BE/APh161: Physical Biology of the Cell
Homework 8: Final Homework
Due Date: Monday, March 13, 2017

"Science is built up of facts as a house is built up of bricks, but a mere accumulation of facts is no more a science than a pile of bricks is a house."
-Henri Poincare

This problem set is in a way a "final" review of everything we have done in the course. My aim is to get you to review all the different topics we have covered and to bring them together as a full toolkit for examining important and exciting biological problems.

1. Cytoskeletal Length Control.

In class we discussed the ways in which the lengths of cytoskeletal filaments are tuned. Work out problem 15.7 from PBOC2. Then, as a new part to the problem now that you figured out the rate at which filament monomers are lost from the end, imitate what we did in class and work out a master equation for this problem. Then, using the same kind of strategy described several times in class, work out the steady-state probability distribution.

2. Cooperative Repression.

In class we considered the regulatory architecture known as simple repression. In this problem, your task is to generalize that treatment to the case of cooperative repression. Imagine a promoter that has two repressor binding sites and that both of them can repress individually, but that when both are present they have a cooperative interaction described by the parameter $\omega = e^{-\beta\epsilon_{int}}$. Write the states and weights for this full promoter and then derive an expression for the fold change and compare your result to the case for simple repression. Make sure you explain the weak-promoter approximation much as we did for the simple repression case. See Figure 2.5 of this paper:
http://www.rpgroup.caltech.edu/publications/Garcia2011a.pdf
in order to see the formula for fold-change you are trying to derive.

3. Practice with Beam Theory.

Do problem 10.2 in PBOC2. This problem gives you much needed practice in thinking about elasticity theory in general and the elastic theory of beams in particular.

4. Tania Baker and the fidelity of replication.

In a wonderful paper about DNA replication, Tania Baker described the process of DNA replication in every day sizes and time scales. In this problem, we will follow her lead and do the estimates ourselves. Stated simply, scale up the DNA double helix such that it has a diameter of 1 m. In light of this, justify her claim that the replisome would be the size of a FedEx truck. Then, figure out using the speed of the replisome how fast this truck would be moving, how frequently it would be making deliveries on both sides of the street, how long its daily journey (to copy the *E. coli* genome) would take and how often the delivery system would make a wrong delivery. The error rate for bacterial replication is roughly 10^{-10} per bp per replication.

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5. Membrane protein census.

Do problem 11.1 of PBOC2. This is a reminder of the artificial view of membranes inspired by thinking of them as lipid bilayers decorated by a few membrane proteins here and there.

6. Proton motive force.

Do problem 18.4 of PBOC2. This problem gives you a chance to think more about the proton-motive force that we discussed in class during our superficial introduction to photosynthesis.

7. Your Turn to Teach 161

RP: all answers to this problem must be submitted electronically to the TAs and me in pdf form.

Some have argued that only by quantitation will we really be able to come to terms with the complexity of living organisms, with the quantitative ap-

proach advocated in this class meant to give you a feel for how such quantitative dissection of biological problems might work. Others have argued that the approach we have taken is a mopping up operation which amounts to dotting the "i"s and crossing the "t"s already worked out by biologists. Write one paragraph defending each of these two points of view. One document you might find interesting to look at is "Bio2010" from the National Academy of Sciences.

Next, make a syllabus for the course. Start with one brief paragraph on the mission of your course. Issues that you might want to consider include: is it important to do hard calculations, or is that the province of other physics courses and our goal here is to illustrate the *style* of thinking? Are estimates a part of the way you will present the material (if yes, why, if no, why not?). How will you organize the material - note that in typical biology books DNA and actin would never be in the same chapter but for PBoC they are both in chap. 10 as examples of "beam theory". The course is only 10 weeks long. What will you cover, what will you skip and why? How will you balance the desire to cover more topics with the resulting superficiality? This is not a look up something in Wikipedia question, nor is it a request to regurgitate what I did in the course. It is asking you how to organize a new and unfinished topic and to present it to advanced Caltech undergrads and to grad students at the beginning of their grad careers. What are the important points? Give a syllabus - state what topics you will consider each week in your lectures and why.