580.439/639 Final Solutions, 2002

Problem 1

Part a) Equilibrium means that there is no thermodynamic potential difference for the ion across the membrane $\mu_A = \mu_B$. For the usual situations, the Nernst equation expresses this condition adequately $V = RT/zF \ln(C_A/C_B)$.

Steady state means quantities are not changing in time. Strictly, this means concentrations and fluxes are constant in time. In order for this to be true, the passive flux of the species must be exactly balanced by active fluxes, so the net flux is zero. Thus a full model involves expressions for passive flux (like the GHK equation or some such) and expressions for active transport (not discussed in this class) and the condition $J_{active}+J_{passive}=0$. Often, a pseudo-steady state is assumed where the active transport is not explicitly included.

Part b) Calcium entering through the surface membrane transfers charge across that membrane and so can be measured with voltage clamp. Calcium entering from an intracellular organelle does not transfer such charge and so has no direct effect on membrane potential or current. However, calcium may have indirect effects through calcium gated channels, so that the membrane potential may change through the calcium-induced changes in other currents.

Problem 2

Part a) As the synapse moves away from the soma, the dendritic branches are smaller in diameter. All other things being equal, that means a higher input impedance, so a given current will produce a larger EPSP. The situation is slightly more complex because synapses produce conductance changes. In class, the membrane potential change produced by a synapse was derived as

$$V = E \frac{g_{syn}/Y_{in}}{1 + g_{syn}/Y_{in}} \qquad (*)$$

where g_{syn} is the synaptic conductance, Y_{in} is the input admittance of the dendritic branch, and E is the synaptic reversal potential. This equation is only strictly true in the D.C. steady state or for some condition in which g_{syn} is constant in time. Speaking approximately of the D.C. steady state, where Y_{in} is real, as Y_{in} decreases (further out in the dendritic tree) V increases. Ultimately, when $g_{syn}/Y_{in} \gg 1$, saturation occurs and no further increases are observed.

Part b) This part will be done assuming $q=1$, i.e. D.C. steady state. The task is to compute Y_{in} at the branch points of the dendritic tree, where the synapses are located. Because the cell can be reduced to an equivalent cylinder, the input admittance Y_0 can be computed as the parallel combination of the input admittances of two cylinders:
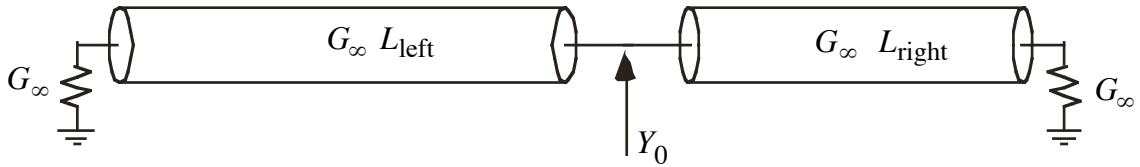
The cylinders are the equivalent cylinders for the part of the tree to the left of Y_0 and for the part of the tree to the right of Y_0. Both cylinders have the G_∞ of the parent part of the original tree, terminated by conductance G_∞, as shown (the sum of the terminating conductances at the 2^n terminal branches). Using the input admittance rule defined in class,

$$Y_0 = G_\infty \frac{\dfrac{G_\infty}{G_\infty} + \tanh(L_{left})}{1 + \dfrac{G_\infty}{G_\infty}\tanh(L_{left})} + G_\infty \frac{\dfrac{G_\infty}{G_\infty} + \tanh(L_{right})}{1 + \dfrac{G_\infty}{G_\infty}\tanh(L_{right})} = 2G_\infty$$

