\text{total}}$ , the range of  $x$  is from  $-N_{\text{total}}/2$  to  $+N_{\text{total}}/2$ . To evaluate the integral, we proceed as follows:

$$\begin{aligned} \int_0^{N_{\text{total}}} \exp\left(-\frac{(N_R - \mu)^2}{2\sigma^2}\right) dN_R &= \int_{-\frac{N_{\text{total}}}{2}}^{\frac{N_{\text{total}}}{2}} \exp\left(\frac{-x^2}{2\sigma^2}\right) dx \\ &= \int_{-\infty}^{+\infty} \exp\left(\frac{-x^2}{2\sigma^2}\right) dx \end{aligned} \quad (A) \quad (17.1.2)$$

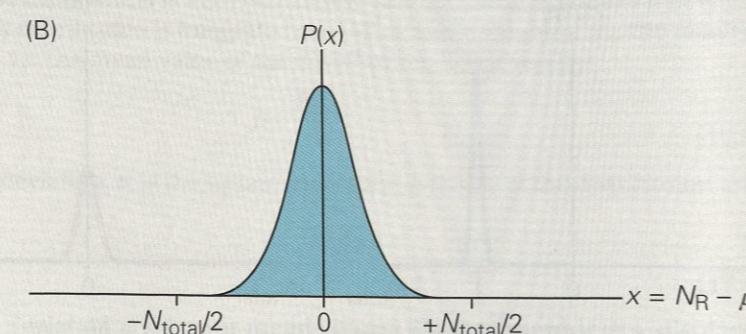
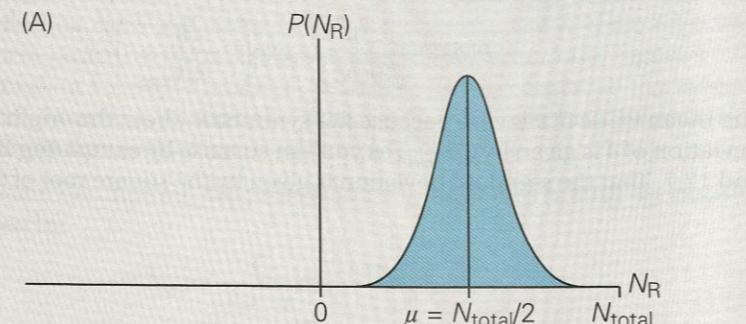
We have extended the range of the integral in Equation 17.1.2 from  $-\infty$  to  $+\infty$  because, as you can see from Figure 17.4B, the function being integrated falls off to zero at  $\pm N_{\text{total}}/2$ , and extending the range of the integration does not change the value of the integral. We can now use the following

expression for the definite integral, given in Table 17.1.1, which you can also find in tables of common integrals:

$$\int_{-\infty}^{+\infty} \exp(-ax^2) dx = 2 \int_0^{+\infty} \exp(-ax^2) dx = \sqrt{\frac{\pi}{a}} \quad (17.1.3)$$

By using Equation 17.1.3 to simplify Equation 17.1.2, we get:

$$\int_{-\infty}^{+\infty} \exp\left(\frac{-x^2}{2\sigma^2}\right) dx = \sqrt{\pi(2\sigma^2)} = \sigma\sqrt{2\pi} \quad (17.1.4)$$



**Figure 17.1.1 Shifting a Gaussian distribution to the origin.** (A) Graph of a Gaussian distribution for the probability of steps to the right ( $N_R$ ) in a random walk where the total number of steps is  $N_{\text{total}}$ . The integral of the probability distribution is the area under the curve, shaded blue. (B) The Gaussian distribution is shifted to the origin (that is, centered about zero) by switching to the variable  $x$ , where  $x = N_R - \mu$ . The range of the probability distribution is now from  $-N_R/2$  to  $+N_R/2$ .

**Table 17.1.1 Standard Gaussian integrals.**

(1)	$\int_0^{\infty} e^{-ax^2} dx = \frac{1}{2} \sqrt{\frac{\pi}{a}}$
(2) ( $a > 0$ )	$\int_0^{\infty} xe^{-ax^2} dx = \frac{1}{2a}$
(3)	$\int_0^{\infty} x^2 e^{-ax^2} dx = \frac{1}{4} \sqrt{\frac{\pi}{a^3}}$
(4) ( $a > 0$ )	$\int_0^{\infty} x^3 e^{-ax^2} dx = \frac{1}{2a^2}$
(5)	$\int_0^{\infty} x^4 e^{-ax^2} dx = \frac{6}{4} \sqrt{\frac{\pi}{a^5}}$

And, by combining Equations 17.1.1, 17.1.2, and 17.1.4, we verify that the probability distribution is indeed normalized:

$$\int_0^{N_{\text{total}}} P(N_R) dN_R = \frac{1}{\sigma\sqrt{2\pi}} \sigma\sqrt{2\pi} = 1 \quad (17.1.5)$$

#### The standard deviation of a Gaussian distribution

It is also useful to review the significance of the **standard deviation**,  $\sigma$ . The standard deviation is the square root of the **variance** of the distribution. The variance is the mean value of the squared displacement from the mean:

$$\text{variance} = \langle (N_R - \mu)^2 \rangle \quad (17.1.6)$$

The angular brackets in Equation 17.1.6 denote an average over the whole distribution. The average value of any variable is calculated by multiplying the variable by the probability distribution and integrating the result:

$$\langle (N_R - \mu)^2 \rangle = \frac{1}{\sqrt{2\pi}\sigma} \int_0^{N_{\text{total}}} (N_R - \mu)^2 \exp\left[-\frac{(N_R - \mu)^2}{2\sigma^2}\right] dN_R \quad (17.1.7)$$

To evaluate the integral in Equation 17.1.7, we again use the shifted variable,  $x$ , which gives:

$$\begin{aligned} \frac{1}{\sigma\sqrt{2\pi}} \int_0^{N_{\text{total}}} (N_R - \mu)^2 \exp\left[-\frac{(N_R - \mu)^2}{2\sigma^2}\right] dN_R &= \\ = \frac{1}{\sigma\sqrt{2\pi}} \int_{-\infty}^{+\infty} x^2 \exp\left(-\frac{x^2}{2\sigma^2}\right) dx & \quad (17.1.8) \end{aligned}$$

By referring to a Table 17.1.1, you will find that:

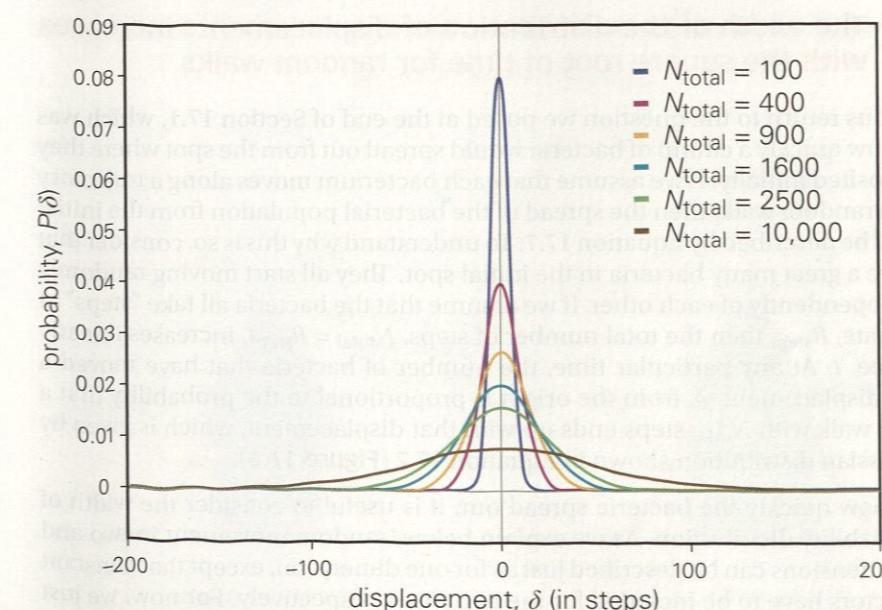
$$\int_{-\infty}^{+\infty} x^2 \exp(-ax^2) dx = 2 \int_0^{+\infty} x^2 \exp(-ax^2) dx = \frac{1}{2} \sqrt{\frac{\pi}{a^3}} \quad (17.1.9)$$

