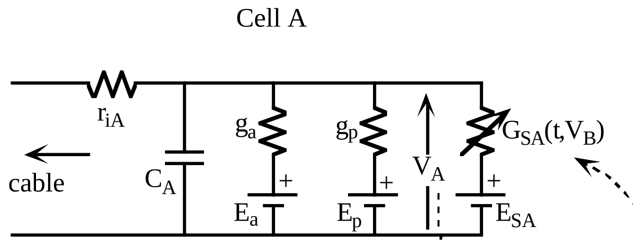
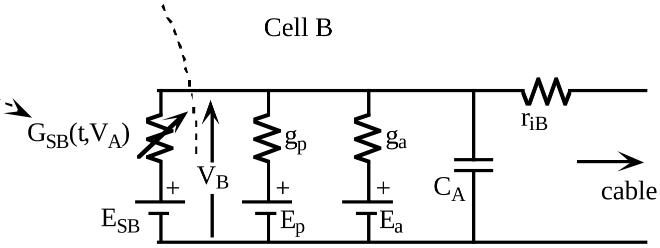
580.439 Final Exam Solutions, 1999

Problem 1

Part a A minimal circuit model is drawn below. The synaptic terminals of cells *A* and *B* are represented by the parallel combination of synaptic conductance (G_S), passive membrane conductance (g_p) and active membrane conductance (g_a), of which there may be several. Each compartment is connected to the main dendritic cable by the resistance r_i. The potentials V_A and V_B in the two terminals control the synaptic conductances in the other terminal, as shown by the dashed lines.





The equations for each terminal are similar and are given below for terminal *A*:

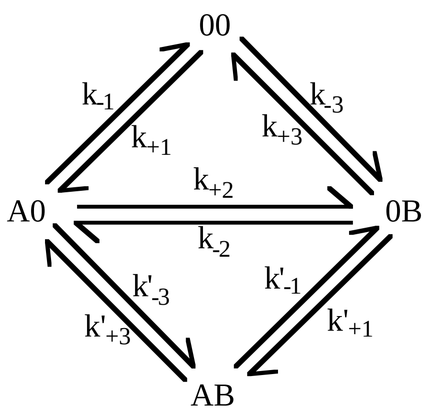
$$\frac{1}{r_{iA}}(V_{cable} - V_A) = C\frac{dV_A}{dt} + g_a(V_A - E_a) + g_p(V_A - E_p) + G_{SA}(t, V_B)(V_A - E_{SA})$$

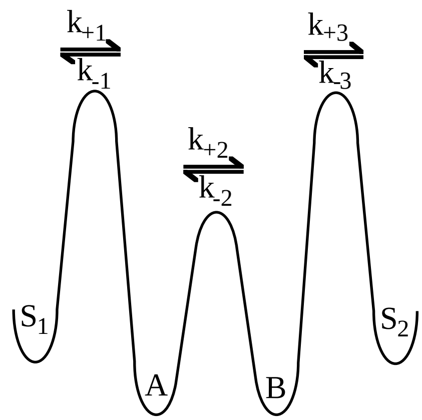
$$G_{SA}(t, V_B) = \sum_{t_{iB} < t} g_{SA}(t - t_{iB} - t_{sd})e^{-(t - t_{iB} - t_{sd})/\tau}$$

The equation for the synaptic conductance is the sum of all the action potentials that occurred in terminal *B* in the past. The spike times are t_{iB} and there is a synaptic delay t_{sd} between each spike and the postsynaptic conductance change. In fact, for reciprocal synapses of this type in the CNS, it is likely that synaptic transmitter release occurs at subthreshold potentials, so a more complicated synaptic model is probably needed.

Part b Molecule *A* is within the membrane's potential field. Therefore if *A* is negatively charged, it will be repelled from the channel by depolarization of the membrane, eliminating the effect on gating. Molecule *B* is not within the membrane potential field, so can only be voltage dependent due to some secondary effect, say due to a change in conformation of the channel molecule when the membrane potential is changed.

Part c The state diagram at left below is helpful in organizing these equations. A channel can be in four states, called *00, A0, 0B,* and *AB,* interpreted as channel with no ion, channel with ion in site *A* only, channel with ion in site *B* only, and channel with ions in both sites. The rate constants in the state diagram correspond to those in the energy barrier diagram at right. Note that the $k_{\pm 1}$ and $k_{\pm 3}$ rate constants have been primed for the *A0* to *AB* and *0B* to *AB* transitions, to handle the general case in which adding an ion to site *A* is different beginning with state *00* as opposed to state *0B*. For part c, these rate constants are explicitly assumed to be the same, i.e. $k_{\pm 1}=k'_{\pm 1}$ and $k_{\pm 3}=k'_{\pm 3}$. Note that simultaneous movement of two ions (e.g. the transition *00* to *AB* are assumed to occur at negligible rates).





