11. Diffusion in a Potential

In this section, we extend the concepts of diffusion and Brownian motion into a regime where the time-evolution is not entirely random. We will refer to this class of problems as diffusion in a potential, although it can also be expressed as diffusion with drift, diffusion in a velocity or force field, or diffusion in the presence of an external force. We will see that these problems can be related to a biased random walk or to motion of a Brownian particle subject to an internal or external potential. Our discussion below will be confined to problems involving diffusion in one dimension.

Diffusion with Drift

If there is an external force or potential acting on a diffusing system (for instance, electrophoresis and sedimentation), or if the diffusion occurs within a moving fluid, the time-dependent concentration profiles will be influenced by the local velocity of the fluid. For these problems, the total flux will have contributions from the diffusive flux and the flux that arises from the external force: $J = J_{\text{diff}} + J_{\text{ext}}$.

Diffusion with drift refers to diffusion in a fluid moving with a drift velocity v_x. This results in an additional flux term in Fick's first law proportional to v_x:

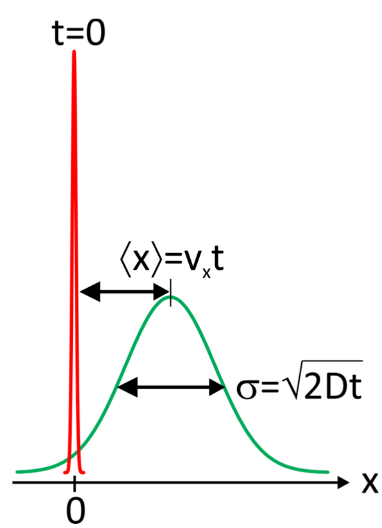
$$J = -D\frac{\partial C}{\partial x} + v_x C \tag{1}$$

Now using the continuity expression $\partial C/\partial t = -\partial J/\partial x$, and assuming a constant drift velocity

$$\frac{\partial C}{\partial t} = D\frac{\partial^2 C}{\partial x^2} - v_x\frac{\partial C}{\partial x} \tag{2}$$

This equation is the same as the normal diffusion equation in the inertial frame of reference. If we shift to a frame moving at v_x, we can define the relative displacement

$$\bar{x} = x - v_x t$$



Remember C is a function of x and t, and expressing eq. (2) in terms of $\bar{x}$ via the chain rule, we find that we can recast it as the simple diffusion equation:

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

Then the solution for diffusion from a point source becomes

$$C(\bar{x},t) = \frac{1}{\sqrt{4\pi Dt}} e^{-\bar{x}^2/4Dt}$$

$$C(x,t) = \frac{1}{\sqrt{4\pi Dt}} e^{-(x-v_x t)^2/4Dt}$$

So the peak of the distribution moves as $\langle x \rangle = v_x t$ and the width grows as $[\langle x^2 \rangle - \langle x \rangle^2]^{1/2} = \sigma = (2Dt)^{1/2}$.

Let's consider the relative magnitude of the diffusive and drift velocity contributions to the motion of a protein in water. A typical diffusion constant is 10^{-6} cm^2/s, meaning that the root mean square displacement in a one nanosecond time period is σ = 1.4 nm. If we compare this with the typical velocity of blood in capillaries, v = 0.3 mm/s, the same protein is pushed $\langle x \rangle$ = 0.3 pm. For this example, diffusive transport dominates, however, with the increase of time scale and transport distance, the drift term will grow in significance due to the $t^{1/2}$ scaling of diffusive transport.

Peclet Number

A unitless hydrodynamic parameter to characterize mass transport processes: Are you in the diffusive transport or advective transport (flow) regime? Language note:

- Convection: internal currents within fluid
- Advection: mass transport due to convection

We characterize this with a ratio of the rates or characteristic time scale for these processes:

$$P_e = \frac{\text{advective flux}\,(J_{\text{ext}})}{\text{diffusive flux}\,(J_{\text{diff}})} \sim \frac{\text{diffusion time}}{\text{advection time}}$$

Limits:

- $P_e > 1$ flow dominated
- $P_e < 1$ diffusion dominated

$$P_e = \frac{vd}{D}$$

v is the flow velocity, d is the characteristic transport length, and D is the diffusion constant. Using Stokes Law for a sphere, we can write this using the characteristic time scales:

$$t_{\text{diff}} = \frac{\langle x^2 \rangle}{D} = \frac{R^2 \zeta}{k_B T} = \frac{R^2 (6\pi\eta R)}{k_B T} \sim \frac{\eta R^3}{k_B T}$$

$$t_{\text{advective}} \sim \frac{R}{V}$$

$$P_e = \frac{R^2 \eta V}{k_B T}$$

For proteins in water $P_e \sim 10^{-6}$

For 1 μm polystyrene bead or bacterium $P_e \sim 50$

Biased Random Walk

The diffusion with drift equation can be obtained from a biased random walk problem. To illustrate, we extend the earlier model for a walker on a 1D lattice that can step left or right by an amount distance Δx for every time interval Δt. However, in this case there is unequal probability ($P_\pm$) of walking right (+) or left (–) during Δt. The change in position for a given time interval is

$$\begin{aligned} x(t+\Delta t) &= x(t) \pm \Delta x\, P_\pm \\ &= x(t) \pm \Delta x\, \Delta t\, k_\pm \end{aligned} \tag{3}$$

