Chapter 2
The Diffusion Equation

We are now ready to study the time dependent solutions of the cable equation which are not separable. We assume you have read the derivation of the cable equation presented in Peterson (2015) so that you are comfortable with that material. Also, we have already studied how to solve the cable equation using the separation of variables technique. This method solved the cable equation with boundary conditions as a product $\hat{v}_m(\lambda, \tau) = u(\lambda)\, w(\tau)$. Then, in order to handle applied voltage pulses or current pulses, we had to look at an infinite series solution of the form $\sum_n A_n u_n(\lambda)\, w_n(\tau)$. Now, we will see how we can find a solution which is not time and space separable. This requires a fair bit of work: first, a careful discussion of how the random walk model in a limiting sense gives a probability distribution which serves as a solution to the classical diffusion model. This is done in this chapter. We follow the standard presentation of this material in for example Johnston and Wu (1995) and others.

The solution of the diffusion model is very important because we can use a clever *integral transform* technique to turn solve a general diffusion model. So in Chap. 3 we discuss the basics of the Laplace and Fourier Transform. Finally, in Chap. 4, we use a change of variables to transform a cable model into a diffusion equation. Then, we use integral transforms to solve the diffusion model. We will get the same solution we obtained using the random walk model which gives us a lot of insight into the structure of the solution.

Now these ideas are important because many second messenger systems are based on the diffusion of a signal across the cytoplasm of the excitable cell. So knowing how to work with diffusion based triggers is necessary.

2.1 The Microscopic Space–Time Evolution of a Particle

The simplest probabilistic model that links the Brownian motion of particles to the macroscopic laws of diffusion is the 1D random walk model. In this model, we assume a particle moves every τ_m seconds along the y axis a distance of either λ_c

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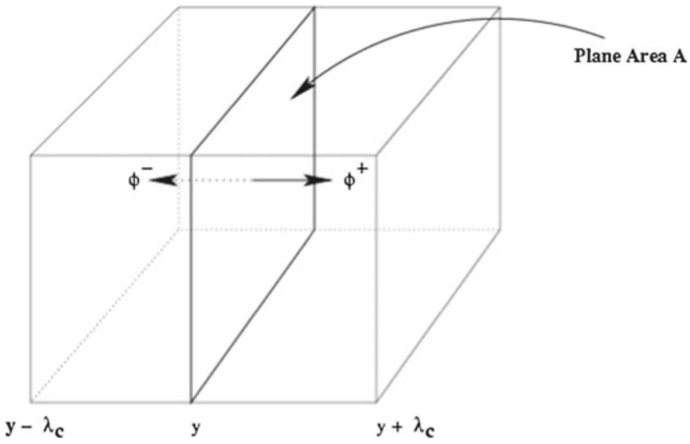


Fig. 2.1 Walking in a volume box

or $-\lambda_c$ with probability $\frac{1}{2}$. Consider the thought experiment shown in Fig. 2.1 where we see a volume element which has length $2\lambda_c$ and cross sectional area A. Since we want to do microscopic analysis of the space time evolution of the particles, we assume that $\lambda_c < y$.

Let $\phi^+(s, y)$ denote the flux density of particles crossing from left to right across the plane located at position y at time s; similarly, let $\phi^-(s, y)$ be the flux density of particles crossing from right to left. Further, $c(s, y)$ denote the concentration of particles at coordinates (s, y). What is the net number of particles that cross the plane of area A?

Since the particles randomly change their position every τ seconds by $\pm\lambda_c$, we can calculate flux as follows: first, recall that flux here is **the number of particles** per unit area and time; i.e., the units are $\frac{particles}{\text{sec}-\text{cm}^2}$. Since the walk is random, half of the particles will move to the right and half to the left. Since the distance moved is λ_c, half the concentration at $c(y - \frac{\lambda_c}{2}, s)$ will move to the right and half the concentration at $c(y + \frac{\lambda_c}{2}, s)$ will move to the left. Now the number of particles crossing the plane is concentration times the volume. Hence, the flux terms are

$$
\begin{aligned}
\phi^+(s, y) &= \frac{1}{2}\,\frac{A\lambda_c\, c\left(y - \frac{\lambda_c}{2}, s\right)}{A\tau_m} \\
&= \frac{\lambda_c}{2\tau_m}\, c\left(y - \frac{\lambda_c}{2}, s\right) \\
\phi^-(s, y) &= \frac{1}{2}\,\frac{A\lambda_c\, c\left(y + \frac{\lambda_c}{2}, s\right)}{A\tau_m} \\
&= \frac{\lambda_c}{2\tau_m}\, c\left(y + \frac{\lambda_c}{2}, s\right)
\end{aligned}
$$

The net flux, $\phi(s, y)$ is thus

$$\begin{aligned}\phi(s, y) &= \phi^+(s, y) - \phi^-(s, y) \\ &= \frac{\lambda_c}{2\tau_m}\left(c\left(s, y - \frac{\lambda_c}{2}\right) - c\left(s, y + \frac{\lambda_c}{2}\right)\right)\end{aligned}$$