Using Equation 17.1.9 in Equation 17.1.7, you will see that:

$$\langle (N_R - \mu)^2 \rangle = \left(\frac{1}{\sigma\sqrt{2\pi}}\right) \left(\frac{1}{2}\right) \sqrt{\pi 2^3 \sigma^6} = \sigma^2 \quad (17.1.10)$$

It follows from Equation 17.1.9 that the standard deviation,  $\sigma$ , is indeed the square root of the variance. The standard deviation is also referred to the **root mean square (r.m.s.) displacement** from the mean.

steps can be appreciated by looking at Figure 17.5, which graphs the probability distributions for random-walk trajectories with different numbers of steps. The longest trajectory in Figure 17.5 has 10,000 steps, and is 100 times longer than the shortest one, which has only 100 steps. The width of the distribution for the longest trajectory, which is related to the standard deviation (see Section 17.5, below), is only 10 times larger than the width of the distribution for the shortest trajectory.



**Figure 17.5 Displacement probability for random walks.** The distribution of displacements,  $\delta$ , from the starting point is shown for increasing numbers of steps,  $N_{\text{total}}$ , for a one-dimensional random walk. These are Gaussian functions, defined in Equation 17.7.

### Box 17.2 Expressing the probability distribution for a random walk in terms of displacements from the mean position

Here we explain how we arrive at the expression for the probability of finding a displacement  $\delta$  from the mean position for a one-dimensional random walk:

$$P(\delta) = \frac{1}{\sqrt{2\pi N_{\text{total}}}} \exp\left(-\frac{\delta^2}{2N_{\text{total}}}\right) \quad (17.7)$$

We begin with Equation 17.5 in the main text, which gives the probability of a trajectory moving  $N_R$  steps to the right:

$$P(N_R) = \frac{2}{\sqrt{2\pi N_{\text{total}}}} \exp\left[\frac{-\left(N_R - \frac{N_{\text{total}}}{2}\right)^2}{\frac{N_{\text{total}}}{2}}\right] \quad (17.5)$$

As we noted in the main text, a trajectory with a displacement  $\delta$  is equivalent to a trajectory that moves  $N_R$  steps to the right, and so the probability of finding such a trajectory must be given by Equation 17.5. We need to express the exponent in Equation 17.5 in terms of  $\delta$  rather than  $N_R$ . To do this, we express  $N_R$  in terms of the displacement,  $\delta$ :

$$N_R = \frac{\delta}{2} + \frac{N_{\text{total}}}{2} \quad (17.2.1)$$

By substituting this expression in Equation 17.5, we get:

$$P(\delta) = K \exp\left[-\frac{\left(\frac{\delta}{2}\right)^2}{\frac{N_{\text{total}}}{2}}\right] = K \exp\left(-\frac{\delta^2}{2N_{\text{total}}}\right) \quad (17.2.2)$$

### 17.5 The width of the distribution of displacements increases with the square root of time for random walks

Now let us return to the question we posed at the end of Section 17.1, which was to ask how quickly a clump of bacteria would spread out from the spot where they are deposited initially. If we assume that each bacterium moves along a trajectory that is a random walk, then the spread of the bacterial population from the initial spot will be described by Equation 17.7. To understand why this is so, consider that there are a great many bacteria in the initial spot. They all start moving randomly and independently of each other. If we assume that the bacteria all take “steps” at a fixed rate,  $R_{\text{step}}$ , then the total number of steps,  $N_{\text{total}} = R_{\text{step}}t$ , increases linearly with time,  $t$ . At any particular time, the number of bacteria that have moved a certain displacement,  $\delta$ , from the origin is proportional to the probability that a random walk with  $N_{\text{total}}$  steps ends up with that displacement, which is given by the Gaussian distribution shown in Equation 17.7 (Figure 17.6).

To see how quickly the bacteria spread out, it is useful to consider the width of the probability distribution. As we explain below, random movement in two and three dimensions can be described just as for one dimension, except that constant scale factors have to be included for the two cases, respectively. For now, we just

Here  $K$  is the normalization constant. To determine its value, we integrate the probability distribution function over all values of  $\delta$ , and set the value of the integral to unity, as explained in Box 17.1.

$$\int_{-\infty}^{+\infty} P(\delta) d\delta = K \int_{-\infty}^{+\infty} \exp\left(-\frac{\delta^2}{2N_{\text{total}}}\right) d\delta = K \sqrt{2\pi N_{\text{total}}} = 1 \quad (17.2.3)$$

And so:

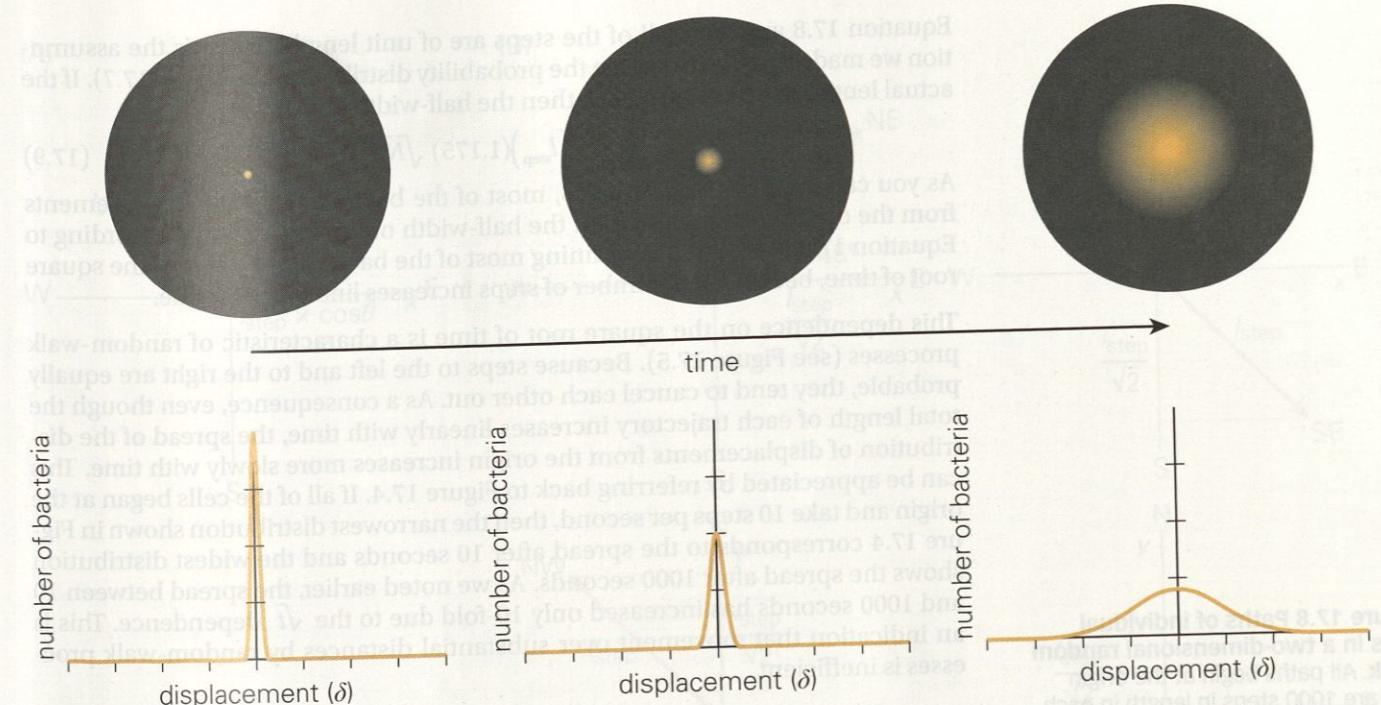
$$K = \frac{1}{\sqrt{2\pi N_{\text{total}}}} \quad (17.2.4)$$

