Biophysics I (BPHS 4080)

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Website: http://www.yorku.ca/cberge/4080W2018.html
According to wikipedia....
Diffusion

- According to wikipedia....

- According to the dictionary....

nomen
1. act of diffusing; state of being diffused.
2. prolixity of speech or writing; discursiveness.
3. Physics.
   a. Also called migration. an intermingling of molecules, ions, etc., resulting from random thermal agitation, as in the dispersion of a vapor in air.
   b. a reflection or refraction of light or other electromagnetic radiation from an irregular surface or an erratic dispersion through a surface; scattering.
4. Movies. a soft-focus effect resulting from placing a gelatin or silk plate in front of a studio light or a camera lens, or through the use of diffusion filters.
5. Meteorology. the spreading of atmospheric constituents or properties by turbulent motion as well as molecular motion of the air.
6. Anthropology, Sociology. Also called cultural diffusion. the transmission of elements or features of one culture to another.
Diffusion
Chapter 1

Diffusion: Microscopic Theory

Diffusion is the random migration of molecules or small particles arising from motion due to thermal energy. A particle at absolute temperature $T$ has, on the average, a kinetic energy associated with movement along each axis of $kT/2$, where $k$ is Boltzmann’s constant. Einstein showed in 1905 that this is true regardless of the size of the particle, even for particles large enough to be seen under a microscope, i.e., particles that exhibit Brownian movement. A particle of mass $m$ and velocity $v_x$ on the $x$ axis has a kinetic energy $mv_x^2/2$. This quantity fluctuates, but on the average $\langle mv_x^2/2 \rangle = kT/2$, where $\langle \rangle$ denotes an average over time or over an ensemble of similar particles. From this relationship we compute the mean-square velocity,

$$\langle v_x^2 \rangle = kT/m,$$  \hfill (1.1)

and the root-mean-square velocity,

$$\langle v_x^2 \rangle^{1/2} = (kT/m)^{1/2}.$$  \hfill (1.2)

We can use Eq. 1.2 to estimate the instantaneous velocity of a small particle, for example, a molecule of the protein lysozyme. Lysozyme has a molecular weight $1.4 \times 10^4$ g. This is the mass of one mole, or $6.0 \times 10^{23}$ molecules; the mass of one molecule is $m = 2.3 \times 10^{-20}$ g. The value of $kT$ at 300°C (273°C) is $4.14 \times 10^{-14}$ g cm$^2$/sec$^2$. Therefore, $\langle v_x^2 \rangle^{1/2} = 1.3 \times 10^3$ cm/sec. This is a sizeable speed. If there were no obstructions, the molecule would cross a typical classroom in about 1 second. Since the protein is not in a vacuum but is immersed in an aqueous medium, it does not go very far before it bumps into molecules of
Some (remarkably deep) ideas right off the bat:

- Random walkers
- Temperature, Boltzmann’s constant
- Einstein and 1905
- Mean-squared velocity, “ensemble”
- “Brownian movement”
- “Microscopic theory” (ch. 2 is “Macroscopic theory”)

→ A kernel of a deep idea is here, the distinction between “lots of little things” versus “big things”
Brownian motion

http://www.microscopy-uk.org.uk/dww/home/hombrown.htm
Diffusion

Each particle undergoes Brownian motion.
Diffusion (1-D)

- Thomas Graham (Scottish chemist, ~1828-1833)
  [pioneered the concept of dialysis]

- Adolf Fick (German physiologist, ~1855)
  [actually was the first to successfully put a contact lens on a person in 1888!]
“A few years ago, Graham published an extensive investigation on the diffusion of salts in water, in which he more especially compared the diffusibility of different salts. It appears to me a matter of regret, however, that in such an exceedingly valuable and extensive investigation, the development of a fundamental law, for the operation of diffusion in a single element of space, was neglected, and I have therefore endeavoured to supply this omission.”

