

BE/APh161: Physical Biology of the Cell  
Homework 5  
Due Date: Wednesday, February 20, 2013

“Often the best way to make progress is to make the mistakes as fast as possible and recognize them.” - John Wheeler

Useful reading can be found in chap. 20 of PBoC2, specifically the section on pattern formation in flies.

**1. Estimate of integration time: Berg-Purcell problem.**

In class I gave a long discussion of the idea that receptors use occupancy measurements as a way to figure out what the external concentration is. We argued that there is a measurement error and the longer the system makes the measurement, the smaller that error. In this problem, we are going to come at this problem from a different angle than I did in class, but arriving at effectively the same result. I am assigning this problem because one of the things I want you to leave this class with is an appreciation of the physical limits to biological detection.

(a) Imagine a receptor with a length scale  $a$  (i.e. molecular dimensions  $a$ ). If the concentration in the neighborhood of the receptor is  $c$ , how many molecules are there in a region with characteristic size  $a$ ? Given this result, what is  $\delta N/N$ ? This is the error in making a single measurement.

(b) The next idea is that we can improve the measurement by repeating it again and again during a total integration time. The argument made by Bialek in his excellent book “Biophysics” is that we need to wait a time given by the diffusion time before making the next measurement. What I mean by this is that there is some characteristic time scale for particles to diffuse out of the region of size  $a$ . What is this time scale?

(c) Now what we want to do is to compute the precision of our measurement by using

$$\frac{\Delta p}{p} = \frac{1}{\sqrt{\text{number of measurements}}} \frac{\delta N}{N}, \quad (1)$$

where the quantity  $\delta N/N$  is the uncertainty in one measurement, and  $\frac{\Delta p}{p}$  is defined as in class. Now figure out how many measurements are made in time  $T$  by figuring out how many diffusion times  $\tau_D$  there are in this period and get a formula for  $\frac{\Delta p}{p}$  and estimate the numerical value for the integration time.

## 2. States and weights and Hill functions.

I am assigning this problem which should be quick in order to make sure everyone gets a chance to think hard about the approximation that is implicit in making a Hill function. As a reminder, the Hill function says that the probability of binding is

$$p_{\text{bound}}(c) = \frac{\left(\frac{c}{K_d}\right)^n}{1 + \left(\frac{c}{K_d}\right)^n}. \quad (2)$$

To see where this comes from, consider a receptor with two binding sites and write the states and weights for all four states (and explain what these states are). Make sure that you include an additional “interaction energy”  $\epsilon$  as you did in an earlier homework for the state that has double occupancy. Consider that the binding energy is  $-3 k_B T$  for the singly bound species. Now, write the formulae for the probability of zero, single and double occupancy and plot the probability of the state with zero ligands, one ligand and two ligands as a function of concentration all on the same graph and make several such graphs. First, do it for the case in which  $\epsilon = -1 k_B T$  and then do it for the case in which  $\epsilon = -10 k_B T$ . What do you observe about the probability of the singly-occupied state for the case in which the interaction energy is large? In light of this, now make an “effective” states and weights diagram for the situation in which you only allow two states - empty or doubly occupied. When you do this, what is the probability of the zero occupancy state and what is the probability of the doubly occupied state? Is that the Hill function?

## 3. Testing the French Flag Model.

Do problem 20.1 of PBoC2.

#### **4. Transcription and Translation in Development.**

Do problem 20.2 of PBoC2.