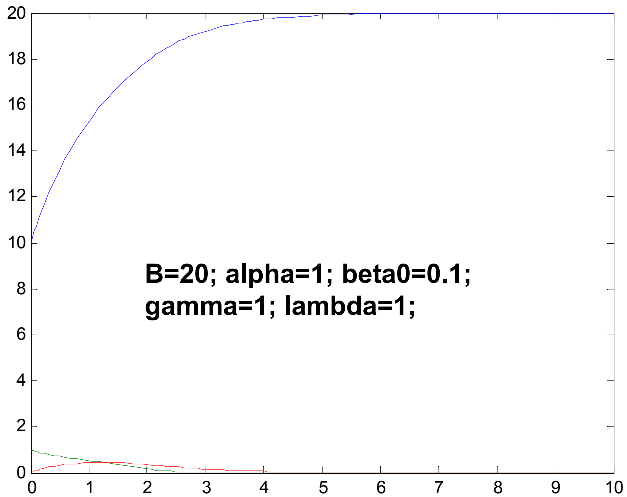
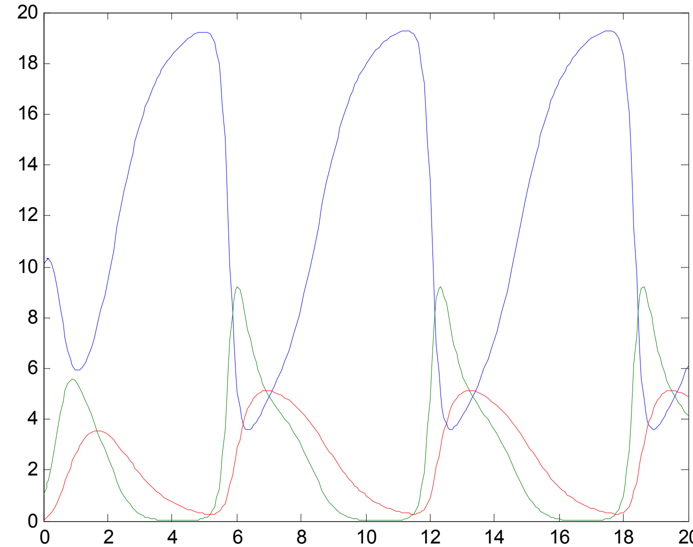




B=20; alpha=1; beta=0.3;
gamma=1; lambda=1; c=1;

$$\frac{dS}{dt} = \underbrace{B}_{\text{birth or immigration}} - \underbrace{\beta_0\left(1+\cos t\right)SI}_{\text{getting sick}} - \underbrace{\alpha S}_{\text{natural death with rate alpha}}$$

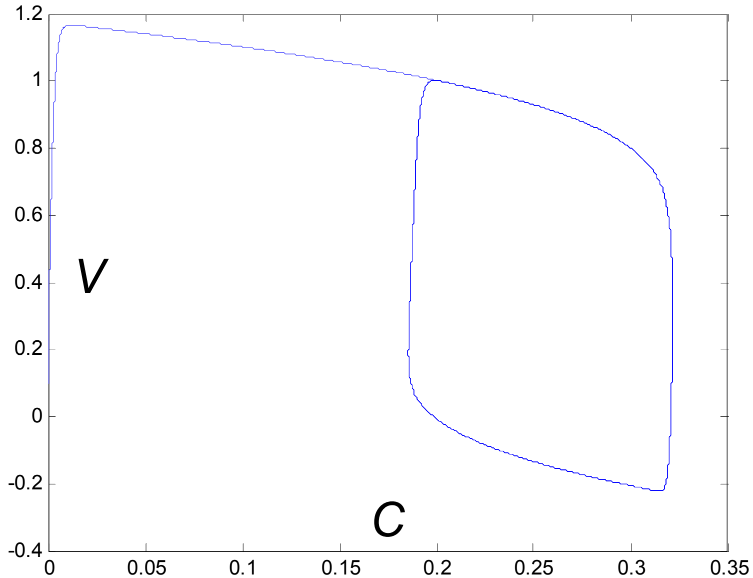
Periodic, as observed!

