580.439/639 Final Solutions, 2014

Question 1

Part a) Equating the electrochemical potentials of H^+ and X on outside and inside:

$$RT \ln H_{out} + zF\,0 + RT \ln X_{out} = RT \ln H_{in} - F\ 60 + RT \ln X_{in}$$

$$60\ \text{mV} = \frac{RT}{F} \ln \frac{X_{in}}{X_{out}} = 26\ \text{mV} \ln \frac{X_{in}}{1\ \mu\text{M}} \quad \Rightarrow \quad X_{in} = 10\ \mu\text{M}$$

Part b) In this case the terms in *zFV* disappear from the electrochemical potential and there is no driving force except the concentration of H^+ which is the same on both sides. Thus X_{in} = 1 μM

Question 2

Part a) Equating electrochemical potentials at equilibrium between the closed and open states in the barrier model gives

$$RT \ln(1-n) + G_C + z_G FV = RT \ln(n)$$

$$RT \ln \frac{n}{1-n} = G_C + z_G FV$$

$$n = \frac{1}{1 + e^{-(G_C + z_G FV)/RT}}$$

With some algebra, this equation is the same as the value of $n_\infty(V)$ from the differential equation (given in the problem question).

Thus, at equilibrium $n=n_\infty$.

Part b) The differential equation is

$$\frac{dn}{dt} = \frac{n_\infty(V) - n}{\tau_n(V)}$$

In the steady state, $dn/dt = 0$, so $n=n_\infty$, the same as for equilibrium.

Part c) The conditions for equilibrium and steady state, derived by (1) equating electrochemical potentials of S_1 and S_2 for equilibrium and (2) using $d(\ )/dt=0$ for steady state are below.

Equilib: $V = \frac{G_C}{zF} + \frac{RT}{zF} \ln \frac{S_1}{S_2}$ Steady state: Flux over the barrier = constant

The difference between the gate model and the S_1/S_2 flux model is in the assumptions. In the gating model, there is a fixed total amount of gates, so a steady state of non-zero flux is not possible and the

only possible steady state is zero flux at equilibrium. In an independence-regime flux model, we assume there are concentrations S_1 and S_2 of solute on the two sides of the model. These are assumed to be held constant by some unstated mechanism (like large volume pools) despite a non-zero flux through the model. In this case, the steady state is different from equilibrium (although equilibrium is still a steady state).

Question 3

Part a) Na currents are inward (negative), so loss of Na currents would make the currents larger, not smaller as in the middle plot. The currents in the middle plot must be K currents and they get smaller when TTX is applied. K channels are not blocked by TTX, so the decrease in K currents must be due to loss of Na currents, consistent with a K_{Na} channel.

Part b) The large inward currents are transient, i.e. inactivating, Na channels of the HH type. They are missing in the middle plot because TTX blocks them.

Part c) At the membrane potentials used here (-90 to +40 mV), sodium currents are inward (negative). Thus the outward currents in both middle and bottom plot are potassium currents. In the bottom plot, they must be currents through the K_{Na} channels mostly, because they are sodium dependent (blocked by TTX). In the middle plot, they are all the other potassium channels, such as voltage gated *K* channels. If the K_{Na} channels are also voltage-gated, then some of the K currents in the middle plot might be Na.

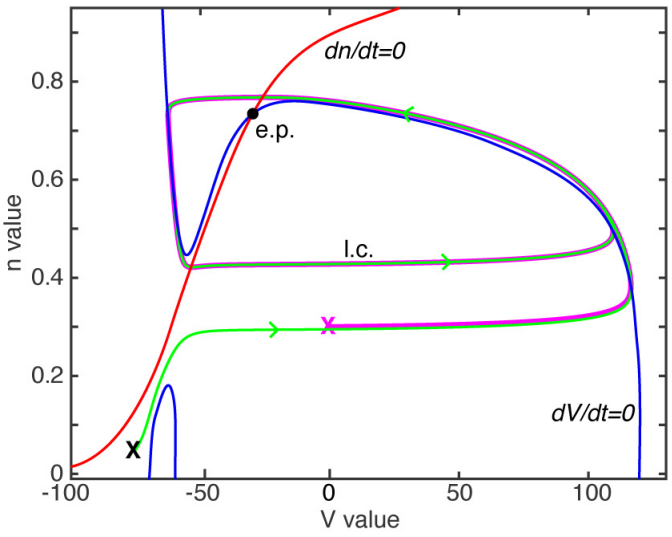
Part d) Based on the duration of the K currents, persistent Na channels are most likely. The alternative is that the transient currents admit sodium which is pumped out very slowly. That seems unlikely given the steady nature of the potassium currents and the speed with which the currents turn off at the end of the voltage clamp. It must be that Na is pumped out rapidly, and a constant flux of sodium is needed to keep the K_{Na} channels open.

