## 8. Diffusion

Continuum Diffusion

In isolated room temperature fluids, we observe that concentration and temperature gradients spontaneously disappear with time, and the properties of the system become spatially uniform. Diffusion refers to the transport of mass and energy that leads toward

equilibrium, and as we will see it is closely related to Brownian motion. Thermodynamically, we can consider the driving force for diffusion as a gradient in the free energy or chemical potential of the system. From this perspective, the driving force for reaching a uniform spatial concentration is entropy of mixing.
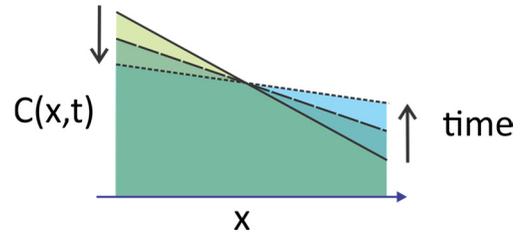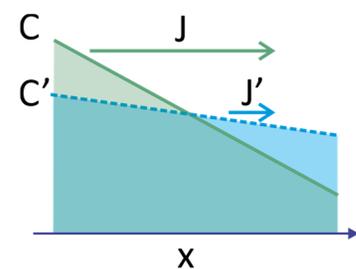
Fick's First Law

We will describe the time evolution of spatially varying concentration distributions $C(x,t)$ as they evolve toward equilibrium. These are formalized in two laws that were described by Adolf Fick (1855). Fick's first law is the "common sense law" that is in line with everyone's physical intuition. Molecules on average will tend to diffuse from regions of higher concentration to regions of lower concentration. Therefore, we say that the flux of molecules through a surface, J, is proportional to the concentration gradient across that surface.

$$J = -D\frac{\partial C}{\partial x}$$

(1)

J is more accurately called a flux density, since it has units of concentration or number density per unit area and time. The proportionality constant between flux density J (mol m^{-2} s^{-1}) and concentration gradient (mol m^{-4}) which sets the time scale for the process is the diffusion constant D (m^2 s^{-1}). The negative sign assures that the flux points in the direction of decreasing concentration. This

relationship follows naturally, when we look at the two concentration gradients in the figure. Both C and C' have a negative gradient that will lead to a flux in the positive direction. C will give a bigger flux than C' because there is more probability for flow to right. The gradient disappears and the concentration distribution becomes constant and time invariant at equilibrium. Note, in a general sense, $\partial C / \partial x$ can be considered the leading term in an expansion of C in x.

Fick's Second Law

Fick's second law is based on the first law, and adds an additional constraint based on the conservation of mass. Consider diffusive transport along x in a pipe with cross-sectional area a, and the change in the total number of particles within a disk of thickness Δt over a time period Δt. If we take this disk to be thin enough that the concentration is a constant at any moment in time, then the total number of particles in the slab at that time is obtained from the concentration times the volume: $N = aC(t)\Delta x$. Within the time interval Δt the concentration can change and therefore the total number of particles within the disk changes by an amount $\Delta N = a\{C(t+\Delta t) - C(t)\}\Delta x$. Now, the change in the number of particles is also dependent on the fluxes of molecules at the two surfaces of the disk. The number of molecules passing into one surface of the disk is $-aJ\Delta t$, and therefore the net change in the number of molecules during Δt is obtained from the difference of fluxes between the left and right surfaces of the disk: $\Delta N = -a\{J(x+\Delta x) - J(x)\}\Delta t$. Setting these two calculations of ΔN equal to each other we see that the flux and concentration gradients for the disk are related as $\{C(t+\Delta t) - C(t)\}\Delta x = -\{J(x+\Delta x) - J(x)\}\Delta t$, or rewriting this in differential form
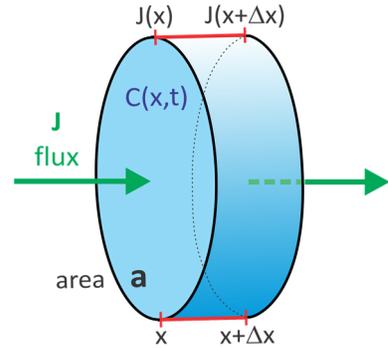
$$\frac{\partial C}{\partial t} = -\frac{\partial J}{\partial x} \tag{2}$$