- A. Fick (1855)
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- A. Fick (1855)
Concentration - of solute in solution \([mol/m^3]\)

Flux - net # of moles crossing per unit time \(t\) through a unit area perpendicular to the \(x\)-axis \([mol/m^2 \cdot s]\)

Position \([m]\), Time \([s]\)

**Diffusion (1-D)**

From Graham’s observations (~1830):

\[c(x, t)\]

\[\phi(x, t)\]
Short Excursion: Microscopic Basis for Diffusion

Brownian motion $\Rightarrow$ ‘Random Walker’ (1-D)

Ensemble of Random Walkers
Fick’s 1st Law (1-D)

\[ \phi(x, t) \propto -\frac{\partial c(x, t)}{\partial x} \]
**Diffusion Constant \( (D) \)**

\[
\phi(x, t) \propto -\frac{\partial c(x, t)}{\partial x}
\]

- diffusion constant is always positive (i.e., \( D > 0 \))
- determines time it takes solute to diffuse a given distance in a medium
- depends upon both solute and medium (solution)
- **Stokes-Einstein relation** predicts that \( D \) is inversely proportional to solute molecular radius
Diffusion Constant ($D$)

$t = 1$

$t = 50$

smaller $D$

larger $D$
Generalizations

**Higher Dimensions:**

\[
\phi(x, t) = -D \frac{\partial c(x, t)}{\partial x} \quad \longleftrightarrow \quad \vec{\phi} = -D \nabla c
\]

where \( \nabla c = \hat{x} \frac{\partial c}{\partial x} + \hat{y} \frac{\partial c}{\partial y} + \hat{z} \frac{\partial c}{\partial z} = \text{grad}(c) \)

**Analogous Flux Laws:**

- **Heat Flow (Fourier):**
  \[
  \phi_h = -\sigma_h \frac{\partial T}{\partial x}
  \]
  heat flow, thermal conductivity, and temperature

- **Electric Conduction (Ohm):**
  \[
  J = -\sigma_e \frac{\partial \psi}{\partial x}
  \]
  current density, electrical conductivity, and electric potential

- **Convection (Darcy):**
  \[
  \Phi_v = -\kappa \frac{\partial p}{\partial x}
  \]
  fluid flow, hydraulic permeability, and pressure

- **Diffusion (Fick):**
  \[
  \phi = -D \frac{\partial c}{\partial x}
  \]
Imagine a cube (with face area $A$ and length $\Delta x$) and a time interval $\Delta t$

\[ A \Delta t \phi(x, t) = A \Delta x \ c(x, t) \]

Solute entering from left - solute exiting from right (during time interval $[t, t+\Delta t]$) = change in amount of solute inside cube (during time interval $[t, t+\Delta t]$)
solute entering from left - solute exiting from right
(during time interval \([t, t + \Delta t]\) )

\[ \text{change in amount of solute inside cube (during time interval \([t, t + \Delta t]\) )} \]

\[ A \Delta t \phi(x, t + \Delta t/2) - A \Delta t \phi(x + \Delta x, t + \Delta t/2) = A \Delta x c(x + \Delta x/2, t + \Delta t) - A \Delta x c(x + \Delta x/2, t) \]

\[ \frac{\phi(x + \Delta x, t + \Delta t/2) - \phi(x, t + \Delta t/2)}{\Delta x} = \frac{c(x + \Delta x/2, t + \Delta t) - c(x + \Delta x/2, t)}{\Delta t} \]
\[
- \frac{\phi(x + \Delta x, t + \Delta t/2) - \phi(x, t + \Delta t/2)}{\Delta x} = \frac{c(x + \Delta x/2, t + \Delta t) - c(x + \Delta x/2, t)}{\Delta t}
\]

\[
\lim_{\Delta t, \Delta x \to 0} \quad \implies \quad \frac{\partial \phi}{\partial x} = -\frac{\partial c}{\partial t}
\]

\[
\Rightarrow \text{conservation of mass within the context of our imaginary cube yielded the \textit{continuity equation}}
\]
1. Fick’s First Law: \[ \phi = -D \frac{\partial c}{\partial x} \]