Part e) Veratridine application should increase the persistent sodium and the K_{Na} current, if the latter depends on the persistent sodium.

Question 4

Part a) There is an unstable limit cycle surrounding the equilibrium point that serves as the inner boundary for the required region *R*. The outer boundary is provided by a rectangle with top and bottom at *w=0* and *1* and left and right boundary outside the lowest and highest equilibrium potential.

Part b) The phase plane is shown at right. The presence of a limit cycle surrounding the unstable equilibrium point can be inferred by index theory and the PB theorem. The limit cycle is shown, as is the trajectory from the point **X**. At right these features are computed, but they can be



inferred approximately from the necessary condition of index theory, the arrows provided in the problem statement and the low-temperature assumption. The flows in the lower left part of the phase plane can also be inferred from the locations of the nullclines. A trajectory near **X** cannot cross the *V* nullcline because there is no horizontal trajectory there. Instead trajectories are dominated by *dn*/*dt* near the **X**.

Question 5

Part a) The cable equation with current injection as its input 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, especially saturation as the input conductance increases.

2. Dendrites contain voltage-gated channels (including NMDA 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. A corollary of #2 is that action potentials can propagate in the forward or backward direction in dendrites.

4. A corollary of #1 and #2 is that summation of inputs is strongest with small inputs spread throughout the tree in a linear dendritic tree but strongest with concentrated inputs, capable of evoking action potentials, in a dendritic tree with voltage-gated channels.

5. A corollary of #1 is that the interaction of excitatory and inhibitory synapses are non-linear, as in shunting inhibition.

Part b) Activating synapses adds conductance to the membrane, decreasing the effective (or average) value of R_m, the membrane resistance. This has the following effects on parameters of the cable equation:

$$\lambda = \sqrt{\frac{R_m a}{R_i 2}} \text{ decreases, } \tau_m = R_m C \text{ decreases, } G_\infty = \sqrt{\frac{2}{R_m R_i}} \pi a^{3/2} \text{ increases}$$

Because of the effect on λ, the electrotonic length from soma to synapses is expected to increase; because of the effect on τ_m the low-pass frequency cutoff of the dendrites is expected to increase; and the increase in G_m should increase the input conductances (i.e. the admittance at zero frequency) in the tree.

The effect on voltage gain and other transfer functions is complex because of competing changes. For voltage gain,

$$A_{synS} = \frac{1}{\cosh qL + \frac{Y_L}{G_\infty q} \sinh qL}$$

The term $Y_L/G_\infty q$ should vary approximately as tanh(*qL)*, from the formula for input admittance of a cable, e.g. if terminated by a zero admittance, $Y_{in} = G_\infty q$ tanh(*qL)*. Because q decreases (following the decrease in τ_m) while L increases (following the decrease in λ), it is not clear what happens to qL and therefore to the cosh, sinh and tanh terms in the equation above. At DC, however, q=1 and

doesn't change with R_m, so the qL terms increase. In that case the denominator of A_{synS} should increase with R_m, meaning that A_{synS} should decrease, making the electrotonic size of the neuron larger (say by the MET measure).

Part c) Inhibition can work by shunting current from excitatory synapses before those currents reach the soma. For this to work, inhibitory synapses must be closer to the soma than the excitatory ones.

Part d) The MET defined as $-\ln A_{01}$ is used as a measure of the effective or functional electrotonic length of a dendritic tree between points 0 and 1. It can be computed from soma (0) to dendrites (1) or in the opposite direction. The larger the MET, the smaller the voltage gain for propagation in the direction 0→1. Those calculations show that the MET is smaller for potentials propagating from soma to dendrites (backpropagation) than for the opposite. Thus backpropagating action potentials should be more robust than forward-propagating ones.

