580.439/639 Final Exam, 2009

Three hours. Do all problems. Closed book except for two sheets of paper. 300 points total.

Problem 1

Part a) (5 points per subpart) A membrane separates two solutions containing different concentrations of ions. There is a potential difference across the membrane. In each case below, can the potential be an equilibrium potential for all the permeant ions? Assume that all ions are permeable except for P^-, a large negatively charged molecule with no membrane transport system.

Subpart 1) Side 1: Na – 100 mM, K – 10 mM, Cl – 110 mM
Side 2: Na – 10 mM, K – 100 mM, Cl – 110 mM

Subpart 2) Side 1: Na – 100 mM, Cl – 100 mM
Side 2: Na – 10 mM, Cl – 10 mM

Subpart 3) Side 1: Na – 100 mM, P – 99 mM, Cl – 1 mM
Side 2: Na – 10 mM, Cl – 10 mM

Subpart 4) Side 1: Na – 100 mM, P – 100 mM
Side 2: Na – 10 mM, P – 10 mM

Subpart 5) Side 1: Ca – 10 mM, P – 9.9 mM, Cl – 0.1 mM
Side 2: Ca – 1 mM, Cl – 1 mM

Part b) A certain organelle of a cell is known to contain an active transport system for Ca^{++} which moves calcium into the organelle from the cytoplasm using energy from a high-energy molecule like ATP. Other than this transporter, nothing else is known to be (or not to be) in the organelle membrane.

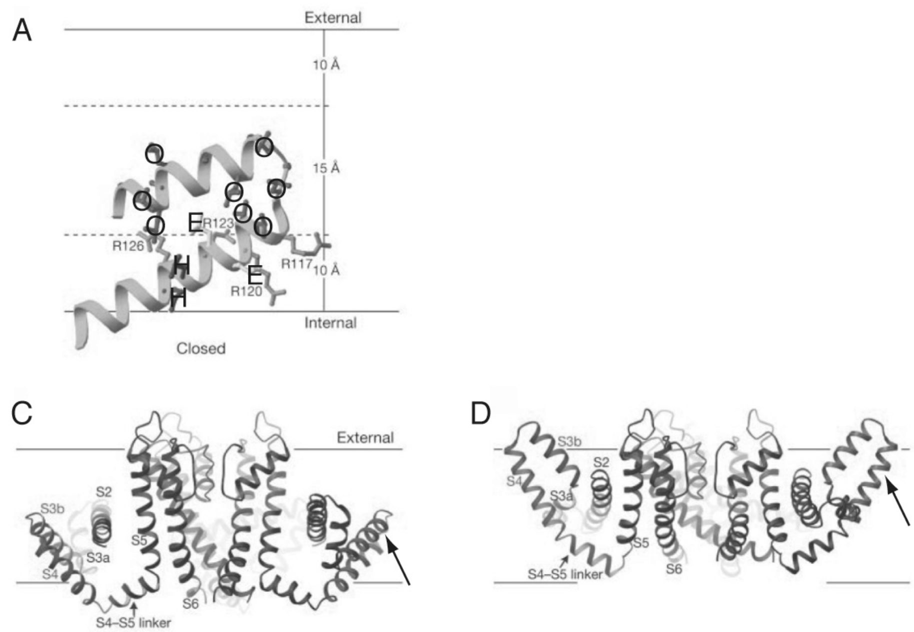
Subpart 1) (20 points) What determines the steady state concentration of Ca^{++} in the organelle, assuming that the concentration in the cell cytoplasm is fixed by other mechanisms? There are at least two possibilities, depending on what else is in the membrane. Give equations to clearly define the steady-state conditions in each case.

Subpart 2) (20 points) Suppose the Ca^{++} concentration in the cytoplasm doubles because of gating on of Ca^{++} channels in the surface membrane of the cell. For each of the mechanisms you listed in subpart 1), tell what would happen to organelle Ca^{++} concentration in this case.

Part c) The figure below shows the hypothesized structure of a voltage-gated potassium channel (like the HH delayed rectifier) with its gate closed (part C) or open (part D; from Jiang et al. Nature 423:42, 2003). The arrows in C and D point to the gating paddle, a pair of alpha helices that move through the membrane when gating occurs.

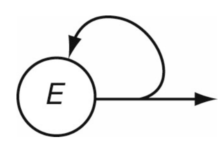
Subpart 1) (20 points) Explain what the various parts labeled on the diagram show, i.e. S1, S2, etc. Identify each of the Sn's with their function in the channel (if known). Explain what is thought to occur in this channel when the gate opens or closes. What is the energy that drives gating?

Subpart 2) (20 points) Part A of the figure shows the gating paddle when it is in the closed state (as in part C of the figure). The letters (*O, H, E*) identify residues of the protein that can be attacked chemically from outside the cell only (*O*), from inside the cell only (*H*), or from either location (*E*). Explain the significance of these data.