This important relationship is known as a continuity expression. Substituting eq. (1) into this expression leads to Fick's Second Law

$$\frac{\partial C}{\partial t} = D\frac{\partial^2 C}{\partial x^2} \tag{3}$$

This is the diffusion equation in one dimension, and in three dimensions:

$$\frac{\partial C}{\partial t} = D\nabla^2 C \tag{4}$$

This equation assumes that D is a constant, but if it is a function of space: $\dot{C} = \nabla(D\nabla C)$.[1] Equation (4) can be used to solve diffusive transport problems in a variety of problems, choosing the appropriate coordinate system and applying the specific boundary conditions for the problem of interest.

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1. In three dimensions, Fick's First Law and the continuity expression are: $\mathbf{J}(\mathbf{r},t) = \mathbf{v}C(\mathbf{r},t) - D\nabla C(\mathbf{r},t)$ and $dC(\mathbf{r},t)/dt = -\nabla \cdot \mathbf{J}(\mathbf{r},t)$ where $\mathbf{v}$ is the velocity of the fluid.

As our first example of how concentration distributions evolve diffusively, we consider the time-dependent concentration profile when the concentration is initially all localized to one point in space, $x = 0$. The initial condition is
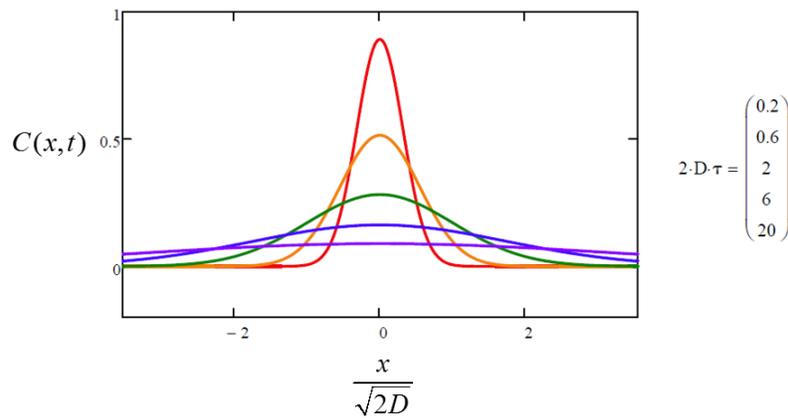
$$C(x, t = 0) = C_0 \, \delta(x)$$

and the solution to eq. (3) is

$$C(x, t) = \frac{C_0}{\sqrt{4\pi D t}} e^{-x^2/4Dt} \tag{5}$$

The concentration profile has a Gaussian form, which is centered on the origin with the mean square displacement broadening with time as:

$$\langle x^2 \rangle = 2Dt$$

$$2 \cdot D \cdot \tau = \begin{pmatrix} 0.2 \\ 0.6 \\ 2 \\ 6 \\ 20 \end{pmatrix}$$

Diffusive transport has no preferred direction. Concentration profiles spread evenly in the positive and negative direction, and the highest concentration observed will always be at the origin. Viewing time-dependent concentrations in space reveal that they reach a peak at $t_{max} = x^2/2D$, before decaying at $t^{-1/2}$ (dashed line below).

$$\frac{\xi}{\sqrt{2 \cdot D}} = \begin{pmatrix} 0 \\ 0.2 \\ 0.4 \\ 0.8 \\ 1.2 \end{pmatrix}$$

