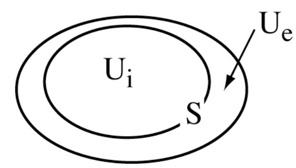
580.439/639 Final Exam 2012

Do all problems, closed book except for 2 pages of notes. Problems marked (**) are hairy, do them last. 20 points per problem plus 20 points for your name.

Problem 1

Consider the transport of an ion *X* with charge *z* between an intracellular compartment with volume U_i and an extracellular compartment with volume U_e as drawn at right. The area of the membrane between the compartments is *S*. The transport occurs through a channel with conductance G_X nA/cm^2 to which the usual HH formalism applies.



$$G_X(t) = \overline{G}_X\, m(t) \quad \text{where } m(t) \text{ is a HH gating variable}$$

Also assume that there is an active transport system for *X* in the membrane $J_{Xactive} = P(X_i, X_e, V)$ where $P(\cdot)$ is a function of the indicated variables with units moles/(s cm^2). The concentration X_e is constant, maintained by transport systems in other cells.

Part a) Assume that there is an energy source that drives the pump $P(\cdot)$ by providing energy up to *H* joules/mole for each mole of ion transported. Write an equation for the concentration X_i at which the pump system is at equilibrium.

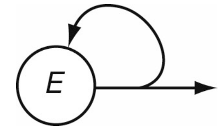
Part b) Write an equation for $P(X_i, X_e, \mathrm{V})$. You won't be able to write the full form of *P* without knowing more about the active transport system, but you should be able to show one important part of the equation (the part that makes it consistent with equilibrium thermodynamics) from your answer to part a).

Part c) Write differential equations that would allow solving for X_i the concentration of *X* inside the cell when it is not at equilibrium. Again, assume that X_e = constant, maintained by other mechanisms in the system. Don't solve anything, just write the equations. (Because there are other ions present, you can't write the equation for *dV/dt*, so don't worry about it.

Part d) Write the condition for steady state for this system at some membrane potential V_{SS}. Is this an equilibrium? (alternatively, under what condition would the steady state be an equilibrium?)

Problem 2

Consider a single neuron with excitatory feedback as sketched at right. The differential equation for this model is



$$\frac{dx}{dt} = -x + b\tanh(x)$$

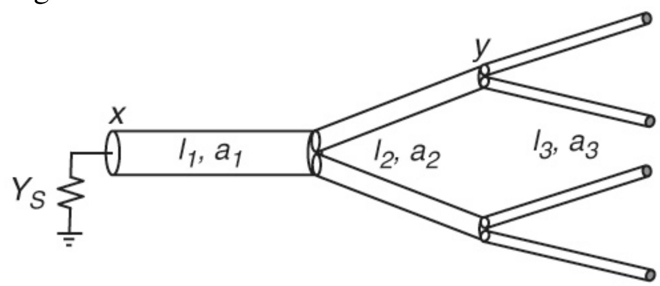
Part a) Find the equilibrium points for this model. Show that the number of equilibrium points varies with *b*. You will not be able to find numerical values of some of the equilibrium points, but you should show sketches of the solutions.

Part b) Classify the equilibrium points according to stability and draw a bifurcation diagram for the system, which plots equilibrium point(s) versus b.

Part c) The phase plane in this system is a line and trajectories are constrained to move along the line. Argue that this precludes any oscillation in this system, in the sense of a limit cycle.

Problem 3

Consider the cell drawn below. The cell has several primary dendrites, each of which branches as shown in the figure below.



There are three levels of branches, with lengths and radii as indicated. The lengths and radii of all branches in each generation are the same. The dendritic membrane has properties $R_m = 1/G_m$, R_i, and C_m as usual and the tree is assumed to be terminated by open circuit boundary conditions (no current out the end of the dendrites). The admittance of the soma is Y_S.

Part a) Write down conditions that allow this tree to be reduced to an equivalent cylinder and give the parameters τ_m, L, and G_∞ of the cylinder.

Part b) One definition of the electrotonic distance between points on a dendritic tree is $L_{xy} = -\ln[A(x,y)]$, where $A(x,y)$ is the complex voltage gain from point x to point y. That is, $A(x,y)$ is the ratio $V(y)/V(x)$ of the (Laplace transformed) voltage produced at y by a voltage clamp at x. Prove the following relationship between the forward and reverse voltage gains between x and y.

$$A(y,x) = \frac{K_{xx}}{K_{yy}} A(x,y) \quad , \qquad (*)$$

K_{xx} is the complex input impedance at point x and similarly for K_{yy}. You do not need the equivalent cylinder for this.

