# Biology 3550: Physical Principles in Biology
# Fall Semester - 2017

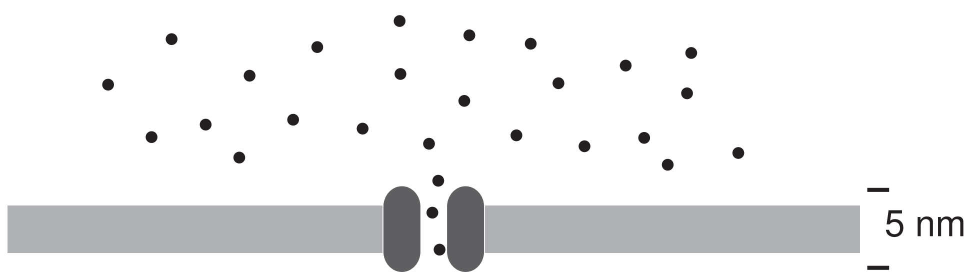
## Problem Set 3

Due: Monday, 16 October, by 11:59 PM. To be submitted as a pdf file via Canvas.

Important note: Work submitted in file formats other than pdf (such as Microsoft Word) will not be graded!

Be sure to show your work and use the proper units. You are encouraged to consult one another, or other resources, but the work that you hand in must be your own!

1. All cells, and the compartments within cells, are bounded by membranes made up of lipid molecules and proteins. The membranes maintain differences in concentrations of a wide variety of molecules and ions. Without going into any of the structural details, we can describe a typical membrane as a thin sheet (made up of the lipids) that is relatively impermeable to most molecules, into which is embedded protein molecules that act as selective pores for different types of molecules. A side view of a membrane section with a single pore is illustrated schematically below:




The small circles represent a molecule that can pass through the idealized pore. Assume that the length of the pore is 5 nm.

Suppose that there is a membrane that establishes a concentration difference for glucose molecules, with 20 mM ($20{\times}10^{-3}$ M) glucose on one side and 10 mM on the other. Assume further that the pore opening has a diameter of 2 nm.

(a) Estimate the concentration gradient across the membrane pore, in units of $\text{mol}\cdot\text{m}^{-4}$.

(b) Assuming a diffusion coefficient of $10^{-9}\ \text{m}^2/\text{s}$, calculate the flux, $J$, of glucose molecules across the pore, with 20 mM glucose on one side and 10 mM on the other.

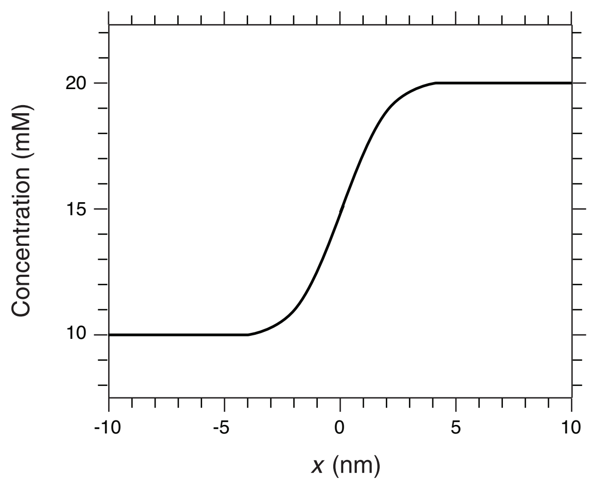
(c) What is the *net* number of molecules of glucose that flow through the pore in 1 second?

(d) If, as we expect, twice as many molecules flow from the high-concentration side to the low-concentration side as flow in the opposite direction, what is the number of molecules that flow in each direction in 1 s?

(Hint: This is a lot like the question: "If Joe gives Sally twice as many apples as Sally gives Joe; and Sally has five more apples than she started with, how many apples did Joe give Sally?")

(e) Suppose that there is a single pore of this type in a bacterial cell. Assume that the cell is 1 $\mu$m in diameter and 2 $\mu$m long, and that the initial concentration inside the cell is 10 mM and outside the cell the concentration is 20 mM. How much would you expect the total inside concentration to change in 1 s? How would you expect the flow of glucose molecules through the pore to change with time?