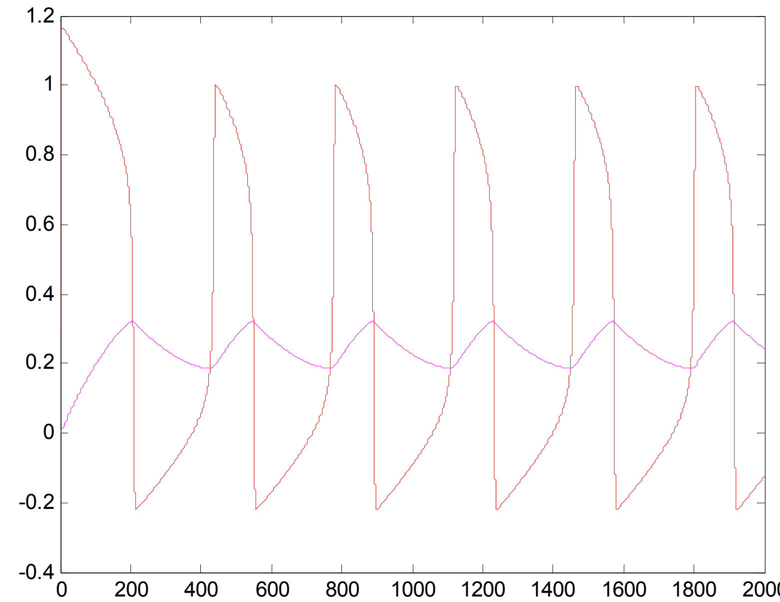
$$\frac{dI}{dt} = \underbrace{\beta_0\left(1+\cos t\right)SI}_{\text{getting sick}} - \underbrace{\alpha I}_{\text{natural death with rate alpha}} - \underbrace{\gamma I}_{\text{recovering}} - \underbrace{\lambda I}_{\text{death from decease with rate lambda}}$$

$$\frac{dR}{dt} = \underbrace{\gamma I}_{\text{recovering}} - \underbrace{\alpha R}_{\text{natural death with rate alpha}}$$

$$\frac{dV}{dt} = I + V(0.2 - V)(V - 1) - C$$

$$\frac{dC}{dt} = 0.002 * (V - C)$$





http://thevirtualheart.org/java/fhn24.html

http://www.scholarpedia.org/article/FitzHugh-Nagumo_model

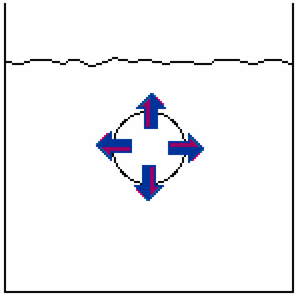
Diffusion, bacterial motility and chemotaxis

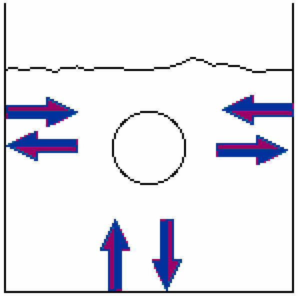
There are two ways that the molecules move: passive transport and active transport. Active transport requires that the cell use energy. Passive transport does not require such energy expenditure, and occurs spontaneously.

The principle means of passive transport is diffusion. Diffusion is the movement of molecules from a region in which they are highly concentrated to a region in which they are less concentrated. It depends on the motion of the molecules and continues until the system in which the molecules are found reaches a state of equilibrium, which means that the molecules are randomly distributed throughout the system.

Diffusion occurs when a system is not at equilibrium. As an example, suppose you drop one drop of ink into a glass of water. At first, all of the ink molecules are in a small space and they are moving around in a random way. They move in straight lines and change direction only when they collide with each other or the surrounding water molecules. Some of the ink molecules near the edge of the drop move away from the center of the drop.

Most of the molecules continue to move away from the original center of the drop. They move in all different directions, and some may even move back toward the center. Still, more are moving away from the drop than toward it until they find the wall of the glass. Then they start moving back toward the center again. More and more molecules bounce off of the glass until they start moving toward the center, then they pass the center and move toward the other side. Eventually the number of molecules moving away from the center equals the number moving toward the center, and equilibrium is established. At this point the molecules are evenly spread throughout the water, and diffusion stops. The molecules do not stop moving - this is a dynamic equilibrium.