Problem 2

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



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

where x is the membrane potential of the neuron and $\tanh(x)$ is the squashing function at the output.

Part a) (25 points) Write an equation for the equilibrium points for this model. Show that the number of equilibrium points varies with b and give the number of points and the critical values of b that determines the number. You will not be able to find numerical values of some of the equilibrium points, but show a rough graph of the solution.

Part b) (25 points) Classify the equilibrium points according to stability and draw a bifurcation diagram for the system, which plots equilibrium point(s) versus b. You may not be able to calculate eigenvalues at some of the equilibrium points, but you should be able to argue for stability or instability, using the fact that this is a 1st-order system.

Part c) (25 points) 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 a one-layer linear network which develops its weights using Oja's rule, discussed in class. The neuron and learning rule are described by the following equations.

$$v = \vec{w}^T \vec{u} \quad \text{and} \quad \Delta\vec{w} = \varepsilon\left[v\vec{u} - v^2\vec{w}\right] \quad \text{where} \quad \vec{w}(n+1) = \vec{w}(n) + \langle \Delta\vec{w} \rangle$$

where $\vec{u}$ is the (column) vector of inputs to the neuron, $\vec{w}$ is the weight vector (column), and v is the neuron's output. It was shown in class that the learning rule given above, when averaged over an ensemble of inputs $\{\vec{u}\}$, gives a weight vector with unit length $\|\vec{w}\| = 1$ which is an eigenvector of the correlation matrix of the inputs $\mathbf{C} = \langle \vec{u}\,\vec{u}^T \rangle$, and it was stated that this is the eigenvector corresponding to the largest eigenvalue. The average $\langle\,\rangle$ in the definition of $\mathbf{C}$ is taken over all the input vectors. Assume for simplicity that $\mathbf{C}$ is full rank so that the eigenvectors form a complete basis set for the N-dimensional input vectors $\vec{u}$.

Part a) (25 points) Assuming that $\vec{w}$ is the largest-eigenvalue eigenvector of $\mathbf{C}$, show that the network maximizes $\langle v^2 \rangle$, the average value of the output-squared across the input ensemble $\{\vec{u}\}$, for all possible weight vectors with $\|\vec{w}\| = 1$.

Now consider a network with two output neurons, both connected to the same input $\vec{u}$. The neurons are described as follows:

$$v_1 = \vec{w}_1^T\vec{u} \quad \text{and} \quad v_2 = \vec{w}_2^T\vec{u} - b\,v_1 \qquad (*)$$

Neuron 1 is equivalent to the neuron considered in part a). Neuron 2 has a similar set of weights $\vec{w}_2$ connected to the same inputs as 1, but also receives a connection from the output of neuron 1 with weight b. Through some magic, the weight b is set to the value $b = \vec{w}_2^T\vec{w}_1$.

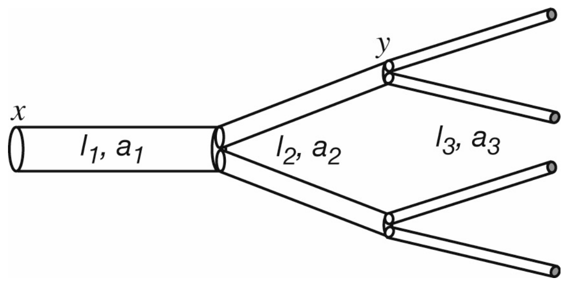
The weights $\vec{w}_1$ and $\vec{w}_2$ are trained in the same unsupervised way as for the neuron in part a). Note that weight b is not trained, but is just set to the value $\vec{w}_2^T\vec{w}_1$ after each update of the input weights.

Part b) (20 points) Argue that neuron 1 will come to the same steady state as the neuron in part a), with $\vec{w}_1$ equal to the largest eigenvector of $\mathbf{C}$.

Part c) (25 points) What value will $\vec{w}_2$ take in steady state? (Hint: rewrite Eqn. (*) in the form $v_2 = \vec{w}_2^T\vec{u}^*$ for some modified input vector $\vec{u}^*$ and then apply the results of Oja's rule.)

Problem 4

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



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).

Part a) (25 points) 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) (25 points) Suppose that this cell has spines in its dendritic tree, but the distribution of spines is non-uniform. To make matters simple, suppose that the secondary dendrites (l_2, a_2) have spines and the other dendrites do not. To add spines to the cable model, one approximate approach is to assume that each spine adds a small conductance g_s and capacitance c_s to the dendritic membrane parameters G_m and C_m. If there are N spines on each secondary dendrite, do the conditions for reduction to an equivalent cylinder worked out in part a) still hold? If not, why not and what change would make them hold (other than N=0)? Assume DC steady state for this part!

Part c) (15 points extra credit) Does your answer to part b change for conditions other than the DC steady state? If so, explain why. (OK, this is an unfair question, since it involves an assumption that was not explicitly discussed while deriving the cable equation. See if you can figure it out for extra credit.)