Since, $\frac{\lambda_c}{y}$ is very small in microscopic analysis, we can approximate the concentration c using a first order Taylor series expansion in two variables if we assume that the concentration is sufficiently smooth. Our knowledge of the concentration functions we see in the laboratory and other physical situations implies that it is very reasonable to make such a smoothness assumption. Hence, for small perturbations $s + a$ and $y + b$ from the base point (s, y), we find

$$c(s + a, y + b) = c(s, y) + \frac{\partial c}{\partial s}(s, y)\, a + \frac{\partial c}{\partial y}(s, y)\, b + e(s, y, a, b)$$

where $e(s, y, a, b)$ is an error term which is proportional to the size of the largest of $|a|$ and $|b|$. Thus, e goes to zero as (a, b) goes to zero in a certain way. In particular, for $a = 0$ and $b = \pm\frac{\lambda_c}{2}$, we obtain

$$\begin{aligned}c\left(s, y - \frac{\lambda_c}{2}\right) &= c(s, y) - \frac{\partial c}{\partial y}(s, y)\, \frac{\lambda_c}{2} + e\left(s, y, 0, -\frac{\lambda_c}{2}\right) \\ c\left(s, y + \frac{\lambda_c}{2}\right) &= c(s, y) + \frac{\partial c}{\partial y}(s, y)\, \frac{\lambda_c}{2} + e\left(s, y, 0, \frac{\lambda_c}{2}\right)\end{aligned}$$

and we note that the error terms are proportional to λ_c^2. Thus,

$$\begin{aligned}\phi(s, y) &= -\frac{\lambda_c}{2\tau_m}\, \frac{\partial c}{\partial y}(s, y)\, \lambda_c + \left(e\left(s, y, 0, -\frac{\lambda_c}{2}\right) - e\left(s, y, 0, \frac{\lambda_c}{2}\right)\right) \\ &\approx -\frac{\lambda_c^2}{2\tau_m}\, \frac{\partial c}{\partial y}(s, y)\end{aligned}$$

as the difference in error terms is still proportional to λ_c^2 at worst and since λ_c is very small compared to y, the error term is negligible.

Recall from Peterson (2015) that Ficke's law of diffusion for particles across a membrane (think of our plane at y as the membrane) can be written as

$$J_{diff} = -D\, \frac{\partial\, [b]}{\partial x}$$

Equating c with $[b]$ and J_{diff} with ϕ, we see that the diffusion constant D in Ficke's Law of diffusion can be interpreted in this context as

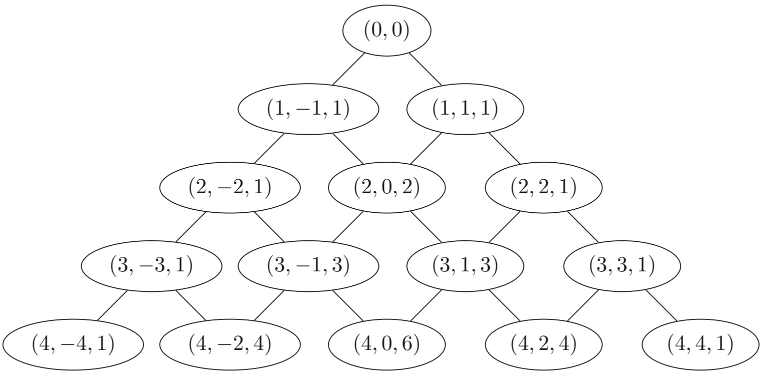
$$D = \frac{\lambda_c^2}{2\tau_m}$$

This will give us a powerful connection between the macroscopic diffusion coefficient of Ficke's Law with the microscopic quantities that define a random walk as we will see in the next section.

2.2 The Random Walk and the Binomial Distribution

In this section, we will be following the discussion presented in Weiss (1996), but paraphrasing and simplifying it for our purposes. More details can be gleaned from a careful study of that volume. Let's assume that a particle is executing a random walk starting at position $x = 0$ and time $t = 0$. This means that from that starting point, the particle can move either $+\lambda_c$ or $-\lambda_c$ at each tick of a clock with time measured in time constant units τ_m. We can draw this as a tree as shown in Fig. 2.2.

In this figure, the labels shown in each node refer to three things: the time, in units of the time constant τ_m (hence, $t = 3$ denotes a time of $3\tau_m$); spatial position in units of the space constant λ_c (thus, $x = -2$ means a position of $-2\lambda_c$ units); and the number of possible paths that read that node (therefore, Paths equal to 6 means there are six possible paths that can be taken to arrive at that terminal node.



A particle starts at $t = 0, x = 0$ and can move with a given probability left or right a distance λ_c in time increments of τ_m. The triple (a, b, c) indicates the time is $t = a\tau_m$, the x location is $x = b\lambda_c$ and the number of paths from the root of the tree to the node is $P = c$.

Fig. 2.2 The random walk of a particle

Since time and space are discretized into units of time and space constants, we have a physical system where time and space are measured as integers. Thus, we can ask what is the probability, $W(m, n)$, that the particle will be at position m at time n? In the time interval of n units, let's define some auxiliary variables: n^+ is the number of time steps where the particle moves to the right—i.e., the movement is $+1$; and n^- is the number of time steps the particle moves to the left, a movement of -1. We clearly see that M is really the net displacement and