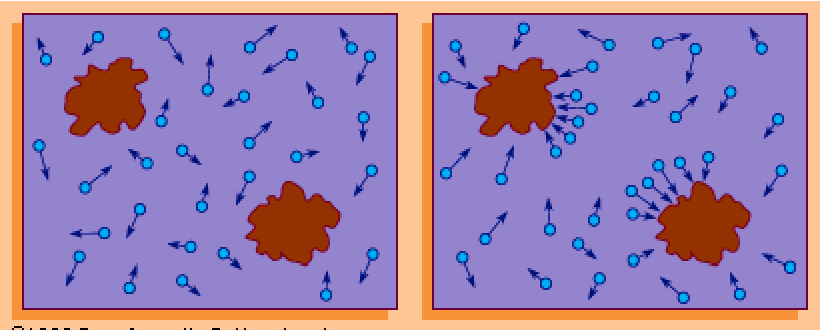
Diffusion
Random movement
No energy needed from the cell
From higher to lower concentration

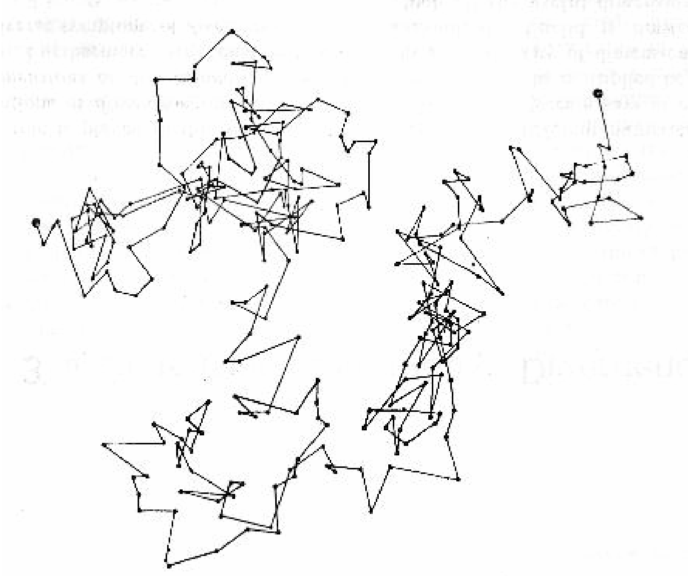
Brownian motion

The radius of a water molecule is about 0.1 nm, while proteins are two orders of magnitude larger, in the range 2 - 10 nm. This size difference suggests that we can view the fluid as a continuum. A protein moving through the fluid is acted on by frequent and uncorrelated momentum impulses arising from the thermal motions of the fluid.

For a protein with $m \simeq 10^{-21}$ kg

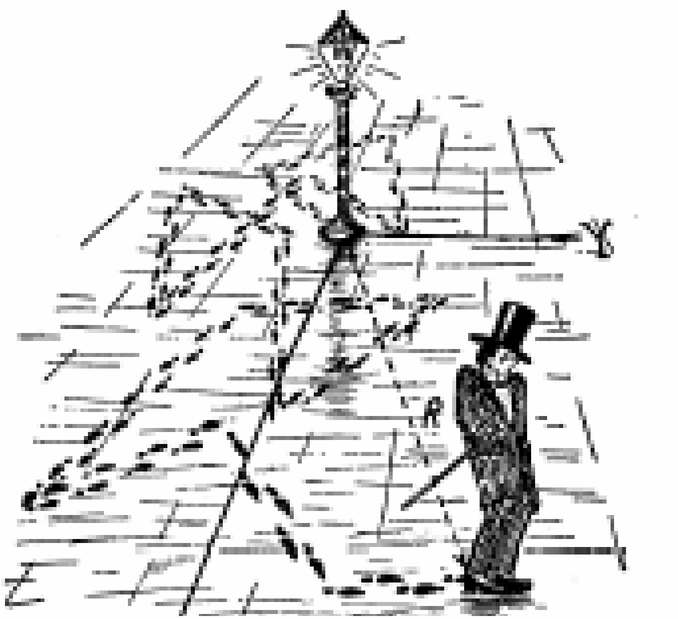
$v \simeq 2$ m/s. However, in a fluid the protein moves at this velocity only for a time $\tau \sim m/\zeta = 10^{-13}$ sec, much shorter than any motion of interest in a molecular motor. During this short time the protein travels a distance $v \cdot \tau \sim 0.01$ nm before it collides with another molecule. This is only a fraction of a diameter of water molecule.





