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 a single particle ~~are~~ over a collection of The same kind of particles. Then

$$\frac{1}{2} m \langle v_x^2 \rangle = \frac{1}{2} kT$$ so particle has RMS velocity

$$\langle v_x^2 \rangle^{1/2} = \sqrt{\frac{kT}{m}}$$

How big is this? Say for hemoglobin

Hemoglobin has molecular weight 64,500 Daltons or 64.5 kDa which means That one mole of hemoglobin has mass 64,500 grams. Since there are approx. $6(10)^{23}$ molecules of any substance in a mole of That substance, each hemoglobin molecule has a mass $m_h = \frac{6.45(10)^4 g}{6(10)^{23}} \approx 10^{-19} g$.

At room temp, $T \approx 300°K$ and $kT = 4.14(10)^{-14}$ dyne-cm $= 4.14(10)^{-14} \frac{g\,cm^2}{sec^2}$, so for hemoglobin

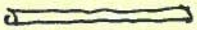
$$\langle v_x^2 \rangle^{1/2} \approx \left(\frac{4(10)^{-14}}{10^{-19}} \right)^{1/2} \frac{cm}{sec} \approx 6(10)^2 \frac{cm}{sec}$$

$$= 6 \text{ m/sec!}$$

If there was nothing in The way, The hemoglobin molecule in a tank of water The size of This room would zip across the room in about 1 sec. But in water, The hemoglobin molecule wouldn't go far before bumping into a H_2O molecule and changing direction. So it keeps changing direction and so wanders about doing what is called a random walk. The typical distance the molecule moves between collisions is 10^{-9} cm, and the molecule makes about 10^{12} collisions/sec.!

Molecular View of Diffusion

We imagine there is a distribution of particles (molecules) along the x-axis and that the particles undergo a random walk. Each particle takes a step Δx to the right, Δx to the left, or sits still every τ time units. Motion in a thin tube:

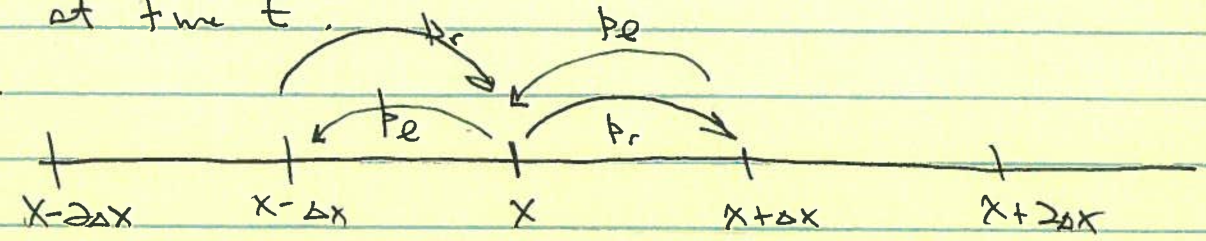


① Suppose probability that particle steps right is p_r and probability it steps left is p_ℓ. So prob. it sits still is $1-(p_r+p_\ell)$.

② We suppose that the step a particle takes in a time step has nothing to do with (ie is independent of) its previous steps.

③ We suppose each particle's steps are independent of each other particle's steps.

Let $N(x,t)$ be the # of particles per unit volume at location x at time t. Then $N(x,t)A\Delta x$ is the # of particles between $x-\frac{\Delta x}{2}$ and $x+\frac{\Delta x}{2}$ at time t.



$$
\begin{aligned}
N(x,t+\tau)A\Delta x &= N(x,t)A\Delta x \\
&\quad + p_r N(x-\Delta x,t)A\Delta x + p_\ell N(x+\Delta x,t)A\Delta x \\
&\quad - p_r N(x,t)A\Delta x - p_\ell N(x,t)A\Delta x .
\end{aligned}
$$

Divide by $A\Delta x$ and rearrange –

$$(\ddagger)\quad \left[\begin{array}{l} N(x, t+\tau) - N(x,t) = \\ \qquad p_r N(x-\Delta x, t) - (p_\ell + p_r) N(x,t) + p_\ell N(x+\Delta x, t) \end{array}\right.$$

This tells us how N changes at each pt x and time t.