3
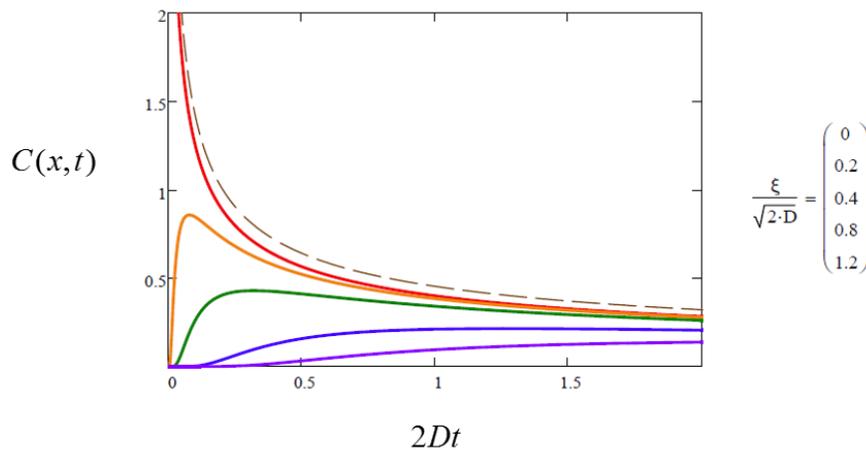
When we solve for 3D diffusion from a point source:

$$C(x,y,z,t=0) = C_0\,\delta(x)\delta(y)\delta(z)$$

the 3D concentration distribution is

$$C(x,y,z,t) = \frac{C_0}{(4\pi Dt)^{3/2}} e^{-r^2/4Dt} \tag{6}$$

where we have assumed that an isotropic medium in which D is identical for diffusion in the x, y, and z dimensions, and $r^2 = x^2 + y^2 + z^2$. Calculating the mean square displacement from $\langle r^2 \rangle = \int_0^\infty dr\, r^2 C(r,t)$, we obtain $\langle r^2 \rangle = 6Dt$, or in d dimensions, $\langle r^2 \rangle = 2^d Dt$.

The characteristic of simple diffusive behavior is the linear relationship between the mean-square displacement and time. Deviation from this behavior is known as anomalous diffusion and is characterized by a scaling relationship $\langle r^2 \rangle \sim t^\nu$. We refer to $\nu < 1$ as sub-diffusive behavior and $\nu > 1$ as super-diffusive. Diffusion in crowded environments can result in sub-diffusion.
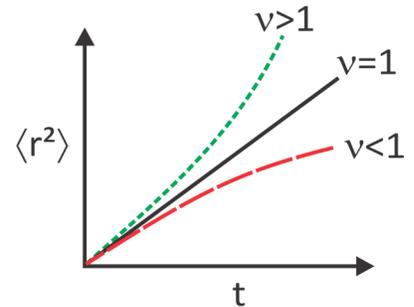
Diffusion Constants

Typical diffusion constants for biologically relevant molecules in water are shown in the graph below, varying from small molecules such as O_2 and glucose in the upper left to proteins and viruses in the lower right. For a typical globular protein, typically diffusion coefficients are:

$$\text{in water} \quad D \sim 10^{-10} \text{ m}^2/\text{s}$$
$$\text{in cells} \quad D \sim 10^{-12} \text{ m}^2/\text{s}$$
$$\text{in lipids} \quad D \sim 10^{-14} \text{ m}^2/\text{s}$$

$$\langle r^2 \rangle^{1/2} = 1\,\mu m, \quad t \sim 0.4 \text{ sec in cells}$$
$$= 10\,\mu m, t \sim 40 \text{ sec in cells}$$

Ions at room temperature usually have a diffusion coefficient of 0.6×10^{-5} to 2×10^{-5} cm^2/s.

Diffusion Coefficients in Water (cm²/s)
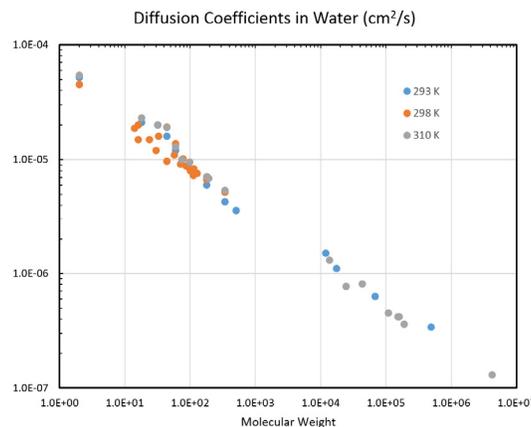
Solving the Diffusion Equation

