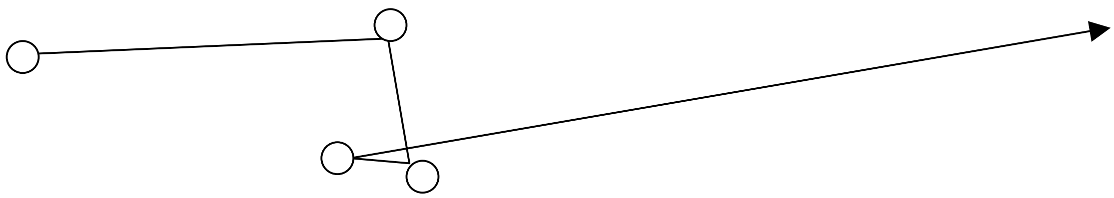
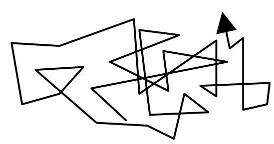
Lecture 31x – Diffusion (extended version)

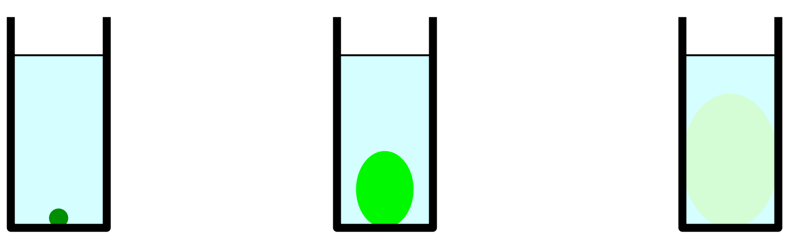
As will be discussed in Lec. 33, the temperature of a body or system reflects the energy of its molecular or other components. For example, the mean kinetic energy of a single particle in an ideal gas is equal to 3/2 $k_B T$, where T is the temperature of the system in Kelvin, and k_B is Boltzmann's constant, equal to 1.38×10^{-23} J/K. As the temperature rises, so does the mean kinetic energy and the mean speed v_{av}. For diatomic molecules like N_2 and O_2 in air, the mean speed is more than 400 m/s, or greater than 1400 km/hr, which is rather fast. At very low densities, a molecule in a gas can travel a considerable distance at this speed without hitting another molecule, so that the displacement covered by the molecule is not too much below the product of the speed and the elapsed time t.



But at high density, a molecule collides frequently with its neighbours, so that the displacement is much lower, even if the distance is still roughly $v_{av}t$.



The path of an individual molecule looks much like the random walk discussed in the previous lecture. Collectively, the molecules *diffuse* through a medium according to a set of macroscopic laws, which use fluid concepts such as concentration densities as their variables. For example, in class we show the diffusion of green food colouring through a beaker of water



---- time --→

Here, we characterize the diffusion of the colouring according to, say, the apparent colour density of a region in the beaker. We don't describe it at a molecular level in terms of the paths taken by the molecules.

The class demo illustrates just how slow diffusion can be in a fluid – it takes about 30-40 minutes before the green colour appears in most regions of the water, and much longer than that for the original shape (such as filaments) of the colouring to disappear.

Diffusion constant

The behaviour of an individual diffusing molecule has the same form as the random walk of the previous lecture. As before, define $\mathbf{r}_{ee}$ as the displacement vector from the origin of the walk to the end-point a time t later. Suppose that the diffusing molecule travels a distance ℓ before it collides with another molecule. Then the random walk tells us that the average end-to-end displacement of the walk is

$$<\mathbf{r}_{ee}^2> = \ell^2 N \qquad (1)$$

where < .. > indicates an average and where N is the number of steps. How big is ℓ? For a gas molecule travelling fast in a dilute environment, ℓ might be very large, but for a protein moving in a crowded cell, ℓ is rather very small. If there is one step per unit time, then $N = t$ and

$$<\mathbf{r}_{ee}^2> = \ell^2 t. \qquad (2)$$

This tells us that $<\mathbf{r}_{ee}^2>$ grows linearly with time, or that the typical size of a diffusing region grows like the square root of time. Now, the units of Eq. (2) aren't quite correct, in that the left-hand-side has units of [$length^2$] while the right hand side has [$length^2$]•[*time*]. We recognize this by writing the displacement as

$$<\mathbf{r}_{ee}^2> = 6D\, t \qquad \text{(diffusion in three dimensions)} \qquad (3)$$

where D is the diffusion constant.

For most fluids, D is in the range 10^{-14} to 10^{-10} m^2/s, depending on the size of the molecule. For the ATP molecule, which is the energy currency of the cell, $D \sim 3 \times 10^{-10}$ m^2/s.

The factor of 6 is dimension-dependent. If an object diffuses in one dimension only (for example, a molecule moves randomly along a track) then

$$<\mathbf{r}_{ee}^2> = 2D\, t \qquad \text{(diffusion in one dimension)}$$

and if it is confined to a plane, such as a protein moving in the lipid bilayer of the cell's plasma membrane

$$<\mathbf{r}_{ee}^2> = 4D\, t \qquad \text{(diffusion in two dimensions)}$$

In all of these cases, D has units of [*length*]^2 / [*time*]. The reason for the 2, 4, 6 should be clear: for each direction, $<\mathbf{r}_{ee}^2>$ is equal to $2Dt$. So in two dimensions, for example

$$<\mathbf{r}_{ee}^2> = <\mathbf{r}_{ee,x}^2> + <\mathbf{r}_{ee,y}^2> = 2Dt + 2Dt = 4Dt.$$

Example How long does it take for a randomly moving protein to travel the distance of a cell diameter, say 10 μm, if its diffusion constant is 10^{-12} m^2/s?

