

Physics/Neuro 141

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Week 5

Abstract

The physics of chemosensation is connected to the physics that governs the particles being sensed and, in some cases, that of the organism doing the sensing. This handout on the physics of diffusion is an abridged version of Chapters 1 and 2 of *Random Walks in Biology* by Howard Berg

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 the movement along each axis of $kT/2$.

A particle of mass m and velocity v_x on the x axis has a kinetic energy mv_x^2 . This quantity fluctuates, but on the average $\langle mv_x^2/2 \rangle$.

We can thus 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 6×10^{23} molecules; the mass of one molecule is $m = 2.3 \times 10^{-20}$ g. The value of kT at 300 °K is 4×10^{-14} g cm²/sec². Therefore, $\langle v_x^2 \rangle^{1/2} = 1.3 \times 10^3$ cm/sec. This is *fast*. If the molecule faced no obstruction, it would move quickly across a room. Since the protein is immersed in water, it does not go far before it bumps into other molecules that slow it down and change its direction. The molecule is forced to undergo a random walk. The overall movement is called diffusion.

1.1 One-dimensional random walk

In order to characterize diffusive spreading, it is convenient to reduce the problem to its essentials, and consider the motion of particles along one axis only such as shown in Figure 1. The particles start at time $t = 0$ at position $x = 0$ and execute a random walk according to a set of rules.

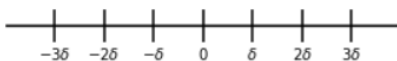


Figure 1. Particles executing a one-dimensional random walk start at the origin, 0, and move in steps of length δ , occupying positions $0, \pm\delta, \pm2\delta, \pm3\delta, \dots$

- Each particle steps to the right or to the left once every τ seconds, moving at velocity $\pm v_x$ a distance $\delta = \pm v_x \tau$. For simplicity, we treat τ and δ as constants. In practice, they will depend on the size of the particle, the liquid, and the absolute temperature T .
- 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 forget what they did on the previous leg of the journey. Successive steps are statistically independent. The walk is not biased.
- Each particle moves independently of all the other particles. The particles do not interact with one another. This will be true if 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 i th particle after the n th step. According to the first rule, the position of a particle after the n th step differs from its position after the $(n - 1)$ th step by $\pm\delta$:

$$x_i(n) = x_i(n - 1) \pm \delta \quad (1)$$

The $+$ sign will apply to roughly half of the particles. The $-$ sign will apply to the rest. The mean displacement of the particles after the n th step can be found by summing over the particle index i and dividing by N :

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

On expressing $x_i(n)$ in terms of $x_i(n - 1)$, we find:

$$\langle x(n) \rangle = \frac{1}{N} \sum_{i=1}^N [x_i(n - 1) \pm \delta] \quad (3)$$

$$= \frac{1}{N} \sum_{i=1}^N x_i(n - 1) \quad (4)$$

$$= \langle x(n - 1) \rangle \quad (5)$$

The second term in the brackets ($\pm\delta$) averages to zero, because its sign is positive for roughly half of the particles and negative for the other half. Because $\langle x(n) \rangle = \langle x(n - 1) \rangle$, the mean position does not change from step to step. If all the particles start at the origin, the mean position remains at the origin. The spreading of particles must be symmetric about the origin.

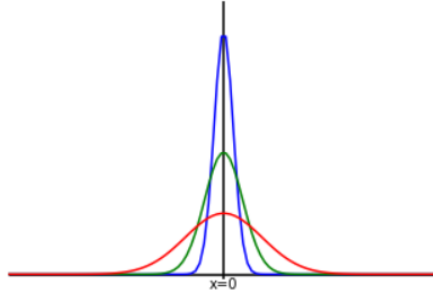


Figure 2. The probability of finding particles at different points x at times $t = 1, 4$, and 16 sec. The standard deviations increase with the square root of time.