Solutions to the diffusion equation, such as eq. (5) and (6), are commonly solved with the use of Fourier transforms. If we define the transformation from real space to reciprocal space as

$$\tilde{C}(k,t) = \int_{-\infty}^{\infty} C(x) e^{ikx} \, dx$$

one can express the diffusion equation in 1D as

$$\frac{d\tilde{C}(k,t)}{dt} = -Dk^2 \tilde{C}(k,t) \tag{7}$$

[More generally one finds that the Fourier transform of a linear differential equation in x can be expressed as in polynomial form: $\mathcal{F}(\partial^n f / \partial x^n) = (ik)^n \tilde{f}(k)$]. This manipulation converts a partial differential equation into an ordinary one, which has the straightforward solution $\tilde{C}(k,t) = \tilde{C}(k,0) \exp(-Dk^2 t)$. We do need to express the boundary conditions in reciprocal space, but then, this solution can be transformed back to obtain the real space solution using $C(x,t) = (2\pi)^{-1} \int_{-\infty}^{\infty} \tilde{C}(k,t) e^{-ikx} \, dk$.

Since eq. (7) is a linear differential equation, sums of solutions to the diffusion equation are also solutions. We can use this superposition principle to solve problems for complex initial conditions. Similarly, when the diffusion constant in independent of x and t, the general solution to the diffusion equation can also be expressed as a Fourier series. If we separate the time and space variables, so that the form of the solution is $C(x,t) = X(x)T(t)$ we find that we can write

$$\frac{1}{DT}\frac{\partial T}{\partial t} = \frac{1}{x}\frac{\partial^2 x}{\partial x^2} = -\alpha^2$$

Where α is a constant. Then $T = e^{-\alpha^2 Dt}$ and $x = A\cos\alpha x + B\sin\alpha x$. This leads to the general form:

$$C(x,t) = \sum_{n=0}^{\infty} \left(A_n \cos\alpha_n x + B_n \sin\alpha_n x \right) e^{-\alpha_n^2 Dt} \tag{8}$$

Here A_n and B_n are constants determined by the boundary conditions.

Examples

Diffusion across boundary

At time $t = 0$, the concentration is uniform at a value C_0 for $x \geq 0$, and zero for $x < 0$, similar to removing a barrier between two homogeneous media. Using the superposition principle, the solution is obtained by integrating the point source solution, eq. (5), over all initial point sources $\delta(x - x_0)$ such that $x_0 = 0 \to \infty$. Defining $y^2 = (x - x_0)^2 / 4Dt$

$$C(x,t) = \frac{C_0}{\sqrt{\pi}} \int_{-\frac{(x-x_0)}{\sqrt{4Dt}}}^{\infty} dy\, e^{-y^2} = \frac{C_0}{2} erfc\left(\frac{-(x-x_0)}{\sqrt{4Dt}}\right)$$
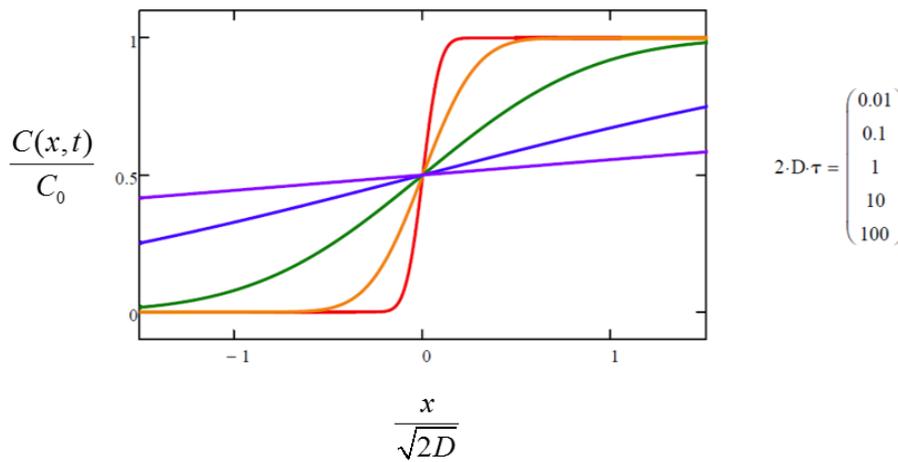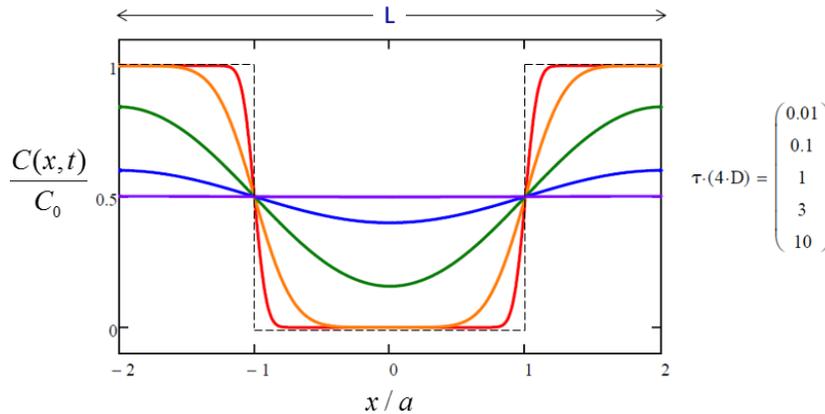

