Physics 360/Math 360 MWF 11:00 - 11:50 PM, Room: Dennis 231

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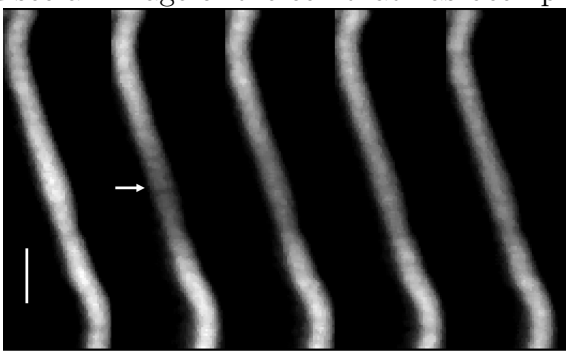
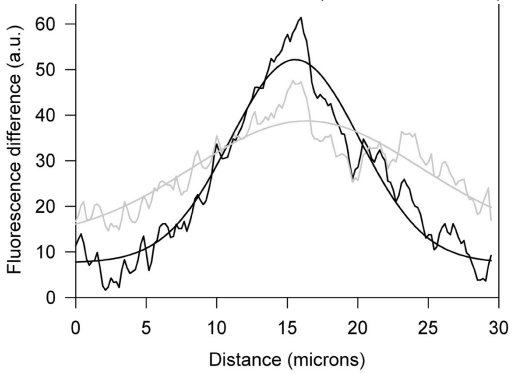
The FRAP problem, with hints

1 FRAP (Adapted from "Physical Biology of the Cell", Ch. 13)

In biology, one often wants to know how quickly various molecules are moving. The standard way of performing these experiments under a wide variety of experimental settings is with Fluorescence Recovery After Photobleaching (FRAP). In the figure below[1], an elongated *E. coli* cell with TorA-GFP (a protein fused with green fluorescent protein) is shown on the far left. A TorA-GPF loses its fluorescent properties when you shine a strong laser on it ("photobleaching"). In the second frame, you see an image of the cell that has been photobleached at the site indicated by the arrow.



As fluorescent proteins from *outside* that area diffuse in (frames 1s to 3s), the bleached area becomes more fluorescent. By measuring the rate at which the fluorescence returns, you can find out how quickly the proteins are diffusing within the cell. The image below shows the difference in fluorescence immediately after bleaching (dark jagged line) and 4 seconds after (light jagged line), along with fits to the data (smooth lines).



Your goal is to write down an equation modeling the concentration of protein over time. We'll split this problem up into three weeks.

[1] C. W. Mulineaux et al., J. Baceriol. 188:3442,2006

1.1 Last week

What PDE will you use to model the system? What are your initial conditions? What are your boundary conditions? Will you be expanding your solution in terms of sin or cos functions?

You should have decided to use the diffusion equation

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} \tag{1}$$

where D is the diffusion constant and $c(x,t)$ is the concentration of fluorescent molecules. There are a couple of ways you could have modeled the initial conditions, depending on how you chose boundary conditions. The simplest thing to do is to decide that you're photobleaching a region from $-a$ to a, and that you have an infinite amount of fluorophores. In that case, you'd get

$$c(x,0) = \begin{cases} c_0 & x < -a \\ 0 & -a < x < a \\ c_0 & x < a \end{cases}$$

but let's be a little more realistic. Let's assume we have a cell of length $2L$, starting with a uniform concentration of c_0, and that we bleach that same region. In this case, we get two restrictions. The first tells us about the concentration:

$$c(x,0) = \begin{cases} c_0 & -L < x < -a \\ 0 & -a < x < a \\ c_0 & a < x < L \end{cases} \tag{2}$$

the second tells us that nothing flows into or out of the cell. If you recall our class discussion, we write that as

$$\frac{\partial c(x,t)}{\partial x} = 0 \text{ for } x = \pm L \tag{3}$$

and, given those boundary conditions, we can guess that we'll expand our solution in cosines:

$$c(x,t) = A_0(t) + \sum_{n=1}^{\infty} A_n(t)\cos\left(\frac{x}{L}n\pi\right) \tag{4}$$

1.2 This week

Your goal this week is to solve (1) subject to (2) and (3). I'll sketch the solution and you can fill in the pieces. Alternatively, you can solve it however you'd like!

1.2.1

First, we plug (4) into (1), yielding

$$\frac{\partial A_0}{\partial t} + \sum_{n=1}^{\infty}(??) = D\sum(??) \tag{5}$$

which gives us an infinite number of differential equations (**why??**)
that look like

$$\frac{\partial A_0}{\partial t} = ??, \tag{6}$$

$$\frac{\partial A_n}{\partial t} = ?? \qquad (n \geq 1) \tag{7}$$

These have solution

$$A_n(t) = A_n(0) \cdot (??) \tag{8}$$

We can use those formulas for A_0 and A_n to rewrite (4) as

$$?? \tag{9}$$

which is our series solution, and has everything we need except for the actual values of the amplitudes $A_n(0)$.

In order to get the amplitudes, we need to use the orthogonality of cosines again. We play the standard trick for these sorts of problems, and multiply both sides of (11) by $\cos(n\pi x/L)$ for different values of n and then integrate over x. What does "the orthogonality of cosines" mean in this case?

$$?? \tag{10}$$

specifically, which integrals will you calculate to find the coefficients?

$$?? \tag{11}$$

Fill in all of the "??" spots above. Next time, we'll finish the solution and plot the results! After all of that, we can evaluate the above integrals to get

$$A_0(0) = c_0 \frac{L-a}{L} \tag{12}$$

$$A_n(0) = -2c_0 \frac{\sin(n\pi a/L)}{n\pi} \qquad (n \geq 1) \tag{13}$$

Put those back into our formula for $c(x,t)$, and we can plot the result! Do it, setting $a = L/2$. What happens at long times? What do we mean by "long times"?

You might want to plot the "FRAP recovery curve" i.e. $N_f(t)$, the number of molecules in the region at time t.