$$n = n^+ + n^-, \quad m = n^+ - n^-$$

Solving, we see

$$n^+ = \frac{n+m}{2}, \quad n^- = \frac{n-m}{2}$$

Let the usual binomial coefficients be denoted by $B_{n,j}$ where

$$B_{n,j} = \binom{n}{j} = \frac{n!}{j!\,(n-j)!}$$

Now look closely at Fig. 2.2. If you look at a node, you can count how many right hand moves are made in any given path to that node. For example, the node for time 4 and space position 2 can be reached by 4 different paths and each of them contains $3 + \lambda_c$ moves. Note three $+\lambda_c$ moves corresponds to $n^+ = 3$ and the number 4 is the same as the binomial coefficient $B_{n=4,n^+=3} = 4$. Hence, at a given node, all of the paths that can be taken to that node have the same n^+ value as shown in Table 2.1. The triangle in Fig. 2.2 has the characteristic form of Pascal's triangle: the root node is followed by two nodes which split into three nodes and so on. The pattern is typically written in terms of levels. At level zero, there is just the root node. This is time 0 for us. At level one or time 1, there are two nodes written as $1 - 1$. At level two or time 2, there are three nodes written as $1 - 2 - 1$ to succinctly capture the branching we are seeing. Continuing, we see the node pattern can be written

Level or Time	Paths
0	1
1	1 - 1
2	1 - 2 - 1
3	1 - 3 - 3 - 1
4	1 - 6 - 4 - 6 - 1

Each of the nodes at a given time then will have some paths leading to it and on each of these paths, there will be the same number of right hand moves. So counting right hand moves, the paths denoted by $1 - 1$ correspond to $n^+ = 0$ for the left node and $n^+ = 1$ for the right node. The number of paths for these are the same as $B_{n=1,n^+=0} = 1$ and

Table 2.1 Comparing paths and rightward movements

Time	Paths	n^+	Binomial coefficient B_{n,n^+}
1	1 - 1	0 - 1	$B_{1,0}$ - $B_{1,1}$
2	1 - 2 - 1	0 - 1 - 2	$B_{2,0}$ - $B_{2,1}$ - $B_{2,2}$
3	1 - 3 - 3 - 1	0 - 1 - 2 - 3	$B_{3,0}$ - $B_{3,1}$ - $B_{3,2}$ - $B_{3,3}$
4	1 - 6 - 4 - 6 - 1	0 - 1 - 2 - 3 - 4	$B_{4,0}$ - $B_{4,1}$ - $B_{4,2}$ - $B_{4,3}$ - $B_{4,4}$

$B_{n=1,n^+=1} = 1$. The next level, $1 - 2 - 1$ corresponds to $n^+ = 0$ for the left node, $n^+ = 1$ for the middle one and $n^+ = 2$ for the right one. The number of paths for these nodes are then $B_{n=2,n^+=0} = 1$ and $B_{n=2,n^+=1} = 2$ and $B_{n=2,n^+=2} = 1$. We can do this for each level giving us the information shown in Table 2.1.

2.3 Rightward Movement Has Probability 0.5 or Less

Let the probability that the particle moves to the right be p and the probability it moves to the left be q. Then we have $p + q = 1$. Let's assume that $p \leq 0.5$. This forces $q \geq 0.5$. Then, in n time units, the probability a given path of length n is taken is $\rho(n)$ where

$$\rho(n) = p^{n^+} q^{n^-} = p^{n^+} q^{n-n^+}$$

and the probability that a path will terminate at position m, $W(m, n)$, is just the number of paths that reach that position in n time units multiplied by $\rho(n)$. We know that for a given number of time steps, certain position will never be reached. Note that if the fraction $0.5(n + m)$ is not an integer, then there will be no paths that reach that position m. Let n_f be the results of the computation $n_f = 0.5(n + m)$. We know n_f need not be an integer. Define the extended binomial coefficients C_{n,n_f} by

$$C_{n,n_f} = \begin{cases} B_{n,n_f} & \text{if } n_f \text{ is an integer} \\ 0 & \text{else} \end{cases}$$

Then, we see

$$W(m, n) = C_{n,n_f}\, p^{n_f}\, q^{n-n_f}$$

From our discussions above, it is clear for any position m that is reached in n time units, that this can be rewritten in terms of n^+ as

$$W(m, n) = B_{n,n^+(m)}\, p^{n^+(m)}\, q^{n-n^+(m)}$$

where $n^+(m)$ is the value of n^+ associated with paths terminating on position m. If you think about this a bit, you'll see that for even times n, only even positions m are reached; similarly, for odd times, only odd positions are reached.

2.3.1 Finding the Average of the Particles Distribution in Space and Time

The expectation $E(m)$ is defined by

$$E(m) = \sum_{m=-n}^{n} m W(m, n)$$

where of course, many of the individual terms $W(m, n)$ are actually zero for a given time n because the positions are never reached. From this, we can infer that

$$E(m) = \sum_{n^+=0}^{n} m \ B_{n,n^+} \ p^{n^+} \ q^{n-n^+}$$

To compute this, first, switch to a simple notation. Let $n^+ = j$. Then, since $n^+ = \frac{m+n}{2}$, $m = 2j - n$ and so

$$\begin{aligned}
E(m) &= \sum_{j=0}^{n} m \ B_{n,j} \ p^j \ q^{n-j} \\
&= \sum_{j=0}^{n} (2j - n) \ B_{n,j} \ p^j \ q^{n-j} \\
&= 2 \ E(j) \ n \ S
\end{aligned}$$

where

$$\begin{aligned}
E(j) &= \sum_{j=0}^{n} j \ B_{n,j} \ p^j \ q^{n-j} \\
S &= \sum_{j=0}^{n} B_{n,j} \ p^j \ q^{n-j}
\end{aligned}$$