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. To find $\langle x^2(n) \rangle$, we write $x_i(n)$ in terms of $x_i(n-1)$ and take the square:

$$x_i^2(n) = x_i^2(n-1) \pm 2\delta x_i(n-1) + \delta^2 \quad (6)$$

Then we compute the mean,

$$\langle x^2(n) \rangle = \frac{1}{N} \sum_{i=1}^N x_i^2(n) \quad (7)$$

which is

$$\langle x^2(n) \rangle = \frac{1}{N} \sum_{i=1}^N x_i^2(n) \quad (8)$$

which is

$$\langle x^2(n) \rangle = \frac{1}{N} \sum_{i=1}^N [x_i^2(n-1) \pm 2\delta x_i(n-1) + \delta^2] \quad (9)$$

$$= \langle x^2(n-1) \rangle + \delta^2 \quad (10)$$

As before, the second term in the brackets averages to zero. Since $x_i(0) = 0$ for all particles i , $\langle x^2(0) \rangle = 0$. Thus, $\langle x^2(1) \rangle = \delta^2$, $\langle x^2(2) \rangle = 2\delta^2$, $\langle x^2(3) \rangle = 3\delta^2$, ..., 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 . 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 is proportional to the square-root of t .

Note that $n = t/\tau$, so that:

$$\langle x^2(t) \rangle = (t/\tau)\delta^2 = (\delta^2/\tau)t \quad (11)$$

, where we write $x(t)$ rather than $x(n)$ to denote the fact that x is being considered as a function of t . For convenience, we define a diffusion coefficient, $D = \delta^2/2\tau$, in units cm^2/sec . This gives us

$$\langle x^2 \rangle = 2Dt \quad (12)$$

and

$$\langle x^2 \rangle^{1/2} = (2Dt)^{1/2} \quad (13)$$

The diffusion coefficient, D , characterizes the migration of particles of a given kind in a given medium at a given temperature.

For a small molecule in water at room temperature, $D = 10^{-5} \text{cm}^2/\text{sec}$. A particle with a diffusion coefficient of this order will diffuse a distance $x = 10^{-4} \text{cm}$ in a time $t \approx x^2/2D = 5 \times 10^{-4} \text{sec}$. It diffuses a distance $x = 1 \text{cm}$ in a time $t \approx 5 \times 10^4 \text{sec}$ or 14 hours.

1.2 Two- and three-dimensional random walk

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

$$\langle r^2 \rangle = 4Dt \quad (14)$$

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

$$\langle r^2 \rangle = 6Dt \quad (15)$$

1.3 The binomial distribution

We have learned that particles undergoing free diffusion have a zero mean displacement and a root-mean-square displacement that is proportional to the square root of time. What 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. 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 . The probability that such a particle steps exactly k times to the right in n trials is given by the binomial distribution

$$P(k; n, p) = \frac{n!}{k!(n-k)!} p^k q^{n-k} \quad (16)$$

The displacement of the particles in n trials, $x(n)$, is equal to the number of steps to the right minus the number of steps to the left times the step length, δ :

$$x(n) = [k - (n - k)] \delta = (2k - n) \delta \quad (17)$$

Sine we know the distribution of k , we know the distribution of x . The two distributions have the same shape. The mean displacement of the particle is:

$$\langle x(n) \rangle = (2 \langle k \rangle - n) \delta \quad (18)$$

where

$$\langle k \rangle = np. \quad (19)$$

The mean-square displacement is

$$\langle x^2(n) \rangle = \langle [2k - n] \delta \rangle^2 \quad (20)$$

$$= (4 \langle k^2 \rangle - 4 \langle k \rangle n + n^2) \delta^2 \quad (21)$$

where

$$\langle k^2 \rangle = (np)^2 + npq \quad (22)$$

For the case $p = q = 1/2$, $\langle x(n) \rangle = 0$ and $\langle x^2(n) \rangle = n\delta^2$ as expected.

