580.439 Final Exam, 1997

3 hours, closed book except for two pieces of paper, do all problems.

Problem 1

20 pts For the model considered in part 15 of Project 1, construct an (n,V) phase-plane for the reduced model with f_{ni} = 0.2. Show nullclines, stable and unstable manifold (if present), compute the equilibrium points and classify them according to type and stability. Show a small number of trajectories to illustrate the behavior of this system. (This should have been prepared before the exam and handed in with the exam).

Problem 2

20 pts **Part a)** On a comet, cells are found with the ionic distribution across their cell membranes given in the table at right. All three ions are potentially permeable through the cell membrane at rest. Draw an electrical circuit for this membrane, assuming that the same general properties of membrane physiology apply to these cells as to the cells with which we are familiar. If there are batteries in your circuit, be sure to compute their values. Write an equation for the resting potential <u>in terms of the parameters of the circuit model</u> (Hint: this is NOT, repeat NOT, the GHK equation).

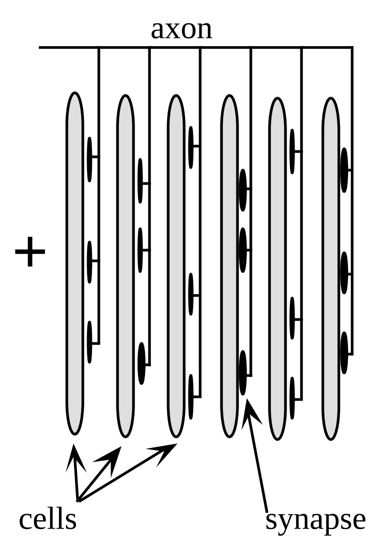
	in	out
Cl^-	80	4
F^-	1	90
K^+	10	94

20 pts **Part b)** The resting potential in this cell is +58 mV. A variety of manipulations of the K^+ concentrations inside and outside the cell do not change the resting potential at all, whereas changes in the Cl^- and F^- concentrations do change the resting potential. What do these facts suggest about the unknown parameters in your circuit model? You should be able to estimate ratios of conductances, like g_K/g_{Cl} and g_F/g_{Cl}. Give these ratios for the resting cell.

20 pts **Part c)** When perturbed, the cells change their membrane potential to -30 mV, which initiates cell defenses. What are the possible mechanisms (at least two) which could cause this change in potential? Do not invent any new ionic conductances for this part. It is observed that the total conductance of the membrane <u>decreases</u> when the potential changes to -30. What does this suggest about the underlying changes in ionic conductances?

20 pts **Part d)** A virus is found on another comet which, when it infects the cells of parts a)-c), changes the membrane potential when the cell is perturbed to about +27 mV (instead of -30); <u>the resting potential is not changed</u>. This is below the threshold of the defense mechanism and ultimately kills the cell. After the virus infection, changing the K^+ concentration outside the cell significantly affects the resting potential. Suggest a way in which the virus could cause these effects by affecting K^+ currents only (Hint: viruses frequently insert genes for new proteins into cells' DNA). Assuming that only K^+ currents are affected, recalculate the conductance ratios.

Problem 3

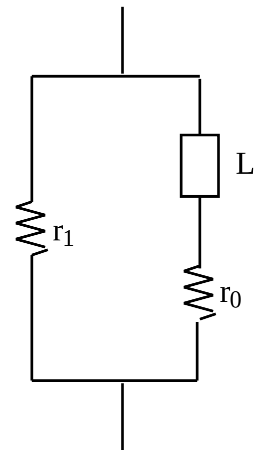


30 pts The electric organ of a certain fish consists of a specialized stack of cells, as drawn at right. The cells have a resting intracellular potential of -60 mV, as usual. They receive a heavy cholinergic innervation by synapses <u>on one side only</u>, as drawn; the synapses are the black blobs on the right side of the cells. The synapses are all activated synchronously by the axon shown. Draw an electrical circuit model for this system with and without synaptic activation and

explain why it produces a potential difference, as indicated by the + and - signs, when the synapse is activated. Approximately how large is the potential produced? Assume for simplicity that the reversal potential of the synapse is 0 mV and that the synapse has a large conductance compared to the resting membrane.

Problem 4

In a homework, it was shown that a delayed rectifier potassium channel of the Hodgkin-Huxley (HH) variety can be linearized to the circuit sketched at right. Only the components of the circuit related to the K^+ channel are shown; in the circuit considered in the homework, the membrane capacitance and the membrane leak conductance were also included. The values of the linearized K channel components are given by the equations below:



$$1/r_1 = \bar{g}_K n_\infty^4(V_r)$$

$$L = \frac{\tau_n(V_r)}{\left.\frac{\partial g_K(t\to\infty)}{\partial V}\right|_{V=V_r}(V_r - E_K)} = \frac{\tau_n(V_r)}{4\,\bar{g}_K\; n_\infty^3(V_r)\left.\frac{\partial n_\infty}{\partial V}\right|_{V=V_r}(V_r - E_K)}$$

$$r_0 = L/\tau_n(V_r)$$

where V_r is the resting potential, $n_\infty(V)$ is the steady state value of the delayed-rectifier's HH gating variable n, and $\tau_n(V)$ is its time constant.