We can also determine the standard deviation directly by calculating the mean square displacement,  $\langle \delta^2 \rangle$ , as follows:

$$\langle \delta^2 \rangle = \int_{-\infty}^{+\infty} \delta^2 P(\delta) d\delta = \frac{1}{\sqrt{2\pi N_{\text{total}}}} \int_{-\infty}^{+\infty} \delta^2 \exp\left(-\frac{\delta^2}{2N_{\text{total}}}\right) d\delta \quad (17.2.5)$$

The integral in Equation 17.2.5 can be evaluated as explained in Box 17.1, yielding:

$$\langle \delta^2 \rangle = \frac{1}{\sqrt{2\pi N_{\text{total}}}} \frac{\sqrt{\pi (2N_{\text{total}})^3}}{2} = N_{\text{total}} \quad (17.2.6)$$

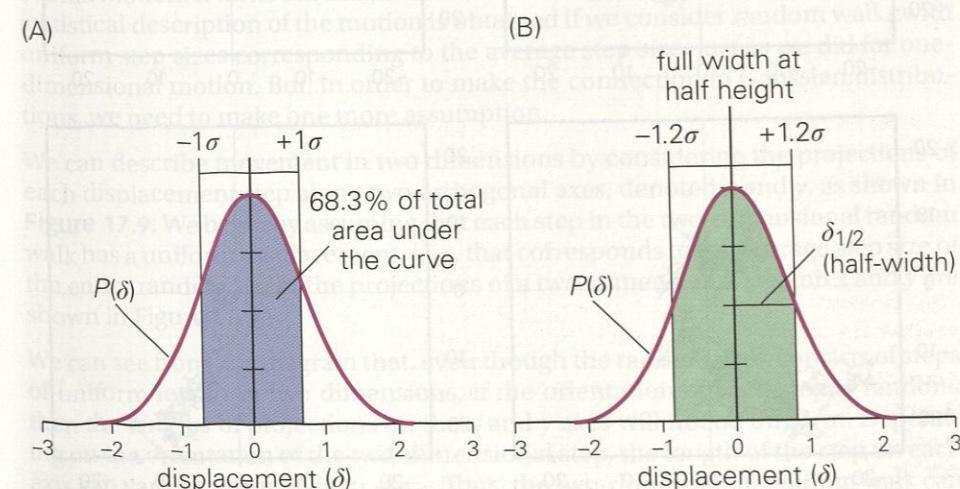


consider the probability distribution for one dimension and assume that the density of bacteria at a certain displacement from the origin will be proportional to the value of the probability distribution for that displacement.

How does the width of the probability distribution change with time? One practical definition of the width is simply the standard deviation of the distribution which, as we saw in the previous section, is  $\sqrt{N_{\text{total}}}$ . Recall from Section 7.14 that ~68% of the displacements will be within  $1\sigma$  of the mean value (Figure 17.7A). Another measure of the width of the distribution is the displacement at which the probability is half of the maximum probability (see Section 7.13). The most probable location is the origin ( $\delta = 0$ ) because steps to the left and to the right are equally probable. The displacement,  $\delta_{1/2}$ , for which the probability drops to half the value at the origin is called the **half-width at half height** (see Figure 17.7B). The population of bacteria starts dropping rapidly when the displacement from the origin is greater than the half-width. This gives us a rough measure of the edge of the spreading spot of bacteria.

As explained in Section 7.13, the half-width of the distribution,  $\delta_{1/2}$ , is given by:

$$\delta_{1/2} \approx 1.175\sigma = 1.175\sqrt{N_{\text{total}}} \quad (17.8)$$



**Figure 17.6 Gaussian functions describe the outward spread of bacteria.** The diagram above shows that a clump of bacteria that is spotted on an agar plate spreads out with time. The graphs show the number of bacteria as a function of distance from the origin.

**Figure 17.7 Two measures of the width of a Gaussian distribution.** (A) The area within  $1\sigma$  of the mean value covers ~68% of the distribution, and so  $1\sigma$  can be considered the width of the distribution. (B) The half-width at half height is another measure of the width, and it is equal to ~ $1.2\sigma$ .

Equation 17.8 applies if all of the steps are of unit length, which is the assumption we made in order to derive the probability distribution (Equation 17.7). If the actual length of each step is  $l_{\text{step}}$ , then the half-width is given by:

$$\delta_{1/2} \approx (l_{\text{step}})(1.175) \sqrt{N_{\text{total}}} \quad (17.9)$$

