should be consulted while reading Chapter 1 and Appendix B while reading Chapter 2. A detailed understanding of differential equations or the methods used for their solution is not required for an appreciation of the main theme of this book.

Chapter 1

Diffusion: Microscopic Theory

Diffusion is the random migration of molecules or small particles arising from motion due to thermal energy. A particle at absolute temperature T has, on the average, a kinetic energy associated with movement along each axis of $kT/2$, where k is Boltzmann's constant. Einstein showed in 1905 that this is true regardless of the size of the particle, even for particles large enough to be seen under a microscope, i.e., particles that exhibit Brownian movement. A particle of mass m and velocity v_x on the x axis has a kinetic energy $mv_x^2/2$. This quantity fluctuates, but on the average $\langle mv_x^2/2\rangle = kT/2$, where $\langle\ \rangle$ denotes an average over time or over an ensemble of similar particles. From this relationship we compute the mean-square velocity,

$$\langle v_x^2\rangle = kT/m, \qquad (1.1)$$

and the root-mean-square velocity,

$$\langle v_x^2\rangle^{1/2} = (kT/m)^{1/2}. \qquad (1.2)$$

We can use Eq.1.2 to estimate the instantaneous velocity of a small particle, for example, a molecule of the protein lysozyme. Lysozyme has a molecular weight 1.4×10^4 g. This is the mass of one mole, or 6.0×10^{23} molecules; the mass of one molecule is $m = 2.3 \times 10^{-20}$ g. The value of kT at 300°K (27°C) is 4.14×10^{-14} g cm²/sec². Therefore, $\langle v_x^2\rangle^{1/2} = 1.3 \times 10^3$ cm/sec. This is a sizeable speed. If there were no obstructions, the molecule would cross a typical classroom in about 1 second. Since the protein is not in a vacuum but is immersed in an aqueous medium, it does not go very far before it bumps into molecules of

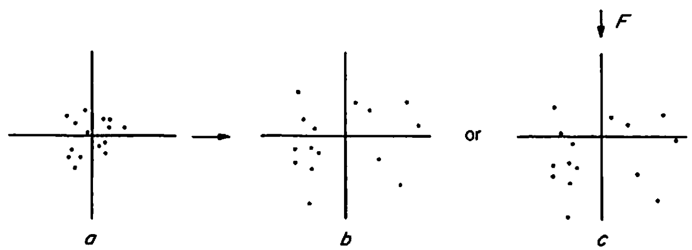

Fig. 1.1. Particles confined initially in a small region of space (a) diffuse symmetrically outward (b) or outward and downward (c) if subjected to an externally applied force, F.

water. As a result, it is forced to wander around: to execute a random walk. If a number of such particles were confined initially in a small region of space, as shown in Fig. 1.1a, they would wander about in all directions and spread out, as shown in Fig. 1.1b. This is simple diffusion. If a force were applied externally, such as that due to gravity, the particles would spread out and move downward, as shown in Fig. 1.1c. This is diffusion with drift. In this chapter, we analyze simple diffusion from a microscopic point of view. We look at the subject more broadly in Chapters 2 and 3. Diffusion with drift is considered in Chapter 4.

One-dimensional random walk

In order to characterize diffusive spreading, it is convenient to reduce the problem to its barest essentials, and to consider the motion of particles along one axis only, say the x axis, as shown in Fig. 1.2. The particles start at time $t = 0$ at position $x = 0$ and execute a random walk according to the following rules:

1) Each particle steps to the right or to the left once every τ seconds, moving at velocity $\pm v_x$ a distance

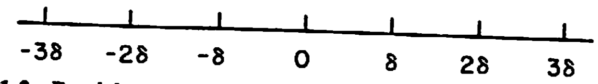

Fig. 1.2. Particles executing a one-dimensional random walk start at the origin, 0, and move in steps of length δ, occupying positions 0, $\pm\delta$, $\pm 2\delta$, $\pm 3\delta$, ...

$\delta = \pm v_x \tau$. For simplicity, we treat τ and δ as constants. In practice, they will depend on the size of the particle, the structure of the liquid, and the absolute temperature T.

2) The probability of going to the right at each step is 1/2, and the probability of going to the left at each step is 1/2. The particles, by interacting with the molecules of water, forget what they did on the previous leg of their journey. Successive steps are statistically independent. The walk is not biased.

3) Each particle moves independently of all the other particles. The particles do not interact with one another. In practice, this will be true provided that the suspension of particles is reasonably dilute.