Δx and τ are small numbers. We can approx. N(x, t+τ) by its Taylor series about (x,t). Similarly, we can approx N(x ± Δx, t) by their Taylor series about (x, t).

$$N(x, t+\tau) = N(x,t) + N_t(x,t)\tau + \frac{1}{2} N_{tt}(x,t)\tau^2 + \cdots$$

$$N(x+\Delta x, t) = N(x,t) + N_x(x,t)\Delta x + \frac{1}{2} N_{xx}(x,t)(\Delta x)^2 + \frac{1}{6} N_{xxx}(x,t)(\Delta x)^3 + \frac{1}{24} N_{xxxx}(x,t)(\Delta x)^4 + \cdots$$

$$N(x-\Delta x, t) = N(x,t) + N_x(x,t)(-\Delta x) + \frac{1}{2} N_{xx}(x,t)(-\Delta x)^2 + \frac{1}{6} N_{xxx}(x,t)(-\Delta x)^3 + \frac{1}{24} N_{xxxx}(x,t)(-\Delta x)^4 + \cdots$$

Substitute these into (‡) to get:

$$N_t(x,t)\tau + \frac{1}{2} N_{tt}(x,t)\tau^2 + \cdots$$

$$= p_r \Big\{ N(x,t) - N_x(x,t)\Delta x + \frac{1}{2} N_{xx}(x,t)(\Delta x)^2 - \frac{1}{6} N_{xxx}(x,t)\Delta x^3$$

$$+ \frac{1}{24} N_{xxxx}(x,t)(\Delta x)^4 + \cdots \Big\} - (p_\ell + p_r) N(x,t)$$

$$+ p_\ell \Big\{ N(x,t) + N_x(x,t)\Delta x + \frac{1}{2} N_{xx}(x,t)(\Delta x)^2 + \frac{1}{6} N_{xxx}(x,t)(\Delta x)^3$$

$$+ \frac{1}{24} N_{xxxx}(x,t)(\Delta x)^4 + \cdots \Big\}$$

$$\Rightarrow N_t \tau + \tfrac{1}{2} N_{tt}\tau^2 + \cdots = \cancelto{0}{\left(p_r - (p_\ell + p_r) + p_\ell\right)} N(x,t)$$

$$+ (-p_r + p_\ell) N_x(x,t)\Delta x + \tfrac{1}{2}(p_\ell + p_r) N_{xx}(x,t)(\Delta x)^2$$

$$+ \cdots$$

Suppose a particle has an equal chance of moving left and moving right, so $\underline{\underline{p_\ell = p_r \equiv p \leq \frac{1}{2}}}$

The coefficient of the N_x term then is 0. Divide resulting equation by τ and factor out $\frac{(\Delta x)^2}{2}(2p)$ on RHS to get:

$$N_t + \tfrac{1}{2}\tau N_{tt} + O(\tau^2) = \text{[illegible]}$$

$$= \frac{(\Delta x)^2}{2\tau}(2p)\left\{ \cancel{2p}\, N_{xx}(x,t) + \frac{1}{12}(\Delta x)^2 N_{xxxx}(x,t) + \cdots \right\}$$

Now, let $\boxed{\mathcal{D} = \frac{(\Delta x)^2}{2\tau}(2p)}$

Imagine $\tau \to 0$ and $\Delta x \to 0$, but this happens in such a way that $\mathcal{D}$ is constant. The equation we get for $N(x,t)$ is

$$\left[\quad N_t(x,t) = \mathcal{D}\, N_{xx}(x,t) \quad\right]$$

the 1D-diffusion eq again.

What if $p_\ell \neq p_r$? We then have the eq.

$$N_t + \frac{1}{2}\tau N_{tt} + \dots = \frac{(p_\ell - p_r)\Delta x}{\tau} N_x + \frac{(p_\ell + p_r)(\Delta x)^2}{2\tau} N_{xx} + \dots$$

So

If p_ℓ and p_r are assumed to be constants, independent of Δx and τ, we have a problem if we let $\tau \to 0$, $\Delta x \to 0$ with $(\Delta x)^2/\tau$ constant as before. Because if $\frac{(\Delta x)^2}{\tau} = C$, say, then $\frac{\Delta x}{\tau} = \frac{C}{\Delta x}$, so the coefficient of N_x, $(p_\ell - p_r)\frac{C}{\Delta x} \to \infty$ as $\Delta x \to 0$.

Suppose that p_ℓ and p_r are close to equal

$$p_r = p + a\Delta x \; ; \; p_\ell = p + b\Delta x$$

Then $p_\ell - p_r = (p + b\Delta x) - (p + a\Delta x) = (b-a)\Delta x$

and so

$$N_t + \frac{1}{2}\tau N_{tt} + \dots = (b-a)\frac{(\Delta x)^2}{\tau} N_x + \frac{(2p+a+b)(\Delta x)^2}{\tau} N_{xx} + \dots$$

If $\Delta x \to 0$ and $\tau \to 0$ with $\frac{\Delta x^2}{\tau} = C$, then the PDE we get is:

$$N_t = \left[(b-a)C\right] N_x + \left[(2p+a+b)C\right] N_{xx}$$

Diffusion coefficient $(2p+a+b)\frac{(\Delta x)^2}{\tau}$

and "drift" coefficient $(b-a)\frac{(\Delta x)^2}{\tau}$.