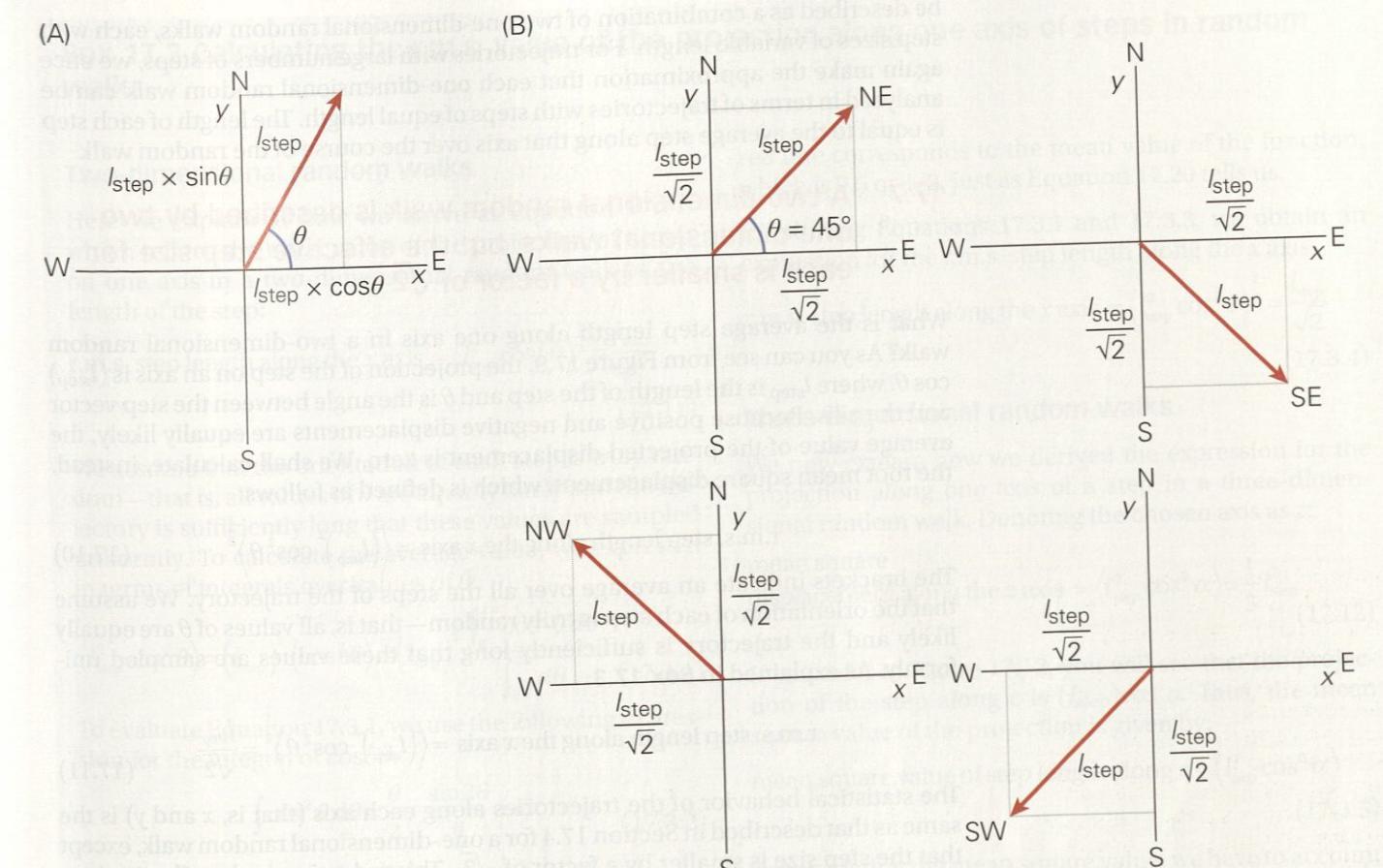
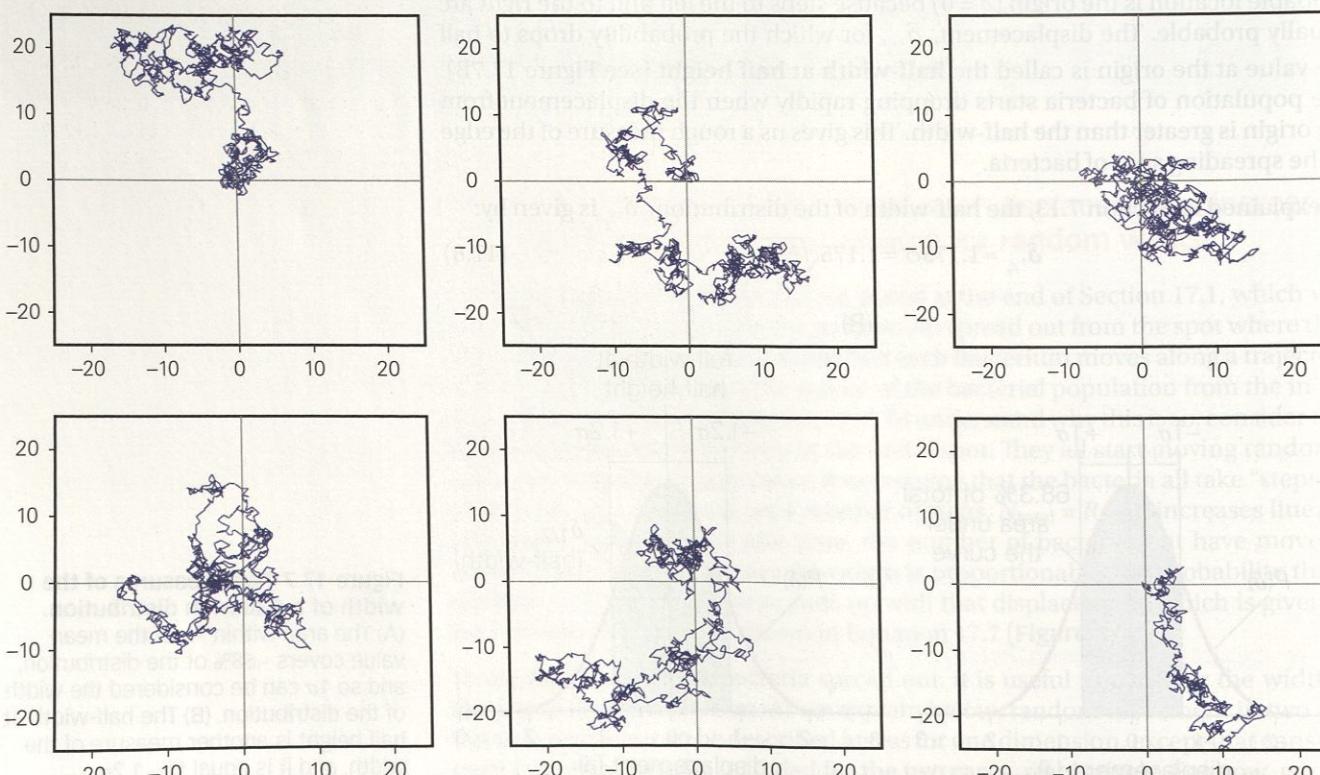
As you can see from Figure 17.7B, most of the bacteria will have displacements from the origin that are less than the half-width of the distribution. According to Equation 17.9, the region containing most of the bacteria will grow as the square root of time, because the number of steps increases linearly with time.

This dependence on the square root of time is a characteristic of random-walk processes (see Figure 17.5). Because steps to the left and to the right are equally probable, they tend to cancel each other out. As a consequence, even though the total length of each trajectory increases linearly with time, the spread of the distribution of displacements from the origin increases more slowly with time. This can be appreciated by referring back to Figure 17.4. If all of the cells began at the origin and take 10 steps per second, then the narrowest distribution shown in Figure 17.4 corresponds to the spread after 10 seconds and the widest distribution shows the spread after 1000 seconds. As we noted earlier, the spread between 10 and 1000 seconds has increased only 10-fold due to the  $\sqrt{t}$  dependence. This is an indication that movement over substantial distances by random-walk processes is inefficient.

### 17.6 Random walks in two dimensions can be analyzed by combining two orthogonal one-dimensional random walks

Several trajectories for cells undergoing random walks in two dimensions are shown in Figure 17.8, in which each trajectory consists of 1000 steps. In these diagrams, each step is in a random direction with respect to the previous one and has a length that is distributed randomly between 0 and 1. For trajectories with such a large number of steps, it is clear from Figure 17.8 that the details of the direction

**Figure 17.8 Paths of individual cells in a two-dimensional random walk.** All paths begin at the origin and are 1000 steps in length in each case. For each step, the direction is random and the size of the step takes a random value between 0 and 1. The net displacement from the origin, averaged over a large number of cells, would give a two-dimensional Gaussian distribution with one-dimensional cross-sections that are equivalent for all directions away from the origin, such as those shown in Figure 17.6.



**Figure 17.9 The projection of a step in a two-dimensional random walk along two orthogonal directions.** (A) A single step, with length  $l_{\text{step}}$ , is shown, with random orientation. The angle between the  $x$  axis and the vector corresponding to the step is denoted by  $\theta$ . The projections of the step on two orthogonal axes are given by  $(l_{\text{step}})\cos\theta$  and  $(l_{\text{step}})\sin\theta$ , respectively. (B) As explained in Section 17.7, r.m.s. length of the projections on

each axis, averaged over many steps in a two-dimensional random walk, is given by  $\frac{l_{\text{step}}}{\sqrt{2}}$ . If we work backwards and construct a two-dimensional random walk from two one-dimensional trajectories, each with this step size, then each step in the resulting two-dimensional random walk is restricted to one of four directions. These are indicated in the diagram using geographical directions (NE, northeast, etc.). See Figure 17.10 for a two-dimensional random walk built up in this way.

and length of each step cannot be made out easily compared to the scale of the overall motion. It turns out that, in the limit of a large number of steps, an accurate statistical description of the motion is obtained if we consider random walks with uniform step sizes corresponding to the average step size, just as we did for one-dimensional motion. But, in order to make the connection to Gaussian distributions, we need to make one more assumption.

We can describe movement in two dimensions by considering the projections of each displacement step along two orthogonal axes, denoted  $x$  and  $y$ , as shown in Figure 17.9. We begin by assuming that each step in the two-dimensional random walk has a uniform displacement,  $l_{\text{step}}$ , that corresponds to the average step size of the entire random walk. The projections of a two-dimensional step on  $x$  and  $y$  are shown in Figure 17.9A.

We can see from this diagram that, even though the random walk consists of steps of uniform length in two dimensions, if the orientation of each step is random, then the lengths of projections on the  $x$  and  $y$  axes will not be uniform. Depending on the orientation of the two-dimensional step, the length of the step on each axis can vary between  $+l_{\text{step}}$  to  $-l_{\text{step}}$ . Thus, the two-dimensional random walk can

be described as a combination of two one-dimensional random walks, each with step sizes of variable length. For trajectories with large numbers of steps, we once again make the approximation that each one-dimensional random walk can be analyzed in terms of trajectories with steps of equal length. The length of each step is equal to the average step along that axis over the course of the random walk.

