

## 580.439/639 Final Exam Solutions, 2011

### Problem 1

**Part a)** In steady state, the net flux of sodium will be zero so that  $3a = p$ . Here  $a$  and  $p$  have units of moles/(s cell), so that  $a$  is the rate of consumption of ATP, but any reasonable flux measure would be OK. The flux of potassium through the right membrane is then  $2a + p = 5a$  moles/(s cell). In steady state, the active potassium flux in the right membrane must equal the passive flux in the left  $I_{KP}$ . Because the latter is a current, the flux units must be converted to electrical units giving  $I_{KP} = 5Fa$  amp/cell (using  $z_K=1$ ).

**Part b)** The charges lining the pore have to be positive if anions like  $\text{Cl}^-$  and  $\text{HCO}_3^-$  are permeable. Negative pore-charges would exclude anions from the pore.

**Part c)** The steady state membrane potential is given by the constant-field equation

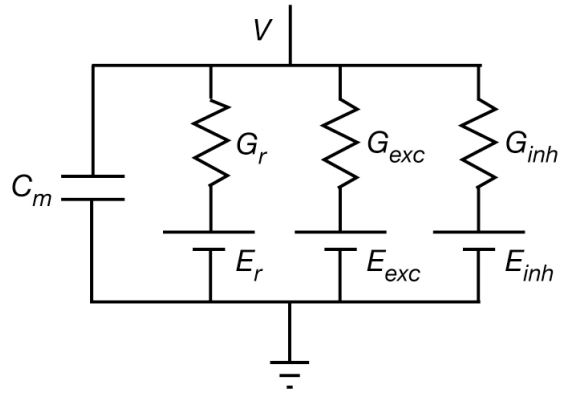
$$V = \frac{RT}{F} \ln \frac{P_{\text{Cl}} \text{Cl}_{\text{in}} + P_{\text{B}} \text{B}_{\text{in}}}{P_{\text{Cl}} \text{Cl}_{\text{out}} + P_{\text{B}} \text{B}_{\text{out}}} = \frac{RT}{F} \ln \frac{\text{Cl}_{\text{in}} + \frac{P_{\text{B}}}{P_{\text{Cl}}} \text{B}_{\text{in}}}{\text{Cl}_{\text{out}} + \frac{P_{\text{B}}}{P_{\text{Cl}}} \text{B}_{\text{out}}},$$

so that

$$\frac{P_{\text{B}}}{P_{\text{Cl}}} = \frac{\text{Cl}_{\text{out}} e^{FV/RT} - \text{Cl}_{\text{in}}}{\text{B}_{\text{in}} - \text{B}_{\text{out}} e^{FV/RT}} = \frac{A1 e^{FV/RT} - A2}{B2 - B1 e^{FV/RT}}$$

where  $B$  stands for bicarbonate ( $\text{HCO}_3^-$ ).

**Part d)** The circuit is at right.  $E_{\text{exc}} \approx -20$  mV and  $E_{\text{inh}} \approx -70$  mV are the reversal potential of the excitatory and inhibitory channels, respectively. Thus voltage clamping at either of these two potentials (i.e. forcing  $V$  to one of the potentials with an external circuit, not shown) eliminates the currents of one of the two channels, allowing the other to be studied. At  $-20$  mV, there is little or no current through the excitatory channels, so the only synaptic currents are inhibitory. At  $-70$  mV, there is little or no current through the inhibitory channels and all synaptic currents are excitatory. Note that  $-20$  and  $-70$  mV are not necessarily exactly the synaptic reversal potentials, but they are close.



