BE/APh161: Physical Biology of the Cell
Homework 3
Due Date: Wednesday, January 25, 2017

"It is better to debate a question without settling it than to settle a question without debating it." - Joseph Joubert

1. Diffusive speed limits: It's not just a good idea, it's the law

In order for a chemical reaction to take place, the reactants must be at the same place at the same time. A very interesting calculation explores the way in which diffusion can control the on rate for reactions. Imagine some reaction in which A and B come together to form the complex AB. To simplify the problem, we are going to imagine B as a sphere of radius a that is fixed at the origin of our coordinate system. Further, we are going to imagine that very far away the concentration of A is held at c_0. What I really mean by this is that $lim_{r\to\infty}c(r) = c_0$, where $c(r)$ is the concentration of reactant A as a function of distance from the origin. Our goal is to compute the so-called "diffusion-limited on rate" for the reaction. We begin by working out the steady-state solution to the diffusion equation with the boundary condition that $c(a) = 0$, which corresponds to the physical statement that the sphere is a "perfect absorber". What this really means is that every time a molecule of A arrives at the sphere, the reaction occurs. (Note that this tells us that the diffusion-limited on rate is the fastest that a reaction could occur. It could be true that after the molecule arrives, it has to wait for some favorable orientation to occur, for example, which would make the rate of the reaction even slower).

(a) Solve the diffusion equation

$$\frac{\partial c(\mathbf{r},t)}{\partial t} = D\nabla^2 c(\mathbf{r},t) \tag{1}$$

in steady state and find the concentration profile $c(r)$ as a function of c_0 and a. Explain why we can write the concentration only as a function of the *scalar* r as opposed to the vector $\mathbf{r}$.

(b) Use that result to compute the diffusive flux $J(a)$ at the surface of the sphere. Here you need to invoke Fick's law relating flux and concentration, but acknowledging that you are working in spherical coordinates.

(c) Use the result of part (b) to write an equation for dn/dt, the rate at which A molecules arrive at the sphere and thus the rate of production of AB. The function $n(t)$ simply tells me how many molecules have arrived at the "perfect absorber" during the time between $t = 0$ and the time t.

(d) Now, use the result of part (c) to write an equation of the form

$$\frac{dn}{dt} = k_{on} c_0, \tag{2}$$

and hence write an expression for k_{on}. This is the so-called Smoluchowski rate.

(e) Find a numerical value for this diffusion limited on rate, k_{on}. Justify the units it has and provide an actual numerical value by estimating the relevant parameters that determine k_{on}.

2. Spread the Butter Diffusion Style.

(a) In class I sketched how to derive the master equation for diffusion as a limiting process by thinking of one-dimensional line as discretized into boxes of width a, and with a jump probability $k\Delta t$. Given that at $t = 0$ we have $p(0, 0) = 1$ (i.e. all the probability is concentrated at the origin), work out the probability after time Δt by hand. That is, figure out $p(0, \Delta t)$, $p(a, \Delta t)$ and $p(-a, \Delta t)$. Why do we not consider any points farther from the origin after a single time step?

(b) In this part of the problem, you will write a code to carry out the discrete spread the butter that you began by hand above. The goal is to work out the time evolution of the probability distribution for the initial condition when all the probability is concentrated at the origin. What you need to hand in is a plot that shows how the probability distribution changes over time.

(c) Now do the same thing as in part (b), but for the case in which the diffusion is in a finite box. The novelty here is figuring out what happens because of the boundaries. Intuitively, what will happen in the long-time limit given that you started out with a delta function at the origin? Hand in a plot of how the probability changes as a function of time. Make sure you explain what is going on in the long-time limit.

(d) One-dimensional FRAP via spread the butter. In this part of the problem, we build on what you did in the previous part to consider fluorescence-recovery-after-photobleaching for a one-dimensional cell. Consider the one-dimensional finite box with an initially uniform distribution of intensity throughout the “cell”. Now, photobleach (i.e. just set the probability to zero) a region symmetrically displaced around the origin. If the cell runs from $-L$ to L then photobleach the region from $-a$ to a. How does the recovery time depend upon the diffusion constant?