580.439/639 Final Exam, 2007

3 hours, closed book except for two-page cheat sheet, do all problems. Problem 4c should be done last.

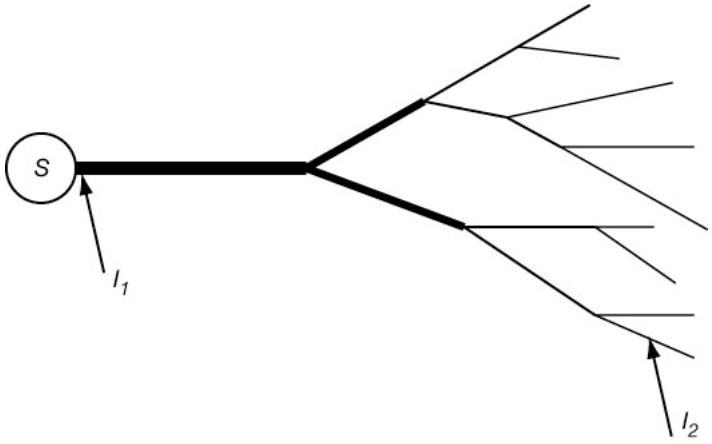
Problem 1 Short answers

Part a) (15 points) Linear cable theory predicts that EPSPs in the soma will be smaller when produced by synapses that are further from the soma along the dendrites. Describe (qualitatively) two ways in which neurons increase the effectiveness of synapses far from the soma.

Part b) (15 points) When a neuron spikes, the action potential often invades the dendritic tree. Explain how this could be useful in neural plasticity.

Part c) (15 points) Explain the difference, in terms of signaling in the neuron, between the Ca^{++} admitted to a spine head by opening synaptic channels and the depolarization of the spine head by those channels.

Part d) (20 points) Suppose that you apply a voltage clamp depolarization of a few mV to a passive dendritic tree at either I_1 or I_2, as indicated in the sketch at right. The voltage clamp is maintained constant to allow membrane potential to come to D.C. steady-state (i.e. $\partial V/\partial t=0$ in the cable equation). Argue that the membrane potential could be (approximately) an exponential function of distance from the site of current injection in one case but not the other. (Hint: the answer has nothing to do with active conductances.)



Part e) (20 points) Consider the differential equations for the harmonic oscillator *(r>0, k>0)*

$$\frac{dx_1}{dt} = x_2 \quad \text{and} \quad \frac{dx_2}{dt} = 1 - kx_1 - rx_2 \ .$$

Find the equilibrium point for this system and show that it is a stable global attractor by showing that the system has a Lyapunov function of the form $U(x_1, x_2) = a(x_1 - b)^2 + (x_2 - c)^2$ for suitable constants *a,b,* and *c*.

Part f) (20 points) Consider a "logic perceptron" which is a linear perceptron as defined in class with a sgn nonlinearity at the output. The inputs x_j, j=1, . . . N are either –1 or +1. The output is defined as

$$V = b + \sum_{j=1}^{N} w_j x_j \qquad y = \text{sgn}(V) \quad ,$$

where sgn(x) = -1 if x<0 and +1 if x≥0. The w_j are weights which can be any real numbers; b is a constant bias. Which of the following logical operations can be computed with this perceptron for two inputs, N=2? In each case, give a set of parameters (b,w_1,w_2) that would work.

(1) AND (output = +1 if both inputs are +1)

(2) OR (output = +1 if either or both input are +1)

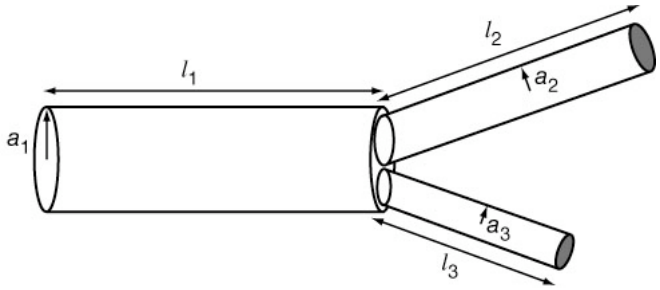
(3) EXOR (output = +1 if either input is +1, but not both)

(4) IMPLICATION (output = -1 only if x_1=+1 and x_2=-1)

(5) SAME (output = +1 if both inputs are –1 or both are +1)

State a rule that allows you to tell whether a particular computation can be done with this perceptron.