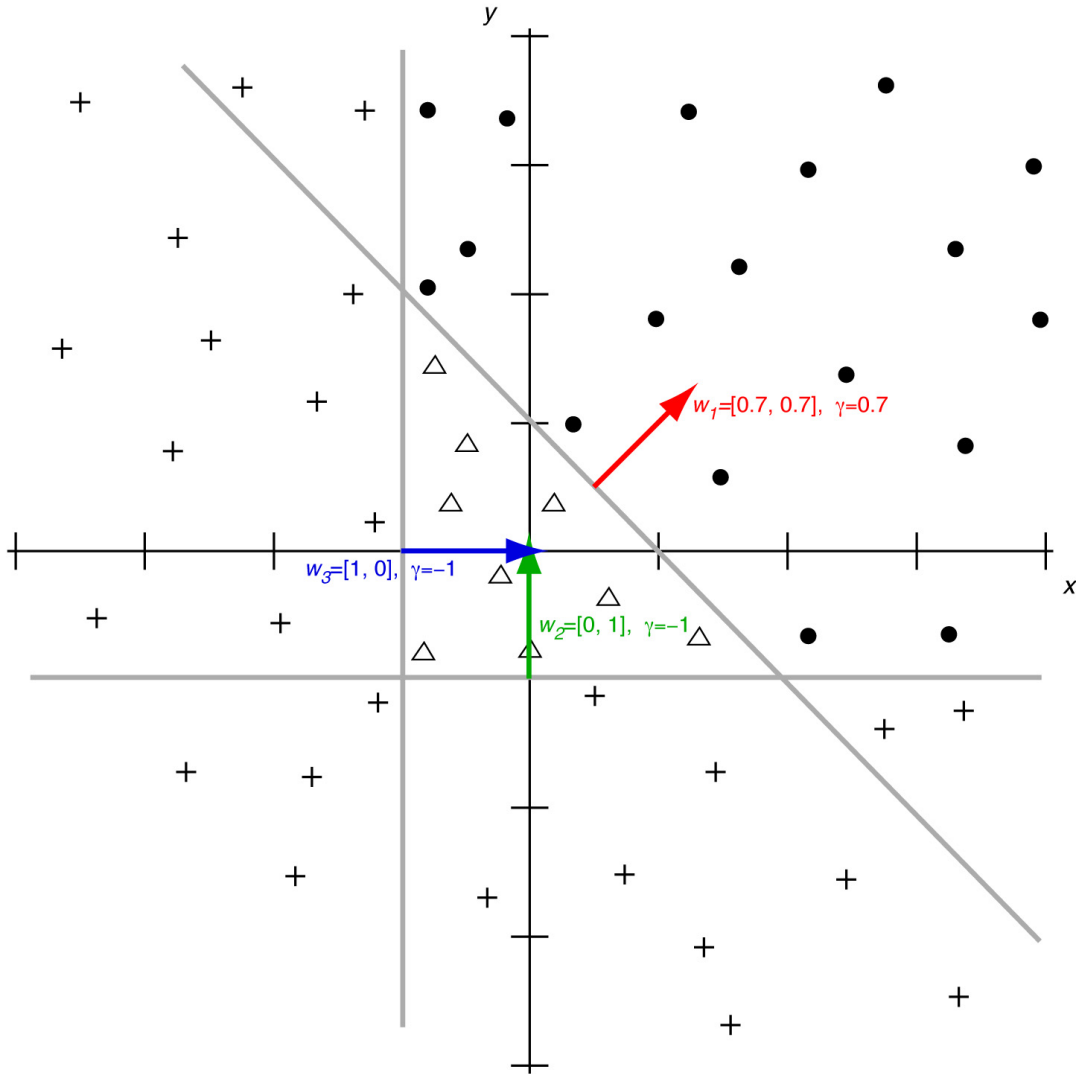
**Part e)** Three hidden-layer perceptrons will suffice. These could implement the separations shown by the thick gray lines in the figure below; the colored vectors show the weight vectors and the gammas are the offset thresholds. The outputs of the hidden-layer then take on the following values:

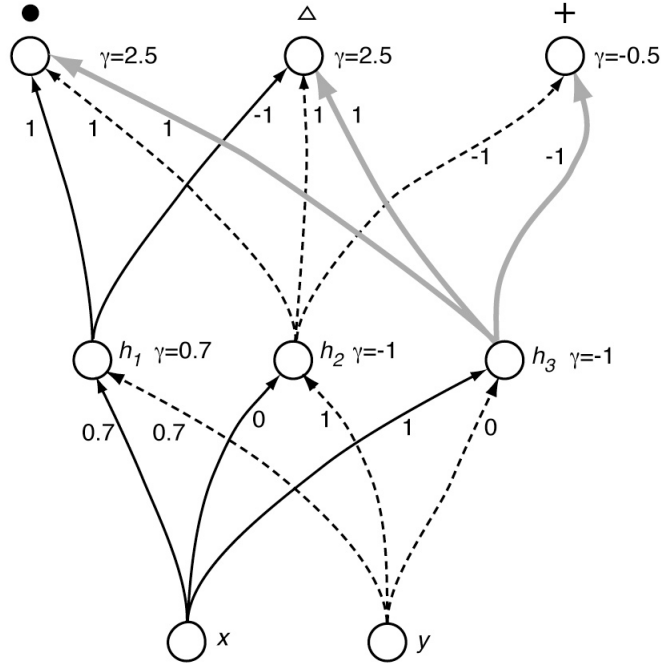
Filled-circle class:  $[h_1, h_2, h_3] = [1, 1, 1]$

Triangle class:  $[h_1, h_2, h_3] = [-1, 1, 1]$

Plus class:  $h_1 = ?, h_2 = -1 \text{ OR } h_3 = -1$

The network on the next page achieves this separation.





**Part f)** The conductance of the postsynaptic receptors increases as the synapse site moves away from the soma. This increase causes EPSPs and EPSCs to be larger in the soma and is assisted by the increased input impedance of smaller dendrites at more distal synapse sites. Further amplification of distal synaptic inputs occurs through NMDA and Ca active processes.

## Problem 2

**Part a)** The Jacobian and characteristic equation are as follows

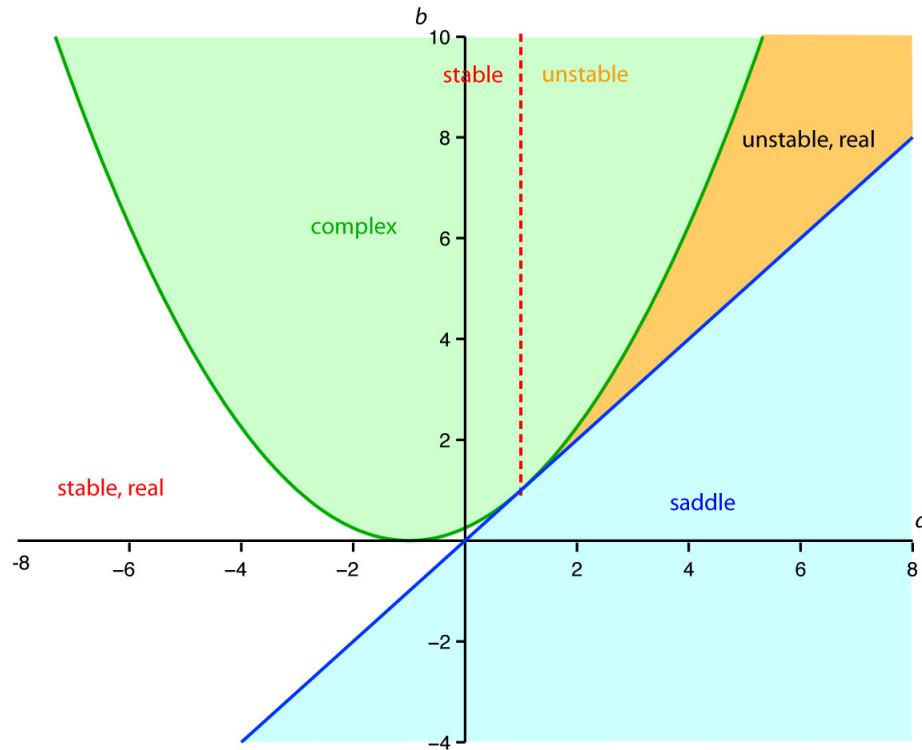
$$\mathbf{Jac} = \begin{bmatrix} a & -b \\ 1 & -1 \end{bmatrix},$$

