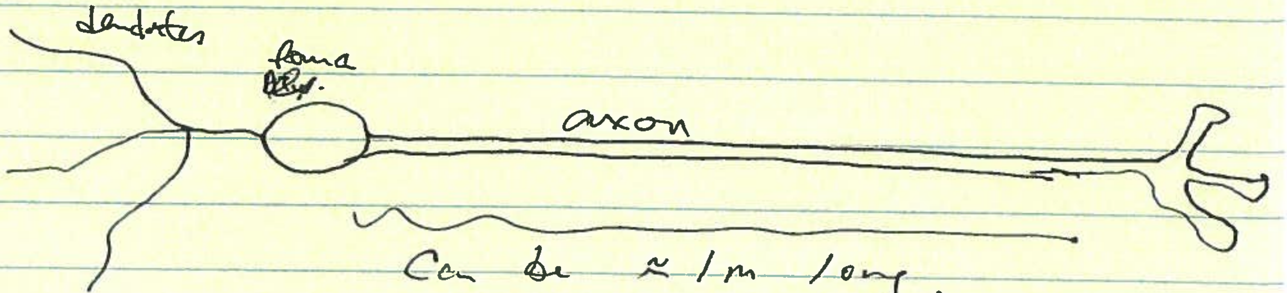
5/20 Rtn.

Nerve Propagation



Can be ≈ 1m long.

Information has to travel down it very quickly – can't survive in the wild with seconds long delays between thinking of moving and the muscle getting a signal to move.

How ~~does the~~ is this accomplished?

Morphogenesis –

How does the shape and structure of our bodies develop from a single fertilized egg?

Too hard – How do simpler spatial patterns arise in biological systems?

– Stripes on my cat's tail

–

Muscles – we know they contract and by so doing generate force – but how does this happen at a microscopic level.

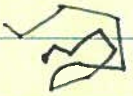
All of these involve things moving in space as well as changes in time.

⇒ Variation in x + t ⇒ $\underline{\underline{\text{PDE}}}$

5120-514

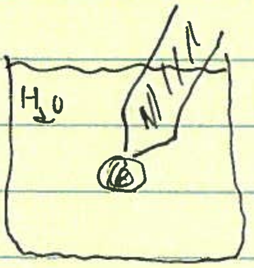
Diffusion

A molecule, say a sugar molecule or a protein molecule, in an aqueous sol'n is constantly moving because of collisions with solvent (H_2O) molecules. If you could fix your vision on a specific molecule it would appear to move randomly, changing direction often. This leads to what we call "diffusion"



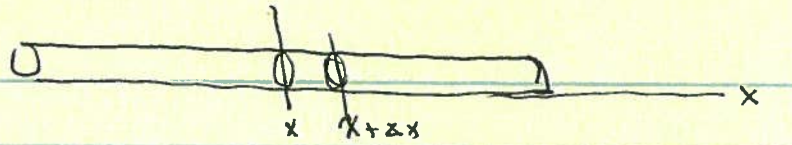
In a little while we'll model this by looking at idealized individual molecules.

First, we take a macroscopic viewpoint - we do not look at individual molecules, but at concentrations or number density of molecules (# / volume)



If we inject a drop of food coloring into a beaker of water, what happens to the food coloring? It spreads out, moving from places where the concentration is high, to places where it is low. Let's consider a simpler version of this process. Suppose we have a long very thin hollow glass tube filled with water and through a tiny hole in the tube we inject some food coloring at some point along the tube.

As in the beaker, the food coloring ~~moves~~ spreads out moving from ~~p~~places of high concentration to places of low concentration. We will model this process.



Let x denote spatial location along the tube at t time. Let $n(x,t)$ denote the number of molecules/volume at location x at time t. In a small section of the tube running from x to $x+\Delta x$, the number of molecules is $n(x,t)\,A\Delta x$.

Because dye molecules move from one location to another, it is useful to introduce the idea of the <u>flux</u> of molecules. The flux is the <u>number of molecules per unit cross-sectional area per unit time</u> crossing a particular tube cross-section. Fluxes have direction, it matters which ~~way~~ direction the molecules are going.

Model: $\boxed{\text{Fick's Law}}$ $\quad \text{Flux} = -D\,\frac{\partial n}{\partial x}(x,t)$
where D is a positive constant. This is the simplest model that captures the motion of dye from places of high conc to places of low concentration.

$$\text{Flux} = -D\,\frac{\partial n}{\partial x}.$$

Consider dimensions of the various terms.