Question 6

Part a) For a single cylinder from 0 to 1, inject a current I_0 that produces potential V_0 and also potential V_1:

$$V_1 = A_{01}V_0 = I_0K_{01} = \frac{V_0K_{01}}{K_{00}} \quad \text{where } V_0 = K_{00}I_0$$

$$V_0 = A_{10}V_1 = I_1K_{10} = \frac{V_1K_{10}}{K_{11}} \quad \text{where } V_1 = K_{11}I_1$$

Combining these

$$A_{01} = K_{01}/K_{00} \quad \text{and} \quad A_{10} = K_{10}/K_{11}$$

$$\text{so} \quad \frac{A_{01}}{A_{10}} = \frac{K_{11}}{K_{00}} \neq 1$$

In the final equation, use has been make of the fact that $K_{01} = K_{10}$.

Part b) The bottom equation above gives the relationship of A_{01} and A_{10}. They are not equal, because K_{11} is unlikely to be equal to K_{00}, nor are they inverses.

Question 7

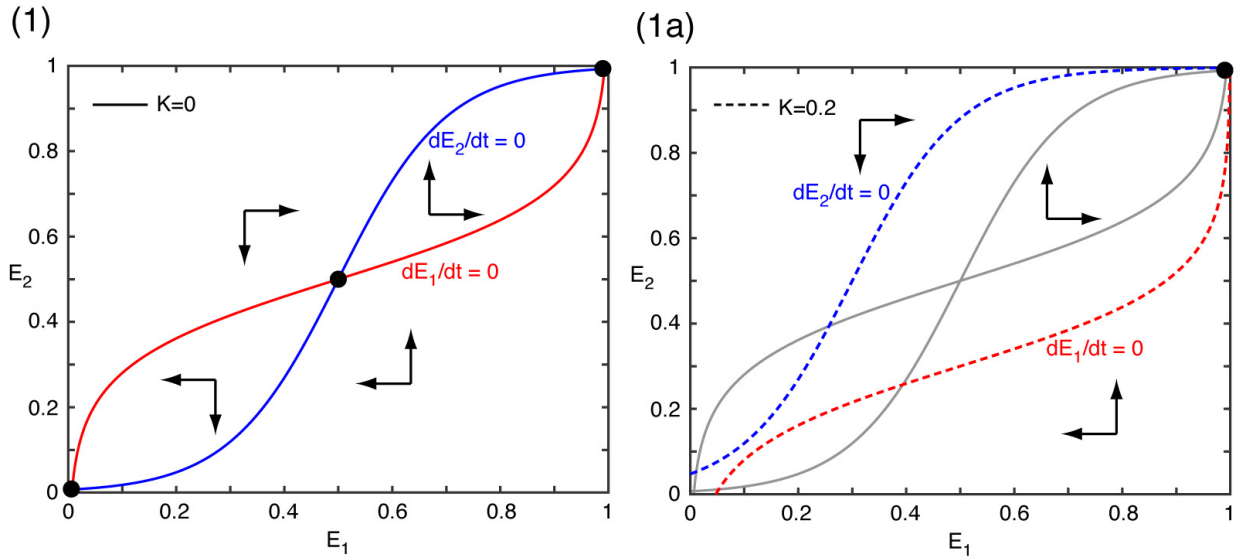
Part a) The phase planes for the model are (1) and (1a). The other two, (2) and (2a)), are for a similar model with negative weights on the connections between the neurons, that is $-E_1$ and $-E_2$ in the arguments of $F()$ in the differential equations. The trajectory directions are indicated below. The nullclines are given by

$$dE_1/dt = 0 \quad \text{at} \quad E_1 = F(E_2 + K) \quad \text{and} \quad dE_2/dt = 0 \quad \text{at} \quad E_2 = F(E_1 + K)$$

The nullcline for $dE_2/dt=0$ is just $E_2 = F(E_1+K)$. For the $dE_1/dt=0$ nullcline, it is useful to have the inverse function $F^{-1}(x)$, where $x = F^{-1}(F(x))$.

$$F^{-1}(x) = 0.5 + K - \frac{1}{10}\ln\left(\frac{1-x}{x}\right)$$

Then the nullcline is $E_2 = F^{-1}(E_1+K)$.



