Physical Sciences 2: Assignments for Nov. 19 – Dec. 1
Homework #10: Statistical Mechanics, Brownian Motion, and Diffusion
Due Friday, Dec. 4 at 5:00 pm

After completing this homework, you should be able to…

• Interpret the meaning of the Boltzmann distribution and describe its applicability
• Describe how temperature affects the Boltzmann distribution
• Explain the connection between Brownian motion and random walks
• Explain how to use a random walk to model Brownian motion
• Show that the mean square displacement is linear in time and directly proportional to the diffusion coefficient
• Understand how the diffusion coefficient indicates how long it takes a molecule or particle in solution to move a given distance
• Use the Stokes-Einstein equation to predict the diffusion coefficient
• Explain how random microscopic motion leads to macroscopic flux (via Fick’s law)
• Understand and be able to use Fick’s first law to describe how flux relates to a concentration gradient
• Understand and be able to use Fick’s second law to describe how concentration changes with respect to both time and space
• Explain why and how concentration gradients relax over time
Boltzmann Distribution
- valid only at thermal equilibrium and for any conservative force
- gives the ratio of the probabilities that a particle will be in a given state compared to another state

\[
\frac{\text{Probability of being in state } 2}{\text{Probability of being in state } 1} = e^{\frac{(U_2 - U_1)}{k_B T}}
\]

* for gravitational force, \( U_2 = mg(h_2) \) and \( U_1 = mg(h) \), so this becomes

\[
\frac{\text{Prob}(2)}{\text{Prob}(1)} = e^{\frac{-mg(h_2 - h)}{k_B T}}
\]

Random Walk
- used to model Brownian motion
- particle has an equal probability of moving to the left or right a distance \( \delta \) (one dimension)
- \( \langle x \rangle \) is the average displacement
  - \( \langle x \rangle = 0 \) since Prob(move left) = Prob(move right)
- \( \langle x^2 \rangle \) is the mean square displacement; this is the actual distance traveled by the particle
  - \( \langle x^2 \rangle = n \delta^2 \), where \( n \) is the number of steps taken and \( \delta \) is the step size

Diffusion
- diffusion coefficient is defined in terms of mean square displacement and total elapsed time \( t \)

\[
\langle x^2 \rangle = 2D t \quad \text{(one dimension)}
\]
- can also be written in terms of step size \( \delta \) and the time \( t \) required for one step

\[
\langle x^2 \rangle = n \delta^2 = 2D t
\]

* NOTE:
  - \( t \) - time for entire random walk
  - \( \tau \) - time for one step

- in 2D: \( \langle x^2 + y^2 \rangle = 4D t \)
- in 3D: \( \langle x^2 + y^2 + z^2 \rangle = 6D t \)
Einstein–Smoluchowski Equation

- This equation relates the diffusion coefficient $D$, drag coefficient $f$, and temperature $T$:

$$Df = k_BT$$

Stokes–Einstein Equation

- Stoke's equation is an expression for the drag force on spherical particles:

$$F_{drag} = 6\pi\eta R \cdot v$$

- Equating this with the general form for a drag force ($F_{drag} = f \cdot v$) gives an expression for $f$:

$$f = 6\pi\eta R \cdot v = f \cdot v$$

- Substituting this result into the Einstein–Smoluchowski equation above yields the Stokes–Einstein equation:

$$D(6\pi\eta R) = k_BT$$

$$D = \frac{k_BT}{6\pi\eta R}$$

Fick's 1st Law

- Relates flux to concentration:

$$J_x = -D \frac{dc}{dx}$$

- Flux $J_x$ is defined as the number of particles passing through some area $A$ in some time $dt$:

$$J_x = \frac{N}{A \cdot dt}$$

Fick's 2nd Law

- Tells how concentration changes with respect to time and space:

$$\frac{dc}{dt} = D \frac{d^2c}{dx^2}$$

- Qualitative understanding only: given a graph of concentration vs. position, determine if concentration will increase or decrease (i.e. if graph has positive concavity, $\frac{d^2c}{dx^2} > 0$ and so $\frac{dc}{dt} > 0$ and concentration increases).
1. **Long axons (5 pts).** The longest cells in the human body are the nerve cells whose cell bodies are located in the base of your spinal cord and whose axons run down to the ends of your toes: these cells are approximately $L = 1$ meter long. Treat the axon as a cylinder with a radius of $r = 1 \ \mu m$.

   a) Consider a neurotransmitter packaged in a spherical vesicle with a radius of $10$ nm. Estimate its diffusion constant. (Assume that the viscosity inside the axon is roughly $\eta = 6 \times 10^{-3} \ \text{kg/m/s}$.)