Problem 2



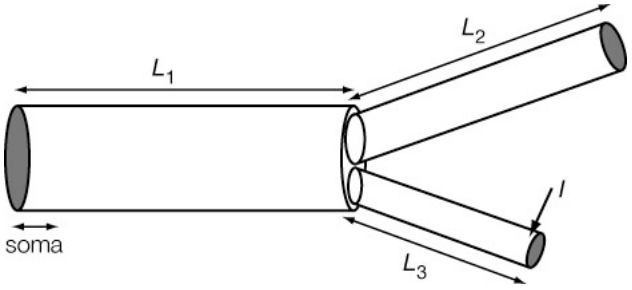
Part a) (15 points) Consider the dendritic branch point sketched at right. State the (nontrivial) conditions that are sufficient to allow this branch point to be represented as a single equivalent cylinder in a passive dendritic tree. Give the properties of the resulting equivalent cylinder (the physical length, radius, electrotonic length and G_∞). Assume that the membrane is uniform with the same properties everywhere. Assume that there is no axial current out of the tips of the dendritic branches, as indicated by the shading. You may have to add some parameters to the problem specification.

Part b) (20 points) Suppose that you add a voltage-gated potassium channel to the dendrites above. The HH model of the channel is as follows:

$$G_K = \bar{G}_K w \qquad \frac{dw}{dt} = \frac{w_\infty(V) - w}{\tau_w(V)} \qquad w_\infty(V) = 0.5\left(1 + \tanh\left(\frac{V+40}{10}\right)\right),$$

(and the details of $\tau_w(V)$ are not important). G_K has units mho/area, the same units as G_m, the resting membrane conductance/area in the absence of G_K. Assuming that V is constant at a potential V_1 everywhere in the dendritic tree, can the equivalent cylinder reduction still be applied? If not, say why not. If so, what effect does adding the potassium channel have on the equivalent cylinder (i.e. how do the parameters of the equivalent cylinder change from the case without G_K) and what is the potential V_1? (Hint: it may be wise to go back to the derivation of the cable equation in your thinking about this problem.)

Problem 3



For this problem, suppose that the soma and dendritic tree of a neuron can be represented as in the single branching structure at right. The soma is incorporated into the first dendritic

branch as indicated; as a result, there is no need to add a somatic load admittance to the model and the tree is assumed to have no axial current at either end, as indicated by the gray shading. Assume a passive, linear tree.

For this problem, assume that the electrotonic lengths $L_1=L_2=L_3$ to simplify the algebra.

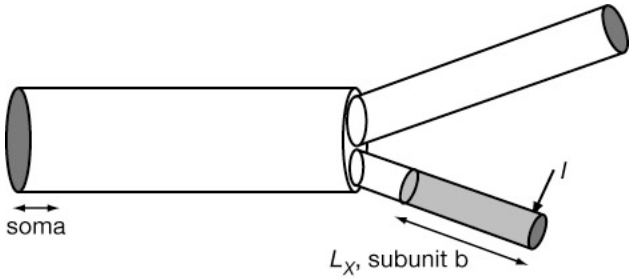
In class, the idea of a subunit of a dendritic tree was developed. For the model above, consider a subunit associated with the end of dendritic branch 3. Suppose current I is injected into the tree at the end of branch 3 as shown by the arrow. The subunit associated with I is the set of points j such that

$$\frac{V_j}{V_I} > C\frac{V_0}{V_I} \ , \qquad \text{(subunit)}$$

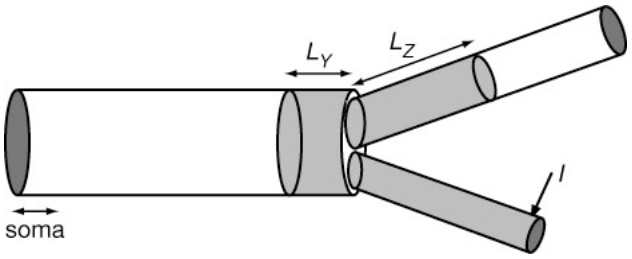
where V_I is the potential produced at the point of current injection, V_j is the potential at point j, and V_0 is the potential at the left end of the first branch, i.e. in the soma. C is a constant (typically 4-10).

Part a) (20 points) Show that the definition of a subunit above can be written in terms of transfer impedances as $K_{Ij}/K_{I0} > C$.