1.4 The Gaussian Distribution

When n and np are both very large, the binomial distribution, $P(k; n, p)$ is equivalent to:

$$P(k)dk = \frac{1}{(2\pi\sigma^2)^{1/2}} e^{-(k-\mu)^2/2\sigma^2} dk \quad (23)$$

where $P(k)dk$ is the probability of finding a value of k between k and $k + dk$, $\mu = \langle k \rangle = np$, and $\sigma^2 = npq$. 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 $D = \delta^2/2\tau$,

$$P(x)dx = \frac{1}{(4\pi Dt)^{1/2}} e^{-x^2/4Dt} dx \quad (24)$$

where $P(x)dx$ is the probability of finding a particle between x and $x + dx$. The variance of this distribution is $\sigma_x^2 = 2Dt$. Its standard deviation is $\sigma_x = (2Dt)^{1/2}$.

2 Diffusion: Macroscopic Theory

2.1 Fick's Laws

Suppose we know the number of particles at each point along the x axis at time t as shown in **Figure 3**. 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 $t + \tau$, 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.

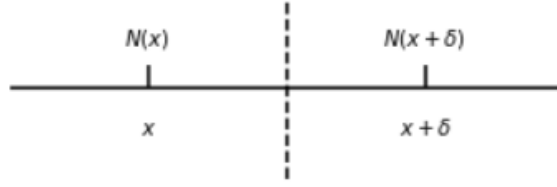


Figure 3. At time t there are $N(x)$ particles at position x , $N(x + \delta)$ particles at $x + \delta$. At time $t + \tau$, half of each set will have stepped to the right and half to the left.

The net number crossing to the right will be:

$$-\frac{1}{2} [N(x + \delta) - N(x)] \quad (25)$$

To obtain the net flux, we divide by the area normal to the x axis and by the time interval, τ ,

$$J_x = -\frac{1}{2} [N(x + \delta) - N(x)] / A\tau \quad (26)$$

Multiplying by δ^2/δ^2 and rearranging, we obtain:

$$J_x = -\frac{\delta^2}{2\tau} \frac{1}{\delta} \left[\frac{N(x + \delta)}{A\delta} - \frac{N(x)}{A\delta} \right] \quad (27)$$

The quantity $\delta^2/2\tau$ is the diffusion coefficient, D . $N(x + \delta)/A\delta$ is the number of particles per unit volume at the point $x + \delta$, i.e., the concentration $C(x + \delta)$. $N(x)/A\delta$ is the concentration $C(x)$. Therefore,

$$J_x = -D \frac{1}{\delta} [C(x + \delta) - C(x)] \quad (28)$$

But δ is very small. In the limit $\delta \rightarrow 0$,

$$J_x = -D \frac{\partial C}{\partial x} \quad (29)$$

This is Fick's first equation. It states that the net flux (at x and t) is proportional to the slope of the concentration function (at x and t). The constant of proportionality is D . If the particles are uniformly distributed, the slope is 0, i.e., $\partial C/\partial x = 0$ and $J_x = 0$. If the slope is constant, i.e., if $\partial C/\partial x$ is constant, J_x is constant. This occurs when C is a linear function of x .

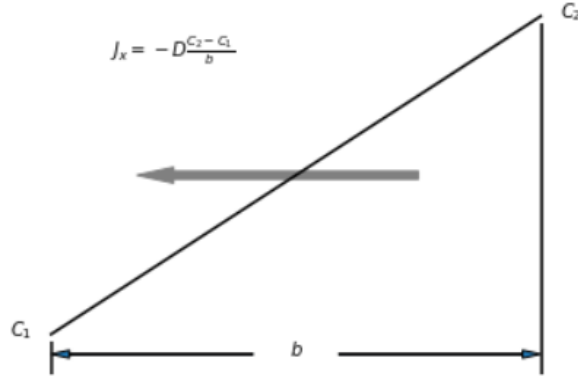


Figure 4. The flux due to a linear concentration gradient $(C_2 - C_1)/b$. There is net movement of particles from right to left solely because there are more particles at the right than at the left.