Here we have defined $k_\pm$ as the rate constant for stepping: $P_\pm = k_\pm \Delta t$ with $k_+ \neq k_-$. Since the walker must take a step, $P_+ + P_- = 1$ and

$$k_+ + k_- = \frac{1}{\Delta t} \tag{4}$$

How does the average position evolve? Performing an ensemble average over eq. (3)

$$\begin{aligned} \langle x(t+\Delta t)\rangle &= \langle x(t)\rangle + (k_+ - k_-)\Delta t \Delta x \\ &= \langle x(t)\rangle + v_x \Delta t \end{aligned} \tag{5}$$

where the drift velocity is related to the difference in hopping rates

$$v_x = (k_+ - k_-)\Delta x$$

Expressing eq. (5) as the result of many steps says that the mean of the position distribution behaves like traditional linear motion: $\langle x(t)\rangle = x_0 + v_x t$.

What about the variance in the distribution? Calculating the mean-square value of x from eq. (3) gives

$$\begin{aligned} \langle x^2(t+\Delta t)\rangle &= \left\langle x^2(t) \pm 2\Delta x\, \Delta t\, k_\pm\, x(t) + (k_+ + k_-)^2\, \Delta x^2 \Delta t^2 \right\rangle \\ &= \langle x^2(t)\rangle + 2 v_x \Delta t \langle x(t)\rangle + (k_+ + k_-)\Delta x^2 \Delta t \end{aligned} \tag{6}$$

where we used $(k_+ + k_-)\Delta t = 1$. Using this to calculate the variance in x: $\sigma^2(t) = (k_+ + k_-)\Delta x^2 t$, and then comparing with $\langle x^2\rangle^{1/2} = 2Dt$, leads to the conclusion that the breadth of the distribution σ spreads as it would in the absence of a drift velocity, and the diffusion coefficient for this biased random walk is given by

$$D = \frac{1}{2}(k_+ + k_-)\Delta x^2$$

When the left and right stepping rates are the same, we recover our earlier result $2D = \Delta x^2/\Delta t$.

Brownian Motion and Diffusion in a Potential

Let's relate diffusion with drift to diffusion of a particle under the influence of an external force or potential.

Brownian Dynamics

The Langevin equation for the motion of a Brownian particle can be modified to account for an additional external force, in addition to the drag force and random force. From Newton's Second Law:

$$m\ddot{x} = f_d + f_r(t) + f_{ext}(t)$$

where the added force is obtained from the gradient of the potential it experiences:

$$f_{\text{ext}} = -\frac{\partial U}{\partial x} \tag{7}$$

With the fluctuation-dissipation relation $\langle f_r(t) f_r(t') \rangle = 2\zeta k_B T\, \delta(t-t')$, the Langevin equation becomes

$$m\ddot{x} + (\partial U / \partial x) + \zeta \dot{x} - \sqrt{2\zeta k_B T}\, R(t) = 0 \tag{8}$$

Here $R(t)$ refers to a Gaussian distributed sequence of random numbers with $\langle R(t) \rangle = 0$ and $\langle R(t) R(t') \rangle = \delta(t - t')$.

Brownian dynamics simulations are performed using this equation of motion in the diffusion-dominated, or strong friction limit $|m\ddot{x}| << |\zeta \dot{x}|$. Then, we can neglect inertial motion, and set the acceleration of the particle to zero to obtain an expression for the velocity of the particle

$$\dot{x}(t) = (\partial U / \partial x) / \zeta - \sqrt{2k_B T / \zeta}\, R(t)$$

We then integrate this equation of motion in the presence of random perturbations to determine the dynamics $x(t)$.

Fokker–Planck Equation

We can also obtain an expression for diffusion of a particle in a velocity field that arises from an external force. When random forces on a particle dominate the inertial ones, we can equate the drift velocity and external force through the friction coefficient

$$f = \zeta v_x \tag{9}$$

The Fokker–Planck equation refers to stochastic equations of motion for the probability density $P(x,t)$ with units of m^{-1}. The corresponding continuity expression for the probability density is

$$\frac{\partial P}{\partial t} = -\frac{\partial j}{\partial x}$$

where j is the flux, or *probability current*, with units of s^{-1}, rather than the flux density we used for continuum diffusion J ($m^{-2}\ s^{-1}$). If the concentration flux is instead expressed in terms of a probability density eq. (1) becomes

$$j = -D\frac{\partial P}{\partial x} + \frac{f(x)}{\zeta}P \tag{10}$$

and the continuity expression is used to obtain the time-evolution of the probability density:

$$\frac{\partial P}{\partial t} = D\frac{\partial^2 P}{\partial x^2} - \frac{\partial}{\partial x}\left[\frac{f(x)}{\zeta}P\right] \tag{11}$$

This is known as a Fokker–Planck equation.