Random walks

Let us now consider a one-dimensional random walk of N particles. A particle always takes a fixed step size Δx towards the left or right with equal probability. The position of the particles is denoted by $x_i(n)$, where the subscript denotes which particles (i=1…N) and n denotes the number of steps that particle I took. All particles start their random walk at x=0: $x_i(0)=0$ for i=1…N. It is easy to show that the position averaged over all particles is always zero independent of how many steps were taken:



$$Mean\left(x(n)\right)=\left\langle x(n)\right\rangle=\frac{1}{N}\sum_{i=1}^{N}x_i(n)=$$
$$=\frac{1}{N}\sum_{i=1}^{N}\left[x_i(n-1)\pm\Delta x\right]=\frac{1}{N}\sum_{i=1}^{N}x_i(n-1)=\frac{1}{N}\sum_{i=1}^{N}x_i(0)=0$$

However individual particles are spreading in both the positive and negative x direction. A convenient way to quantify the spreading is to calculate the variance of the distribution of positions. The variance is defined as $Var(x(n))=\left\langle x^2(n)\right\rangle-\left\langle x(n)\right\rangle^2$:

$$Var\left(x(n)\right) = \left\langle x^2(n)\right\rangle - \left\langle x(n)\right\rangle^2 = \left\langle x^2(n)\right\rangle - 0 = \frac{1}{N}\sum_{i=1}^{N} x_i^{\,2}(n) =$$

$$\frac{1}{N}\sum_{i=1}^{N}\left[x_i(n-1) \pm \Delta x\right]^2 = \frac{1}{N}\sum_{i=1}^{N}\left[x_i^{\,2}(n-1) \pm 2\Delta x x_i(n-1) + \Delta x^2\right] =$$

$$\frac{1}{N}\sum_{i=1}^{N}\left[x_i^{\,2}(n-1) + \Delta x^2\right] = \frac{1}{N}\sum_{i=1}^{N} x_i^{\,2}(n-1) + \frac{1}{N}\sum_{i=1}^{N}\Delta x^2 = Var\left(x(n-1)\right) + \Delta x^2$$

As expected the variance is non-zero. For each extra step the variance grows by Δx^2 and since the variance is zero for n=0 we can write: $\left\langle x^2(n)\right\rangle = n\Delta x^2$

$$Var\left(x(0)\right) = \left\langle x^2(0)\right\rangle = 0$$

$$Var\left(x(1)\right) = Var\left(x(0)\right) + \Delta x^2 = \Delta x^2$$

$$Var\left(x(2)\right) = Var\left(x(1)\right) + \Delta x^2 = 2\Delta x^2$$

....

$$Var\left(x(n)\right) = n\Delta x^2$$

$$std(x) = \sqrt{Var(x)}$$

Standard deviation

During one step the particle moves at a constant velocity $v = \Delta x/\tau$. This means that a time t the particle performed $n = t/\tau$ steps, therefore the variance is proportional to t:

$$\langle x^2(n) \rangle = t\frac{\Delta x^2}{\tau} \equiv 2Dt$$

$$D = \frac{\Delta x^2}{2\tau}$$ - diffusion coefficient

$$v \sim 1\frac{m}{s}, \tau \sim 10^{-12}s, D = \frac{\Delta x^2}{2\tau} \sim \frac{(v\tau)^2}{\tau}$$

$$\sim v^2\tau \sim 10^{-12}\frac{m^2}{s} \sim 1\frac{\mu m^2}{s}$$

$$L = \sqrt{\langle x^2 \rangle} = \sqrt{2Dt}$$

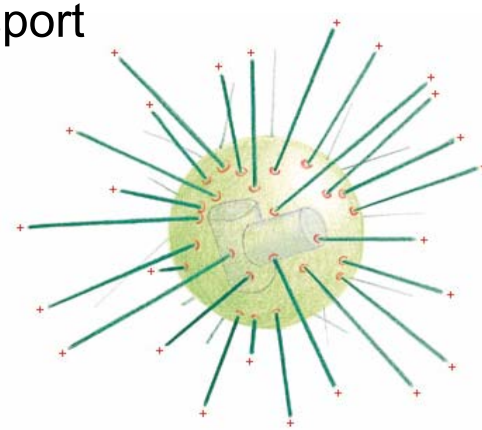
Cells also use molecular motors for *active* transport