   We use the Stokes-Einstein equation with a body temperature of about $310 \ \text{K}$ for $T$:
   
   $$D = \frac{kT}{6\pi\eta R} = \frac{(1.38 \times 10^{-23} \ \text{J/K})(310 \ \text{K})}{6\pi (6 \times 10^{-3} \ \text{Pa} \cdot \text{s})(10^{-8} \ \text{m})} = 4 \times 10^{-12} \ \text{m}^2/\text{s}.$$  

   b) Under passive diffusion, how long would it take on average for this package to move from the cell body to the end of the axon? Is diffusion a reasonable method for transport in this case?

   The package has to move in a specific direction, so we need to apply the equation for 1d diffusion. If we plug in $1 \ \text{m}$ for $y_{\text{RMS}}$ and the given diffusion constant, we get a time of
   
   $$t = \frac{y_{\text{RMS}}^2}{2D} = \frac{(1 \ \text{m})^2}{2(4 \times 10^{-12} \ \text{m}^2/\text{s})} = 1.3 \times 10^{11} \ \text{s}.$$  

   How long is that? About $4,000$ years. In other words, it’s not a good idea to wait around for passive diffusion to move things around on the scale of a meter. Luckily, complex organisms have developed active transport techniques for large-scale movement.

   Suppose that the cell body manufactures these neurotransmitters such that the concentration at the top of the axon is kept constant at $c_0 = 1 \ \text{mM}$ (1 millimolar, i.e. $10^{-3}$ moles per liter). At the bottom of the axon, the neurotransmitter is consumed at a steady rate, so that its concentration is zero.

   c) Assuming that the concentration decreases linearly from the cell body ($y = L$) to the bottom of the axon ($y = 0$), write an expression for $c(y)$, the concentration of the neurotransmitter as a function of position.

   The function $c(y)$ is a linear function satisfying $c(L) = c_0$ and $c(0) = 0$. From this information we can write down the correct answer by inspection:
   
   $$c(y) = c_0 \left( \frac{y}{L} \right).$$  

   You can see from the form of this function that a) $c(y)$ is linear, and b) it has the correct values at the endpoints, $c(0) = 0$ and $c(L) = c_0$. There is only one line that passes through two different given points, so this must be the correct answer. Another approach is to notice that the $y$-intercept is 0, and the slope is $c_0/L$ (over the “run” from 0 to $L$, the “rise” is $c_0$). So the equation for the line is
\[ c(y) = 0 + \left( \frac{c_0}{L} \right) y, \]

which is equivalent to the boxed answer above.

d) Calculate the flux (in molecules per unit area per unit time) of neurotransmitter at the bottom of the axon.

The flux is given by Fick’s first equation:

\[ J_y = -D \frac{dc}{dy} = -D \left( \frac{c_0}{L} \right) = -4 \times 10^{-12} \text{ mol/m}^2 \cdot \text{s} = \boxed{-2 \times 10^{12} \text{ molecules/m}^2 \cdot \text{s}}. \]

where we have used the slope of \( c(y) \) for the concentration gradient \( dc/dy \). \( J_y \) is negative, indicating that the net movement of neurotransmitter molecules is towards smaller \( y \) (down the axon length towards the toes).

e) To send a signal to a muscle cell, the bottom of the axon must release about \( 3 \times 10^6 \) molecules of the neurotransmitter. If the axon relied on diffusion alone, how often could the neuron send a signal?

The number of molecules that are consumed at the bottom of the axon each second is the flux multiplied by the cross-sectional area of the axon:

\[ J_y A = \left( -2 \times 10^{12} \text{ molecules/m}^2 \cdot \text{s} \right) \pi \left( 10^{-6} \text{ m} \right)^2 = -7 \text{ molecules/s}. \]

In order to get \( 3 \times 10^6 \) molecules, you’d have to wait for \( 4 \times 10^5 \) seconds, which is about 5 days. This reinforces the idea that passive diffusion is not the most efficient way to transport things over macroscopic length scales.

2. The diffusion equation (1 pts). Suppose that the concentration of a solute as a function of position at a particular time is given by the graph below. Re-draw that graph, and superimpose on it a graph of the concentration a short time later.

![Graph of concentration vs position](image)

The diffusion equation says that
\[ \frac{dc}{dt} = D \frac{d^2c}{dx^2}. \]

So the concentration will increase at the places where \( c(x) \) is concave up (positive \( d^2c/dx^2 \)), and decrease where it is concave down. We’ll mark the points where the concavity changes (known as inflection points, where \( d^2c/dx^2 = 0 \)) with a dot in the diagram below. The red curve is what the concentration might look like a short time later.

As you can see, diffusion causes the “peaks” to come down and the “valleys” to come up. If we wait long enough, the concentration will become completely uniform.

