580.439/639 Final Exam solutions

Problem 1

Part a) No direct potential change because no charge is carried across the surface membrane of the cell.

Part b) Calcium-activated channels could indirectly change the membrane potential. The calcium-dependent potassium channels were studied in class; in increase in Ca would hyperpolarize the cell through them. There are other calcium-dependent processes including inactivation of calcium channels, activation of Cl⁻ channels, and activation of 2nd-messenger systems that could change the membrane potential of the cell.

Problem 2

Part a) Any step that translates a charge through some fraction of the membrane potential (between the heavy lines in the sketch) will be voltage-dependent. For this case the following should be voltage-dependent:

k_1 and k_{-1} with gating charge $\lambda_1 z_L$ where λ_1 is the fraction of the membrane potential through which L^+ moves.

k_3 and k_{-3} with gating charge $\lambda_2 z_L$ where λ_2 is the fraction of the membrane potential through which L^+ moves and $\lambda_3 z_E$ where λ_3 is the fraction of membrane potential through which fixed charges on the protein move.

k_4 and k_{-4} with gating charge $\lambda_4 z_L$ where λ_4 is the fraction of the membrane potential through which L^+ moves.

k_6 and k_{-6} with gating charge $\lambda_5 z_E$ where λ_5 is the fraction of membrane potential through which fixed charges on the protein move.

The rest ($k_{\pm 2}$, $k_{\pm 6}$) should not be voltage-dependent.
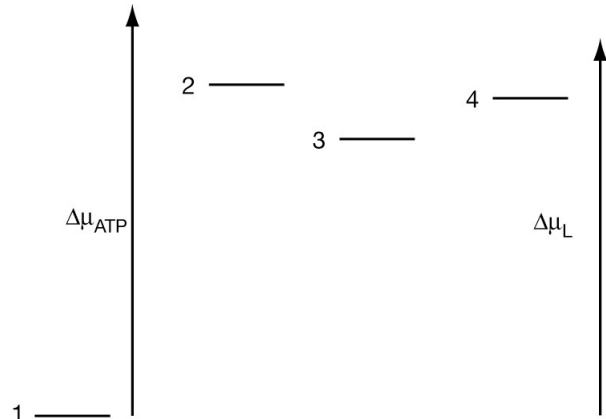
Part b) The net reaction is

$$L_1 + ATP \rightleftharpoons L_2 + ADP + P,$$

with free energy change as follows:

$$\Delta\mu = \mu_{L2} - \mu_{L1} + \mu_{ADP} + \mu_P - \mu_{ATP} = \Delta\mu_L + \Delta\mu_{ATP}$$

The change in free energy of L^+ is $RT \ln L_2/L_1 + z_L F(V_2 - V_1)$. The free energy change of ATP is the energy of hydrolysis of ATP to ADP.

Part c) Δμ<0.

Part d) One such diagram is shown at right. Remember that this is the free energy of E plus L^+ and does not include the ATP molecule This diagram assumes that the membrane potential is negative as usual. From state 1 to 2, $\Delta\mu_{ATP}$ is transferred to E. Presumably the process is not 100% efficient so the energy level of state 2 is lower than it would be if all energy were transferred. From state 2 to 3 there is a change in conformation of E and a translation of charges through some fraction of the membrane potential. The net free energy change is drawn as negative, but it need not be. From 3 to 4 L^+ moves out of E and through the final part of the membrane potential, so the free energy should increase somewhat. $\Delta\mu_L$ is shown at right. It is larger than the relative energy of state 4 versus state 1 because L^+ is translated partway through the membrane potential in state 1.

Problem 3

Part a) For the nullclines:

$$\frac{dx}{dt} = 0 \quad \Rightarrow \quad y = d(x-a)^2 + b$$

$$\frac{dy}{dt} = 0 \quad \Rightarrow \quad y = c(x-a) + b$$

The constant d is needed to obtain the point $(3a/2, b+a^2d/4)$ as shown in the graph in the problem statement. The slope c of the line was given in the problem statement.

A convenient set of differential equations with these nullclines is as follows:

$$\tau\frac{dx}{dt} = I + d(x-a)^2 + b - y$$

$$\frac{dy}{dt} = c(x-a) + b - y$$

The current I has been added to the equation for membrane potential (x) as requested. A useful degree of freedom is the time constant τ in the first equation. This can be any finite non-zero number, including negative numbers without changing the nullclines. This is an illustration that the nullclines don't fully-specify the dynamics of a system. There is no need for a second time constant in the equation for dy/dt because it can be set to 1 by a change in the time variable.

Part b) With the change of variables $v = \sqrt{d}(x-a)$ and $u = y - b$ and defining $\tau = \sqrt{d}$, the differential equations become

$$\tau \frac{dx}{dt} = \sqrt{d} \frac{1}{\sqrt{d}} \frac{dv}{dt} = \frac{dv}{dt} = I + v^2 - u$$
$$\frac{dy}{dt} = \frac{du}{dt} = \frac{c}{\sqrt{d}} v - u$$

(1)

This is the form specified in the problem set. For an arbitrary value of τ, the differential equations are

$$\frac{\tau}{\sqrt{d}} \frac{dv}{dt} = I + v^2 - u$$
$$\frac{du}{dt} = \frac{c}{\sqrt{d}} v - u$$

(2)

Part c) The Jacobian for the system in Eqn. 2 at the equilibrium point (0,0) is

$$J = \begin{bmatrix} 0 & -\dfrac{\sqrt{d}}{\tau} \\ \dfrac{c}{\sqrt{d}} & -1 \end{bmatrix},$$

which gives the following eigenvalues:

$$\lambda = \frac{-1 \pm \sqrt{1 - 4c/\tau}}{2}.$$

The eigenvalues have the following characteristics:

$c/\tau > 0.25$ λ are complex, giving stable spirals

$0 < c/\tau \le 0.25$ negative real λ, stable eq. pt.

