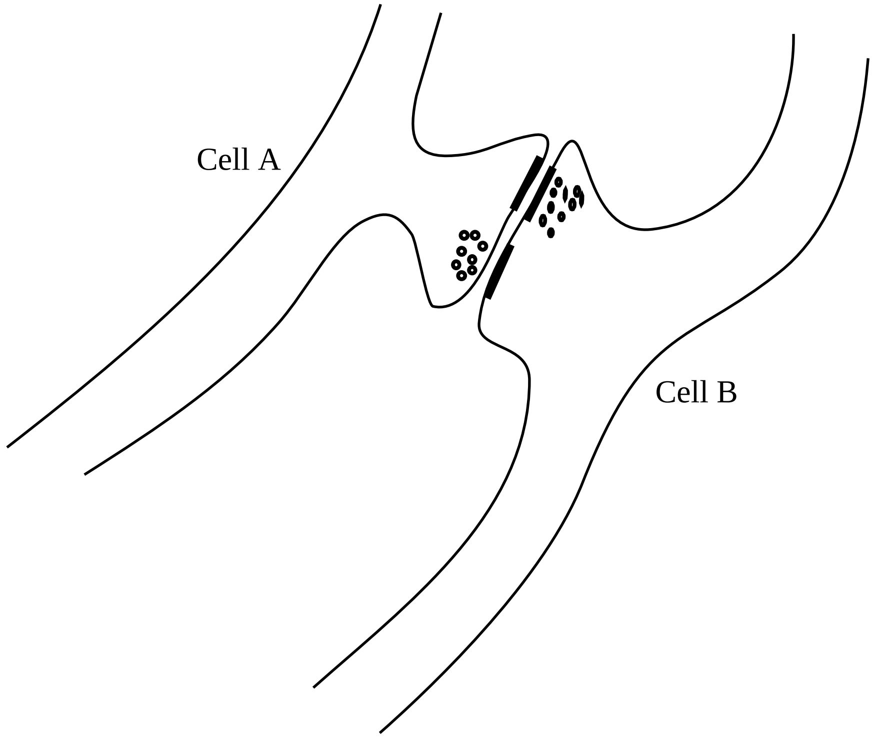
580.439 Final Exam, 1999

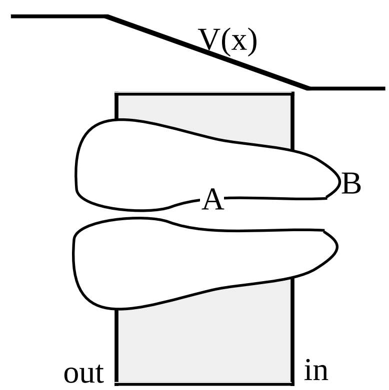
Answer all questions. Closed book except for two 8.5” x 11” sheets of paper.

Problem 1



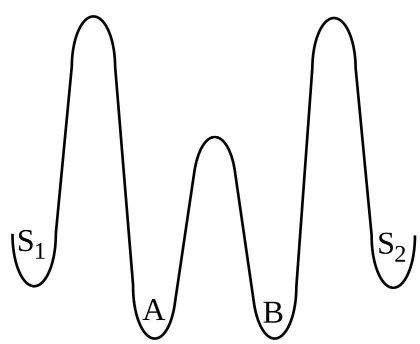
9 pts

Part a Consider the reciprocal synapse drawn at right. Cells A and B contact each other at the synapse, making what appear to be functional synapses going in both directions. Draw an electrical circuit diagram modeling this situation and sketch the sort of equations that you would write and solve to model the effects of a depolarization in either cell on that cell and the other cell.



9 pts

Part b Consider the channel sketched at right. There are two molecules *A* and *B* that modify voltage-dependent gating in the channel. It is known that the binding sites for the two molecules are located as drawn in the figure. Both of the modifications are <u>voltage dependent</u>, i.e. depolarizing the cell reduces or eliminates either gating modification. It is apparent, however, that the voltage dependence is different for *A* and *B*. Give qualitative hypotheses that could explain the voltage dependence of the two modifications in terms of different hypotheses. The likely potential field in the membrane is sketched at the top of the membrane.



9 pts

Part c Consider an ion channel with two binding sites in the membrane, as sketched in the energy diagram at right. Suppose that this channel can hold 0, 1, or 2 ions, i.e. both sites within the channel (*A* and *B*) can be occupied at the same time. Write a set of equations to describe steady state permeation through this channel (<u>don’t solve for the flux, just set up the equations that you would have to solve to get the flux</u>). Write these in terms of rate constants only, do not bother to define the rate constants in terms of barrier heights (do define the rate constants, however). Assume for this part that ions do not interact within the channel, i.e. the presence of an ion in site *A* does not affect the kinetics or probability of occupancy of site *B* in the same channel. (Hint: you will have to consider explicitly the following states of the channel: no ion in the channel, ion in site *A* only, ion in site *B* only, and ion in both sites.)