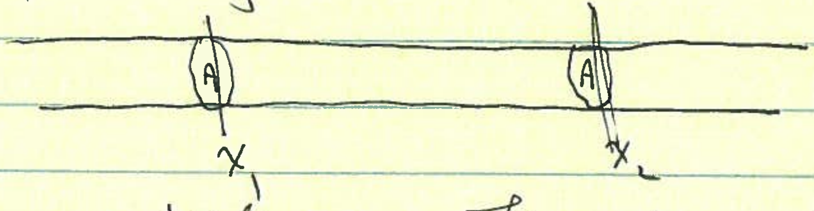
$$\text{Flux} \quad \frac{\#}{\text{Area Time}}, \qquad \frac{\partial n}{\partial x} \quad \frac{\#/\text{volume}}{\text{length}}$$

Since dimensions on two sides of an equation must match, this tells us that D has dimensions

of L^2/T. We denote flux by J, so Fick's Law has $J = -D \frac{\partial n}{\partial x}$.
$J > 0$ means molecules move to the right. Since $D > 0$, This happens if $\frac{\partial n}{\partial x} < 0$, ie The concentration is lower as we ~~move to the~~ look further to the right. So the formula is consistent with dye moving from high conc locations to low conc. locations.

We will derive an equation (a PDE) for the number density $n(x,t)$ of dye molecules.

Consider an arbitrary piece of the tube (not necessarily short) running from $x = x_1$ to $x = x_2 > x_1$



How many molecules are in the section of the tube at time t?

$$\int_{x_1}^{x_2} n(x,t)\, A\, dx$$

What about at time $t + \Delta t$ a little while later?

$$\int_{x_1}^{x_2} n(x,t+\Delta t)\, A\, dx .$$

How can these two quantities be different? No new food coloring molecules are added during this time and none are removed.

Molecules can move around from one part of the tube to another. Only molecules crossing the cross-section at x_1 or x_2 affect the # of molecules in the section $x_1 < x < x_2$. The two quantities before can differ only if molecules cross x_1 or x_2 between times t and $t + \Delta t$.

Between these times the number of molecules crossing x_1 is

$$\int_t^{t+\Delta t} J(x_1, t')\, A\, dt' \qquad \text{Why?}$$

and the number crossing x_2 is

$$\int_t^{t+\Delta t} J(x_2, t')\, A\, dt' .$$

So simple book keeping tells us that

$$\int_{x_1}^{x_2} n(x, t+\Delta t)\, A\, dx = \int_{x_1}^{x_2} n(x,t)\, A\, dx$$

$$+ \int_t^{t+\Delta t} J(x_1, t')\, A\, dt' \underset{\substack{\uparrow \\ \text{Why?}}}{-} \int_t^{t+\Delta t} J(x_2, t')\, A\, dt'$$

Rearranging, we have

$$\int_{x_1}^{x_2} \frac{n(x, t+\Delta t) - n(x,t)}{\Delta t}\, A\, dx$$

$$= \frac{1}{\Delta t} \int_t^{t+\Delta t} J(x_1, t')\, A\, dt' - \frac{1}{\Delta t} \int_t^{t+\Delta t} J(x_2, t')\, A\, dt'$$

What happens if we consider $\Delta t \to 0$?

LHS $\longrightarrow$ $\displaystyle\int_{x_1}^{x_2} \frac{\partial n}{\partial t}(x,t)\, A\, dx$.

RHS $\longrightarrow$ $J(x_1,t)A - J(x_2,t)A$ (Why?)

FTC

So we find that $\displaystyle\int_{x_1}^{x_2} \frac{\partial n}{\partial t}(x,t)\, A\, dx = \left(J(x_1,t) - J(x_2,t)\right)A$

But $\displaystyle J(x_2,t) - J(x_1,t) = \int_{x_1}^{x_2} \frac{\partial J}{\partial x}(x,t)\, dx$.