### 17.7 A two-dimensional random walk is described by two one-dimensional walks, but the effective step size for each is smaller by a factor of $\sqrt{2}$

What is the average step length along one axis in a two-dimensional random walk? As you can see from Figure 17.9, the projection of the step on an axis is  $(l_{\text{step}}) \cos \theta$ , where  $l_{\text{step}}$  is the length of the step and  $\theta$  is the angle between the step vector and the axis. Because positive and negative displacements are equally likely, the average value of the projected displacement is zero. We shall calculate, instead, the root mean square displacement, which is defined as follows:

$$\text{r.m.s. step length along the } x \text{ axis} = \langle (l_{\text{step}})^2 \cos^2 \theta \rangle^{\frac{1}{2}} \quad (17.10)$$

The brackets indicate an average over all the steps of the trajectory. We assume that the orientation of each step is truly random—that is, all values of  $\theta$  are equally likely and the trajectory is sufficiently long that these values are sampled uniformly. As explained in Box 17.3:

$$\text{r.m.s. step length along the } x \text{ axis} = \langle (l_{\text{step}})^2 \cos^2 \theta \rangle^{\frac{1}{2}} = \frac{l_{\text{step}}}{\sqrt{2}} \quad (17.11)$$

The statistical behavior of the trajectories along each axis (that is,  $x$  and  $y$ ) is the same as that described in Section 17.4 for a one-dimensional random walk, except that the step size is smaller by a factor of  $\sqrt{2}$ . This reduction in the effective step size occurs because the motion is broken down into two orthogonal and independent components. For each step, only part of the movement is in the radial direction, away from the origin. The time dependence of the outward movement (that is, the movement of the “edge” of the distribution) remains the same as for the one-dimensional distribution and scales as  $\sqrt{t}$ .

### 17.8 The assumption of uniform step lengths along each axis means that the random walk occurs on a grid

It turns out that, by assuming that we can treat movement along each axis in terms of a uniform step length given by Equation 17.21, we are assuming that each step in the two-dimensional random walk occurs on a grid, with only diagonal steps allowed. This is made clear in Figure 17.9B, which shows that, if the step along each axis is  $\frac{l_{\text{step}}}{\sqrt{2}}$ , then the actual step must lie exactly midway between each

axis. Thus, only four kinds of steps are possible, corresponding to moves in the northwest, northeast, southeast, and southwest directions (assuming that  $x$  and  $y$  correspond to “east” and “north,” respectively). This idea is illustrated in Figure 17.10, which shows how a two-dimensional random walk is broken down into two orthogonal one-dimensional random walks.

The random walk shown in Figure 17.10C is restricted to lie on the nodes of a two-dimensional grid or lattice. You can readily appreciate that it is straightforward to write computer algorithms that generate such random walks, given a small set of parameters such as the step size and the time constant. Indeed, such algorithms find powerful application in the analysis of a very diverse range of problems in which random steps influence some kind of aggregate behavior. In addition to the study of diffusion and Brownian motion, which is our particular focus here, random walks are used to study things as apparently unrelated as the structure of polymers and the variation in stock market prices.

### Box 17.3 Calculating the r.m.s. value of the projection along one axis of steps in random walks

#### Two-dimensional random walks

Here we explain at how we arrive at Equation 17.11, which relates the r.m.s. value of the projection of a step on one axis in a two-dimensional random walk to the length of the step:

$$\text{r.m.s. step length along the } x \text{ axis} = \langle l_{\text{step}}^2 \cos^2 \theta \rangle^{\frac{1}{2}} = \frac{l_{\text{step}}}{\sqrt{2}} \quad (17.11)$$

We assume that the orientation of each step is truly random—that is, all values of  $\theta$  are equally likely and the trajectory is sufficiently long that these values are sampled uniformly. To calculate the average value, we express it in terms of integrals over values of  $\theta$ :

$$\langle l_{\text{step}}^2 \cos^2 \theta \rangle = \langle l_{\text{step}}^2 \rangle \langle \cos^2 \theta \rangle = \langle l_{\text{step}}^2 \rangle \frac{\int_0^{2\pi} \cos^2 \theta d\theta}{\int_0^{2\pi} d\theta} \quad (17.3.1)$$

To evaluate Equation 17.3.1, we use the following expression for the integral of  $\cos^2 \theta$ :

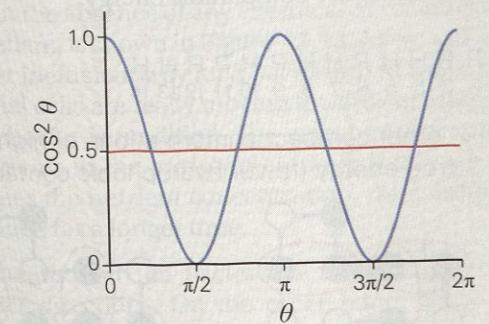
$$\int \cos^2 \theta d\theta = \frac{\theta}{2} + \frac{\sin 2\theta}{4} + C \quad (17.3.2)$$

where  $C$  is a constant of the integration.

Using Equation 17.3.2, we evaluate the definite integral in Equation 17.3.1 as follows:

$$\int_0^{2\pi} \cos^2 \theta d\theta = \frac{\left[ \frac{\theta}{2} + \frac{\sin 2\theta}{4} \right]_0^{2\pi}}{2\pi} = \frac{1}{2} \quad (17.3.3)$$

Although Equation 17.3.3 may look complicated, its meaning may be appreciated intuitively by looking at Figure 17.3.1, which shows a graph of  $\cos^2 \theta$  over the interval 0 to  $2\pi$ . The figure shows a horizontal red line that cuts the graph of the function exactly in half. This



**Figure 17.3.1** The mean value of  $\cos^2 \theta$  over a full cycle is equal to 1/2. The value of the function  $\cos^2 \theta$  is graphed in the interval 0 to  $2\pi$ . Notice that the horizontal red line cuts the function into two equal halves. The red line marks the mean value of the function over the interval, which is 1/2.

red line corresponds to the mean value of the function, which is 0.5 or  $1/2$ , just as Equation 17.20 tells us.

Combining Equations 17.3.1 and 17.3.3, we obtain an expression for the r.m.s. step length along the  $x$  axis:

$$\text{r.m.s. step length along the } x \text{ axis} = \langle l_{\text{step}}^2 \cos^2 \theta \rangle^{\frac{1}{2}} = \frac{l_{\text{step}}}{\sqrt{2}} \quad (17.3.4)$$

#### Three-dimensional random walks

We now explain how we derived the expression for the projection along one axis of a step in a three-dimensional random walk. Denoting the chosen axis as  $z$ :

$$\text{mean square displacement along the } z \text{ axis} = \langle l_{\text{step}}^2 \cos^2 \alpha \rangle = \frac{1}{3} l_{\text{step}}^2 \quad (17.12)$$

If you refer to Figure 17.12, you will see that the projection of the step along  $z$  is  $(l_{\text{step}}) \cos \alpha$ . Thus, the mean square value of the projection is given by:

$$\text{mean square value of step length along } z = \langle l_{\text{step}}^2 \cos^2 \alpha \rangle \quad (17.3.5)$$

In calculating the mean square value, we have to account for the different weighting of vectors with different values of  $\alpha$ . This is because for each value of  $\alpha$  there are a different number of vectors with the same value of  $\alpha$ . We do this by multiplying the projection of the vector by the circumference of the circle traced out by the tips of vectors with the same value of  $\alpha$  (see Figure 17.12), which is  $(2\pi)(l_{\text{step}}) \sin \alpha$ , and integrating over the range of  $\alpha$ :

$$\begin{aligned} \text{mean square value} &= \int_0^\pi (l_{\text{step}})^2 (\cos^2 \alpha) (2\pi) (l_{\text{step}}) (\sin \alpha) d\alpha \\ &= \int_0^\pi (2\pi) (l_{\text{step}}) (\sin \alpha) d\alpha \\ &= \frac{l_{\text{step}}^2 \int_0^\pi (\cos^2 \alpha) (\sin \alpha) d\alpha}{\int_0^\pi \sin \alpha d\alpha} \end{aligned} \quad (17.3.6)$$