Since $p + q = 1$, we know that

$$(p + q)^n = S = \sum_{j=0}^{n} B_{n,j} \ p^j \ q^{n-j} = 1$$

Further, by taking derivatives with respect to p, we see that

$$p\,\frac{d}{dp}\,\left((p+q)^n\right) = p\,n\,(p+q)^{n-1} = p\,n$$

Thus,

$$\begin{aligned}
E(j) &= \sum_{j=0}^{n} j\ B_{n,j}\ p^j\ q^{n-j} \\
&= \sum_{j=0}^{n} j\ p\ B_{n,j}\ p^{j-1}\ q^{n-j} \\
&= \sum_{j=0}^{n} p\ \frac{d}{dp}\left(B_{n,j}\ p^j\ q^{n-j}\right) \\
&= p\ \frac{d}{dp}\left(\sum_{j=0}^{n} B_{n,j}\ p^j\ q^{n-j}\right) \\
&= p\ \frac{d}{dp}\left((p+q)^n\right) \\
&= p\,n
\end{aligned}$$

by our calculations above. We conclude that

$$\begin{aligned}
E(m) &= 2\ E(j)\ nS \\
&= 2\ pn - n
\end{aligned}$$

2.3.2 Finding the Standard Deviation of the Particles Distribution in Space and Time

We compute the standard deviation of our particle's movement through space and time in a similar way. First, we find the second moment of m,

$$E(m^2) = \sum_{m=-n}^{n} m^2 W(m,n)$$

Our earlier discussions still apply and we find we can rewrite this as

$$\begin{aligned} E(m^2) &= \sum_{j=0}^{n} (2j - n)^2 \; B_{n,j} \; p^j \; q^{n-j} \\ &= \sum_{j=0}^{n} (4j^2 - 4jn + n^2) \; B_{n,j} \; p^j \; q^{n-j} \\ &= 4E(j^2) - 4\,n\;E(j) + n^2\;S \end{aligned}$$

where $E(j^2)$ is the second moment of the binomial distribution. We know S is 1 and $E(j)$ is pn. So we only have to compute $E(j^2)$. Note that

$$p^2 \, \frac{d^2}{d^2 p} \, \left((p+q)^n\right) = p^2 \, n\,(n-1)\,\left((p+q)^{n-2}\right) = p^2 \, n\,(n-1)$$

Also

$$\begin{aligned} p^2\,n\,(n-1) &= p^2 \, \frac{d^2}{d^2 p} \left((p+q)^n\right) \\ &= p^2 \, \frac{d^2}{d^2 p} \left(\sum_{j=0}^{n} B_{n,j} \; p^j \; q^{n-j} \right) \\ &= \sum_{j=0}^{n} \; p^2 \, \frac{d^2}{d^2 p} \; \left(B_{n,j} \; p^j \; q^{n-j}\right) \\ &= \sum_{j=0}^{n} \; p^2 \; j\;(j-1) \;\; B_{n,j} \; p^{j-2} \; q^{n-j} \\ &= \sum_{j=0}^{n} (j^2 - j) \; B_{n,j} \; p^j \; q^{n-j} \\ &= E(j^2) - E(j) \end{aligned}$$

We conclude that

$$E(j^2) = p^2 \, n\,(n-1) + p\,n$$

Since, we also have a formula for $E(m^2)$, we see

$$E(m^2) = 4E(j^2) - 4\,n\;E(j) + n^2$$

Now recall the standard formula from Statistics: the square of the standard deviation of our distribution is $\sigma^2 = E(m^2) - (E(m))^2$. Hence,

$$\begin{aligned}
\sigma^2 &= E(m^2) - (E(m))^2 \\
&= 4E(j^2) - 4\,n\,E(j) + n^2 - (2E(j) - n)^2 \\
&= 4(E(j^2) - (E(j))^2) \\
&= 4\Big(p^2\,n\,(n-1) + pn - (pn)^2\Big) \\
&= 4\,np(1-p) = 4\,npq.
\end{aligned}$$

Hence, the standard deviation is

$$\sigma = \sqrt{4pqn}.$$

2.3.3 *Specializing to an Equal Probability Left and Right Random Walk*

Here, p and q are both 0.5. We see that $4pq = 1$ and

$$\begin{aligned}
E(m) &= 2\,p\,n - n = 0 \\
\sigma &= \sqrt{n}
\end{aligned}$$

Note, that if the random walk is skewed, with say $p = 0.1$, then we would obtain

$$\begin{aligned}
E(m) &= 2\,p\,n - n = -0.8n \\
\sigma &= .6\sqrt{n}
\end{aligned}$$

so that for large n, the standard deviation of our particle's movement would be approximately $0.6n$ rather than n.