2. The figure below shows a graph of concentration versus distance, at a particular time after the pore opened, for the membrane pore described above. The $x$-axis represents the direction of the pore axis and extends about 7 nm beyond the pore in each direction. The position $x = 0$ represents the middle of the pore along its axis.




An enlarged version of this graph is provided on page 4.

(a) From the graph above, make a plot of the concentration gradient, $dc/dx$, as a function of $x$. This graph doesn't have to be super precise, but it should have enough points to define the curve and the correct units and values on its axes.

(b) From your graph of $dc/dx$, make a graph of $d^2c/dx^2$ versus $x$. The same guidelines for the plot of $dc/dx$, versus $x$ appy to this one.

(c) From your graph of $d^2c/dx^2$, estimate the values of $x$ at which the concentration of glucose will increase and decrease most rapidly, assuming (unrealistically) that diffusion is only along the $x$-axis. Making the same assumptions, estimate the rates of concentration change at these points.

(d) Considering the situation more realistically, a pore embedded in a lipid bilayer, how would you expect the rates of concentration change, at the points identified above, to differ from those that you calculated? Explain your reasoning.

(e) The rates of concentration that you estimated are likely to be substantially larger in absolute value than you expected. Suggest an explanation for these large rates of concentration change.

Note: The plots of $dc/dx$ and $d^2c/dx^2$ can be made in a variety of ways, the simplest being to estimate the derivative of $C$ with respect to $x$ directly from the plot, using a pencil and ruler. After drawing the graph of $dc/dx$ versus $x$, you can then do the same thing to generate the plot of $d^2c/dx^2$ versus $x$. If you want to take advantage of a computer, there are a number of programs for "ungraphing" data, that is extracting data values from an image of the graph. This is sometimes handy when trying to look closely at published graphs. Some programs of this type include:

- GraphClick (now free, but not under active development). For Mac only. Nice interface and easy to use. This is the program I use for un-graphing.
  `http://www.arizona-software.ch/graphclick/tour.html?page=4`
- Enguage Digitizer (Free, open source). Now available for Windows, Mac and Linux.
  `http://markummitchell.github.io/engauge-digitizer/`
- Plot Digitizer (Free, open source). Java program with executables for Mac, Windows and Linux. I haven't tried it.
  `http://plotdigitizer.sourceforge.net/`
- WebPlotDigitizer (Free) As the name implies, this is a web application. I played with this just a little bit, and it looks pretty neat.
  `http://arohatgi.info/WebPlotDigitizer/app/`

Once you have the data digitized, you can calculate the derivative, $dc/dx$, and $d^2c/dx^2$. Some graphing programs, such as SciDAVis, include a derivative function. It's also not too difficult to set up a formula to calculate the derivative in Microsoft Excel. Graphs generated this way are likely to be rather jagged, and a further refinement is to apply a smoothing function. However, reasonable graphs produced in any way will be accepted, provided that they have proper units and values.

3. Now, consider the movement of molecules through the pore from the perspective of a random walk.

   (a) What is the average velocity of a glucose molecule in water at 25°C?

   (b) As a glucose molecule takes a random walk, how far, on average, does it move before colliding with another molecule (of either water or glucose) and changing directions?