To evaluate this expression, we use the following integrals, which you can look up in a table of standard integrals:

$$\int (\cos^2 \alpha) (\sin \alpha) d\alpha = -\frac{1}{3} \cos^3 \alpha + C \quad (17.3.7)$$

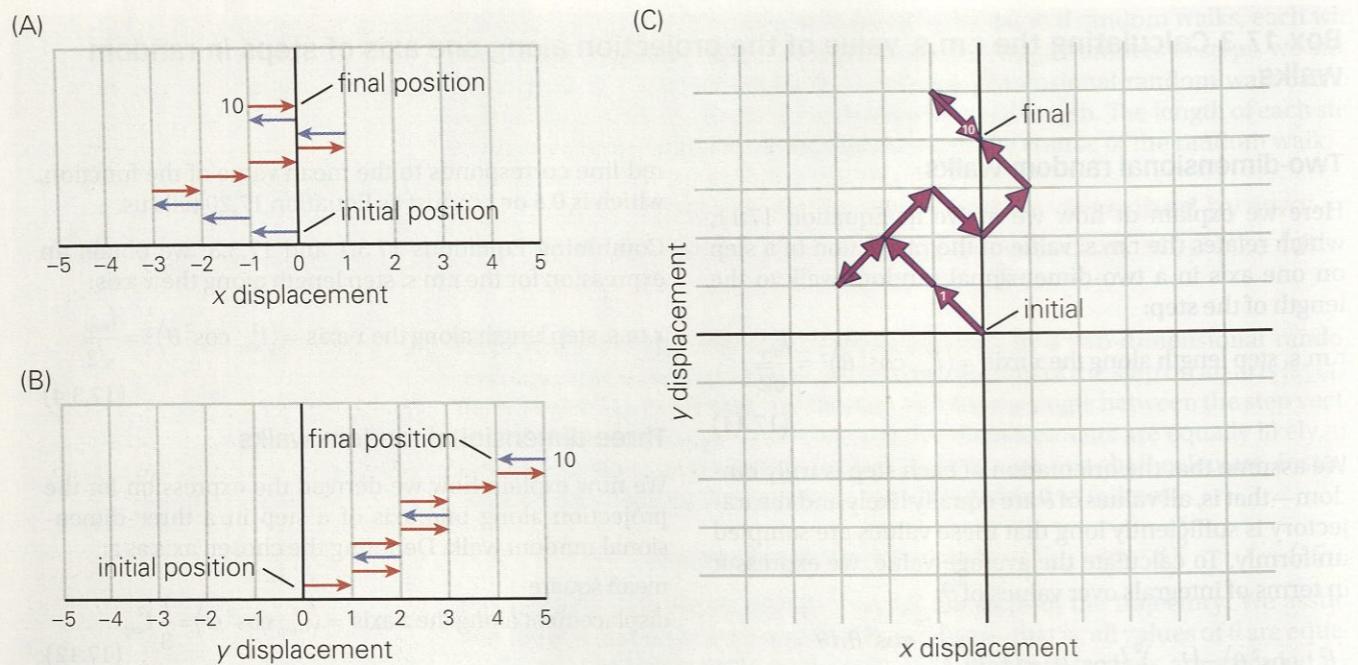
$$\int \sin \alpha d\alpha = -\cos \alpha + C \quad (17.3.8)$$

By using these equations to evaluate the definite integrals in Equation 17.3.6, we get:

$$\text{mean square value} = \langle l_{\text{step}}^2 \cos^2 \alpha \rangle = \frac{1}{3} l_{\text{step}}^2 \quad (17.3.9)$$

Thus, the r.m.s. value of the projection of the displacement on any one of the axes is given by:

$$\text{r.m.s. step length along any axis} = \frac{l_{\text{step}}}{\sqrt{3}} \quad (17.3.10)$$

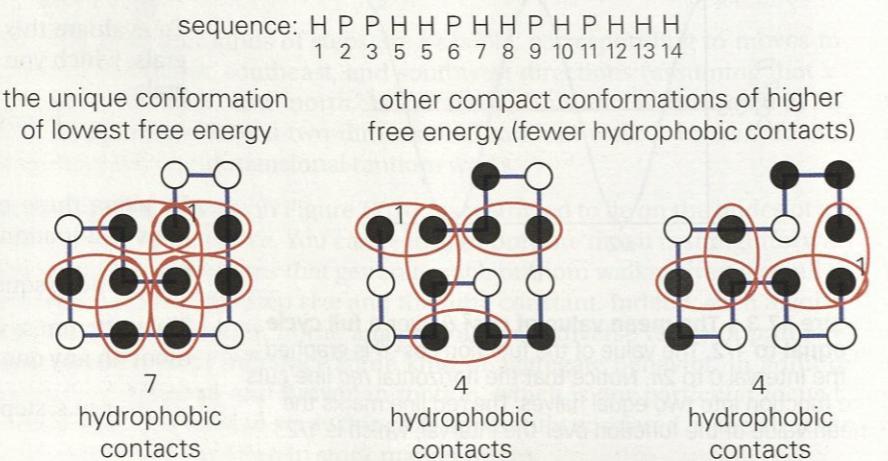


**Figure 17.10 Construction of a two-dimensional random walk from two orthogonal one-dimensional random walks.** (A, B) Displacements along the  $x$  and  $y$  directions during a 10-step random walk. Compare with Figure 17.2, and note that the trajectories for  $x$  and  $y$  displacements end up at 0 and +4, respectively. (C) A two-dimensional random walk generated by combining the sequential steps shown in (A) and (B). As expected, the trajectory ends up at  $x = 0$  and  $y = +4$ .

As an example, consider the application of a two-dimensional random walk to the analysis of protein folding. One interesting question is whether there are particular patterns of amino acids that are capable of folding into a stable structure and others that are not. To study this question, scientists have analyzed the behavior of proteins that consist of just two kinds of amino acids, one hydrophobic and the other polar. A simple computational model for such a protein considers each residue to be a ball that is connected to two adjacent residues in a chain. Any particular conformation of the protein corresponds to a random-walk trajectory, in which the starting point is the first residue and the number of steps is simply the number of residues in the chain.

Three conformations of a 14-residue protein modeled in this way in two dimensions are shown in Figure 17.11. Using the random-walk algorithm, modified to prevent the chain from running into itself, all possible conformations of the protein can be generated very quickly on a computer. Different patterns of amino acids can then be placed on these chains, and the energies of the different structures can be evaluated using simple schemes. In the example shown in Figure 17.11, every time two hydrophobic residues are next to each other, the energy is deemed to be favorable. This kind of strategy has allowed scientists to understand what features allow proteins to adopt unique folded structures without being trapped in alternative conformations that have comparable energy.

**Figure 17.11 Protein structure modeled by random walks.** A two-dimensional representation of a protein with 14 residues is shown here. The residues of the protein are constrained to lie on the points of a grid, and all possible conformations are generated by the trajectories of a two-dimensional random walk. The trajectories are self-avoiding, because two residues cannot lie on the same point. There are only two kinds of residues, hydrophobic (black) and polar (white). Favorable contacts between hydrophobic residues are outlined in red. Highly simplified protein models such as this help us to understand what kinds of sequence patterns lead to unique folded structures. (Adapted from K.A. Dill, *Biochemistry* 29: 7133–7155, 1990. With permission from Elsevier.)



### 17.9 A three-dimensional random walk is described by three orthogonal one-dimensional walks, and the effective step size for each is smaller by a factor of $\sqrt{3}$

The extension of our analysis of random walks to three dimensions is done in a way that is analogous to the extension to two dimensions, but with a further reduction in the rate of outward movement due to the fact that the steps can have components along the  $x$ ,  $y$ , and  $z$  directions. This reduces the effective step size in each direction to  $\frac{l_{\text{step}}}{\sqrt{3}}$ . The spread of the distribution in each direction has the same time dependence as before, increasing with the square root of time.