2.4 Macroscopic Scale

For a very large number of steps, the probability distribution, $W(m, n)$, will approach a limiting form. This is done by using an approximation to $k!$ that is know as the Stirling Approximation. It is known that for very large k,

$$k! \approx \sqrt{2\pi k}\,\left(\frac{k}{e}\right)^k.$$

The distribution of our particle's position throughout space and time can be written as

$$W(m,n) = B_{n,\frac{n+m}{2}}\ p^{\frac{n+m}{2}}\ q^{\frac{n-m}{2}}$$

using our definitions of n^+ and n^- (it is understood that $W(m,n)$ is zero for non integer values of these fractions). We can apply Stirling's approximation to $B_{n,\frac{n+m}{2}}$:

$$\begin{aligned}
n! &\approx \sqrt{2\pi n}\left(\frac{n}{e}\right)^n \\
\left(\frac{n+m}{2}\right)! &\approx \sqrt{2\pi\frac{n+m}{2}}\left(\frac{n+m}{2e}\right)^{\frac{n+m}{2}} \\
&\approx \sqrt{\pi(n+m)}\left(\frac{n}{2e}\right)^{\frac{n+m}{2}}\left(1+\frac{m}{n}\right)^{\frac{n+m}{2}} \\
\left(\frac{n-m}{2}\right)! &\approx \sqrt{2\pi\frac{n-m}{2}}\left(\frac{n-m}{2e}\right)^{\frac{n-m}{2}} \\
&\approx \sqrt{\pi(n-m)}\left(\frac{n}{2e}\right)^{\frac{n-m}{2}}\left(1-\frac{m}{n}\right)^{\frac{n-m}{2}}
\end{aligned}$$

From this, we find

$$\left(\frac{n+m}{2}\right)!\left(\frac{n-m}{2}\right)! \approx \pi\, n\sqrt{1-\frac{m^2}{n^2}}\left(\frac{n}{2e}\right)^n\left(1-\frac{m^2}{n^2}\right)^{\frac{n}{2}}\left(1-\frac{m}{n}\right)^{\frac{-m}{2}}\left(1+\frac{m}{n}\right)^{\frac{m}{2}}$$

Hence, we see

$$\begin{aligned}
B_{n,\frac{n+m}{2}} &\approx \frac{\sqrt{2\pi n}}{\pi n}\left(\left(\frac{n}{e}\right)^n\right)\left(\frac{n}{2e}\right)^{-n}\left(1-\frac{m^2}{n^2}\right)^{-\frac{1}{2}}\left(1-\frac{m^2}{n^2}\right)^{-\frac{n}{2}}\left(1-\frac{m}{n}\right)^{\frac{m}{2}}\left(1+\frac{m}{n}\right)^{-\frac{m}{2}} \\
&\approx \sqrt{\frac{2}{\pi n}}\,2^n\left(1-\frac{m^2}{n^2}\right)^{-\frac{1}{2}}\left(1-\frac{m^2}{n^2}\right)^{-\frac{n}{2}}\left(1-\frac{m}{n}\right)^{\frac{m}{2}}\left(1+\frac{m}{n}\right)^{-\frac{m}{2}}
\end{aligned}$$

Thus,

$$\begin{aligned}
\ln\left(B_{n,\frac{n+m}{2}}\right) \approx \frac{1}{2}\ln\left(\frac{2}{\pi n}\right) + n\ln(2) + -\frac{1}{2}\ln\left(1-\frac{m^2}{n^2}\right) + \frac{-n}{2}\ln\left(1-\frac{m^2}{n^2}\right) \\
+ \frac{m}{2}\ln\left(1-\frac{m}{n}\right) + \frac{-m}{2}\ln\left(1+\frac{m}{n}\right)
\end{aligned}$$

Now, for small x, the standard Taylor's series approximation gives $\ln(1+x) \approx x$; hence, for $\frac{m}{n}$ sufficiently small, we can say

$$\begin{aligned} \ln\left(B_{n,\frac{n+m}{2}}\right) &\approx \frac{1}{2}\ln\left(\frac{2}{\pi n}\right) + n\ln(2) + \frac{1}{2}\frac{m^2}{n^2} + \frac{n}{2}\frac{m^2}{n^2} - \frac{m}{2}\frac{m}{n} - \frac{m}{2}\frac{m}{n} \\ &\approx \frac{1}{2}\ln\left(\frac{2}{\pi n}\right) + n\ln(2) + \frac{1}{2}\frac{m^2}{n^2} - \frac{m^2}{2n} \end{aligned}$$

For very large n (i.e. after a very large number of time steps $n\tau_m$), since we assume $\frac{m}{m}$ is very small, the term $\frac{m^2}{n^2}$ is negligible. Hence dropping that term and exponentiating, we find

$$B_{n,\frac{n+m}{2}} \approx \sqrt{\frac{2}{n\pi}}\,\exp\left(\frac{-m^2}{2n}\right)\,2^n$$

This implies that

$$\begin{aligned} W(m,n) &\approx \sqrt{\frac{2}{n\pi}}\,\exp\left(\frac{-m^2}{2n}\right)\,2^n\,p^{\frac{n+m}{2}}\,q^{\frac{n-m}{2}} \\ &\approx \sqrt{\frac{2}{n\pi}}\,\exp\left(\frac{-m^2}{2n}\right)(4pq)^{\frac{n}{2}}\left(\frac{p}{q}\right)^{\frac{m}{2}} \end{aligned}$$

Note that if the particle moves with equal probability 0.5 to the right or the left at any time tick, this reduces to

$$W(m,n) \approx \sqrt{\frac{2}{n\pi}}\,e^{\frac{-m^2}{2n}}$$

and for $p = \frac{1}{3}$ and $q = \frac{2}{3}$, this becomes

$$W(m,n) \approx \sqrt{\frac{2}{n\pi}}\,\exp\left(\frac{-m^2}{2n}\right)\left(\frac{8}{9}\right)^{\frac{n}{2}}\left(\frac{1}{2}\right)^{\frac{m}{2}}$$