Part b) The Jacobian is the partial derivative of the rhs of the differential equations with respect to the state vector, giving

$$J = \begin{bmatrix} -1 & F'(eq.pt.) \\ F'(eq.pt.) & -1 \end{bmatrix} \quad \text{where} \quad F'(eq.pt.) = \left.\frac{10e^{-10(x-0.5)}}{\left(1+e^{-10(x-0.5)}\right)^2}\right|_{eq.pt.} \left.\frac{\partial x}{\partial E}\right|_{eq.pt.}$$

where x is the argument of $F(x)$ so $\partial x / \partial E = 1$. Because of the symmetry of this phase plane, the equilibrium points must by on the main diagonal (E_1=E_2), so J is symmetric on both diagonals.

The symmetry of J leads to a simple form of the eigenvalues at equilibrium points; such eigenvalues must be $\lambda = -1 \pm a$, where $a = F'(eq.pt.)$. Thus they are stable nodes if $|a|<1$ and saddles if $|a|>1$.

At the three equilibrium points the Jacobians and eigenvalues are as follows:

$$\text{At (0,0) and (1,1):} \quad J = \begin{bmatrix} -1 & -0.0665 \\ -0.0665 & -1 \end{bmatrix} \quad \lambda = -1.06, -0.993$$

$$\text{At (0.5,0.5):} \quad J = \begin{bmatrix} -1 & -2.5 \\ -2.5 & -1 \end{bmatrix} \quad \lambda = -3.5, 1.5$$

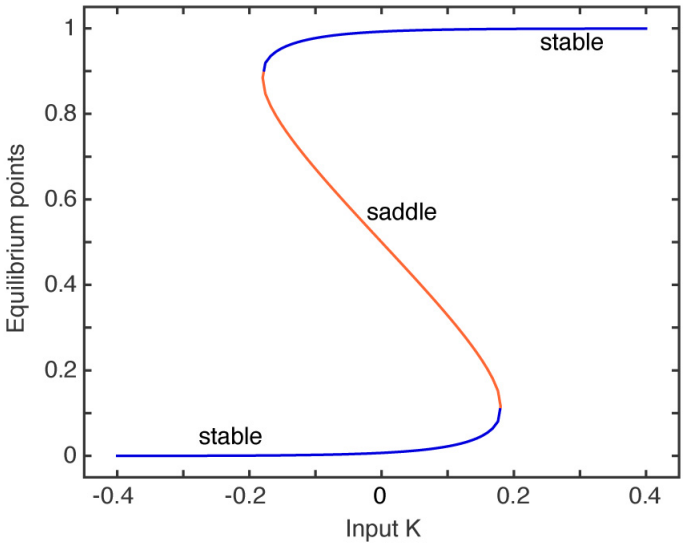
So, the equilibrium points at (0,0) and (1,1) are stable and the one at (0.5,0.5) is a saddle. From the arrows in the phase plane, one can see that the unstable manifolds of the saddle lead to the stable equilibrium points and the stable manifolds enter the phase plane at upper left and lower right and terminate in the saddle. Thus, in the plane (1), the stable equilibrium points each are attracting for half the phase plane. The arrows also show that no trajectory can escape from the phase plane.

Part c) With an input *K=0.2* the phase plane is (1a) with nullclines at the colored dashed lines. The gray lines are the nullclines from (1) for comparison. The movement of the nullclines along the axes can be inferred by adding K to the E_i in the differential equations. A saddle node bifurcation has occurred and the lower equilibrium point and saddle have merged and disappeared. The upper equilibrium point remains,

$$\text{At } (1,1) \text{ with } K = 0.2: \quad \mathbf{J} = \begin{bmatrix} -1 & -0.0091 \\ -0.0091 & -1 \end{bmatrix} \quad \lambda = -1.009, -0.991$$

which is stable; from the arrows above, it is clear that all trajectories flow into the phase plane across its boundaries, so the equilibrium point is globally attracting.

Part d) The bifurcation diagram is shown below.



For large negative or positive values of K only one stable equilibrium point exists and the system is attracted to it, as in part b) above. The system is stable in that state as K changes over (-0.181, 0.181); at either endpoint of this domain, there is a saddle node bifurcation and the system switches to the other state. In this way, the network has memory for the recent history of K.