The equations below describe this system:

$$\frac{d00}{dt} = -(k_{+1} \cdot S_1 + k_{-3} \cdot S_2)OO + k_{-1}AO + k_{+3}OB$$

$$\frac{dA0}{dt} = k_{+1} \cdot S_1 \cdot OO - (k_{-1} + k_{+2} + k_{-3} \cdot S_2)AO + k_{-2}OB + k_{+3}AB$$

$$\frac{d0B}{dt} = k_{-3} \cdot S_2 \cdot OO + k_{+2}AO - (k_{+3} + k_{-2} + k_{+1} \cdot S_1)OB + k_{-1}AB \qquad (*)$$

$$\frac{dAB}{dt} = k_{-3} \cdot S_2 \cdot AO + k_{+1} \cdot S_1 \cdot OB - (k_{-1} + k_{+3})AB$$

$$Q = OO + AO + OB + AB$$

This seems to be five equations in four unknowns; however the equations are redundant and *dAB*/*dt* can be derived by adding the previous three equations and using the fifth equation. Thus there are only four independent equations.

In the steady state, all time derivatives in (*) are zero and a solution can be found for the concentrations *00*, *A0*, *0B*, and *AB* (four algebraic equations in four unknowns). The flux can then be computed from any one of the equations below:

$$J = k_{+1} \cdot S_1 \cdot OO + k_{+1} \cdot S_1 \cdot OB - k_{-1} \cdot AO - k_{-1}AB$$

$$J = k_{+2}AO - k_{-2}OB \qquad (**)$$

$$J = k_{+3}OB + k_{+3}AB - k_{-3} \cdot S_2 \cdot OO - k_{-3} \cdot S_2 \cdot AO$$

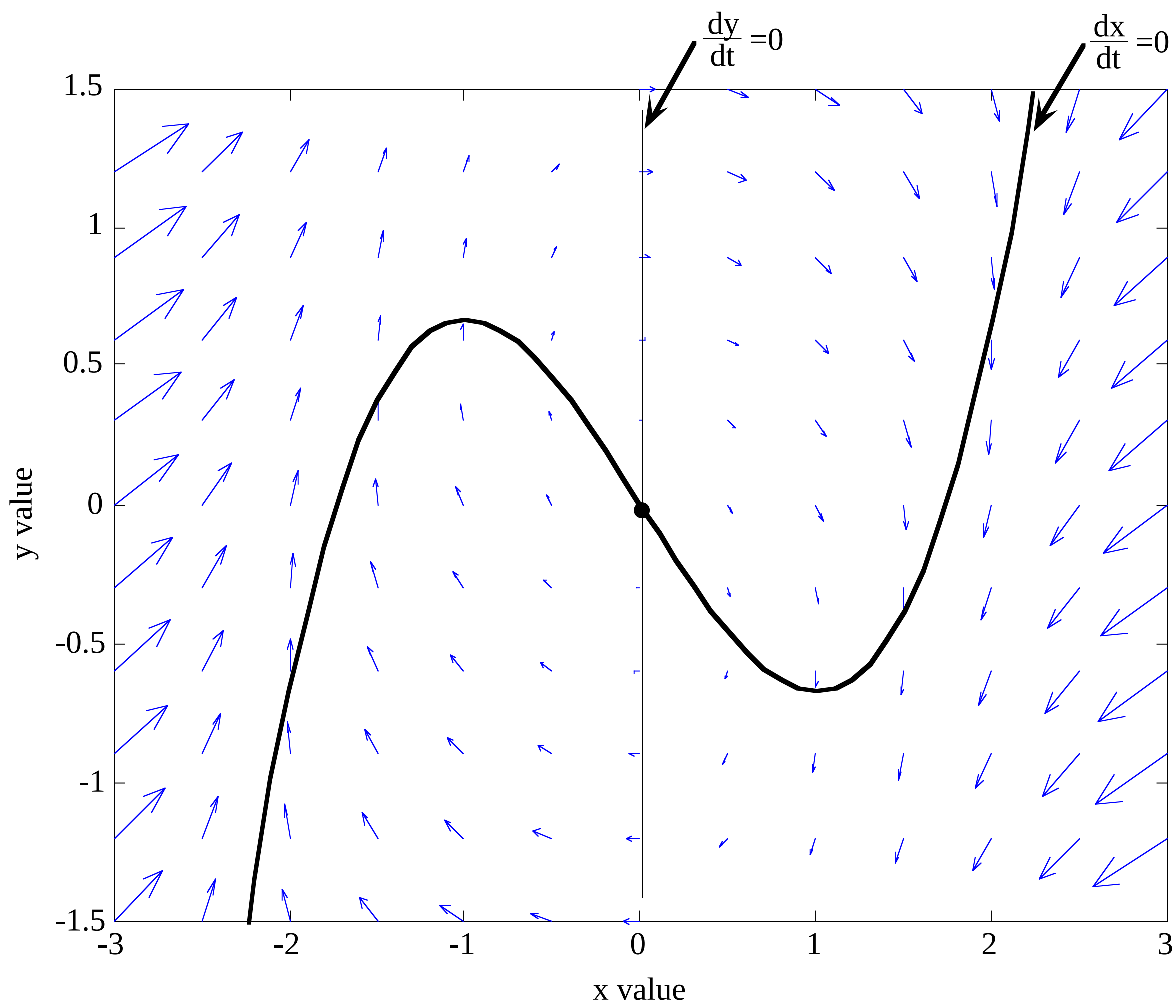
Each of these equations expresses the flux over one of the three barriers, in terms of the rate constants and the state transitions that lead to a flux over that barrier. From the steady state assumption, the three fluxes must be equal. A little algebra on the equations in (*) will show that this is so.