At Y_1, the structure is slightly more complex:
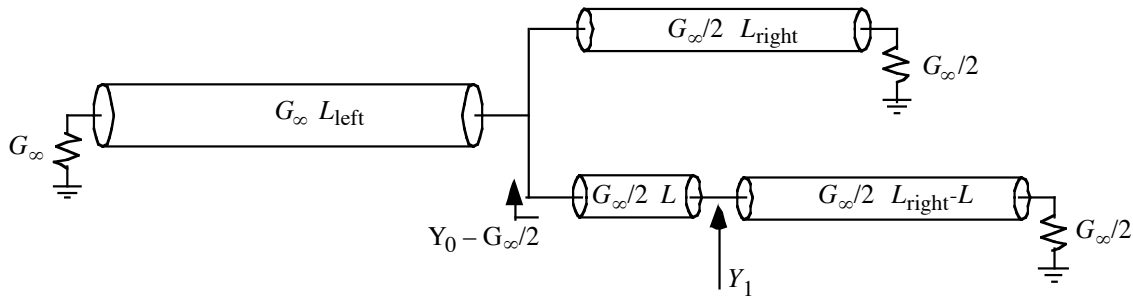
Now the right-hand cylinder has been broken into two parallel cylinders, with $G_\infty/2$ and length L_{right}. The lower one has been split into the cylinder between Y_0 and Y_1 and the rest. Now Y_1 is the sum of the input conductance of the L-length cylinder looking leftward and the remainder cylinder looking right (which is $G_\infty/2$). This can also be expressed as $Y_0–G_\infty/2$ Again using the conductance rule:

$$Y_1 = \frac{G_\infty}{2} \frac{\dfrac{Y_0 - G_\infty/2}{G_\infty/2} + \tanh(L)}{1 + \dfrac{Y_0 - G_\infty/2}{G_\infty/2}\tanh(L)} + \frac{G_\infty}{2} = \frac{G_\infty}{2} \frac{\dfrac{3G_\infty/2}{G_\infty/2} + \tanh(L)}{1 + \dfrac{3G_\infty/2}{G_\infty/2}\tanh(L)} + \frac{G_\infty}{2} = \frac{G_\infty}{2}\left[\frac{3 + 0.2}{1 + 3\cdot 0.2} + 1\right]$$

$$= \frac{3G_\infty}{2}$$

where Y_0-$G_\infty/2$ is the load admittance seen by the length-L cylinder at its left end, equal to the input admittance Y_0 at that point, minus the contribution from the length-L cylinder itself. Alternatively, this is G_∞ from the length-L_{lewft} main cylinder plus $G_\infty/2$ for the upper branch of the length L_{right} cylinder.

Proceeding similarly for Y_2
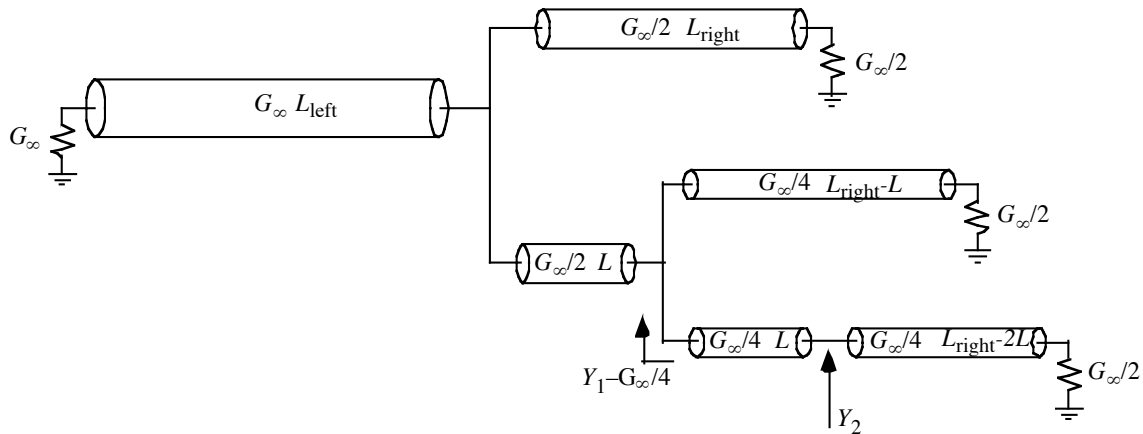
$$Y_2 = \frac{G_\infty}{4} \frac{\dfrac{Y_1 - G_\infty/4}{G_\infty/4} + \tanh(L)}{1 + \dfrac{Y_1 - G_\infty/4}{G_\infty/4}\tanh(L)} + \frac{G_\infty}{4} = \frac{G_\infty}{4}\frac{5+0.2}{1+5\cdot 0.2} + \frac{G_\infty}{4}$$

$$= 0.9\cdot G_\infty$$

This algorithm can be continued and generalized using induction. At the next branch point, for example, $Y_3 = 0.48 G_\infty$.