These rules have two striking consequences. The first is that the particles go nowhere on the average. The second is that their root-mean-square displacement is proportional not to the time, but to the square-root of the time. It is possible to establish these propositions by using an iterative procedure. Consider an ensemble of N particles. Let $x_i(n)$ be the position of the ith particle after the nth step. According to rule 1, the position of a particle after the nth step differs from its position after the $(n-1)$th step by $\pm\delta$:

$$x_i(n) = x_i(n-1) \pm \delta. \tag{1.3}$$

According to rules 2 and 3, the $+$ sign will apply to roughly half of the particles, the $-$ sign to the other half. The mean displacement of the particles after the nth step can be found by summing over the particle index i and dividing by N:

$$\langle x(n) \rangle = \frac{1}{N} \sum_{i=1}^{N} x_i(n). \tag{1.4}$$

On expressing $x_i(n)$ in terms of $x_i(n-1)$, Eq. 1.3, we find

$$\langle x(n) \rangle = \frac{1}{N} \sum_{i=1}^{N} [x_i(n-1) \pm \delta]$$

$$= \frac{1}{N} \sum_{i=1}^{N} x_i(n-1) = \langle x(n-1) \rangle. \tag{1.5}$$

The second term in the brackets averages to zero, because its sign is positive for roughly half of the particles, negative for the other half. Eq. 1.5 tells us that the mean position of the particles does not change from step to step. Since the particles all start at the origin, where the mean position is zero, the mean position remains zero. This is the first proposition. The spreading of the particles is symmetrical about the origin, as shown in Fig. 1.3.

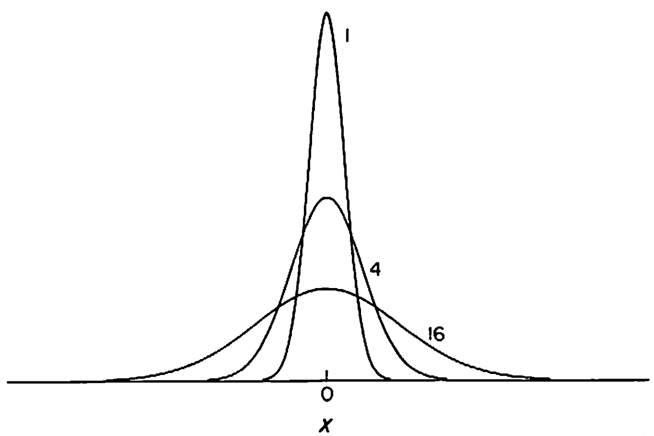

Fig. 1.3. The probability of finding particles at different points x at times $t = 1, 4$, and 16. The particles start out at position $x = 0$ at time $t = 0$. The standard deviations (root-mean-square widths) of the distributions increase with the square-root of the time. Their peak heights decrease with the square-root of the time. See Eq. 1.22.

How much do the particles spread? A convenient measure of spreading is the root-mean-square displacement $\langle x^2(n) \rangle^{1/2}$. Here we average the square of the displacement rather than the displacement itself. Since the square of a negative number is positive, the result must be finite; it cannot be zero. To find $\langle x^2(n) \rangle$, we write $x_i(n)$ in terms of $x_i(n-1)$, as in Eq. 1.3, and take the square:

$$x_i^2(n) = x_i^2(n-1) \pm 2\delta x_i(n-1) + \delta^2. \tag{1.6}$$

Then we compute the mean,

$$\langle x^2(n) \rangle = \frac{1}{N} \sum_{i=1}^{N} x_i^2(n), \tag{1.7}$$

which is

$$\langle x^2(n) \rangle = \frac{1}{N} \sum_{i=1}^{N} [x_i^2(n-1) \pm 2\delta x_i(n-1) + \delta^2]$$

$$= \langle x^2(n-1) \rangle + \delta^2. \tag{1.8}$$

As before, the second term in the brackets averages to zero; its sign is positive for roughly half of the particles, negative for the other half. Since $x_i(0) = 0$ for all particles i, $\langle x^2(0) \rangle = 0$. Thus, $\langle x^2(1) \rangle = \delta^2$, $\langle x^2(2) \rangle = 2\delta^2, \ldots,$ and $\langle x^2(n) \rangle = n\delta^2$. We conclude that the mean-square displacement increases with the step number n, the root-mean-square displacement with the square-root of n. According to rule 1, the particles execute n steps in a time $t = n\tau$; n is proportional to t. It follows that the mean-square displacement is proportional to t, the root-mean-square displacement to the square-root of t. This is the second proposition. The spreading increases as the square-root of the time, as shown in Fig. 1.3.