Diffusion into "hole"

A concentration "hole" of width *2a* is inserted into a box of length *2L* with an initial concentration of C_0. Let's take *L = 2a*. Concentration profile solution:

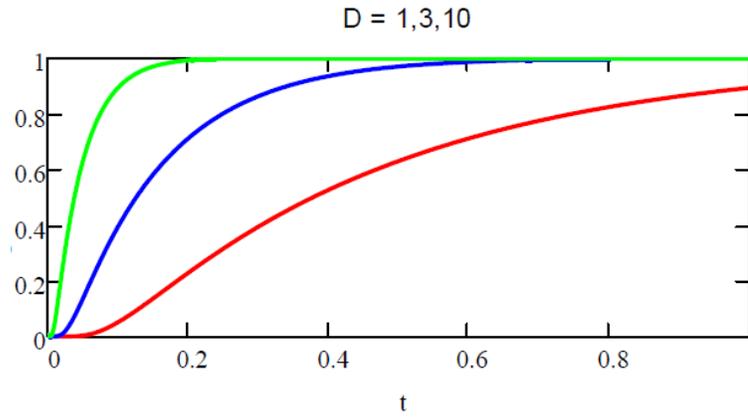$$C(x,t) = C_0\left[\left(\frac{L-a}{L}\right) - \sum_{n=1}^{\infty} A_n \cos(\alpha_n x) e^{-\alpha_n^2 Dt}\right]$$

$$A_n = \frac{2\sin(\alpha_n a)}{n\pi} \qquad \alpha_n = \frac{n\pi}{L}$$

Fluorescence Recovery after Photobleaching (FRAP)

We can use this solution to describe the diffusion of fluorescently labeled molecules into a photobleached spot. Usually observe the increase of fluorescence with time from this spot. We integrate concentration over initial hole:

$$N_{FRAP}(t) = \int_{-a}^{+a} C(x,t)dx$$

$$= C_0 \left[\frac{2a}{L}(L-1) - L\sum_{n=1}^{\infty} A_n^2 e^{-\alpha_n Dt} \right]$$

D = 1,3,10

Steady-State Solutions

Steady-state solutions can be applied when the concentration gradient may vary in space but does not change with time, $\partial C / \partial t = 0$. Under those conditions, the diffusion eq. (4) simplifies to Laplace's equation $\nabla^2 C = 0$. For certain conditions this can be integrated directly, and the flux is obtained from Fick's first law, eq. (1).

Diffusion through a Membrane

The steady-state solution to the diffusion equation in one dimension can be used to describe small molecule (i.e., O_2) diffusion through a cell plasma membrane. The membrane resists flow more than the fluid.