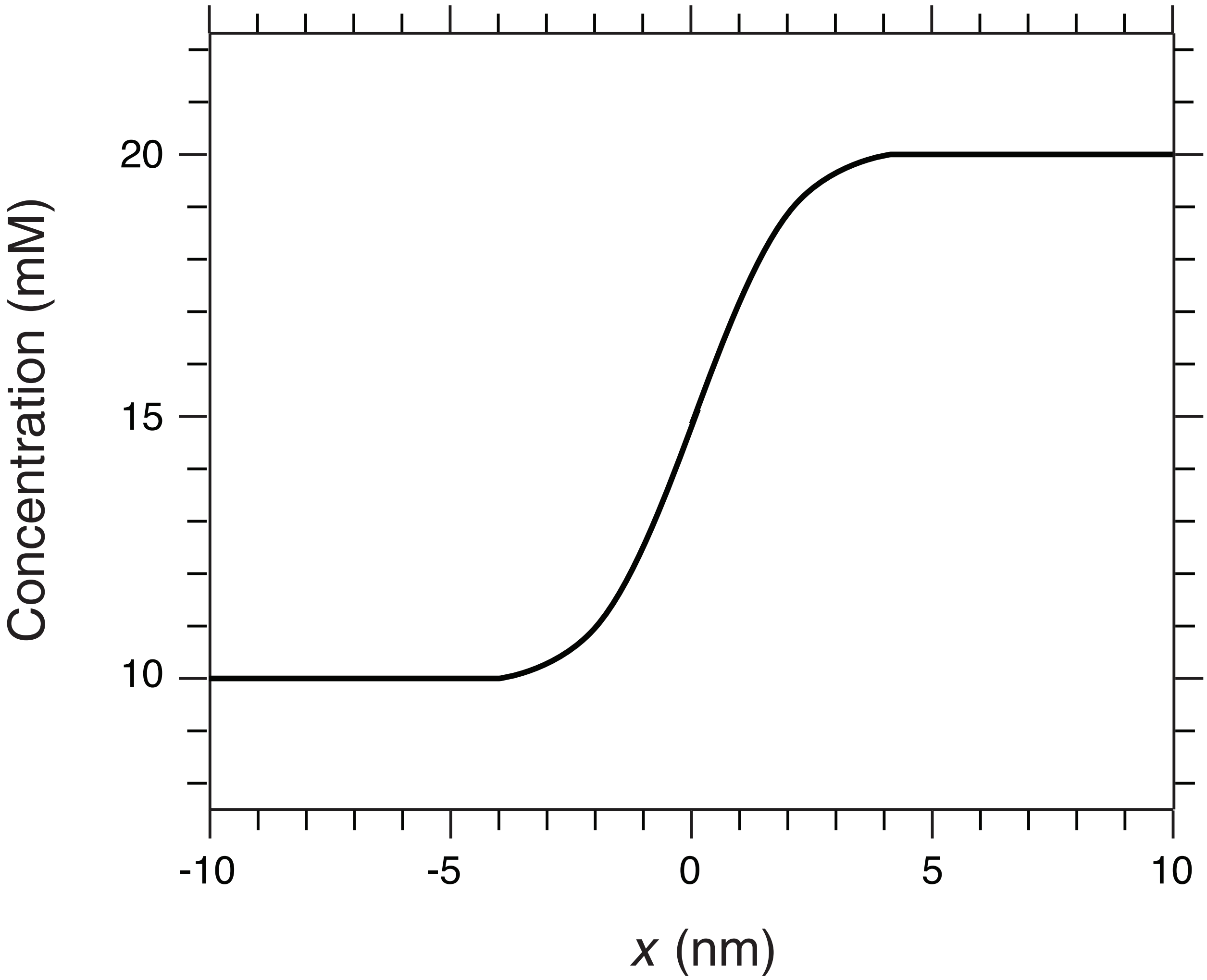
   (c) What is the average time interval between collisions?

   (d) On average, how long do you expect it to take for a glucose molecule to diffuse, via a random walk, through a pore that is 5 nm long? Does this number seem to be consistent with the flux that you calculated in the previous question? If not, how could you reconcile the difference?

   (e) If you were to take all of the random-walk steps required for an average crossing of the pore and add them together, what is the total distance moved by the molecule? How much longer is this than the net distance of 5 nm?

   (f) Once the molecule enters the cell, what is the average time that it would take for it to diffuse across the length of a bacterial cell (2 $\mu$m)?

   (g) Suppose that the pore was in one end of a human motor neuron, with a length of 1 m. What is the average time required to diffuse from one end of this cell to the other?



20
15
10
Concentration (mM)
-10
-5
0
5
10
x (nm)