Note that Eqns. (**) could be written with the last equation in (*) ($Q = . . .$), yielding four equations in five unknowns, but it does not appear that a solution for flux can be obtained from these equations alone.

Part d If the ions interact within the channel, then the potential wells at sites *A* and *B* will have higher energies when both sites *A* and *B* are occupied. That is, the repulsion of ions can be modeled as an increase in energy at sites *A* and *B* when both are occupied, the amount of energy increase being the electrical potential seen from the other ion. This has the effect of changing the rate constants $k_{\pm 1}$ and $k_{\pm 3}$ for transitions to and from sites*A* and *B*. The primed rate constants in the figure above reflect this change in the model. Equations (*) and (**) can be rewritten in a straightforward way using the primed rate constants.

Problem 2

Part a The phase plane is drawn below (for the purposes of the exam, it is sufficient



to just draw a few arrows to show the general direction of the trajectories. The nullclines are shown. There is one equilibrium point, at the origin. The vectors show directions of trajectories for μ=1.

Part b The Jacobian of this system is

$$J = \begin{bmatrix} \mu(-x^2+1) & \mu \\ -\dfrac{1}{\mu} & 0 \end{bmatrix} \qquad J(0,0) = \begin{bmatrix} \mu & \mu \\ -\dfrac{1}{\mu} & 0 \end{bmatrix}$$