To understand how the factor of  $\sqrt{3}$  arises, consider a three-dimensional random walk with uniform step size, but with random direction at each step. The projection of such a step on to one of the three orthogonal axes is shown in Figure 17.12. The vector corresponding to the step makes an angle  $\alpha$  with the vertical axis. The projection of the vector on to the vertical axis is given by  $(l_{\text{step}}) \cos \alpha$ .

Each value of  $\alpha$  defines a set of displacement vectors, the tips of which trace out a circle of radius  $(l_{\text{step}}) \sin \alpha$ , as shown in Figure 17.12. The number of such vectors is proportional to  $\sin \alpha$ , and therefore increases as  $\alpha$  increases from 0 to 90 and then decreases again. The range of  $\alpha$  is from 0° to 180° ( $2\pi$ ). As explained in Box 17.3,

$$\text{mean square displacement along the } z \text{ axis} = \langle (l_{\text{step}})^2 \cos^2 \alpha \rangle = \frac{1}{3} l_{\text{step}}^2 \quad (17.12)$$

Thus, the r.m.s. value of the projection of the displacement on any one of the axes is given by:

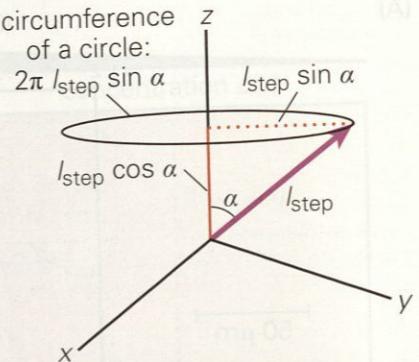
$$\text{r.m.s. step length along any axis} = \frac{l_{\text{step}}}{\sqrt{3}} \quad (17.13)$$

According to Equation 17.13, for a molecule diffusing in three dimensions, its rate of movement along any one direction is slower by a factor of  $\sqrt{3}$  than its overall movement. We implicitly used this result earlier in Section 11.19, when we compared the rate of diffusion of potassium ions in water (that is, in three dimensions) to the rate at which they translocate through the potassium channel (in one dimension). The significance of this point will be made clear in Section 17.14, below, where we relate a parameter known as the diffusion constant to the r.m.s. displacement.

### 17.10 The movement of bacteria in the presence of attractants or repellents is described by biased random walks

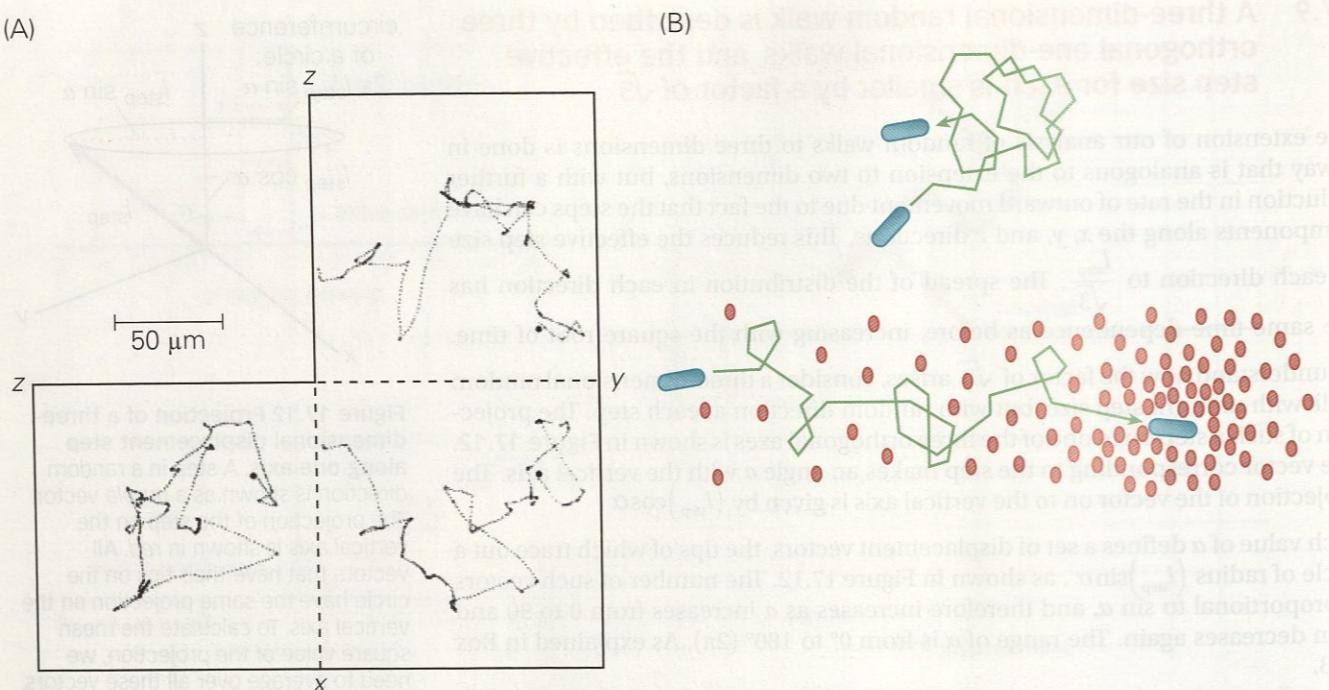
The random-walk model provides a satisfactory description of the behavior of bacterial swimming. The actual movement of a single *E. coli* over a period of 30 seconds, in the absence of any chemical attractant (for example, nutrient molecules) or repellent, is shown in Figure 17.13. As we saw earlier, this random movement is a rather inefficient way for a bacterium to travel over substantial distances. When bacterial cells are really moving towards a nutrient source (or away from a toxin), this behavior is modified. The cells have receptors on the surface that respond to nutrients in the environment and, if the cell is swimming in a direction that increases the nutrient concentration, then the periods of straight swimming are continued for a longer time.

This means that the bacterium takes longer steps towards the nutrient than in other directions. On the other hand, if the concentration of the attractant decreases, then the cell tumbles and then sets off in a new direction to try its luck again. This leads to a biased random walk (still random in the sense that the new direction after a period of tumbling is always arbitrary), but with a larger step size in the direction of increasing nutrients. In the completely random walk, the center of the distribution always stays at the starting point, but in the biased case there is a net motion of the whole distribution in the favorable direction.



**Figure 17.12 Projection of a three-dimensional displacement step along one axis.** A step in a random direction is shown as a purple vector. The projection of the step on the vertical axis is shown in red. All vectors that have their tips on the circle have the same projection on the vertical axis. To calculate the mean square value of the projection, we need to average over all these vectors, and over all values of  $\alpha$ , the angle made by the vector with the vertical axis (see Box 17.3).

**Figure 17.13 Fick's first law.** A cross-section of a three-dimensional volume is shown, with the variation in the concentration of solute molecules indicated. As in Figure 17.14, the dotted line denotes an imaginary plane, and the magnitude of the flux across this plane is proportional to the width of the plane. According to Fick's first law, the flux is proportional to the concentration gradient. The gradient is shallower in (a) than in (b), so the flux is correspondingly smaller.



**Figure 17.13 Unbiased and biased random walks.** (A) Trajectory of an actual *E. coli* bacterium, observed over 30 seconds in a microscope. The diagram shows three orthogonal projections of the three-dimensional movement of the bacterium. There are no attractant or repellent molecules in the solution, and the random walk is unbiased. (B) Shown at the top is a schematic representation of an unbiased random walk, such as the trajectory depicted in (A), in which no particular direction is preferred. The diagram at the bottom shows what happens if there is a concentration gradient of attractant molecules (red). The steps that move the bacterium up the gradient are longer than steps in other directions, leading to a random walk that is biased towards the source of the attractant. (A, adapted from H.C. Berg and D.A. Brown, *Nature* 239: 500–504, 1972. With permission from Macmillan Publishers Ltd; B, adapted from B. Alberts et al., *Molecular Biology of the Cell*, 5th ed. New York: Garland Science, 2008.)