2.5 Obtaining the Probability Density Function

From our discrete approximations in previous sections, we can now derive the probability density function, $P(x,t)$ at position x at time t. In what follows, we will assume that $p \leq 0.5$. Let Δx be a small number which is approximately $m\lambda_c$ for some m. The probability that the particle is in an interval $[x - \frac{\Delta x}{2}, x + \frac{\Delta x}{2}]$ can then be approximated by

$$P(x,t)\,\Delta x \approx \sum_k W(k,n)$$

where the sum is over all indices k such that the position $k\lambda_c$ lies in the interval $[x - \frac{\Delta x}{2}, x + \frac{\Delta x}{2}]$. Hence,

$$\left[x - \frac{\Delta x}{2}, x + \frac{\Delta x}{2}\right] \equiv \{(m - j)\lambda_c, ..., m\lambda_c, ..., (m + j)\lambda_c\}$$

for some integer j. Now from the way the particle moves in a random walk, only half of these tick marks will actually be positions the particle can occupy. Hence, half of the probabilities $W(m - i, n)$ for i from $-j$ to j are zero. The number of nonzero probabilities is thus $\approx \frac{\Delta x}{2\lambda_c}$. We can therefore approximate the sum by taking the middle term $W(m, n)$ and multiplying by the number of nonzero probabilities.

$$P(x, t)\ \Delta x \approx W(m, n)\ \frac{\Delta x}{2\lambda_c}$$

which implies, since $x = m\lambda_c$ and $t = n\tau_m$, that for very large n,

$$\begin{aligned} P(x, t) &= \frac{1}{2\lambda_c}\ W(m, n) \\ &= \frac{1}{\sqrt{4\pi \frac{\lambda_c^2}{2\tau_m}\ t}}\ \exp\left(\frac{-x^2}{4\frac{\lambda_c^2}{2\tau_m}\ t}\right)\ (4pq)^{\frac{t}{2\tau_m}}\ \left(\frac{p}{q}\right)^{\frac{x}{2\lambda_c}} \end{aligned}$$

Note that the term $\frac{\lambda_c^2}{2\tau_m}$ is the diffusion constant D. Thus,

$$P(x, t) = \frac{1}{\sqrt{4\pi D\, t}}\ \exp\left(\frac{-x^2}{4D\, t}\right)\ (4pq)^{\frac{t}{2\tau_m}}\ \left(\frac{p}{q}\right)^{\frac{x}{2\lambda_c}}$$

Next, rewrite all the power terms as exponentials:

$$P(x, t) = \frac{1}{\sqrt{4\pi D\, t}}\ \exp\left(\frac{-x^2}{4D\, t}\right)\ \exp\left(\ln(4pq)\ \frac{t}{2\tau_m}\right)\ \exp\left(\ln\left(\frac{p}{q}\right)\ \frac{x}{2\lambda_c}\right)$$

2.5.1 *p Less Than 0.5*

Note since $p + q = 1$, $4pq$ is between bigger than zero and strictly less than 1 for all nonzero p and q with p not 0.5. So for us, if we let ξ be the value $\frac{1}{4pq}$, we know that $\ln(\xi) > 0$. Let $A = \ln(\xi)$. Next, let ζ be the value $\frac{q}{p}$. Since p is less than $1/2$ here, this means $\zeta > 1$. Let $B = \ln(\zeta)$. Then, we know A and B are both positive in this case unless the probability of movement left and right is equal. In the case of equal probability, $\xi = 1$, $\zeta = 1$ and $A = B = 0$. However, with unequal probability, we have

$$(4pq)^{\frac{t}{2\tau_m}} = (\xi)^{\frac{-t}{2\tau_m}} = \exp\left(\frac{-t\ln(\xi)}{2\tau_m}\right).$$

Also,

$$\left(\frac{p}{q}\right)^{\frac{x}{2\lambda_c}} = (\zeta)^{\frac{-x}{2\lambda_c}} = \exp\left(\frac{-x\ln(\zeta)}{2\lambda_c}\right)$$

Rewriting the density function, we obtain

$$P(x,t) = \frac{1}{\sqrt{4\pi D\,t}}\exp\left(\frac{-x^2}{4D\,t} - \ln(\xi)\,\frac{t}{2\tau_m} - \ln(\zeta)\,\frac{x}{2\lambda_c}\right)$$

We thus have

$$P(x,t) = \frac{1}{\sqrt{4\pi D\,t}}\exp\left(\frac{-x^2}{4D\,t} - A\,\frac{t}{2\tau_m} - B\,\frac{x}{2\lambda_c}\right)$$

After manipulation, we can complete the square on the quadratic term and rewrite it as

$$\frac{-x^2}{4D\,t} - A\,\frac{t}{2\tau_m} - B\,\frac{x}{2\lambda_c} = -\frac{1}{4Dt}\left(x + \frac{BD}{\lambda_c}\,t\right)^2 + \frac{B^2 - 4A}{8\tau_m}\,t$$

and thus

$$P(x,t) = \frac{1}{\sqrt{4\pi D\,t}}\exp\left(-\frac{1}{4Dt}\left(x + \frac{BD}{\lambda_c}\,t\right)^2\right)\exp\left(\frac{B^2 - 2A}{4\tau_m}\,t\right)$$

The case where p is larger than $1/2$ is handled in a symmetric manner. We simply reverse the role of p and q in the argument above.