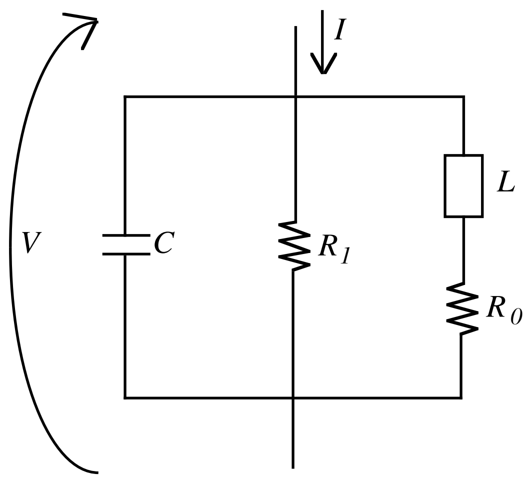
Part c) The third conclusion of the equivalent-cylinder theorem as discussed in class amounts to saying that K_{yx} in the figure above is the same as K_{zx} where z is the point in the equivalent cylinder that corresponds to y, i.e. a point at equal electrotonic distance from the soma. This relationship was not proven in class. It can be proven using the symmetry of the transfer impedance and the first part of the equivalent-cylinder theorem, which says that the potential is the same, as a function of electrotonic distance, in the original dendritic tree and the equivalent cylinder, if the potential is produced by a current injected at the soma (or a voltage clamp at the soma). Show that $K_{yx} = K_{zx}$.

Problem 4

Consider a dendritic membrane which consists of a membrane capacitance, a linear (i.e. constant-conductance) leakage channel, and a Hodgkin-Huxley style voltage-gated sodium channel. This problem considers the effect of the sodium channel on the cable properties of the dendrite.

Part a) This system has 2 differential equations, one for V and one for m. Compute a linearized approximation of the system around the resting potential V_R (don't worry about what V_R is, just assume that there is one). To make this algebraically tractable, assume that the inactivation variable h can be ignored, so that the sodium conductance is given by $g_{Na} = \overline{g}_{Na} m^3 h_\infty(V_R)$, with the inactivation gate held fixed at the h_∞ value at the resting potential.

Hint: you have seen this problem before; the linear approximation should take the form $d\vec{x}/dt = \mathbf{J}\vec{x} + \vec{i}$, where $\mathbf{J}$ is the Jacobian of the system at the resting potential and $\vec{i}$ is a vector containing external current excitation. Hint: Use $dm/dt = \alpha_m(1-m) - \beta_m m$, not the τ, m_∞ version of the equation.



(**) **Part b)** Show that the linearized model is equivalent to the linear circuit at right. Write expressions for C, R_0, R_1, and L (an inductance) in terms of the parameters of the Hodgkin-Huxley model derived in part a). (Hint: express the linearized model from a) in terms of Laplace transformed variables, from 0 initial conditions).

Part c) Write the cable equation for a membrane cylinder with the membrane conductance in the figure above. That is, use the circuit above instead of the usual linear cable with a capacitance and resistor as its transmembrane impedance. Express the result in Fourier transformed form, i.e. consider the system in sinusoidal steady state. The result should look like

$$\frac{d^2\mathbf{V}}{dx^2} = \gamma^2(j\omega)\mathbf{V}$$

Give an expression for γ.

(**) **Part d)** Write the boundary conditions for this cable model for a semi-infinite cylinder with a current $I_0\exp(j\omega_0 t)$ applied at $x=0$. That is, the cylinder runs from $x=0$ to positive infinity. Solve the cable equation for potential in the cylinder $V(x,t)$ with this boundary condition and the usual regularity condition that V is finite as x goes to ∞. (Hint: use the Fourier transform pair $\exp(j\omega_0\tau) \leftrightarrow 2\pi\,\delta(\omega-\omega_0)$).

The complex exponential is used to make the problem easier. Usually one is interested in the results of applying a sinusoidal current $I_0\cos(\omega t)$, which can be done by applying a sum of complex exponentials.