$$\det(\mathbf{Jac} - \lambda \mathbf{I}) = \det \begin{bmatrix} a - \lambda & -b \\ 1 & -1 - \lambda \end{bmatrix} = \lambda^2 + (1 - a)\lambda + (b - a) = 0,$$

so that

$$\lambda = \frac{-(1 - a) \pm \sqrt{(1 - a)^2 - 4(b - a)}}{2} = \frac{a - 1}{2} \left[ 1 \pm \sqrt{1 + \frac{4(a - b)}{(1 - a)^2}} \right].$$

The eigenvalues are a saddle (positive and negative real) if  $a > b$  so that  $(a - b) > 0$  and the value of the radical is larger than 1. They are complex if  $4(a - b)/(1 - a)^2 < -1$ , so the number within the radical is negative. In this case,  $b > (1 + a)^2/4$ . The remaining values of  $a$  and  $b$  give real eigenvalues of the same sign. For these complex and real, non-saddle cases, the roots have a negative real part (stable) for  $a < 1$ . Thus the  $a - b$  plane can be divided up as follows.



An interesting case occurs when  $b=1$ . In this case, the roots are either stable or saddles. Unstable real or complex roots don't occur.

**Part b)** For case (1),  $a/b > 1$ , so that this is always a saddle (blue region above). For case (2), the slope is negative so  $a < 0$  and  $a/b < 1$ , so that the point is not a saddle. The equilibrium point is stable in this case because  $a < 1$ .

**Part c)** To use the  $a$ - $b$  plane, the values of  $a$  and  $b$  must be computed from the derivatives of the r.h.s. of the differential equations at the equilibrium points.  $b=2$  for all cases.

For case (1):  $a = -3 \cdot 0.11 \cdot 0.77^2 + 2 \cdot 0.77 = 1.34$  and  $b = 2$ . So  $b > a$  and there are several possibilities. Because  $a > 1$ , the EP is unstable with complex eigenvalues.

For case (2):  $a > b$  and the equilibrium point must be a saddle.

For case (3): the slope is negative, so  $a < 0$  and the point is stable. To check,  $a = -3 \cdot 0.11 \cdot 6.51^2 + 2 \cdot 6.51 = -0.97$  and  $b = 2$ . This point is stable with complex eigenvalues.

For case (4):  $a = -3 \cdot 0.2 \cdot 1.72^2 + 2 \cdot 1.72 = 1.65$  and  $b = 2$ . This point is unstable with complex eigenvalues.

**Part d) EXTRA CREDIT** The Jacobian of the MLE is given by the following matrix, where  $V_\theta$  and  $w_\theta$  are the values of the state variables at the equilibrium point.

$$J = \begin{bmatrix} -\frac{1}{C} \left( G_{Ca} \frac{dm_{\infty}(V_0)}{dV} (V_0 - E_{Ca}) + G_{Ca} m_{\infty}(V_0) + G_K w_0 + G_L \right) & -\frac{G_K}{C} (V_0 - E_K) \\ \frac{\phi}{\tau_w(V_0)} \frac{dw_{\infty}(V_0)}{dV} & -\frac{\phi}{\tau_w(V_0)} \end{bmatrix} = \begin{bmatrix} e & -f \\ g & -h \end{bmatrix}.$$