So, at the first four branch points, the input conductances are 2, 1.5, 0.9, and 0.5 times G_∞. Clearly K_{ii} is increasing with branching, so the injection of fixed current will lead to larger EPSPs.

Part c) If the synapses are modeled correctly, as conductance changes, then Eqn. (*) should be used. This equation is a monotonic function of g_{syn}/Y_{in}, so the same qualitative effect will be seen, but the saturation of Eqn. (*) when $g_{syn} > Y_{in}$ will limit the extent of the rise distally.

Problem 3

Part a) The usual cable equation applies. Writing it in dimensional form:

$$\lambda^2 \frac{\partial^2 V}{\partial x^2} = \tau\frac{\partial V}{\partial t} + v$$

$$-\frac{1}{r_i}\frac{\partial V}{\partial x} = I_0 u(t) \qquad V(x\to\infty,t) = 0 \qquad\qquad (**)$$

$$V(x,0) = 0$$

Part b) The total charge on the cable, as defined in the problem statement, can be computed by integrating the cable equation in (**) and using the boundary conditions in space. Multiplying both sides by c_m first,

$$c_m \lambda^2 \int_0^\infty \frac{\partial^2 V}{\partial x^2} dx = c_m \tau \int_0^\infty \frac{\partial V}{\partial t} dx + c_m \int_0^\infty V dx$$

$$c_m \lambda^2 \left[\frac{\partial V}{\partial x}\bigg|_{x=\infty} - \frac{\partial V}{\partial x}\bigg|_{x=0} \right] = \tau \frac{\partial Q}{\partial t} + Q$$

$$c_m \lambda^2 \left[0 - (-r_i I_0 u(t)) \right] = \tau \frac{\partial Q}{\partial t} + Q$$

$$\tau \frac{\partial Q}{\partial t} + Q = c_m \lambda^2 r_i I_0 \, u(t) = c_m \frac{r_m}{r_i} r_i I_0 \, u(t) = \tau I_0 \, u(t)$$

Part c) Because the membrane potential $V(0)=0$, clearly $Q(0) = 0$, from the definition of Q.

Part d) The solution is a sum of a homogeneous part ($A \exp(-t/\tau)$) and a particular solution, which is constant B, since the input is constant for $t>0$. From the boundary condition

$$Q(0) = 0 = A + B \quad \Rightarrow \quad A = -B \quad \text{so that } Q(t) = A(1 - e^{-t/\tau})$$

Substituting in the differential equation gives

$$\tau A \frac{1}{\tau} e^{-t/\tau} + A - A e^{-t/\tau} = \tau I_0 \quad \text{for } t > 0$$

$$A = \tau I_0$$

so $Q(t) = \tau I_0 \left(1 - e^{-t/\tau} \right)$

Part e) Charge flows into the cable at $x=0$ at rate I_0, but is dissipated by flowing through the resistors in the cable membrane. Using the fact that the resistance per unit length of cable membrane is r_m and that the steady-state membrane potential is $I_0 \exp(-x/\lambda)/G_\infty$, the total current I_{leak} flowing through the cable wall can be computed by integrating

$$I_{leak} = \int_0^\infty \frac{V}{r_m} dx = \frac{I_0}{r_m G_\infty} \int_0^\infty e^{-x/\lambda} dx = \frac{I_0 \lambda}{r_m G_\infty} = I_0 \frac{\sqrt{r_m / r_i}}{r_m / \sqrt{r_m r_i}} = I_0$$

So, in the steady state, the current leaking through the cable wall just equals the current injected at $x=0$,

Problem 4

Part a) Writing the usual equations:

$$\tau_E \frac{dE}{dt} = -E + S(K + w_{EE}E - w_{IE}I)$$

$$\tau_I \frac{dI}{dt} = -I + S(w_{EI}E)$$

where $S(x)$ is given in the problem statement at the weights are specified in the figure in the problem.