To see this more explicity, note that $n = t/\tau$, so that

$$\langle x^2(t) \rangle = (t/\tau)\delta^2 = (\delta^2/\tau)t, \tag{1.9}$$

where we write $x(t)$ rather than $x(n)$ to denote the fact that x now is being considered as a function of t. For convenience, we define a diffusion coefficient, $D = \delta^2/2\tau$, in units cm²/sec. The reason for the factor 1/2 will become clear in Chapter 2. This gives us

$$\langle x^2 \rangle = 2Dt \tag{1.10}$$

and

$$\langle x^2 \rangle^{1/2} = (2Dt)^{1/2}, \tag{1.11}$$

where, for simplicity, we drop the explicit functional reference (t). The diffusion coefficient, D, characterizes the migration of particles of a given kind in a given medium at a given temperature. In general, it depends on the size of the particle, the structure of the medium, and the absolute temperature. For a small molecule in water at room temperature, $D \simeq 10^{-5}$ cm²/sec.

A particle with a diffusion coefficient of this order of magnitude diffuses a distance $x = 10^{-4}$ cm (the width of a bacterium) in a time $t \simeq x^2/2D = 5 \times 10^{-4}$ sec, or about half a millisecond. It diffuses a distance $x = 1$ cm (the width of a test tube) in a time $t \simeq x^2/2D = 5 \times 10^4$ sec, or about 14 hours. The difference is dramatic. In order for a particle to wander twice as far, it takes 4 times as long. In order for it to wander 10 times as far, it takes 100 times as long. Therefore, there is no such thing as a diffusion velocity; displacement is not proportional to time but rather to the square-root of the time. What happens if we try to define a diffusion velocity by dividing the root-mean-square displacement by the time? The result is an explicit function of the time. Dividing both sides of Eq. 1.11 by t, we find

$$\frac{\langle x^2 \rangle^{1/2}}{t} = \left(\frac{2D}{t}\right)^{1/2}. \tag{1.12}$$

Thus, the shorter the period of observation, t, the larger the apparent velocity. For values of t smaller than τ, the apparent velocity is larger than $\delta/\tau = v_x$, the instantaneous velocity of the particle. This is an absurd result.

In Chapter 2 we will speak of adsorption rates or diffusion currents. These expressions refer to the number of particles that are adsorbed at, or cross, a given boundary in unit time. They are bulk properties of an ensemble of particles, proportional to their number. They are not rates that tell us how long it takes a particle, by diffusion, to go from here to there. This time depends on the square of the distance, as defined by Eq. 1.10. When next you come across the expression "diffusion rate," think twice! This phrase is ambiguous, at best, and often used incorrectly.

Two- and three-dimensional random walks

Rules 1 to 3 apply in each dimension. In addition, we assert that motions in the x, y, and z directions are statistically independent. If $\langle x^2 \rangle = 2Dt$, then $\langle y^2 \rangle = 2Dt$ and $\langle z^2 \rangle = 2Dt$. In two dimensions, the square of the distance from the origin to the point (x,y) is $r^2 = x^2 + y^2$; therefore,

$$\langle r^2 \rangle = 4Dt. \tag{1.13}$$

In three dimensions, $r^2 = x^2 + y^2 + z^2$, and

$$\langle r^2 \rangle = 6Dt. \tag{1.14}$$

A computer simulation of a two-dimensional random walk is shown in Fig. 1.4. Steps in the x and y directions were made at the same times, so the particle always moved diagonally. The simulation makes graphic a remarkable feature of the random walk, discussed further in Chapter 3. Since explorations over short distances can be made in much shorter times than explorations over long

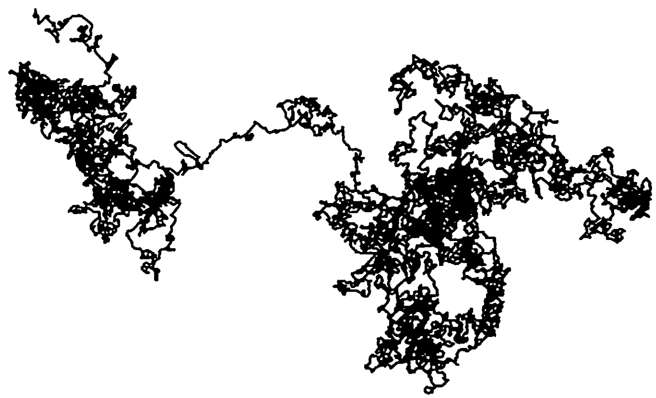

Fig. 1.4. An x, y plot of a two-dimensional random walk of n = 18,050 steps. The computer pen started at the upper left corner of the track and worked its way to the upper right edge of the track. It repeatedly traversed regions that are completely black. It moved, as the crow flies, 196 step lengths. The expected root-mean-square displacement is $(2n)^{1/2}$ = 190 step lengths.