3. **Vacuoles (3 pts)**. We can model a vacuole as a sphere of radius \( r \) surrounded by a very thin semi-permeable membrane of thickness \( w \). A particular enzyme can diffuse across the membrane with diffusion constant \( D \). At \( t = 0 \), the concentration of the enzyme in the vacuole is \( c_0 \). Assume that the enzymes are distributed uniformly throughout the interior of the vacuole, and that the outside world is large enough that the enzyme concentration outside the vacuole is always essentially zero.

a) Find an expression for \( J \), the flux of enzyme molecules across the vacuole membrane, in terms of \( D \), \( w \), and \( c \). Use the sign convention that positive values of \( J \) correspond to a net outflux of enzyme molecules.

\[
J = -D \frac{c_{\text{out}} - c_{\text{in}}}{w} = -D \frac{0 - c(t)}{w}
\]

\[
J = \frac{Dc(t)}{w}
\]

b) Let \( N(t) \) be the total number of enzyme molecules inside the vacuole as a function of time. Derive an expression for the derivative \( dN/dt \) in terms of \( r \) and \( J \). What is the physical interpretation of \( dN/dt \)?

\( dN/dt \) is the time rate of change of \( N \); a positive value indicates that \( N \) is increasing, and a negative one indicates that \( N \) is decreasing. We know from part a) that there is a net flux of
enzyme molecules out of the vacuole (because $J$ is positive). In fact, the number of enzyme molecules leaving the vacuole each second is just $J$ times the surface area of the vacuole membrane. This quantity corresponds to minus $dN/dt$, so $dN/dt$ is minus the number of enzyme molecules leaving the vacuole per unit time, and can be expressed as

$$\frac{dN}{dt} = -4\pi r^2 J.$$ 

\[d)\text{ Combining the results of parts a) and c) yields a differential equation for } c(t). \text{ Show that } c(t) = c_0 e^{-t/\tau} \text{ is a solution to this equation, where } \tau \text{ is a constant. Determine the value of } \tau \text{ in terms of } D, r, \text{ and } w.\]

Taking the result of part c) and plugging in $J = \frac{Dc(t)}{w}$ gives

$$\frac{D}{w} c(t) = -\frac{r}{3} \frac{dc}{dt} \text{ gives }$$

$$\frac{dc}{dt} = -\frac{3D}{r w} c(t).$$

This is a differential equation. Recall the two best ways of solving a differential equation:

1. Know the answer already
2. Guess the answer, and plug it in to check if it works

Here, we’re using method 2, and the guess has already been given to us: $c(t) = c_0 e^{-t/\tau}$, with $\tau$ as a free parameter. To plug it into the differential equation for $c(t)$, we need to use the chain rule to evaluate the derivative:
\[
\frac{dc}{dt} = c_0 e^{-t/\tau} \left( \frac{-1}{\tau} \right)
\]
\[
= -\frac{1}{\tau} c(t).
\]
Comparing this to the differential equation above, \( c(t) \) will satisfy the equation for all \( t \) if (and only if)
\[
\frac{3D}{rw} = \frac{1}{\tau}.
\]
Solving for \( \tau \), we get
\[
\tau = \frac{rw}{3D}.
\]

4. Take a Walk (1 pt) Suppose you embark on an unbiased random walk along a straight line (1 dimension) and take 4 steps, each of length 1 ft.

a) What is your average displacement?
Because the walk is unbiased, the probability of taking a step to the right is equal to the probability of taking a step to the left. Therefore, the average displacement will be equal to zero:
\[
< x > = 0
\]

b) What is your mean square displacement?
The mean square displacement is defined as the number of steps multiplied by the square of the step size. We have a step size of 1 ft and take a total of 4 steps. This means the mean square displacement will be
\[
< x^2 > = n\delta^2 = 4 \times (1\text{ft})^2 = 4\text{ ft}^2
\]

c) If each step took you 1 minute and you moved under the influence of diffusion, what would your diffusion constant be?
The diffusion constant can be found based on the total time for the walk, \( t \), and the mean square displacement, \( < x^2 > \), via
\[
D = \frac{< x^2 >}{2t} = \frac{4\text{ ft}^2}{2 \times (4\text{ min})} = 0.5\frac{\text{ft}^2}{\text{min}}
\]

d) What is the probability that your walk will end a distance greater than 2 ft from your starting location? Hint: there are 16 possible, unique walks of 4 steps.
To answer this question, we will first list all possible random walks of 4 steps. We will define a step to the right to be positive and a step to the left to be negative. In the following chart, “+” denotes a step to the right and “-” denotes a step to the left. The last column tells us how many steps we are from our starting location.
As we can see from the table, there are only 2 walks that take us beyond 2 ft from the starting location. These are when we take either 4 steps to the right or 4 steps to the left. The probability of ending more than 2 ft from the starting location is therefore

\[
\frac{2 \text{ walks}}{16 \text{ possibilities}} = \frac{2}{16} = \frac{1}{8} = 0.125
\]

e) What is the probability that your walk will end exactly where you started? Hint: there are 16 possible, unique walks of 4 steps.

Looking at the above table, we see that 6 of the 16 possible walks end 0 ft from the starting location. This means the probability of this occurring is

\[
\frac{6 \text{ walks}}{16 \text{ possibilities}} = \frac{3}{8} = 0.375
\]