The nullclines can be worked out from the equations above. For the dI/dt equation

$$I = S(w_{EI}E) = \frac{M(w_{EI}E)^2}{\sigma^2 + (w_{EI}E)^2} \qquad (***)$$

For the dE/dt equation $E = S(K + w_{EE}E - w_{IE}I)$. To write this with variables I and E separated, it is necessary to have the inverse of $S()$

$$S(x) = \frac{Mx^2}{\sigma^2 + x^2} \qquad \Rightarrow \qquad x = \sqrt{\frac{S\sigma^2}{M - S}}$$

and the positive root is taken, since neural activation cannot be negative. Note also that $S<M$. Now

$$K + w_{EE}E - w_{IE}I = \sqrt{\frac{E\sigma^2}{M - E}} \qquad \text{or} \qquad I = \frac{1}{w_{IE}}\left[K + w_{EE}E - \sqrt{\frac{E\sigma^2}{M - E}}\right] \qquad (****)$$

Part b) The left phase plane has an equilibrium point at (0,0). Clearly this can only be so if $K=0$, since Eqn. (****) is satisfied at (0,0) only if $K=0$. In both phase planes, the solid line has the form of Eqn. (***), so is the dI/dt nullcline.

Part c) Differentiating the r.h.s. of the equations developed in a) gives:

$$\frac{\partial F_E}{\partial E} = \frac{1}{\tau_E}\left[-1 + S'(x_{E0})w_{EE}\right] \qquad \frac{\partial F_E}{\partial I} = -\frac{1}{\tau_E}S'(x_{E0})w_{IE}$$

$$\frac{\partial F_I}{\partial E} = \frac{1}{\tau_I}S'(x_{I0})w_{EI} \qquad \frac{\partial F_I}{\partial I} = -\frac{1}{\tau_I}$$

where the notation $S'(x_{E0})$ and $S'(x_{I0})$ means the derivative of S evaluated at the equilibrium point, with $x_{E0} = K + w_{EE}E_{eqpt} - w_{IE}I_{eqpt}$ and $x_{I0} = w_{EI}E_{eqpt}$. With some algebra

$$S'(x) = \frac{2M\sigma^2 x}{\left(\sigma^2 + x^2\right)^2}$$

Part d) For the phase plane at left, the Jacobian at the equilibrium point at (0,0) has eigenvalues (-0.2, -0.1), so it is stable. For the phase plane at right, the Jacobian at the equilibrium point at (12.7, 28.9) has eigenvalues (0.16 ± j*0.24), so it is unstable.

Part e) The system for $K=20$ has a limit cycle by the Poincare Bendixson theorem. Inspection of the differential equations shows that $dE/dt>0$ for $E=0$ and $dI/dt>0$ for $I=0$ because $S(x)$ is always positive. Further $dE/dt<0$ and $dI/dt<0$ for $E>M$ or $I>M$, respectively. This so because $S(x)\leq M$, regardless of x. Thus trajectories beginning in the first quadrant are guaranteed to stay there. That plus the unstable equilibrium point guarantees a limit cycle.

The system for $K=0$ cannot have a limit cycle, because any such cycle would have to surround the origin, but, from dE/dt and dI/dt on the abscissa and ordinate, such a trajectory is not possible.

Part f) For the three equilibrium points:

Eigenvalues at (18.0, 44.7):   0.19 ± j*0.18   unstable

(61.4, 90.4):   0.175, -0.074   saddle

(84.9, 94.7):   -0.092 ± j*0.028   stable

Part g) Any limit cycle would have to encircle 1 or 3 equilibrium points. It cannot encircle one equilibrium point because each equilibrium point will have at least one manifold of the saddle node connected to it. The trajectory shown in the problem set, which is an unstable maniforld of the saddle, rules out the saddle and the stable node. While a limit cycle around the unstable node cannot be eliminated for certain, the direction of the trajectories in the plot makes such a limit cycle very unlikely. In fact, a stable manifold of the saddle begins in the unstable node, ruling it out. There also cannot be a limit cycle outside all three equilibrium points because of the second stable manifold of the saddle, which must ener at about $E=70$, $I=100$ and go to the saddle. That manifold will block a limit cycle around all three equilibrium points.

Thus, it is unlikely that a limit cycle will exist, but without actually calculating the other three manifolds of the saddle, one does not know for sure.