Fick's second equation follows from the first, provided that the total number of particles is conserved, i.e., that the particles are neither created nor destroyed. Consider the box shown in **Figure 5**. In a period of time τ , $J_x(x)A\tau$ particles will enter from the left and $J_x(x + \delta)A\tau$ particles will leave from the right. The volume of the box is $A\delta$. If particles are neither created nor destroyed, the number of particles per unit volume in the box must increase at the rate

$$\frac{1}{\tau} [C(t + \tau) - C(t)] = -\frac{1}{\tau} [J_x(x + \delta) - J_x(x)] \frac{A\tau}{A\delta} \quad (30)$$

$$= -\frac{1}{\delta} [J_x(x + \delta) - J_x(x)] \quad (31)$$

In the limit $\tau \rightarrow 0$ and $\delta \rightarrow 0$, this means that

$$\frac{\partial C}{\partial t} = -\frac{\partial J_x}{\partial x} \quad (32)$$

or, when we combine Fick's First Law:

$$\frac{\partial C}{\partial t} = D \frac{\partial^2 C}{\partial x^2} \quad (33)$$

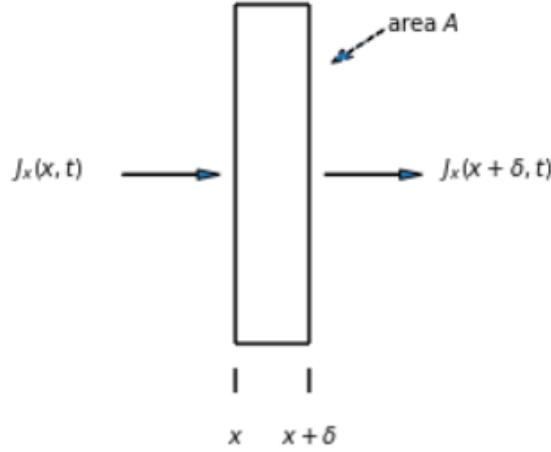


Figure 5. Fluxes through the faces of a thin box extending from position x to position $x + \delta$. The area of each face is A . The faces are normal to the x axis.

Fick's second equation states that the time rate of change in concentration (at x and t) is proportional to the curvature of the concentration function (at x and t); the constant of proportionality is D . The diffusion equation tells us how a nonuniform distribution of particles will redistribute itself over time. If we know the initial distribution and other boundary conditions, we can figure out all later distributions.

In three dimensions, we have $J_x = -D\partial C/\partial x$, $J_y = -D\partial C/\partial y$, and $J_z = -D\partial C/\partial z$. These are components of a flux vector:

$$\mathbf{J} = -D\nabla C \quad (34)$$

The concentration changes with time as

$$\frac{\partial C}{\partial t} = D\nabla^2 C \quad (35)$$

where ∇^2 is the three dimensional Laplacian.

If the problem is spherically symmetric, the flux is radial,

$$J_r = -D\partial C/\partial r \quad (36)$$

and

$$\frac{\partial C}{\partial t} = D \frac{1}{r^2} \frac{\partial}{\partial r} \left(r^2 \frac{\partial C}{\partial r} \right) \quad (37)$$

2.2 Diffusion to a spherical absorber

Consider a spherical adsorber of radius a in an infinite medium. Every particle reaching the surface of the sphere is gobbled up, so the concentration at $r = a$ is 0. The concentration at $r = \infty$ is C_0 . With these boundary conditions, the diffusion equation has the solution:

$$C(r) = C_0 \left(1 - \frac{a}{r} \right) \quad (38)$$

The flux is

$$J_r = -DC_0 \frac{a}{r^2} \quad (39)$$

The net migration of molecules is radially inward, as shown by the dashed arrows in **Figure 6**. The particles are adsorbed by the sphere at a rate equal to the area, $4\pi a^2$ times the inward flux $-J_r(a)$:

$$I = 4\pi DaC_0 \quad (40)$$

We will refer to this adsorption rate, I , as a diffusion current. Note that this current is proportional not to the area of the sphere, but its radius. As the radius increases, the area increases as a^2 but the concentration gradient decreases as $1/a$.