9 pts **Part d** Suppose, in the channel model of part c above, that when both sites *A* and *B* are occupied, the ions interact electrostatically with one another, i.e. each ion is within the electric field generated by the other ion, so the ions repel each other. How can this fact be incorporated into the model? (Hint: consider a change in the energy barrier diagram). Show how the equations you wrote in part c would be modified for this case.

Problem 2

A simple two state-variable system which resembles nerve action potentials in some ways is the Van der Pol oscillator, defined by the equations:

$$\frac{dx}{dt} = \mu\left(y - \frac{x^3}{3} + x\right) \quad \text{and} \quad \frac{dy}{dt} = -\frac{x}{\mu}$$

for a positive constant μ.

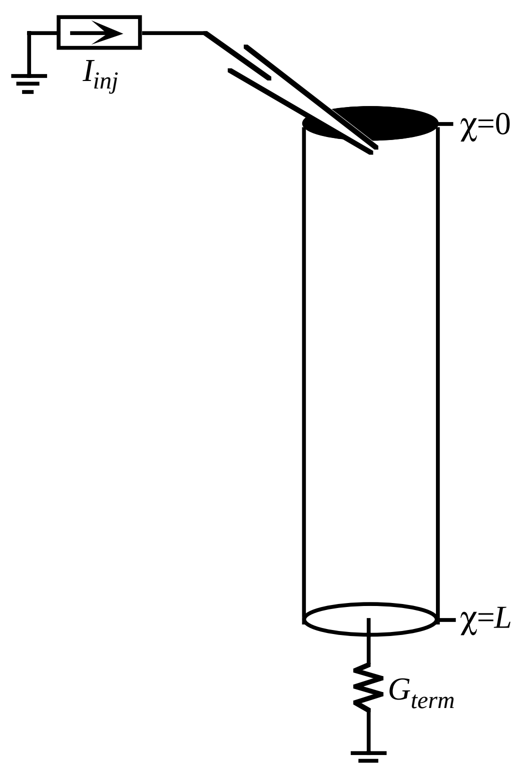
9 pts **Part a** Draw a phase plane for this system. Include the nullclines and equilibrium points. Sketch vectors to indicate the general direction of trajectories in the plane.

9 pts **Part b** Work out the stability of the system at its equilibrium point(s). Can you conclude, from this analysis, that the system does or does not have a stable limit cycle? Could it have a limit cycle?

9 pts **Part c** Suppose that the system does have a limit cycle for a large enough value of μ. Sketch the limit cycle on the phase plane, assuming that μ is large enough that the time scale of one equation is substantially faster than the other.

Problem 3

Consider the cell diagrammed at right. This is a model for a certain glial cell in the retina. The cell is equivalent to a single cylinder and is terminated at one end by a closed-end boundary condition (Y=0 at χ=0) and at the other end with a conductance G_{term} (at χ=L). In fact, what has been done is to incorporate the cell body into the cable at the χ=0 end. A microelectrode is placed in the cell at the χ=0 end as drawn and a step of current $I_{inj}(t) = I_0\text{u}(t)$ is injected into the cell through the microelectrode.



9 pts **Part a** Set up the cable equation and appropriate boundary conditions which would allow you to solve for the potential in the cylinder. Assume that the membrane is linear and passive. Write the equations in transformed form, i.e. in a form that is suitable for using the Laplace transform from zero initial conditions or the D.C. steady state.

10 pts **Part b** Solve the equations for membrane potential $\overline{V}(\chi,q)$. Warning, this is a bit messy.

9 pts **Part c** Show that $\overline{V}(L,q)$, the potential at L, can be written as below. Note that there is an easy way and a hard way to do this (Hint: transfer impedance).

$$\overline{V}(L,q) = \bar{I}_{inj}\,\frac{1}{G_{term}\cosh(qL) + G_{\infty}q\sinh(qL)}$$

9 pts **Part d** Consider the potential recorded at χ=0 when a step of current is injected. Can G_{term} be determined from this potential in the absence of knowledge of G_{∞} and L? Is there any special case when G_{term} could be measured from the response to the step current without knowledge of G_{∞} and L? Is there any special case in which G_{term} could not be measured from properties at χ=0? (Hint: L very small or very large.)