2. Continuity Equation: \[ \frac{\partial \phi}{\partial x} = -\frac{\partial c}{\partial t} \]

\( \frac{\partial c}{\partial t} = D \frac{\partial^2 c}{\partial x^2} \) (Fick’s Second Law)
1. **Equilibrium**: Zero flux and concentration is independent of time

\[
\frac{\partial \phi}{\partial x} = 0 \quad \Rightarrow \quad \int \phi_0 \, dx = \int -D \, dc \quad \Rightarrow \quad c(x) = c(x_0) - \frac{\phi_0}{D} (x - x_0)
\]

[integrate Fick’s 1st Law]

D ≠ 0 ⇒ concentration is independent of space and time

D = 0 ⇒ non-diffusible solute is automatically at equilibrium

2. **Steady-state**: Flux can be non-zero, but flux and concentration are independent of time

\[
\frac{\partial \phi}{\partial x} = 0 \quad \Rightarrow \quad \int \phi_0 \, dx = \int -D \, dc \quad \Rightarrow \quad c(x) = c(x_0) - \frac{\phi_0}{D} (x - x_0)
\]

[x₀ is a reference location where the concentration is known]

\[c(x)\]

\[c(x_0)\]

\[-\frac{\phi_0}{D}\]
3. Impulse Response: Point-source of particles \( (n_0 \text{ mol/cm}^2) \) at \( t = 0 \) and \( x = 0 \)

[Dirac delta function \( \delta(x) \)]

Given the initial/boundary conditions:

\[
c(x, t) = n_0 \delta(x) \quad \text{at} \quad t = 0 \quad \text{where} \quad \int_{-\infty}^{\infty} \delta(x) \, dx = 1
\]

Need to solve:

\[
\frac{\partial c}{\partial t} = D \frac{\partial^2 c}{\partial x^2}
\]

[Aside: solution can be found by a # of different methods, one being by separation of variables and using a Fourier transform]

\[
c(x, t) = \frac{n_0}{\sqrt{4\pi Dt}} e^{-x^2 / 4Dt}
\]

Solution (for \( t > 0 \))
solution to diffusion equation!

\[ f(x, y) = \frac{1}{\sqrt{y}} e^{-x^2/y} \]
Importance of Scale

\[ c(x, t) = \frac{n_0}{\sqrt{4\pi D t}} e^{-x^2/4D t} \]

Gaussian function with zero mean and standard deviation:

\[ \sigma = \sqrt{2D t} \]

Question: How long does it take \((t_{1/2})\) for \(\sim 1/2\) the solute to move at least the distance \(x_{1/2}\)?

\[ \frac{x_{1/2}}{\sqrt{2D t_{1/2}}} \approx \frac{2}{3} \implies t_{1/2} \approx \frac{x_{1/2}^2}{D} \]

For small solutes (e.g. \(K^+\) at body temperature)

\[ D \approx 10^{-5} \ \frac{\text{cm}^2}{\text{s}} \]

<table>
<thead>
<tr>
<th>Size</th>
<th>(x_{1/2})</th>
<th>(t_{1/2})</th>
</tr>
</thead>
<tbody>
<tr>
<td>membrane sized</td>
<td>10 nm</td>
<td>(\frac{1}{10} \ \mu\text{sec})</td>
</tr>
<tr>
<td>cell sized</td>
<td>10 \ \mu\text{m}</td>
<td>(\frac{1}{10} \ \text{sec})</td>
</tr>
<tr>
<td>dime sized</td>
<td>10 \ \text{mm}</td>
<td>(10^6 \ \text{sec} = 1 \ \text{day})</td>
</tr>
</tbody>
</table>
Exercise

At a junction between two neurons, called a synapse, there is a 20 nm cleft that separates the cell membranes. A chemical transmitter substance is released by one cell (the pre-synaptic cell), diffuses across the cleft, and arrives at the membrane of the other (post-synaptic) cell. Assume that the diffusion coefficient of the chemical transmitter substance is \( D = 5 \times 10^{-6} \text{ cm}^2/\text{s} \).

