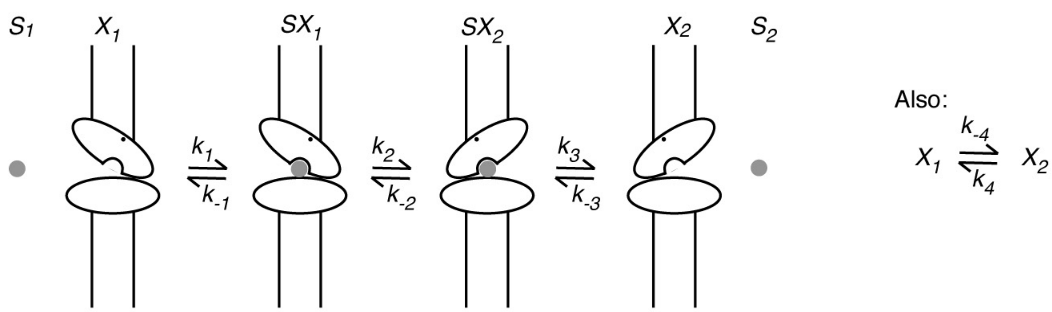
580.439/639 Midterm 2011

1 hour, closed book except for one sheet of paper. Do all problems, 12 points/problem plus 4 points for your name.

Problem 1

The figure below shows a transporter model similar to the lactose transporter discussed in class. Transport consists of binding of the substrate (S, gray ball) to the transporter (X), a change in conformation of the transporter that opens the substrate to the opposite side of the membrane ($SX_1 \leftrightarrow SX_2$), and then unbinding of the substrate. Assume that the substrate does not move through the membrane during the conformational change of the transporter, only during the binding and unbinding steps. Also, as shown at right, the transporter can change states while empty.



Part a) Write a set of flux equations for this model <u>assuming that flux is in steady state</u>. Also assume that there is a <u>fixed total amount of transporter</u> T and that the concentrations S_1 and S_2 are constant. Do not attempt to solve the equations, as the result is quite messy, but make sure that your equations can be solved (i.e. there are as many equations as unknowns and the equations are not degenerate).

Part b) If you had solved the equations for the flux, which of the following equations is the most likely result, given the assumptions made above? Answer this assuming that S is uncharged. Justify your choice.

$$(1)\ \ J = F(K,V)\frac{S_1 - S_2 e^{-zFV/RT}}{1-e^{-zFV/RT}}$$

$$(2)\ \ J = \frac{S_1 - \dfrac{k_{-1}k_{-2}k_{-3}k_{-4}}{k_1k_2k_3k_4}S_2}{F(K,S_1,S_2,\ldots)}$$

$$(3)\ \ J = \frac{S_1 - \dfrac{k_{-1}k_{-2}k_{-3}k_{-4}}{k_1k_2k_3k_4}S_2}{F(K)}$$

where K stands for various functions of the rate constants k_i (sums, products and ratios of the rate constants, etc.). $F(\cdot\,)$ is a function of the variables listed in the parentheses.

(Hint: remember microscopic reversibility requires that $k_1k_2k_3k_4 = k_{-1}k_{-2}k_{-3}k_{-4}$ for a non-charged substrate.

Part c) Suppose that the substrate is charged with charge z_S per ion. Which rate constants will become functions of the membrane potential? Write an equation showing the effect of the membrane potential on these rate constants. To do this, you will have to define a barrier diagram for the rate constants and make assumptions about the way membrane potential affects this barrier diagram. Make a simple assumption about the membrane potential. If you chose either model (2) or (3) in Part b) above, show the value of ratio of rate constants ($k_{-1}k_{-2}k_{-3}k_{-4} / k_1k_2k_3k_4$) with the incorporation of membrane-potential effects, <u>assuming that the ratio is 1 for z_S=0.</u>

Part d) Suppose the reaction $X_1 \leftrightarrow X_2$ does not occur; that is, the transporter cannot change conformation unless a substrate molecule is bound. What effect would this have on the flux J?

Problem 2

Consider the system defined by the following two equations. This is an approximation to the near-threshold region of a neuron model.

$$\frac{dx}{dt} = -y + x^2 - 2$$

$$\frac{dy}{dt} = -y + x$$

Part a) Draw a phase plane for this system, showing the nullclines and equilibrium points. Please draw this on the phase-plane plot on the following page. The dotted lines on this plot are four trajectories made by a simulation of this system. These may be helpful.

Part b) Classify the equilibrium points using linearizations around each one. You should find one stable point and one saddle. Compute the stable and unstable manifolds near the saddle and sketch them on the phase plane.

Part c) Does this system have a limit cycle? If not tell why not. If it does, draw an approximation to where it might be.

Part d) From the directions in which trajectories point in various regions of the phase plane, you should be able to specify a domain of attraction for the stable equilibrium point, that is a region in which you can argue that all initial values will lead to the equilibrium point. Tell whether you have found the entire domain of attraction of the equilibrium point and why.

Note: the four trajectories are shown in their entirety, from initial value until end, except for the effects of falling off the page.