$c/\tau \le 0$ saddle nodes, unstable (allowed if $\tau < 0$)

If $\tau = \sqrt{d}$, then only the first two apply. Again, this analysis shows that the nullclines by themselves don't specify the dynamics of the system.

Problem 4

Part a) Applying the boundary conditions specified to the solution given in the problem statement:

$$\overline{V}(0,q) = \overline{V}_0 = A + B$$

$$\overline{I}_i(L,q) = \overline{I}_1 = -G_\infty \frac{\partial \overline{V}}{\partial \chi}\bigg|_{\chi=L} = -G_\infty q \left[A e^{qL} - B e^{-qL} \right].$$

Solving for A and B gives

$$A = \frac{e^{-qL} \overline{V}_0 - \dfrac{1}{qG_\infty} \overline{I}_1}{2\cosh qL} \qquad B = \frac{e^{qL} \overline{V}_0 + \dfrac{1}{qG_\infty} \overline{I}_1}{2\cosh qL}$$

Then substituting for A and B in the equations for $\overline{V}$ and $\overline{I}_i$ gives

$$\begin{aligned}
\overline{V}(\chi,q) &= \frac{e^{-qL}\overline{V}_0 - \dfrac{1}{qG_\infty}\overline{I}_1}{2\cosh qL} e^{q\chi} + \frac{e^{qL}\overline{V}_0 + \dfrac{1}{qG_\infty}\overline{I}_1}{2\cosh qL} e^{-q\chi} \\
&= \overline{V}_0 \frac{\cosh\big(q(L-\chi)\big)}{\cosh qL} - \overline{I}_1 \frac{\dfrac{1}{qG_\infty}\sinh(q\chi)}{\cosh qL}
\end{aligned} \tag{3}$$

and

$$\begin{aligned}
\overline{I}_i(\chi,q) &= -G_\infty \frac{\partial \overline{V}}{\partial \chi} = -qG_\infty \frac{e^{-qL}\overline{V}_0 - \dfrac{1}{qG_\infty}\overline{I}_1}{2\cosh qL} e^{q\chi} + qG_\infty \frac{e^{qL}\overline{V}_0 + \dfrac{1}{qG_\infty}\overline{I}_1}{2\cosh qL} e^{-q\chi} \\
&= qG_\infty \overline{V}_0 \frac{\sinh\big(q(L-\chi)\big)}{\cosh qL} + \overline{I}_1 \frac{\cosh(q\chi)}{\cosh qL}
\end{aligned} \tag{4}$$

Part b) In the open circuit case, $\overline{I}_i(\chi = L, q) = 0$, so the potential and current at χ=0 can be computed from substituting in Eqns. 3 and 4, giving

$$\overline{V}(0,q) = \overline{V}_0 \quad \text{and} \quad \overline{I}_i(0,q) = \overline{V}_0 q G_\infty \tanh(qL) .$$

The input admittance of the cable at χ=0 is the ratio of these;

$$\overline{Y}_{in}(\chi = 0, q) = \frac{\overline{I}_i(\chi = 0, q)}{\overline{V}(\chi = 0, q)} = qG_\infty \tanh qL$$

Part c) The point of all the hints is that the equivalent cylinder theorem (ECTh) applies here. The problem statement said that all cylinders have electrotonic length L, making the first condition of the ECTh true. The 3/2 branching power rule also holds, as verified by computation:

$$a_0^{3/2} = (0.38\,a_0)^{3/2} + (0.84\,a_0)^{3/2}$$

and all termination conditions are equivalent. Thus this tree is equivalent to a single cylinder of length $2L$ with the G_∞ value of the parent cylinder. The result of part b) applies to this equivalent cylinder, so $\overline{Y}_{in} = qG_\infty \tanh(q2L)$.

Problem 5

Part a) The cable equation with current injection as its inputs is linear. Real dendritic trees are nonlinear in the following ways. Each was discussed in class.

1. The inputs are conductances, not currents, producing nonlinear interactions among inputs.

2. Dendrites contain voltage-gated channels, so the membrane currents are not linear, as assumed in the cable equation. This leads to saturation due to K currents or active processes (action potentials) due to Na and Ca channels.

3. Related to the previous, the action potential of the cell can invade the dendritic tree through backpropagation. This plays a role in synaptic plasticity, so that the conductances are not constants.

Part b) Adding synaptic conductances increases the membrane conductance G_m. Thus the length constant decreases since $\lambda = \sqrt{a/(2R_i G_m)}$. When λ decreases, the cell's electrotonic length increases. Also G_∞ increases since $G_\infty = \sqrt{2G_m/R_i}\,\pi a^{3/2}$, so that the cell's input admittance increases. The cell's time constant $\tau_m = C_m/G_m$ decreases. Because the electrotonic length of the cell increases, voltage gains from synapse to soma are expected to get smaller.

Part c) Injecting currents into the dendrites activates the dendritic tree in a linear way, so the properties of the cable equation should apply. If the same current is injected at various points, the potential in the soma should be exponential with the distance of the synapse. This is most easily seen if the ECTh applies. As discussed in class, synaptic conductances increase with distance from the soma in many cells, so that the cable properties of the dendrites are counteracted.