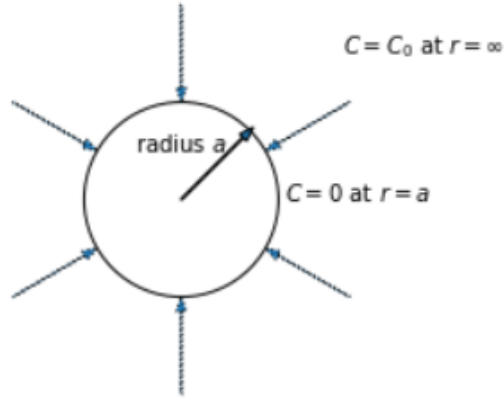


Figure 6. A spherical adsorber of radius a in an infinite medium containing particles at an initial concentration C_0 . The dashed arrows are lines of flux.

2.3 Probability of capture

Suppose a particle is released near a spherical adsorber of radius a at a point $r = b > a$? What is the probability that the particle will be adsorbed at $r = a$ rather than wander away for good?

Consider a spherical shell source of radius b between a spherical adsorber of radius a and a spherical shell adsorber of radius c as shown in **Figure 7**. The concentration rises from 0 at $r = a$ to a maximum value C_m at $r = b$ and then falls again to 0 at $r = c$. With these boundary conditions, the diffusion equation has the solution:

$$C(r) = \begin{cases} \frac{C_m}{1 - a/b} \left(1 - \frac{a}{r}\right) & \text{if } a \leq r \leq b, \\ \frac{C_m}{c/b - 1} \left(\frac{c}{r} - 1\right) & \text{if } b \leq r \leq c \end{cases} \quad (41)$$

The radial flux is

$$J_r(r) = \begin{cases} \frac{-DC_m}{1 - a/b} \frac{a}{r^2} & \text{if } a \leq r \leq b, \\ \frac{DC_m}{c/b - 1} \frac{c}{r^2} & \text{if } b \leq r \leq c \end{cases} \quad (42)$$

Thus, the diffusion current from the spherical shell source to the inner adsorber is

$$I_{in} = 4\pi DC_m \frac{a}{1 - a/b} \quad (43)$$

and the diffusion current from the spherical shell source to the outer adsorber is

$$I_{out} = 4\pi DC_m \frac{c}{c/b - 1} \quad (44)$$

The ratio

$$\frac{I_{in}}{I_{in} + I_{out}} = \frac{a(c - b)}{b(c - a)} \quad (45)$$

is the probability that a particle released at $r = b$ will be adsorbed at $r = a$. In the limit $c \rightarrow \infty$, this probability is just a/b . This is the probability of capture for the sphere of radius a immersed in an infinite medium. As b increases, this probability decreases as $1/b$.

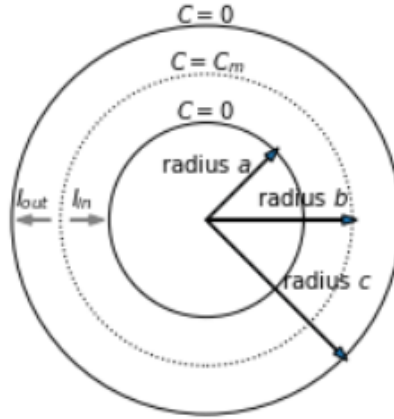


Figure 7. A spherical shell source, radius b , between a spherical adsorber of radius a and a spherical shell adsorber of radius c . Particles released at $r = b$ move inward and are adsorbed at $r = a$ at rate I_{in} or move outward and are adsorbed at $r = c$ at rate I_{out} . Their steady-state concentration rises from 0 at $r = a$ to C_m at $r = b$ and then falls again to 0 at $r = c$.