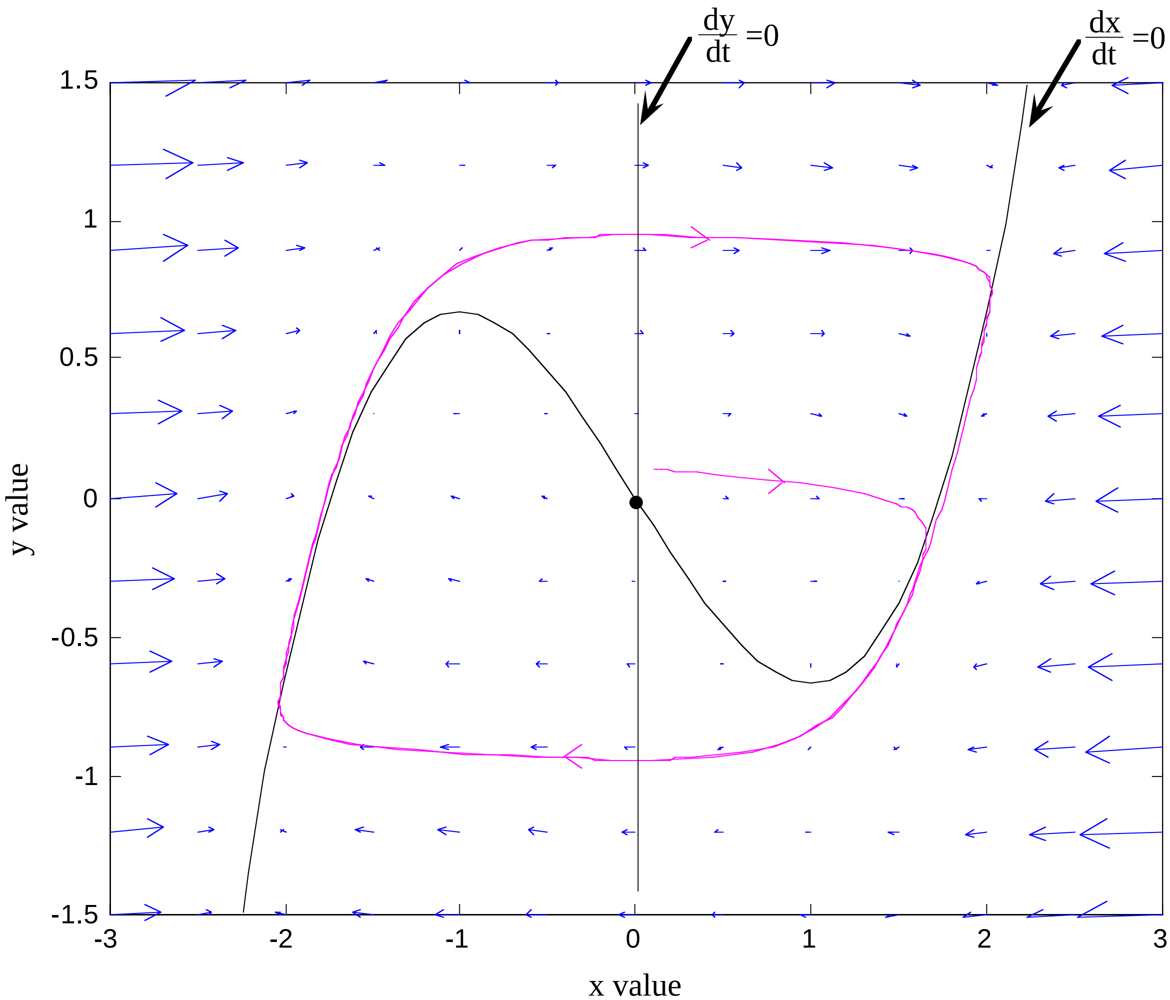
The eigenvalues of $J(0,0)$ are

$$\lambda = \frac{\mu}{2} \pm \sqrt{\frac{\mu^2-4}{4}}$$

for μ positive, the eigenvalues have positive real parts. They are complex for $\mu<2$ and real for $\mu \geq 2$. The equilibrium point at zero is therefore unstable for all positive μ.

The index of any closed curve surrounding the origin is +1, so it is possible that there is a limit cycle enclosing the origin. None of the methods considered in this course can be used to rule out (or prove the existence of) a limit cycle. Thus all we can conclude is that there could be a limit cycle surrounding the origin. The trajectories drawn in the phase plane above are consistent with this idea.

Part c As μ increases, the system becomes a low-temperature or relaxation oscillator. *dx*/*dt* becomes large compared to *dy*/*dt* and the trajectories become approximately horizontal, as shown in the phase plane below. The magenta line shows a limit cycle displayed by the system in this case (for μ=4). As μ increases, the trajectories become more and more horizontal and the limit cycle increasingly has two portions: a slow creep along the *dx*/*dt* nullcline, followed by a rapid transition from one side of the plane to the other.



Problem 3

Part a The cable equation takes its usual transformed form:

$$\frac{d^2\overline{V}}{d\chi^2} = q^2\,\overline{V} \tag{1}$$

where $\overline{V}$ is the transformed membrane potential $\overline{V}(\chi,q)$ and q is the transformed variable, e.g. $\sqrt{s+1}$ for Laplace transform problems.

The boundary conditions are that the axial current at χ=0 is the injected current and the axial current at χ=L is the current through the termination conductance G_{term}.

$$\bar{I}_{inj} = -G_\infty \left.\frac{\partial\overline{V}}{\partial\chi}\right|_{\chi=0} \quad \text{and} \quad G_{term}\overline{V}(L,q) = -G_\infty \left.\frac{\partial\overline{V}}{\partial\chi}\right|_{\chi=\text{L}} \tag{2}$$

where $\bar{I}_{inj}$ is the appropriate transform of the injected current, e.g. I_0/s for the current step in the case of a Laplace transform solution.