This Jacobian has four terms, none of which is likely to be 1. Inspection of the terms one by one shows that  $e$  can have either sign and the other three terms have the signs given in the matrix at right above, where  $f$ ,  $g$ , and  $h$  are positive. Making the suggested changes of variables  $V' = V/l$  and  $w' = w/k$  gives the following linearized differential equations:

$$\frac{d}{dt} \begin{bmatrix} lV' \\ kw' \end{bmatrix} = \begin{bmatrix} e & -f \\ g & -h \end{bmatrix} \begin{bmatrix} lV' \\ kw' \end{bmatrix} \quad \text{so that} \quad \frac{d}{dt} \begin{bmatrix} V' \\ w' \end{bmatrix} = \begin{bmatrix} e & -kf/l \\ lg/k & -h \end{bmatrix} \begin{bmatrix} V' \\ w' \end{bmatrix}.$$

Now choose  $k$  and  $l$  to make  $lg/k = h$ , so that  $l/k = h/g$  (note that  $h$  and  $g$  are not zero). Then

$$\frac{d}{dt} \begin{bmatrix} V' \\ w' \end{bmatrix} = \begin{bmatrix} e & -fg/h \\ h & -h \end{bmatrix} \begin{bmatrix} V' \\ w' \end{bmatrix}.$$

Finally, change the time variable so that  $t' = ht$ . Then

$$\frac{d}{dt'} \begin{bmatrix} V' \\ w' \end{bmatrix} = \begin{bmatrix} e/h & -fg/h^2 \\ 1 & -1 \end{bmatrix} \begin{bmatrix} V' \\ w' \end{bmatrix} \quad \text{same equations as} \quad \frac{d}{dt} \begin{bmatrix} x \\ y \end{bmatrix} = \begin{bmatrix} a & -b \\ 1 & -1 \end{bmatrix} \begin{bmatrix} x \\ y \end{bmatrix}.$$

Note that the signs assumed above ( $a$  either sign,  $b$  positive) still hold.

The result of part a) of this problem depends on the particular distribution of signs in the differential equations. For example the same nullclines are obtained from the following

$$\frac{d}{dt} \begin{bmatrix} x \\ y \end{bmatrix} = \begin{bmatrix} -a & b \\ -1 & 1 \end{bmatrix} \begin{bmatrix} x \\ y \end{bmatrix}$$

although the behavior of the linearized equation is different (stable and unstable are interchanged without changing the boundaries of complex and saddle in the  $a$ - $b$  plane. This is the reason for the warning in the problem statement. See if you can find a neural model that has this form of the linearized equations. There are plenty.

### Problem 3

**Part a)** Some calculation verifies that the  $3/2$  power branching law applies at each branchpoint, as follows:

$$\text{branchpoint 1: } \text{parent} = a_1^{3/2} = \text{children} = a_1^{3/2} (0.89^{3/2} + 0.3^{3/2}) = a_1^{3/2} 1$$

$$\text{branchpoint 2: parent} = 0.3^{3/2} a_1^{3/2} = 0.16 a_1^{3/2} = \text{children} = a_1^{3/2} (0.18^{3/2} + 0.2^{3/2}) = 0.16 a_1^{3/2}$$

$$\text{branchpoint 3: parent} = 0.2^{3/2} a_1^{3/2} = 0.089 a_1^{3/2} = \text{children} = a_1^{3/2} (0.15^{3/2} + 0.1^{3/2}) = 0.089 a_1^{3/2}$$