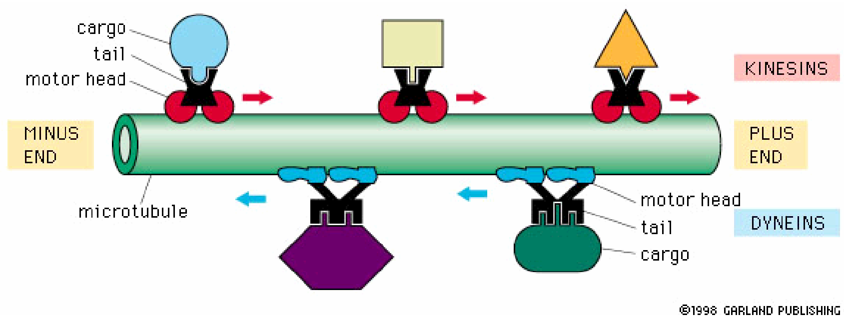
Active transport
Directed movement
Energy is needed from the cell
Could be from lower to higher concentration

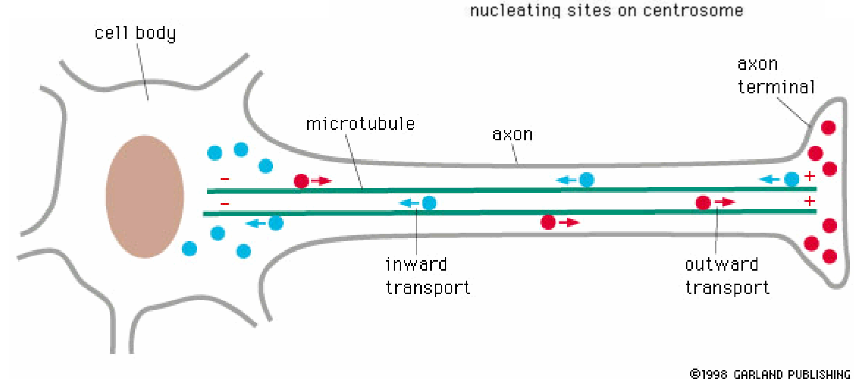
$$L = Vt$$

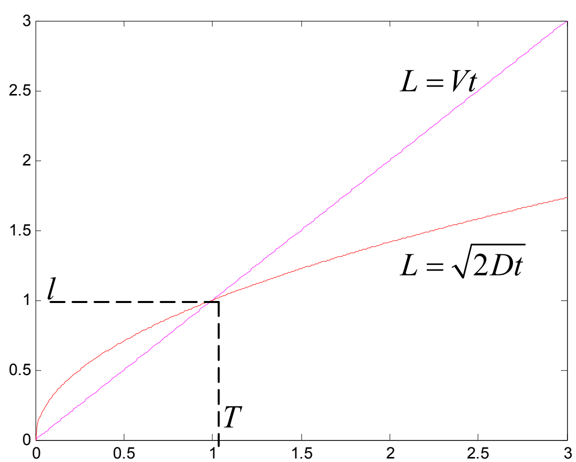
Diffusion
Random movement
No energy needed from the cell
From higher to lower concentration

$$L = \sqrt{2Dt}$$









What to use – active or passive transport?

$$VT = \sqrt{2DT}$$

$$V^2T^2 = 2DT$$

$$T = 2D/V^2$$

$$l = VT = 2D/V$$

$$V \sim 0.1\frac{\mu m}{s}, D \sim 1\frac{\mu m^2}{s},$$

$$l \sim \frac{D}{V} \sim 10\,\mu m; T \sim \frac{D}{V^2} \sim 100s$$

Fick's first law

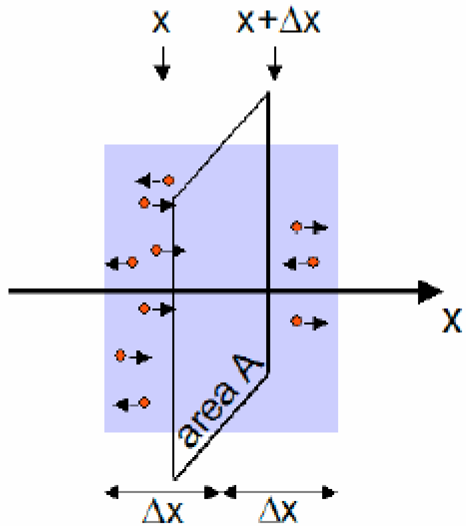


Figure Particles randomly moving along one-dimension crossing an area A

Consider Fig. illustrating particles moving along one dimension x. The particles are randomly moving. Assume there are $N(x)$ particles in the gray region on the left of area A and $N(x+\Delta x)$ particles in the gray region on the right of area A. How many particles will cross the area A to the right? Since the probability to travel to right or the left is identical $0.5N(x)$ particles will travel to the right. However $0.5N(x+\Delta x)$ will travel to the left and cross area A. Therefore the net number of crossing to the right is: $-\frac{1}{2}\left(N(x+\Delta x)-N(x)\right)$. The flux of molecules J through the area A during a short time interval τ is defined as:

$$J=\frac{-\frac{1}{2}\left(N\left(x+\Delta x\right)-N\left(x\right)\right)}{A\tau}$$

$$J = \frac{-\frac{1}{2}\left(N\left(x+\Delta x\right) - N\left(x\right)\right)}{A\tau}$$

$$C\left(x\right) = \frac{N\left(x\right)}{A\Delta x}$$

$$J = \frac{-A\Delta x\left(C\left(x+\Delta x\right) - C\left(x\right)\right)}{2A\tau} = -\frac{\Delta x^2}{2\tau}\frac{C\left(x+\Delta x\right) - C\left(x\right)}{\Delta x}$$

$$\boxed{J = -D\frac{C\left(x+\Delta x\right) - C\left(x\right)}{\Delta x}}$$

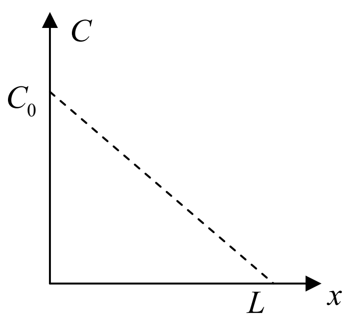
flux

concentration gradient

$$J = \frac{D}{L} C_0$$

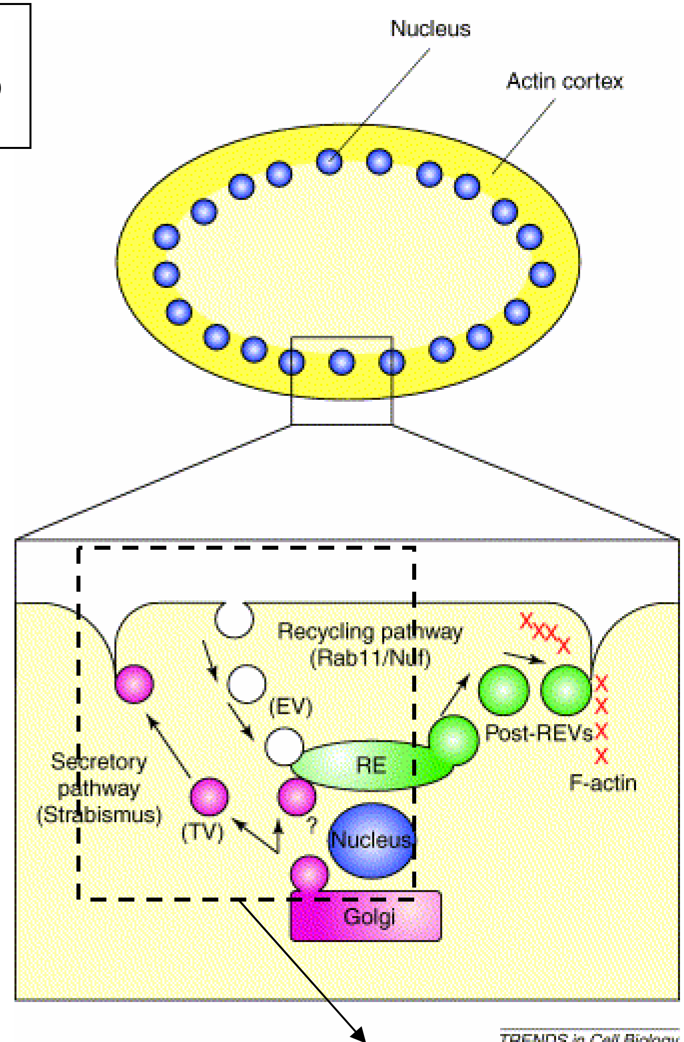
$$J = -D \frac{\left(C\left(x+\Delta x\right) - C\left(x\right)\right)}{\Delta x}$$

$$\frac{C\left(x+\Delta x\right) - C\left(x\right)}{\Delta x} = const = -\frac{C_0}{L}$$