Part b) (20 points) Supppose that the subunit is confined to branch 3 of the dendritic tree, as shown by the shaded cylinder at right. Write the equation that would have to be solved to find the length of the subunit L_X. Just write the equation, you don't need to solve it.



Part c) (25 points) Suppose the subunit extends into branches 1 and 2 as in the shaded regions in the figure at right. Again, write the equations necessary to find the electrotonic distances L_Y and L_Z.



Problem 4

Mammalian outer hair cells have a specialized transporter molecule in their membranes called prestin. Prestin contains a site to which Cl^- can bind in a first-order reaction. When the chloride binds, it increases the cross sectional area of the prestin, which can do mechanical work in the membrane, i.e. change the length of the cell or its stiffness. Although this mechanical effect is important in hearing, in this problem we consider only the electrical effects of prestin on the membrane current-voltage characteristic. (Note that some aspects of this problem are controversial and are still being researched).

Part a) (20 points) Suppose that binding Cl^- to prestin is a first-order process described by

$$P + Cl^- \underset{k_r}{\overset{k_f}{\rightleftharpoons}} PCl \ .$$

Cl^- enters prestin from the inside of the cell and does not pass all the way through the membrane. When Cl^- binds to prestin, the free energy of the system changes for three reasons:

(1) Cl^- moves through a fraction λ of the membrane potential V; the resting potential of the hair cell is –50 mV or so, typical of neurons.

(2) There is a free energy of interaction between Cl^- and the binding site in prestin, an amount G^*.

(3) A certain amount of work W is done expanding the cross sectional area of the prestin.

Draw a barrier diagram for this system containing two sites, Cl^- free in solution and Cl^- bound to prestin, separated by a barrier. Write an equation for G_S, the difference in free energies between Cl^- free in solution and bound to the site.

Also, write a differential equation for the PCl state in the reaction sketched above, assuming there is a fixed total amount of prestin available, but an excess of Cl^- so that $[Cl^-]$ = constant. Write equations for the forward and reverse rate constants k_f and k_r from the barrier diagram. Assume that the Cl^- has passed over $\lambda/2$ of the membrane potential at the barrier peak and that no work has been done at that point.

Part b) (15 points) Now consider the effects of small changes of membrane potential on the fraction of prestins with bound chloride. We want to do a small-signal analysis from a steady state of membrane potential V_0 with bound prestin fraction Π_0. The deviations from the steady state are v and π, so that

$$V = V_0 + v \quad \text{and} \quad \Pi = \Pi_0 + \pi$$

Assume that the system is in steady state where $d\Pi/dt = 0$ and write an equation relating V_0 and Π_0.

Part c) (30 points) (a hairy mess, do this last) Differentiate the steady-state relationship derived in Part b) to obtain a relationship between v and π. This can be done in several ways. Start by substituting the voltage dependence into the rate constants. The easiest way to proceed is to differentiate the steady-state relationship after substituting the voltage dependence and use the steady-state relationship to simplify terms. A second approach is to substitute V_0+v and $\Pi_0+\pi$ into the steady state relationship and cancel the terms that relate V_0 and Π_0 in the steady state, and also cancel the second order terms (in $v\pi$).

Note that either method is the same as assuming that the chloride movements are rapid (in equilibrium) compared to the slower electrical potential changes that drive the charge movements.

The result should be in the form

$$-\pi = C_{NL} v \qquad (*)$$

where C_{NL} is a function of V_0, Π_0, and the parameters only. Of course Π_0 can be written as a function of V_0 from the steady-state relationship, so C_{NL} is really only a function of V_0.

Part d) (15 points) Argue that the $-d\pi/dt$ is proportional to the current carried out of the cell by chloride. You should then conclude that Eqn. (*) in part c) is exactly the current-voltage relationship of a capacitor C_{NL} (*NL* for nonlinear).

Part e) (15 points) When the capacitance C_{NL} is measured as a function of V_0 by setting a steady D.C. membrane potential equal to V_0 and using a small sinusoidal v to measure the capacitance, it is found to have a form something like the plot at right. This is actually a measure of the total capacitance of the cell, which is the sum of the usual membrane capacitance C equal to 1 μfd/cm^2 (the dashed line) and C_{NL}. Explain why the nonlinear capacitance goes to zero (total capacitance goes to 1 μfd/cm^2) at large positive or negative holding membrane potentials (V_0). This can be done with C_{NL} computed in part c) above or from a consideration of the state of the prestin molecules and the steady state relationship.