One can ask why the bacterial cells tumble at all if there is a nutrient gradient. Why don't they simply move directly towards the attractant? As discussed in following sections, molecules and cells are constantly buffeted by random collisions with their surroundings, and this means that the cells cannot maintain a straight line for very long and will invariably be diverted from the correct direction. They must, as a consequence, reset their direction of travel over and over again just to be sure that they are moving in the best direction. Imagine a small rowboat in strong winds and high waves—even a rorer who could maintain a perfect line on calm water would have to turn to look for a landmark and correct the course of the boat to have a chance of reaching the target in rough conditions.

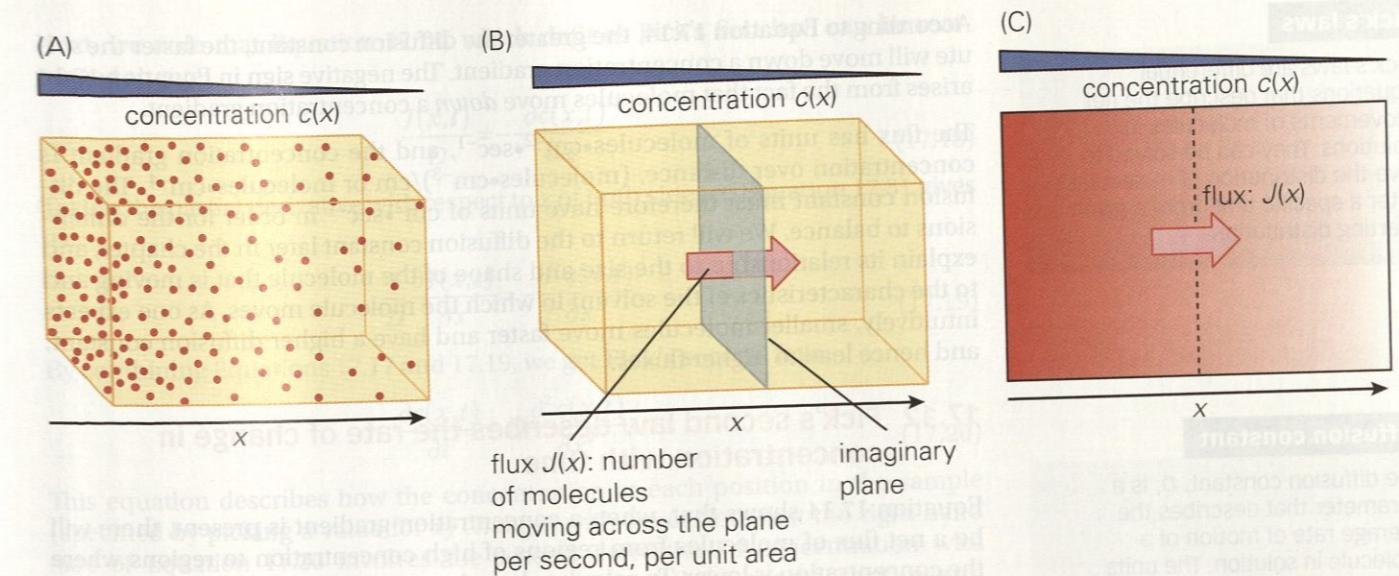
## B. MACROSCOPIC DESCRIPTION OF DIFFUSION

In the first part of this chapter we described the diffusive movement of bacteria with a focus on individual random trajectories, from which we built up a description of the aggregate behavior of many trajectories. In this part of the chapter we shall approach diffusion from a macroscopic perspective, instead, in which we do not consider individual trajectories at all.

### 17.11 Fick's first law states that the flux of molecules is proportional to the concentration gradient

A molecule in a solution is buffeted constantly by other molecules and therefore undergoes random motion. Instead of following the trajectories of individual molecules, we shall use differential equations, called **Fick's laws**, to describe changes in concentration due to molecular motion. These differential equations were developed by Adolf Fick, in the middle of the nineteenth century. If different parts of the solution have different concentrations of the solute, then the net movement of the solute molecules will be towards equalizing concentration throughout space. We first consider a case in which the concentration gradient is along one axis only, taken as the *x* direction. The concentration profile along *x* is defined by the function *c(x)*.

Imagine that the concentration decreases from left to right, as shown in Figure 17.14. The system is clearly not at equilibrium, and there will be a net movement of molecules from left to right, along the *x* axis. The extent of movement is



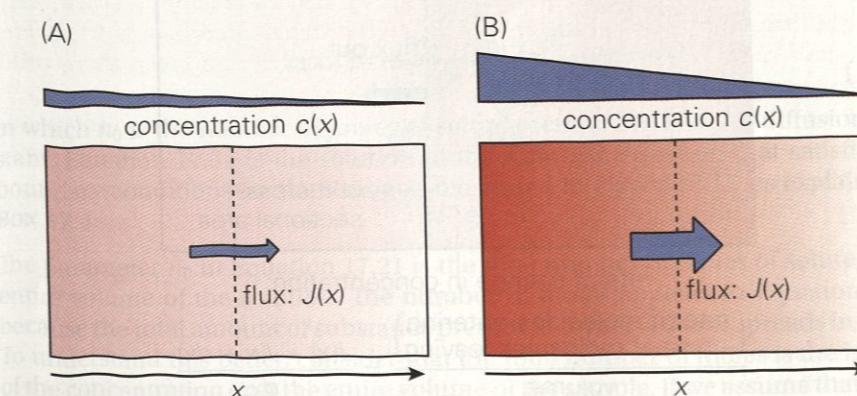
characterized by the **molecular flux** along *x*, which is denoted *J(x)*. Consider an imaginary plane that is perpendicular to the *x* axis at position *x*, as shown in Figure 17.14B. The concentration of the solute is higher on the left side of the plane than the other, due to the gradient. The flux at position *x* is the net number of molecules crossing a unit area of the plane per unit time.

As molecules move randomly in the solution, there will be some that cross the imaginary plane. If the concentration is equal on each side of the plane, then the average number of solute molecules that cross from left to right will be equal to the number going from right to left, and there will be no net flux across the plane. When the concentration on one side is higher, however, more molecules will cross the plane from that side. There will be a net flux of molecules across the plane, and the difference in concentration will decrease with time.

**Fick's first law** simply states that the flux, *J(x)*, at position *x* is proportional to the concentration gradient at *x* (Figure 17.15). Fick's first law is stated mathematically as follows:

$$J(x) = -D \left[ \frac{\partial c(x)}{\partial x} \right]_{y,z} \quad (17.14)$$

The derivative  $\left( \frac{\partial c}{\partial x} \right)_{y,z}$  is the difference in concentration across the virtual plane at position *x* (that is, the concentration gradient along the *x* direction). The proportionality constant, *D*, is called the **diffusion constant**, and its value depends on the properties of the solute and the nature of its interactions with the solvent.



**Figure 17.14 Concentration gradient and flux of molecules in solution.** (A) A section of a three-dimensional volume of a solution with the solute in red. The concentration of the solute decreases from left to right, which is defined as the *x* axis. (B) Schematic representation of the flux of solute molecules across an imaginary plane that is perpendicular to the *x* axis. Because the concentration is higher on the left side of the plane, there is a net flux of molecules from left to right. (C) A one-dimensional projection of the concentration gradient. The imaginary plane is indicated by a dashed line.

### Molecular flux, *J(x)*

The flux of molecules in a direction *x* is the rate at which molecules cross a unit area of an imaginary plane perpendicular to the *x* axis.

**Figure 17.15 Fick's first law.** A cross section of a three-dimensional volume is shown, with the variation in the concentration of solute molecules indicated, as in Figure 17.14C. The dotted line denotes an imaginary plane, and the magnitude of the flux across this plane is shown by the width of the arrow. According to Fick's first law, the flux is proportional to the concentration gradient. The gradient is shallower in (A) than in (B), and the flux is correspondingly smaller.