→ Make a rough estimate of the delay caused by diffusion of the transmitter substance across the cleft. What are the limitations of this estimate? Explain.
Exercise

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Answer

Consider the time it takes for \( \frac{1}{2} \) to cross the cleft, then we have approximately 1 us (1 \( \times \) 10\(^{-6}\) s). However, this calculation:

- Ignores the cleft geometry (e.g., not infinite baths)
- There is nothing special about \( \frac{1}{2} \) the solute here (perhaps only a few molecules are needed, or perhaps a lot are)
Exercise

To wiggle your big toe, neural messages travel along a single neuron that stretches from the base of your spine to your toe. Assume that the membrane of this neuron can be represented as a uniform cylindrical shell that encloses the intracellular environment, which is represented as a simple saline solution. The diameter of the shell is 10 μm and the length is 1 m. Assume that $10^{-15}$ moles of dye are injected into the neuron at time $t = 0$ and at a point located in the center of the neuron, which we will refer to as the point $z = 0$. Assume that the dye diffuses across the radial dimension so quickly that the concentration of dye $c(z,t)$ depends only on the longitudinal direction $z$ and time $t$. Assume that the diffusivity of the dye in the intracellular saline is $D = 10^{-7}$ cm$^2$/s and that the membrane is impermeant to the dye.

→ Determine the amount of time $t_1$ required for 5% the injected dye to diffuse to points outside the region $-1$ mm $< z < 1$ mm.

→ Determine the amount of time $t_2$ required for half the injected dye to diffuse to points outside the region $-1$ mm $< z < 1$ mm. Determine the ratio of $t_2$ to $t_1$. Briefly explain the physical significance of this result.

→ Determine the amount of time $t_3$ required for 5% the injected dye to diffuse to points outside the region $-10$ mm $< z < 10$ mm. Determine the ratio of $t_3$ to $t_1$. Briefly explain the physical significance of this result.
Answers

→ Determine the amount of time $t_1$ required for 5% the injected dye to diffuse to points outside the region $-1 \, \text{mm} < z < 1 \, \text{mm}$.

3.5 hours

→ Determine the amount of time $t_2$ required for half the injected dye to diffuse to points outside the region $-1 \, \text{mm} < z < 1 \, \text{mm}$. Determine the ratio of $t_2$ to $t_1$. Briefly explain the physical significance of this result.

1.3 days

→ Determine the amount of time $t_3$ required for 5% the injected dye to diffuse to points outside the region $-10 \, \text{mm} < z < 10 \, \text{mm}$. Determine the ratio of $t_3$ to $t_1$. Briefly explain the physical significance of this result.

14.5 days
Exercise

To wiggle your big toe, neural messages travel along a single neuron that stretches from the base of your spine to your toe. Assume that the membrane of this neuron can be represented as a uniform cylindrical shell that encloses the intracellular environment, which is represented as a simple saline solution. The diameter of the shell is 10 μm and the length is 1 m. Assume that $10^{-15}$ moles of dye are injected into the neuron at time $t = 0$ and at a point located in the center of the neuron, which we will refer to as the point $z = 0$. Assume that the dye diffuses across the radial dimension so quickly that the concentration of dye $c(z,t)$ depends only on the longitudinal direction $z$ and time $t$. Assume that the diffusivity of the dye in the intracellular saline is $D = 10^{-7}$ cm$^2$/s and that the membrane is impermeant to the dye.

The following plot shows the concentration of dye as a function of time for a particular point at $z0 > 0$.

$\rightarrow$ Determine $z0$. 