2.5.2 *p and q Are Equal*

The equal probability random walk has $A = B = 0$ and so the probability density function reduces to

$$P(x,t) = \frac{1}{\sqrt{4\pi D\,t}}\exp\left(-\frac{x^2}{4Dt}\right)$$

2.6 Understanding the Probability Distribution of the Particle

It is important to get a strong intuitive feel for the probability distribution of the particle under the random walk and skewed random walk protocols. A normal distribution has the form

$$P(x) = \frac{1}{\sqrt{2\pi\sigma}}\, e^{-\frac{x^2}{2E(m^2)}}$$

Hence, comparing, we see the standard deviation of our particle can be interpreted as

$$\sigma = \lambda_C^2 \frac{t}{\tau_m}.$$

Note, in general, for fixed time, we can plot the particle's position. We show this in Fig. 2.3 for three different standard deviations, σ. In the plot, the standard deviation is labeled as D. Now if we skew the distribution so that the probability of moving to the right is now $\frac{1}{6}$, we find

$$P(x,t) = \frac{1}{\sqrt{4\pi D\, t}} \exp\left(-\frac{1}{4Dt}\left(x - \frac{1.61Dt}{\lambda_c}\right)^2\right) \exp\left(\frac{0.35t}{\tau_m}\right)$$

which generates the plot shown in Fig. 2.4.

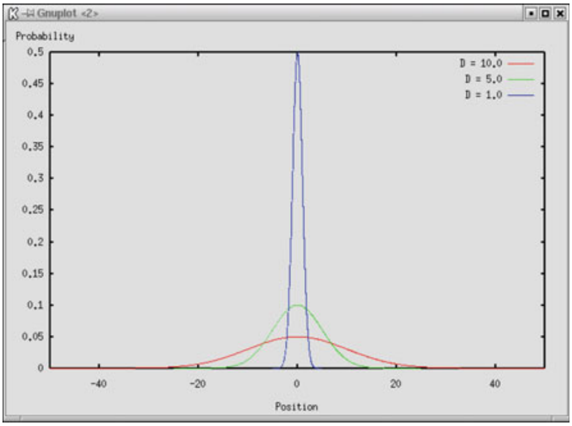


Fig. 2.3 Normal distribution: spread depends on standard deviation

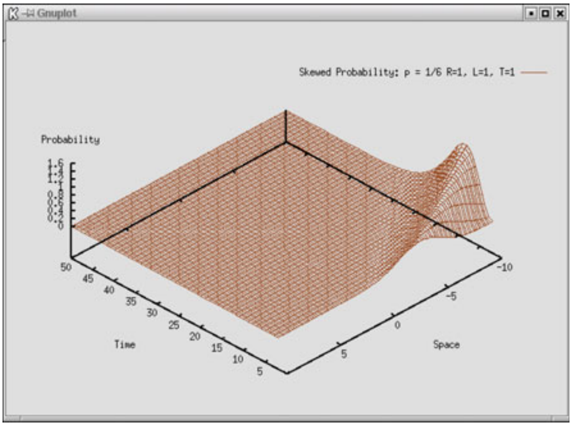


Fig. 2.4 Skewed random walk probability distribution: p is 0.1666

2.7 The General Diffusion Equation

We will now show that the probability density function $P(x, t)$ given by Eq. 2.1

$$P(x,t) = \frac{1}{\sqrt{4\pi D\, t}}\, e^{-\frac{x^2}{4Dt}} \tag{2.1}$$

solves the diffusion equation

$$\frac{\partial \Phi}{\partial t} = D \frac{\partial^2 \Phi}{\partial x^2}.$$

where D is the diffusion constant. A more general diffusion equation would not assume the diffusion constant D is independent of position x. The diffusion equation in that case would be

$$\frac{\partial u}{\partial t} = \frac{\partial}{\partial x}\left[D \frac{\partial u}{\partial x} \right]$$

However, often the term D is independent of the variable x allowing us to write the simpler form

$$\frac{\partial u}{\partial t} = D \frac{\partial^2 u}{\partial x^2}$$

in the time and space variables (t, x). In this model, we assume x is one dimensional, although it is easy enough to extend to higher dimensions. In 3 dimensions, u has units of mM per liter or cm^3, but in a one dimensional setting u has units of mM per cm. However, the diffusion coefficient D will always have units of length squared per time unit; i.e. $\frac{cm^2}{s}$. Note in our earlier discussions, we found $P(x, t)$ had to have units of particles per cm or simple cm^{-1}. We also assume the diffusion coefficient

D is positive. We can now show a typical solution for positive time is given by our $P(x, t)$ and let's do it by direct calculation. With a bit of manipulation, we find

$$\frac{\partial P}{\partial t} = \frac{1}{\sqrt{4\pi D}}\, t^{-3/2}\, e^{-x^2/(4Dt)} \left(-\frac{1}{2} + \frac{x^2}{4Dt} \right).$$