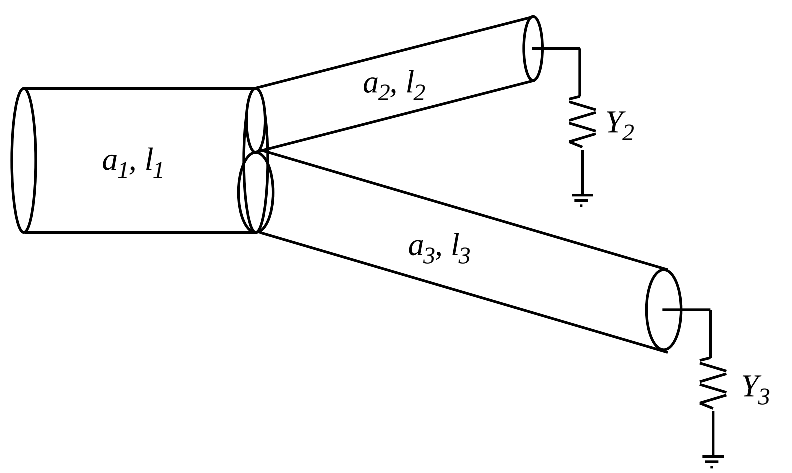
Part a) Argue that the same circuit and similar equations would result if this analysis were
30 pts repeated for a persistent Na channel, i.e. a Na channel with only an m gate and no inactivation (h) gate Do this by writing a HH model for the persistent Na channel and comparing it to the HH model for the K channel. You can do this part by considering only the equations above, without having to rederive the linearization. Write the equations for r_0, r_1 and L for your persistent Na model.

20 pts **Part b)** Some components in the linearized circuit of part a) should be negative for the persistent Na channel. Which ones? Clearly justify your answer, using your equations from part a).

Part c) Draw a circuit for a linearized compartmental model of a dendrite containing only membrane capacitance, a leakage conductance, and a persistent Na conductance. It turns out that
20 pts $|r_1| >> |r_0|$ at the resting potential. If this is so, what effect will addition of persistent Na channels have on the D.C. space constant λ of a dendritic cylinder?

Problem 5

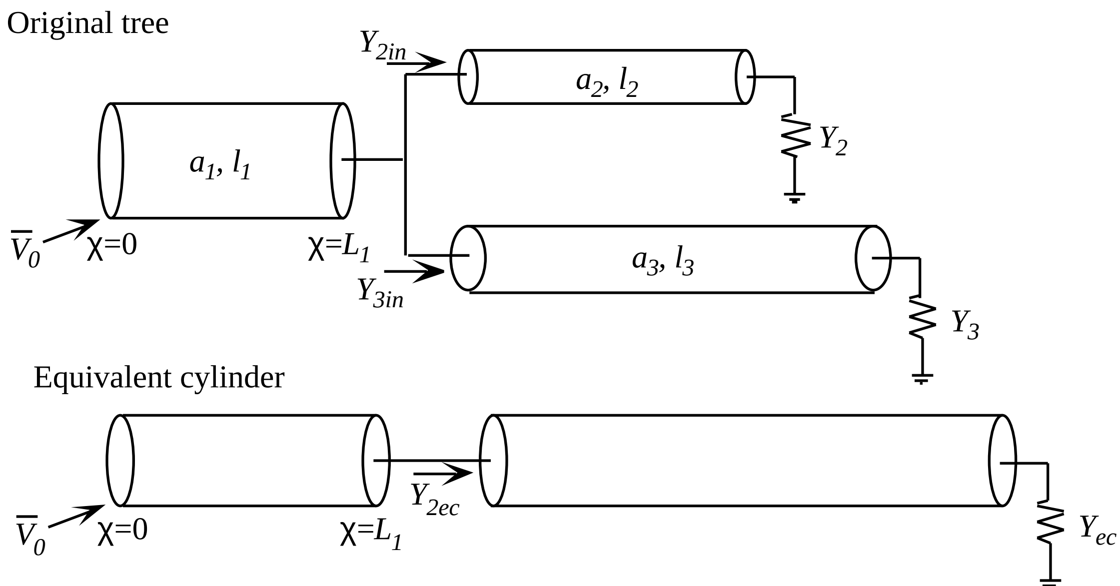
Consider the dendritic branchpoint sketched at right. The radii a_i and physical lengths l_i are given, along with the termination admittances Y_2 and Y_3. Note that $a_2 \neq a_3$, $l_2 \neq l_3$, and $Y_2 \neq Y_3$.



Part a) Under what conditions is it possible to reduce this tree to an
20 pts equivalent cylinder? Give the conditions in terms of the parameters in the figure and the electrical parameters R_i, R_m, and C_m.

20 pts **Part b)** Sketch the equivalent cylinder and give its parameters in terms of the parameters defined in part a); specify the radius a_{ec}, length l_{ec}, electrotonic length L_{ec}, G_∞ value, and termination admittance for the equivalent cylinder.

30 pts **Part c)** Show that if the tree is voltage clamped to potential $\bar{V}_0$ at the left end of the parent branch, then the potential $\bar{V}(\chi)$ is the same in the parent branch of the original tree and in the corresponding portion of the equivalent cylinder, i.e. $\bar{V}(\chi)$ is the same for $\chi=[0,L_1]$, where L_1 is the electrotonic length of the parent branch in the original tree. (of course, the equivalent cylinder theorem guarantees this, but in this problem you are asked to show that the theorem is correct); in doing this, you may assume that $Y_{2ec} = Y_{2in}+Y_{3in}$ in the drawing below. This fact is part of the equivalent cylinder theorem and was proved in class.



30 pts **Part d)** Extend the results above to show that $\bar{V}(\chi)$ is the same throughout the original tree and the equivalent cylinder.