Part b The solution to Eqn. 1 is

$$\bar{V} = A\cosh(q\chi) + B\sinh(q\chi) \tag{3}$$

Using the boundary condition at χ=0 gives

$$\bar{I}_{inj} = -G_\infty \frac{\partial \bar{V}}{\partial \chi}\bigg|_{\chi=0} = -G_\infty qB\cosh q\chi\big|_{\chi=0} \quad \text{so that} \quad B = -\frac{\bar{I}_{inj}}{G_\infty q} \tag{4}$$

Writing the boundary condition at χ=L gives

$$G_{term}\,\bar{V}(L,q) = G_{term}\left[A\cosh(qL) - \frac{\bar{I}_{inj}}{G_\infty q}\sinh(qL)\right] = -G_\infty\left[Aq\sinh(qL) - \frac{\bar{I}_{inj}}{G_\infty q}q\cosh(qL)\right] \tag{5}$$

Solving for A gives

$$A = \frac{\bar{I}_{inj}}{G_\infty\, q}\frac{\frac{G_{term}}{G_\infty q}\sinh(qL)+\cosh(qL)}{\frac{G_{term}}{G_\infty q}\cosh(qL)+\sinh(qL)} = \frac{\bar{I}_{inj}}{G_\infty\, q}\frac{1+\frac{G_{term}}{G_\infty q}\tanh(qL)}{\frac{G_{term}}{G_\infty q}+\tanh(qL)} = \frac{\bar{I}_{inj}}{Y_{in}} \tag{6}$$

where Y_{in} is the input admittance of the cable at the electrode.

Using Eqns. 4 and 5, the solution in Eqn. 3 can be written as follows:

$$\bar{V}(\chi,q) = \bar{I}_{inj}\left[\frac{1}{Y_{in}}\cosh(q\chi) - \frac{1}{G_\infty q}\sinh(q\chi)\right] \tag{7}$$

Part c The easy way to do this is to note that the transfer impedance equation applies to this situation. That is,

$$\frac{\bar{V}(L,q)}{\bar{I}_{inj}} = \frac{1}{(Y_0+Y_L)\cosh(qL) + \left(\frac{Y_0 Y_L}{G_\infty q} + G_\infty q\right)\sinh(qL)}$$

$$\bar{V}(L,q) = \bar{I}_{inj}\,\frac{1}{G_{term}\cosh(qL) + G_\infty q\sinh(qL)} \tag{8}$$

where Y_0 is the load admittance at χ=0, which is 0, and Y_L is the load admittance at χ=L. Equation 8 can also be derived from Eqn. 7 with some algebra.

Part d The transform of the potential at χ=0 is (from Eqn. 7):

$$\overline{V}(\chi = 0, q) = \frac{\bar{I}_{inj}}{Y_{in}} = \frac{\bar{I}_{inj}}{G_\infty q} \frac{1 + \frac{G_{term}}{G_\infty q} \tanh(qL)}{\frac{G_{term}}{G_\infty q} + \tanh(qL)} \tag{9}$$

In general, there is no way to pull G_{term} out of this equation without simultaneously solving for G_∞ and L. However, if L<<1, then tanh(qL)≈qL and

$$\overline{V}(\chi = 0, q) = \frac{\bar{I}_{inj}}{G_\infty q} \frac{1 + \frac{G_{term}}{G_\infty q} \tanh(qL)}{\frac{G_{term}}{G_\infty q} + \tanh(qL)} \approx \frac{\bar{I}_{inj}}{G_\infty q} \frac{1 + \frac{G_{term}}{G_\infty q} qL}{\frac{G_{term}}{G_\infty q} + qL} \approx \frac{\bar{I}_{inj}}{G_\infty q} \frac{1}{\frac{G_{term}}{G_\infty q}} = \frac{\bar{I}_{inj}}{G_{term}} \tag{10}$$

In this case, the cable properties of the cylinder become unimportant and the input conductqance of the cylinder is just G_{term}. On the other hand, if L>>1, then tanh(qL)≈1 and

$$\overline{V}(\chi = 0, q) = \frac{\bar{I}_{inj}}{G_\infty q} \frac{1 + \frac{G_{term}}{G_\infty q} \tanh(qL)}{\frac{G_{term}}{G_\infty q} + \tanh(qL)} \approx \frac{\bar{I}_{inj}}{G_\infty q} \frac{1 + \frac{G_{term}}{G_\infty q}}{\frac{G_{term}}{G_\infty q} + 1} = \frac{\bar{I}_{inj}}{G_\infty q} \tag{11}$$

In this case, the cylinder approximates a cylinder of infinite length and G_{term} does not affect its input admittance.