Next,

$$\begin{aligned}
\frac{\partial P}{\partial x} &= \frac{1}{\sqrt{4\pi D t}}\, e^{-x^2/(4Dt)} \left(-\frac{2x}{4Dt} \right) \\
\frac{\partial^2 P}{\partial x^2} &= \frac{1}{\sqrt{4\pi D t}} \left(e^{-x^2/(4Dt)} \left(-\frac{2}{4Dt} \right) \right. \\
&\qquad \left. + \left(-\frac{2x}{4Dt} \right) \left(-\frac{2x}{4Dt} \right) e^{-x^2/(4Dt)} \right) \\
&= \frac{1}{\sqrt{4\pi D t}} e^{-x^2/(4Dt)}\, \frac{2}{4Dt} \left(-1 + \frac{2x^2}{4Dt} \right) \\
&= \frac{1}{D}\, \frac{1}{\sqrt{4\pi D}} t^{-3/2} e^{-x^2/(4Dt)} \left(-\frac{1}{2} + \frac{x^2}{4Dt} \right) \\
&= \frac{1}{D}\, \frac{\partial P}{\partial t}.
\end{aligned}$$

Hence, we see P solves $\frac{\partial P}{\partial t} = D \frac{\partial^2 P}{\partial x^2}$. From our previous discussions, we see we can interpret the motion of our particle as that of a random walk for space constant λ_c and time constant τ_m as the number of time and position steps gets very large.

Note the behavior at $t = 0$ seems undefined. However, we can motivate the interpretation of the limiting behavior as $t \to 0$ as an impulse injection of current as follows. Note using the substitution, $y = \frac{1}{t}$, for x not zero,

$$\lim_{t \to 0} u(t, x) = \lim_{y \to \infty} \sqrt{y}\, \exp\left(\frac{-x^2 y}{4D} \right)$$

and so at $x = 0$, we find $u(t, 0) = \frac{1}{\sqrt{t}}$. This behaves qualitatively like an impulse. Thus, we interpret this solution as an impulse injection of essentially unbounded magnitude at $t = 0$. This corresponds to the usual delta function input $\delta(0)$. If the amount of current injected is $I\delta(0)$, the solution is

$$u(t, x) = \frac{I}{\sqrt{4\pi D t}} \exp\left(\frac{-x^2}{4Dt} \right).$$

Since for $x \neq 0$, $\lim_{x \to \infty} u(t, x) = 0$ and $\lim_{t \to 0} u(t, x) = 0$, we know $u(t, x)$ has a maximum value at some value of t. The generic shape of the solution can be seen in Fig. 2.5. The solution at $x = 0$ behaves like the curve $\frac{1}{\sqrt{t}}$ as is shown. The solutions for non zero values of x behave like spatially spread and damped pulses. In fact, the

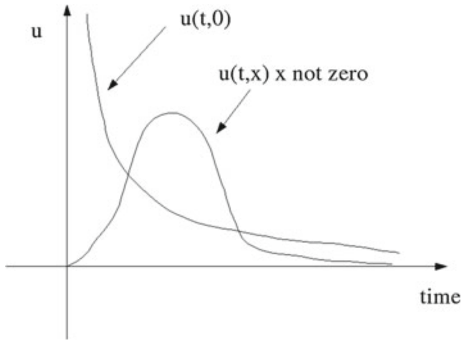


Fig. 2.5 The generic diffusion solution behavior

solution to the diffusion equation for nonzero x provides a nice model of the typical excitatory pulse we see in a dendritic tree. Also, if $I < 0$, this is a good model of an inhibitory pulse as well. Letting

$$I(t) = \frac{1}{\sqrt{4\pi Dt}} \exp\left(-\frac{x^2}{4Dt}\right)$$

we find for nonzero t, that

$$I'(t) = \frac{1}{\sqrt{4\pi D}}\, t^{\frac{-3}{2}} \exp\left(-\frac{x^2}{4Dt}\right) \left\{-\frac{1}{2} + \frac{x^2}{4Dt}\right\}$$

For $t \neq 0$, $f'(t) = 0$ implies $-\frac{1}{2} + \frac{x^2}{4Dt} = 0$. Thus, the maximum of the injection pulse occurs at $t = \frac{x^2}{2D}$. The maximum value of the current is then

$$\begin{aligned} I\left(\frac{x^2}{2D}\right) &= \frac{1}{\sqrt{4\pi D\,(x^2/(2D))}}\, e^{\left(-\frac{x^2}{4D}\frac{2D}{x^2}\right)} \\ &= \frac{1}{\sqrt{2\pi}\,|x|}\, e^{-\frac{1}{2}}. \end{aligned}$$

it follows that the current pulses become very sharply defined with large heights as x approaches 0 and for large x, the pulse has a low height and is spread out significantly. We show the qualitative nature of these pulses in Fig. 2.6. In both curves shown, the maximum is achieved at the time point $\frac{x^2}{2D}$. These general solutions can also be centered at the point (t_0, x_0) giving the solution

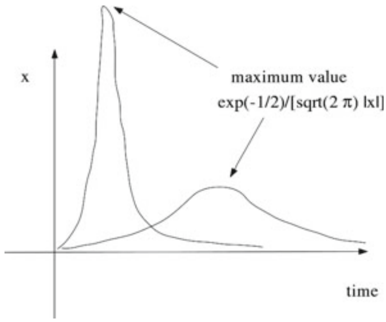


Fig. 2.6 The generic diffusion solution maximum

$$u(t, x) = \frac{I}{\sqrt{4\pi D(t - t_0)}} \exp\left(\frac{-(x - x_0)^2}{4D(t - t_0)}\right).$$

which is not defined at t_0 itself.

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