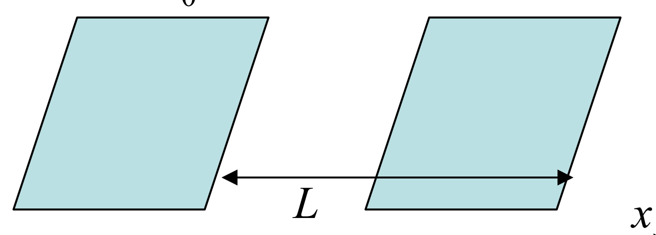


$$J = VC_0$$

$$V = \frac{D}{L}$$



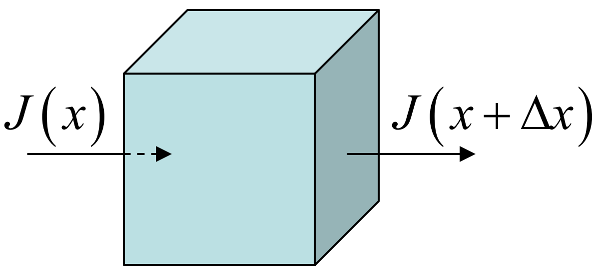
$C = C_0$ $\quad$ $C = 0$



$$J = \frac{-\frac{1}{2}\left(N(x+\Delta x) - N(x)\right)}{A\tau} \qquad C(x) = \frac{N(x)}{A\Delta x}$$

$$J = \frac{-A\Delta x\left(C(x+\Delta x) - C(x)\right)}{2A\tau} = -\frac{\Delta x^2}{2\tau}\frac{C(x+\Delta x) - C(x)}{\Delta x}$$

flux → $\boxed{J = -D\frac{C(x+\Delta x) - C(x)}{\Delta x} \rightarrow -D\frac{\partial C}{\partial x}}$ ← concentration gradient



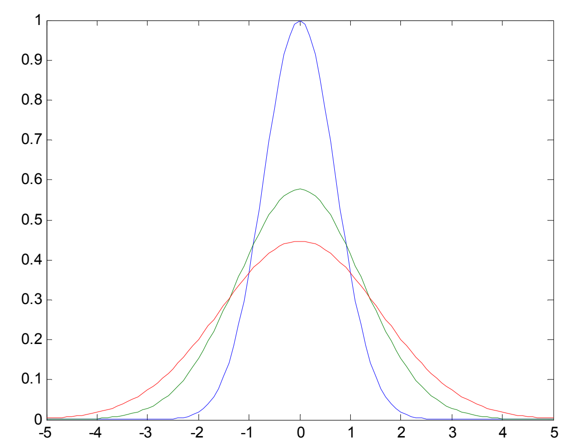
$$\frac{\Delta N}{\Delta t} = \frac{A\Delta x\Delta C}{\Delta t} = A\left[J(x) - J(x+\Delta x)\right]$$

$$\frac{\Delta C}{\Delta t} = -\frac{J(x+\Delta x) - J(x)}{\Delta x} \rightarrow \boxed{\frac{\partial C}{\partial t} = -\frac{\partial J}{\partial x}}$$

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

$$C = \frac{C_0}{\sqrt{4Dt}}e^{-x^2/4Dt}$$

$$\boxed{\langle x \rangle = \sqrt{2Dt}}$$

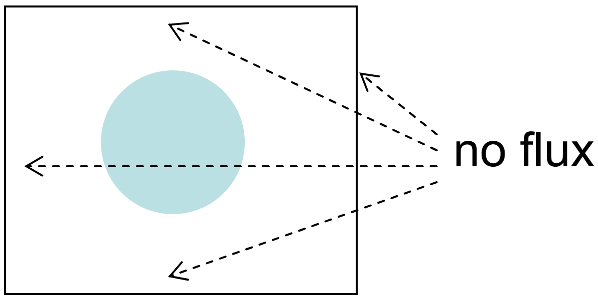


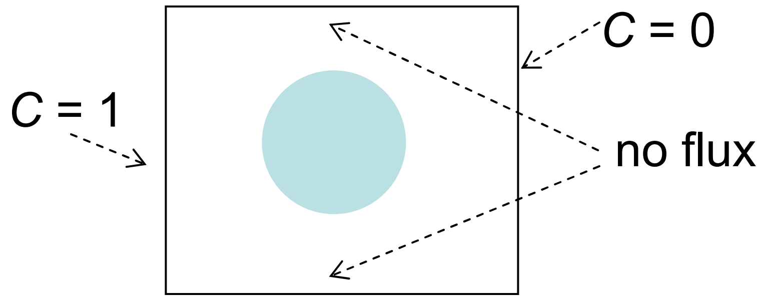
$$\frac{\partial C}{\partial t} = D\left(\frac{\partial^2 C}{\partial x^2} + \frac{\partial^2 C}{\partial y^2}\right)$$