Membrane thickness, h; concentrations of small molecule in the fluid on left and right side of membrane, C_l and C_r. The partition coefficient between membrane and fluid:

$$K = \frac{C_{\text{membrane}}}{C_{\text{fluid}}}$$
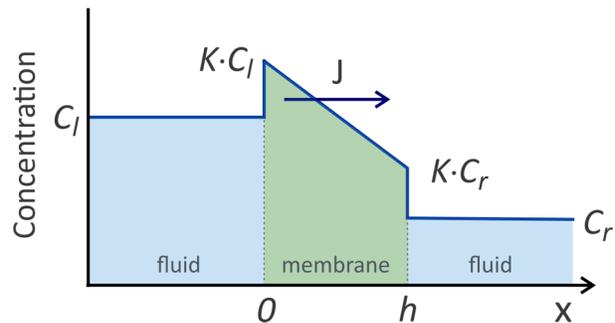
Applying steady-state approximation for the diffusion equation inside the membrane: $\partial^2 C / \partial x^2 = 0$. Solutions will take the form $C(x) = A_1 x + A_2$. Applying boundary conditions for the concentration of small molecule in the membrane at the two boundaries, we find

$$A_1 = \frac{K(C_r - C_l)}{h} \qquad A_2 = KC_l$$

Then we can write the flux of the small molecule across the membrane as

$$J = -D_{\text{mol}} \frac{\partial C}{\partial x} = \frac{KD_{\text{mol}}}{h}(C_\ell - C_r) = \frac{KD_{\text{mol}}\Delta C}{h}$$
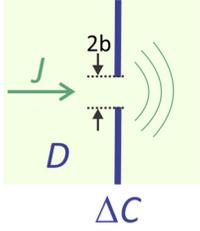
The membrane permeability is:

$$P \equiv \frac{J}{\Delta C} = \frac{KD_{\text{mol}}}{h}$$

Membrane resistance to flow $R = 1/P$. The rate of transport $dn/dt = J\,a$, where a is area.

We can also treat this as diffusion through a solid membrane with holes.

One pore

$$J = -D\frac{b}{2r^2}\Delta C$$

$$-\frac{dN}{dt} = Ja = \pi bD\Delta C$$

n pores

$$-\frac{dN}{dt} = n\pi bD\Delta C$$

Not proportional to pore area, just pore radius!

Diffusion to Capture by Sphere

What is the flux of a diffusing species onto a spherical surface from a solution with a bulk concentration C_0? This problem appears often for diffusion limited reaction rates. To find this, we calculate the steady-state radial concentration profile $C(r)$ around a perfectly absorbing sphere with radius b, i.e., $C(b) = 0$. At steady state, Fick's Second Law is $\nabla^2 C = 0$ and we take diffusion to depend only on the radial coordinate r and not the angular ones.
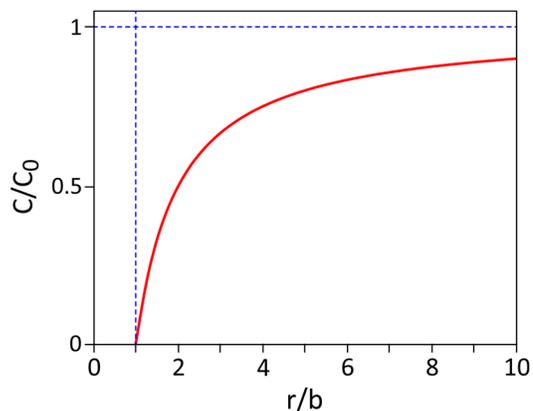
$$\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial C}{\partial r}\right) = 0$$

Let's look for the simplest solution. We begin by assuming that the quantity in parenthesis is a constant and integrate twice to give

$$C(r) = -\frac{A_1}{r} + A_2$$

Where A_1 and A_2 are constants of integration. Now, using the boundary conditions $C(b) = 0$ and $C(\infty) = C_0$ we find:

$$C(r) = C_0\left(1 - \frac{b}{r}\right)$$

Next, we use this expression to calculate the flux of molecules incident on the surface of the sphere ($r=b$).

$$J(b) = -D\frac{\partial C}{\partial r}\bigg|_{r=b} = \frac{DC_0}{b} \tag{9}$$

Here J is the flux density in units of (molecules area^{-1} sec^{-1}) or [(mol/L) area^{-1} sec^{-1}]. We then calculate the rate of collisions of molecules with the sphere (the flux) by multiplying J by the surface area of the sphere ($a = 4\pi b^2$):

$$\frac{dN}{dt} = Ja = 4\pi \, Db \, C_0$$

This shows that the rate constant, which expresses the proportionality between rate of collisions and concentration is $k = 4\pi Db$.