Smoluchowski Equation

Similarly, we can express diffusion in the presence of an internal interaction potential using eq. (7) and the Einstein relation

$$\zeta = \frac{k_B T}{D} \tag{12}$$

Then the total flux with contributions from the diffusive flux and potential flux can be written as

$$J = -D\frac{\partial C}{\partial x} - \frac{DC}{k_B T}\left(\frac{\partial U}{\partial x}\right) \tag{13}$$

and the corresponding diffusion equation is

$$\frac{\partial C}{\partial t} = D\left[\frac{\partial^2 C}{\partial x^2} - \frac{C}{k_B T}\left(\frac{\partial U}{\partial x}\right)\right] \tag{14}$$

This is known as the Smoluchowski Equation.

Linear Potential

For the case of a linear external potential, we can write the potential in terms of a constant external force $U = -f_{\text{ext}}x$. This makes eq. (14) identical to eq. (2), if we use eqs. (9) and (12) to define the drift velocity as

$$v_x = \frac{f_{\text{ext}}D}{k_B T} \equiv \underset{\sim}{f}D$$

Here I defined $\underset{\sim}{f}$ as the constant external force expressed in units of k_BT. Then the probability distribution that describes the position of particles released at x_0 after a time t is

$$P(x,t) = \frac{1}{\sqrt{4\pi Dt}} \exp\left[-\frac{\left(x - x_0 - \underset{\sim}{f} Dt\right)^2}{4Dt} \right]$$

As expected, the mean position of the diffusing particle is given by $\langle x(t) \rangle = x_0 + v_x t$.

To make use of this, let's calculate the time it takes a monovalent ion to diffuse freely across the width of a membrane (d) under the influence of a linear electrostatic potential of $\Phi = 0.3\text{V}$. With $U = e\Phi$

$$t = \frac{d}{v_x} = \frac{k_B T d}{f_{\text{ext}} D} = \frac{k_B T d^2}{e\Phi D}$$

Using $d = 4$ nm, $D = 10^{-5}$ cm^2/s, and $e = 1.6\times10^{-19}$ C, we obtain $t = 1.4$ ns.

Steady-State Solutions

For steady-state solutions to the Fokker–Planck or Smoluchowski equations, we can make use of a commonly used mathematical manipulation. As an example, let's work with eq. (10), re-writing it as

$$j = -D\left[\frac{\partial P}{\partial x} - \frac{P}{k_B T}\left(\frac{\partial U}{\partial x} \right) \right] \tag{15}$$

We can rewrite the quantity in brackets as:[1]

$$j = -De^{-U(x)/k_B T} \frac{d}{dx}\left[P e^{U(x)/k_B T} \right]$$

Separating variables, we obtain

$$-\frac{j}{D} e^{U(x)/k_B T} dx = d\left(P e^{U(x)/k_B T} \right)$$

This is an expression that can be manipulated in various ways and integrated over different boundary conditions. For instance, recognizing that j is a constant under steady state conditions, and integrating from x to a boundary b:

$$\begin{aligned} -\frac{j}{D}\int_x^b e^{U(x)/k_B T} dx &= \int_x^b d\left(P e^{U(x)/k_B T} \right) \\ &= P(b) e^{U(b)/k_B T} - P(x) e^{U(x)/k_B T} \end{aligned}$$

This leads one to an important expression for the steady state flux in the diffusive limit:

1. The general three-dimensional expression is $\mathbf{J}(\mathbf{r},t) = -\mathrm{D}\, e^{-U(\mathbf{r})/k_B T} \nabla \cdot [e^{U(\mathbf{r})/k_B T} P(\mathbf{r},t)]$.

$$j = \frac{-D\left[P(b)e^{U(b)/k_BT} - P(x)e^{U(x)/k_BT}\right]}{\int_x^b e^{U(x)/k_BT}dx}$$

The boundary chosen depends on the problem, for instance *b* is set to infinity in diffusion to capture problems or set as a fixed boundary for first-passage time problems.

For problems involving an absorbing boundary condition, $P(b) = 0$, and we can solve for the probability density as

$$P(x) = \frac{j}{D}e^{-U(x)/k_BT}\left[\int_x^b e^{U(x')/k_BT}dx'\right]$$

If we integrate both sides of this expression over the entire space, the left hand side is just unity, so we can express the steady-state flux as

$$j = D^{-1}\left[\int_0^b e^{-U(x)/k_BT}\left[\int_x^b e^{U(x')/k_BT}dx'\right]dx\right]^{-1}$$