APh161: Physical Biology of the Cell
Homework 7
Due Date: Tuesday, March 8, 2005

"Lack of willpower has caused more failure than lack of intelligence or ability." - Flower Newhouse

1. Miscellany Relevant to Molecular Motors.

(a) In class I used simple equilibrium arguments to derive the Michaelis-Menten equation for the rate of an enzyme reaction as a function of the substrate concentration. In this part of the problem, we will use rate equation in steady-state to derive this same result. Write a rate equation for the concentration $[ES]$ in terms of the rate constants k_1, k_{-1} and k_p that we used in class. Note that this rate equation should have three terms. Next, set this rate equal to zero (i.e. steady state) and replace the concentration of enzyme $[E]$ with $([E_{tot}] - [ES])$. Solve the resulting equation for $[ES]$ and then use $v = k_p[ES]$ and $v_{max} = k_p[E_{tot}]$ to write the Michaelis-Menten equation. Make sure to relate the constants in your rate formulation to the formulation I gave in class. For kicks, work out how much change in substrate concentration needed to increase the reaction rate from $0.1v_{max}$ to $0.9v_{max}$. Take a look at the data from the Block group on kinesin that I showed in class and see how well you can fit the ATP dependence of the velocity using the Michaelis-Menten fit you have derived. (Note: I have not tried this fit myself and am not clear on how well it will work.)

(b) In class I have repeatedly shown single molecule experiments in which motor molecules are attached to polystyrene beads which are used to monitor the motion of the motor. In this part of the problem I want you to estimate the force acting on such a motor as a result of the Stokes drag on the bead. Use a characteristic speed for a motor like kinesin and work out the drag force resulting from an attachment to a one micron bead. Comment on the magnitude of this drag force relative to the stall force of such motors.

(c) Repeat the entirety of the derivation given in class for the one-state motor. That is, discuss the nature of the model, derive the relevant rate equation and reproduce the derivation of the driven diffusion equation. Then,

show how the driven diffusion equation can be solved and see if you can find choices of v and D (and hence $k_+(F)$ and $k_-(F)$) that best describe the motion of kinesin. As I mentioned in class, Fisher and Kolomeisky find that even the two-state model is not sufficient to fit kinesin data so we should not be too surprised if the fit doesn't work out too well.

2. Myosin and Muscles: Some Estimates.

In class, I described (very briefly) the organization of muscles. In this problem, we will examine all of this in more detail.

a) Give a "multiscale" description of muscles. That is, describe the various levels in the structural hierarchy of muscles starting with the entire muscle itself (at the largest scales) and ending with the individual myosin molecules (at the smallest scales). Make sure you discuss each structural feature in some detail, making sure to describe the relevant length scales.

b) Make an estimate of the cross-sectional area of a muscle and work your way through to the maximum force available during contraction of the muscle by figuring out the force available per molecule (again, think about a cross section). You will probably have to refer to some of the single molecule work on myosin to really carry out a correct estimate (see Howard, pg. 267, for example). In particular, once you have your estimate of the number of myosins per cross section and the force available per myosin, you will be able to make a preliminary estimate (although not all myosins are attached at all times and you may want to consider that also).

3. Polymerization Rates.

In class we discussed a variety of different polymerization scenarios. In this problem I want you to tell the full story of the case in which the rates on the two ends are different, but there is no polymerization. In particular, write the rate equations for the plus and minus ends. Next, show that the equilibrium condition demands that the ratio of the rates on the two ends (or the critical concentration) is the same. Explain the significance of this result and its physical origins. Make a plot of the growth rate on the two ends as a function of the monomer concentrations.