distances, the particle tends to explore a given region of space rather thoroughly. It tends to return to the same point many times before finally wandering away. When it does wander away, it chooses new regions to explore blindly. A particle moving at random has no tendency to move toward regions of space that it has not occupied before; it has absolutely no inkling of the past. Its track does not fill up the space uniformly.

The binomial distribution

We have learned so far that particles undergoing free diffusion have a zero mean displacement and a root-mean-square displacement that is proportional to the square-root of the time. What else can we say about the shape of the distribution of particles? To find out, we have to work out the probabilities that the particles step different distances to the right or to the left. While doing

so, it is convenient to generalize the one-dimensional random walk and suppose that a particle steps to the right with a probability p and to the left with a probability q. Since the probability of stepping one way or the other is 1, $q = 1 - p$. The probability that such a particle steps exactly k times to the right in n trials is given by the binomial distribution

$$P(k;n,p) = \frac{n!}{k!(n-k)!}\, p^k q^{n-k}. \tag{1.15}$$

This equation is derived in Appendix A; see Eqs. A.17, A.18. The displacement of the particle in n trials, $x(n)$, is equal to the number of steps to the right less the number of steps to the left times the step length, δ:

$$x(n) = [k - (n - k)]\delta = (2k - n)\delta. \tag{1.16}$$

Since we know the distribution of k, we know the distribution of x. The two distributions have the same shapes. The probability machine shown in Fig. A.3 converts one into the other.

The mean displacement of the particle is

$$\langle x(n)\rangle = (2\langle k\rangle - n)\delta, \tag{1.17}$$

where

$$\langle k\rangle = np; \tag{1.18}$$

see Eq. A.22. The mean-square displacement is

$$\begin{aligned}\langle x^2(n)\rangle &= \langle[(2k - n)\delta]^2\rangle \\ &= (4\langle k^2\rangle - 4\langle k\rangle n + n^2)\delta^2,\end{aligned} \tag{1.19}$$

where

$$\langle k^2\rangle = (np)^2 + npq; \tag{1.20}$$

see Eq. A.23. For the case $p = q = 1/2$, Eqs. 1.17 and 1.19 yield $\langle x(n)\rangle = 0$ and $\langle x^2(n)\rangle = n\delta^2$, as expected.

The Gaussian distribution

A small particle, such as lysozyme, steps an enormous number of times every second. Given the instantaneous velocity estimated from Eq. 1.2, $v_x = \delta/\tau \simeq 10^3$ cm/sec, and a diffusion coefficient, $D = \delta^2/2\tau \simeq 10^{-6}$ cm²/sec, we can compute the step length, δ, and the step rate, $1/\tau$. The step length is $2D/v_x \simeq (10^{-6}$ cm²/sec)/(10^3 cm/sec) = 10^{-9} cm, and the step rate is $v_x/\delta \simeq (10^3$ cm/sec)/(10^{-9} cm) = 10^{12} sec^{-1}. Of these $n = 10^{12}$ steps taken each second, $np = 0.5 \times 10^{12}$ are taken to the right. The standard deviation in this number is $(npq)^{1/2} = 0.5 \times 10^6$; see Eq. A.25. So, to a precision of about a part in a million, half of the steps taken each second are made to the right and half to the left. What happens to the distribution of x in this limit? As stated in Appendix A, when n and np are both very large, the binomial distribution, $P(k;n,p)$, is equivalent to

$$P(k)dk = \frac{1}{(2\pi\sigma^2)^{1/2}} e^{-(k-\mu)^2/2\sigma^2} dk, \qquad (1.21)$$

where $P(k)dk$ is the probability of finding a value of k between $k + dk$, $\mu = \langle k \rangle = np$, and $\sigma^2 = npq$; see Eq. A.27. This is the Gaussian or normal distribution. By substituting $x = (2k - n)\delta$, $dx = 2\delta dk$, $p = q = 1/2$, $t = n/\tau$, and $D = \delta^2/2\tau$, we obtain

$$P(x)dx = \frac{1}{(4\pi Dt)^{1/2}} e^{-x^2/4Dt} dx, \qquad (1.22)$$

where $P(x)dx$ is the probability of finding a particle between x and $x + dx$. This is the function plotted in Fig. 1.3. The variance of this distribution is $\sigma_x^2 = 2Dt$; its standard deviation is $\sigma_x = (2Dt)^{1/2}$.

