BE/APh 161: Physical Biology of the Cell, Winter 2019
Homework #2
Due at the start of lecture, 2:30 PM, January 23, 2019.

Problem 2.1 (Mathematizing a cartoon for ciliar growth, 50 pts)**.**
Another model for flagellar/ciliar growth was proposed in Howard, et al., *Nat. Rev. Mol. Biol.*, **12**, 393–398, 2011. The cartoon is shown in Fig. 1, along with the text from the caption in the paper.

Let $c(x,t)$ be the concentration of active growth factors in the cilium and let $\ell(t)$ be the length of the cilium.

a) Write down a set of differential equations to describe the dynamics of c and ℓ. If you like, you may assume a constant number of cargo-carrying motors as we did in lecture for the *Chlamydomonas* flagella, or you may assume that the density of motors is constant. Be sure to state any other assumptions or decisions you made in mathematizing the cartoon.

b) Nondimensionalize your dynamical equation(s) and comment on any physical insight this procedure provides.

c) If you can, solve for $\ell(t)$ analytically. If cannot, solve it numerically. Use your solution to also plot the growth rate, $\mathrm{d}\ell/\mathrm{d}t$, over time.

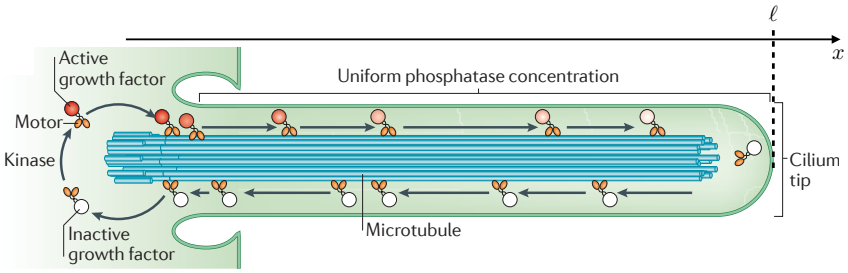

Figure 1: A cartoon describing a possible mechanism for ciliar growth adapted from Howard, et al., *Nat. Rev. Mol. Biol.*, **12**, 393–398, 2011. The text from the caption in the paper reads as follows. "Schematic of an advection-reaction model, a hypothetical mechanism for the length control of cilia and microvilli. Cargoes, for example growth factors, carried along cilia and microvilli are inactivated over time by phosphatases, which may provide a length-dependent signal to the growing tip."

Problem 2.2 (Boltzmann's grave, 5 pts)**.**
Boltzmann's tomb is in Zentralfriedhoff in Vienna, a beautiful cemetery that also contains the graves of some of the world's greatest composers, including Beethoven,

Brahms, Schubert, Strauss, Ligeti, and Falco. Boltzmann's tomb is shown in Fig. 2. Not the equations, $S = k \log W$, at the top of the stone.

Figure 2: Boltzmann's tomb in Zentralfriedhoff in Vienna. Photo from Daderot, licensed under CC-BY-SA-3.0.

Here, S is entropy, k is the Boltzmann constant, log refers to the natural logarithm, and W is the number of microstates. In class on January 17, we derived the famous Boltzmann distribution by maximizing the Shannon entropy, given that we knew an average energy of our system of interest. Derive the equation on Boltzmann's grave using the same technique. To do so, assume we do not know anything about the energy of the system.

Problem 2.3 (Ligand-receptor binding and small numbers of molecules, 45 pts)**.** In this problem, we will explore the effect of having small number of ligands and receptors in a small volume, as is often the case in cells. Imagine we have a cell with volume V_{cell} that contains L total ligands and R total receptors. (Of course here we mean copies of specific ligand-receptor pair; cells have lots of ligands and receptors of different type.) The receptors and ligands are all free to move about in the cell. Each receptor can bind a single ligand. Let n be the number of receptors that are bound to ligands.

a) Compute the expected number of bound receptors, n, as a function of L, R, and $W \equiv K_{\text{d}} V_{\text{cell}}$. In doing the calculation, assume that R and L are large, which enables you to use

$$K_{\text{d}} = \frac{c_L c_R}{c_{LR}}. \tag{2.1}$$

b) W is a dimensionless number. What is its physical meaning?

c) When L and R are not large, just knowing the expected number of bound receptors is not enough to fully understand what the molecules are doing in our system. We therefore would like to know $P(n)$, the probability mass function of n. I.e., $P(n)$ is the probability that there are n bound receptors at equilibrium. Show that

$$P(n) = \frac{[W^n\, n!(R-n)!(L-n)!]^{-1}}{\displaystyle\sum_{n=0}^{\min(R,L)} [W^n\, n!(R-n)!(L-n)!]^{-1}}. \tag{2.2}$$

d) Plot $P(n)$ for various values of L, R, and W. Comment on what you see, especially for small L and R. By "small," I mean between 1 and 100. (Are there ligands and receptors with these sorts of copy numbers in cells?) Think carefully about how to represent your plot so that you can highlight the important physical consequences of your analysis. Be sure to discuss your plots. *Hint:* It will be difficult to compute the statistical weights and the partition function. Work with logarithms of the statistical weights when you can. If you are using Python, `scipy.special.gammaln()` and `scipy.misc.logsumexp()` might be useful functions.

e) The coefficient of variation is the ratio of the standard deviation of a distribution to its mean. Plot the coefficient of variation of $P(n)$ for $W = 1000$, R going from 1 to 10^5, and $L = 2R$. What does this say about variability in number of of species? When can you just use your result from part (a), and when should be think more carefully about the full distribution?