Solving

$$t = \langle \mathbf{r}_{ee}^2 \rangle / 6D,$$

and

$$t = (10^{-5})^2 / 6 \cdot 10^{-12} = 16 \text{ seconds}$$

So it takes a protein less than a minute to diffuse across a cell at this diffusion constant; it would take much longer if the protein were large and $D \sim 10^{-14}$ m^2/s.

Einstein-Stokes equation

The diffusion constant can be determined analytically for a few specific situations. One case is the random motion of a sphere of radius R moving in a fluid of viscosity η, which Einstein solved using Stokes' Law: $F = 6\pi\eta R\, v$. We saw this formula for viscous drag back at the beginning of the course. The so-called Einstein relation reads:

$$D = k_B T / 6\pi\eta R \qquad (4)$$

where k_B is Boltzmann's constant, having the numerical value $k_B = 1.38 \times 10^{-23}$ J/K. We'll see k_B in the kinetic theory of gases in Lec. 33. At room temperature (20 °C) where $T = 293$ K, the combination

$$k_B T = 293 \cdot 1.38\text{x}10^{-23} = 4\text{x}10^{-21} \text{ J}.$$

Now, $k_B T$ is close to the mean kinetic energy of a molecule, so the Einstein equation tells us that:

*the higher the temperature, the more kinetic energy an object has, the faster it diffuses.

*the larger an object is, or the more viscous its environment, the slower it diffuses.

Example A biological cell contains internal compartments with radii in the range 0.3 to 0.5 μm. Estimate their diffusion constant.

Solution. Suppose a cellular object like a vesicle has a radius of 0.3 μm and moves in a medium with viscosity $\eta = 2\text{x}10^{-3}$ kg / m•s. At room temperature, the Einstein relation predicts

$$D = 4\text{x}10^{-21} / (6\pi \cdot 2\text{x}10^{-3} \cdot 3\text{x}10^{-7}) = 4\text{x}10^{-13} \text{ m}^2/\text{s}.$$

Rotational diffusion

Although the *translation* of a molecule – its linear motion – is the most common example of diffusion, it's not the only one. For example, a large molecule like a protein can rotate around its axis at the same time as it travels. Although this rotation could be driven with a particular angular speed ω, it could also just be random, such that ω changes in both magnitude and direction constantly and randomly. When we talk about a protein docking onto a substrate or receiving site, it may be undergoing rotational diffusion before the optimal orientation is achieved. A random "walk" in angle θ as the molecule rotates around its axis can be written as

$$<\theta^2> = 2D_r t, \qquad (5)$$

where D_r is the rotaional diffusion constant. Once again, the mean change in θ from its original value at $t = 0$ grows like the square root of the elapsed time.

For a sphere rotating in a viscous medium, there is an expression for D_r just like the translational diffusion of Eq. (4), namely

$$D_r = k_B T / 8\pi\eta R^3. \qquad (6)$$

Note the units of D, compared to D_r: the units of D_r are [*time* $^{-1}$], whereas D is [*length*^{2}]/[*time*]. Hence, the extra factor of R^2 in the denominator of Eq. (6).

Microscopic picture

As we discussed intuitively, the diffusion constant D depends on both the speed of the diffusing particle and on the distance between collisions. Using a model like the kinetic theory of gases leads to an expression for D in terms of microscopic variables, namely

$$D = v_{av}\ell /3, \qquad \text{(low density gas)} \qquad (7)$$

where

v_{av} is the mean speed of the diffusing particle

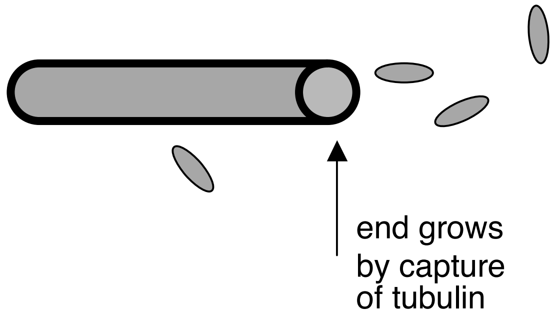
ℓ is the mean free path (i.e., the mean distance between collisions.

It's easy to verify that the units are correct.

Biological applications

We have alluded to several molecular effects of diffusion in biology, namely the random translation and rotation of proteins. There are *many* other examples, as are described in Howard Berg's book *Random Walks in Biology*. Among other important biological techniques, Berg describes sedimentation in a centrifuge and electrophoresis.

Although we've tended to describe diffusion mathematically in terms of an object moving *away* from its original location, it is also important to describe the *capture* of randomly moving molecules. For example, a growing cellular filament like a microtubule captures its protein building blocks (tubulin) from its environment:



In this case, one is interested in the rate at which a collection of randomly diffusing molecules strikes the growing end of the microtubule. See Berg's book for more details.