The Gaussian or normal distribution is the distribution encountered most frequently in discussions of propagation of errors. It is tabulated, for example, in the *Handbook of Chemistry and Physics*, as the "normal curve of error"; see Fig. A.5. About 68% of the area of the curve is within one standard deviation of the origin. Thus, if the root-mean-square displacement of the particles is $(2Dt)^{1/2}$, the chances are 0.32 that a particle has wandered that far or farther. The chances are 0.045 that it has wandered twice as far or farther and 0.0026 that it has wandered three times as far or farther. These numbers are the areas under the curve for $|x| \geq \sigma_x$, $2\sigma_x$, and $3\sigma_x$, respectively.

Visualizing the Gaussian distribution: It is instructive to generate the distributions shown in Fig. 1.3 experimentally. This can be done by layering aqueous solutions of a dye, such as fluorescein or methylene blue, into water. For a first try, layer the dye at the center of a vertical column of water in a graduated cylinder. The dye promptly sinks to the bottom! It does so because it has a higher specific gravity than the surrounding medium. For a second try, match the specific gravity of the medium to the dye by adding sucrose to the water. Now the dye drifts about and becomes uniformly dispersed in a matter of minutes or hours. It does so because there is nothing to stabilize the system against convective flow. Any variation in temperature that increases the specific gravity of regions of the fluid that are higher in the column relative to those that are lower drives this flow. For a final try, layer the dye into a column of water containing more sucrose at the bottom than at the top, i.e., into a sucrose density gradient; a 0-to-2% w/v solution will do. Match the specific gravity of the solution of the dye to that at the midpoint of the gradient and layer it there. Now, patterns of the sort shown in Fig. 1.3 will evolve over a period of many days. The diffusion coefficients of fluorescein, methylene blue, and sucrose are all about

5×10^{-6} cm²/sec. A sucrose gradient $x = 10$ cm high will survive for a period of time of order $t = x^2/2D = 10^7$ sec, or about 4 months. The dye will generate a Gaussian distribution with a standard deviation $\sigma_x = 2.5$ cm in a time $t = \sigma_x^2/2D \simeq 6 \times 10^5$ sec, or in about 1 week. Try it!

It is evident from this experiment that diffusive transport takes a long time when distances are large. Here is another example: The diffusion coefficient of a small molecule in air is about 10^{-1} cm²/sec. If one relied on diffusion to carry molecules of perfume across a crowded room, delays of the order of 1 month would be required. Evidently, the makers of scent owe their livelihood to close encounters, wind, and/or convective flow.

Chapter 2

Diffusion: Macroscopic Theory

Fick's equations

Most discussions of diffusion start with Fick's equations, differential equations that describe the spatial and temporal variation of nonuniform distributions of particles. I find it more illuminating to derive these equations from the model of the random walk. Suppose we know the number of particles at each point along the x axis at time t, as shown in Fig. 2.1. How many particles will move across unit area in unit time from the point x to the point $x + \delta$? What is the net flux in the x direction, J_x? At time $t + \tau$, i.e., after the next step, half the particles at x will have stepped across the dashed line from left to right, and half the particles at $x + \delta$ will have stepped across the dashed line from right to left. The net number crossing to the right will be

$$-\frac{1}{2}[N(x+\delta) - N(x)].$$

To obtain the net flux, we divide by the area normal to the

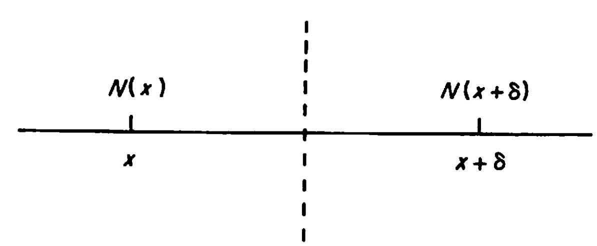

Fig. 2.1. At time t, there are $N(x)$ particles at position x, $N(x + \delta)$ particles at position $x + \delta$. At time $t + \tau$, half of each set will have stepped to the right and half to the left.