Why? FTC

So
$$\int_{x_1}^{x_2} \frac{\partial n}{\partial t}(x,t)\, A\, dx = -\int_{x_1}^{x_2} \frac{\partial J}{\partial x}(x,t)\, A\, dx$$

or
$$\int_{x_1}^{x_2} \left(\frac{\partial n}{\partial t} + \frac{\partial J}{\partial x} \right) A\, dx = 0 .$$

This can be true only if (Why?)

$$(*) \qquad \frac{\partial n}{\partial t} + \frac{\partial J}{\partial x} = 0$$

Now, according to Fick's law, $J = -D\frac{\partial n}{\partial x}$, so
$$\frac{\partial n}{\partial t} + \frac{\partial}{\partial x}\left(-D\frac{\partial n}{\partial x}\right) = 0$$

or
$$\frac{\partial n}{\partial t} = \frac{\partial}{\partial x}\left(D\frac{\partial n}{\partial x}\right).$$

If D is constant, this becomes
$$\frac{\partial n}{\partial t} = D\frac{\partial^2 n}{\partial x^2}$$

which is a PDE called the 1-D diffusion eq.

Note that in our derivation of (*), we made no use of the specific form of the flux fn $J(x,t)$. So Eq (*) is true whatever causes the motion of molecules across the cross-sections at x_1 and x_2!

Ex Suppose that the water in the tube was moving say with speed u to the right. So the dye molecule would then be moving both ~~by~~ along with the water and by diffusion.

$$J = un - D\frac{\partial n}{\partial x}.$$

$$\Rightarrow \quad \frac{\partial n}{\partial t} = -\frac{\partial}{\partial x} J = -u\frac{\partial n}{\partial x} + D\frac{\partial^2 n}{\partial x^2}$$

ie
$$\frac{\partial n}{\partial t} = -u\frac{\partial n}{\partial x} + D\frac{\partial^2 n}{\partial x^2}$$

This is called an <u>advection - diffusion equation</u>

Diffusion Coefficient

[1905 Special Relativity, Photoelectric Effect, Brownian Motion

A. Einstein gave a quantitative understanding of diffusion in his 1906 paper on Brownian motion. He used his theory to give estimates of the sizes of molecules. He showed that for a spherical solute molecule which is large compared to the solvent molecules :

$$D = \frac{kT}{6\pi\mu a}$$ Stokes-Einstein Formula

where a is the molecule's radius, μ is the viscosity of the solvent, T is the absolute temp, and k is a constant called Boltzmann's constant. The expression kT appears in a lot of the science of small (nano-sized) things; it has dimensions of energy.

For a nonspherical molecule, $6\pi\mu a$ is replaced by a friction coefficient f called the Stokes friction coefficient; it depends on the size and shape of the molecule.

For a spherical molecule of radius a and mass density ρ, the molecule has mass – ← molecular weight

$$M = \frac{4\pi}{3}\rho a^3 .$$

$a = \left(\frac{3M}{4\pi\rho}\right)^{1/3}$

Solving for a and using this in the S-E formula gives

$$D = \frac{kT}{6\pi\mu}\left(\frac{4\pi\rho}{3M}\right)^{1/3} = \frac{kT}{3\mu}\left(\frac{\rho}{6\pi^2 M}\right)^{1/3} .$$

Most large protein molecules have about the same mass density 1.3 - 1.4 g/cm^3, so at a fixed temperature $DM^{1/3} = \left(\frac{kT}{3\mu}\right)\left(\frac{\rho}{6\pi^2}\right)^{1/3}$ is approximately constant.

So for these proteins, D scales like $M^{-1/3}$.

For small molecules, like O_2 or CO_2, the diffusion is different $D \sim M^{-1/2}$.

In aqueous sol'n, like inside cells or the blood, some typical diffusion coefficients are

O_2 (Mwt 32)	$2.1(10)^{-5}$ cm²/sec
Glucose (Mwt 182)	$6.6(10)^{-6}$ cm²/sec
Hemoglobin (Mwt 64500)	$6.9(10)^{-7}$ cm²/sec.
Myosin (524,800)	$1.05(10)^{-7}$ cm²/sec

Molecular View of Diffusion

The origin of diffusion of a molecule is ultimately due to thermal motion. It is a fact from physics that any particle has an average kinetic energy from thermal motion associated with each coordinate direction (x, y, z) of $kT/2$ (Einstein again).

For a particle with mass m and velocity V_x along the x-axis, its KE is $\frac{1}{2} m V_x^2$. This fluctuates in time, but on average it is $\frac{1}{2} kT$. Let < > denote an average over time following