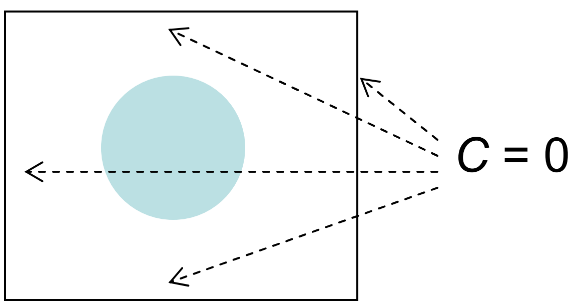
+ need initial conditions and…

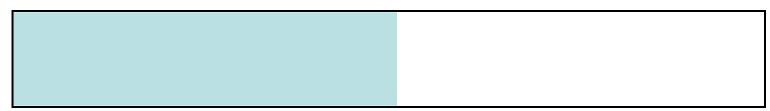
…possible boundary conditions:
- fixed concentration at the boundary
- no flux (boundary is impermeable)

Tomorrow you will see how to simulate:

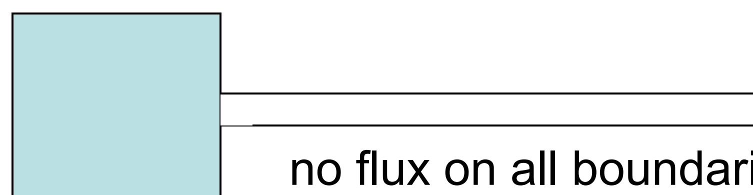






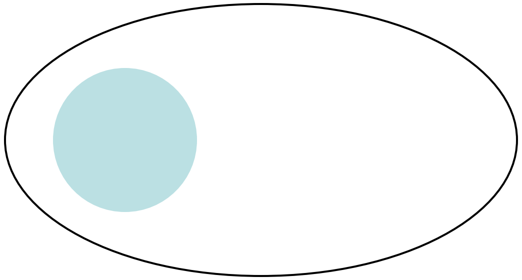


no flux on all boundaries

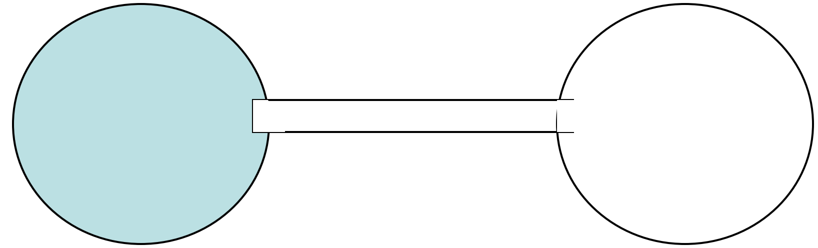


no flux on all boundaries

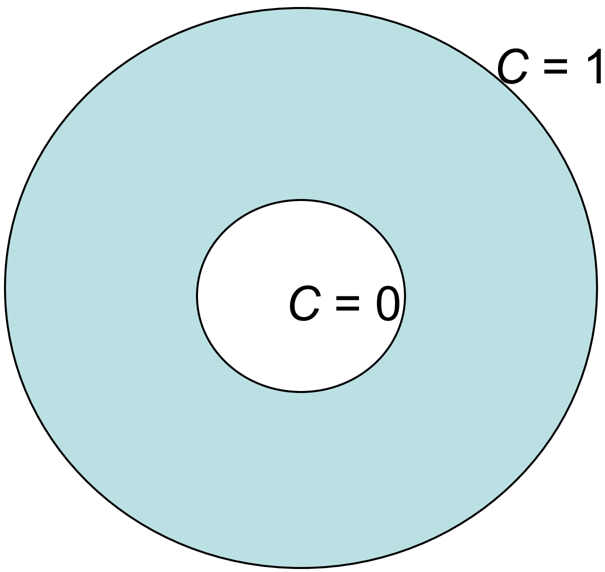
Do yourself:



C = 0 on the whole boundary



no flux an all boundaries



(diffusion only goes on in the ‘ring’ space between two circles)

In all cases, make surface color plots of the concentration in the cell at different moments of time, learn how to make line plots, determine how fast the concentration spreads, and in general think about the meaning of the results.