The total lengths of the dendritic tree by each path are also similar. Let  $K = \sqrt{2R_i/R_m}$  so that the electrotonic length of a branch is  $Kl/\sqrt{a} = l/\lambda$ . Then

$$\text{top branch: } K(l_1/\sqrt{a_1} + 5.7l_1/\sqrt{0.89a_1}) = 7.04Kl_1/\sqrt{a_1}$$

$$\text{middle branch: } K(l_1/\sqrt{a_1} + 2l_1/\sqrt{0.3a_1} + l_1/\sqrt{0.18a_1}) = 7.01Kl_1/\sqrt{a_1}$$

$$\text{lower branches: } K(l_1/\sqrt{a_1} + 2l_1/\sqrt{0.3a_1} + 0.5l_1/\sqrt{0.2a_1} + 0.5l_1/\sqrt{0.15a_1}) = 7.06Kl_1/\sqrt{a_1}$$

$$\text{and: } K(l_1/\sqrt{a_1} + 2l_1/\sqrt{0.3a_1} + 0.5l_1/\sqrt{0.2a_1} + 0.4l_1/\sqrt{0.1a_1}) = 7.03Kl_1/\sqrt{a_1}$$

Thus the equivalent cylinder theorem holds for a cylinder of physical length  $\sim 7l_1$  and radius  $a_1$ . Because the termination admittance is 0, the input admittance  $Y_{in}$  is thus

$$Y_{in} = G_{\infty} q \tanh qL = \sqrt{\frac{2}{R_m R_i}} \pi a_1^{3/2} q \tanh \frac{q7l_1}{\sqrt{R_m a_1/2R_i}} \quad (**)$$

$q$  is as usual the Fourier or Laplace transform variable or 1 for DC steady state.

**Part b)** If  $|qL| \ll 1$ , then  $\tanh()$  in Eqn. (\*\*) can be approximated by its first term as follows:

$$Y_{in} \approx \sqrt{\frac{2}{R_m R_i}} \pi a_1^{3/2} q \frac{q7l_1}{\sqrt{R_m a_1/2R_i}} = \frac{2\pi a_1 7l_1}{R_m} (1 + s)$$

The term  $2\pi a_1 7l_1/R_m$  is the area of the equivalent cylinder divided by the resistance of a unit area of membrane, so equals the conductance  $G_D$  of the dendritic membrane.  $s$  is the transformed Laplace transform variable, i.e. it is the Laplace variable for a time variable of  $T = t/\tau$ . Thus  $s$  is equal to  $\tau s'$ , where  $s'$  is the Laplace variable corresponding to non-normalized time  $t$ . The time constant  $\tau$  equals the capacitance divided by the conductance of the membrane of the cylinder, so

$$Y_{in} = G_D (1 + \tau s') = G_D + G_D \frac{C_D}{G_D} s' = G_D + C_D s'$$

which is the conductance of the membrane in the equivalent cylinder, ignoring cable effects.

#### Problem 4

**Part a)** In steady state, the flux across the barrier must be zero so that

$$k_c Mg \cdot C = k_o MgC \quad .$$

Assuming a fixed number of channels so that  $T = C + MgC$  gives

$$C = \frac{T}{1 + \frac{k_c}{k_o} Mg}$$

The rate constants are given by the following, taken from the barrier diagram in the exam.

$$k_c = \alpha e^{-(G_0 + \lambda_1 z F V)/RT} \quad \text{and} \quad k_o = \alpha e^{-(G_0 + \lambda_1 z F V - G_1 - \lambda_2 z F V)/RT} .$$

Then the fraction of channels available is

$$\frac{C}{T} = \frac{1}{1 + e^{-(G_1 + \lambda_2 z F V)/RT} Mg} .$$

where  $z=2$  (for  $Mg^{++}$ ). The values in the exam problem are then  $a = Mg e^{-G_1/RT}$  and  $b = \lambda_2 F/RT$ .

**Part b)** Assuming that Glu binding and Mg block are independent the NMDA conductance can be written as  $G_{NMDA} = \bar{G}_{NMDA} f g$  where  $f$  is the fraction of channels not blocked by  $Mg^{++}$  and  $g$  is the fraction of channels with their glutamate gate open.

For the  $Mg^{++}$  block, the dynamics are described as in the barrier diagram, giving

$$f = \frac{C}{T} \quad \text{and} \quad \frac{dC}{dt} = k_o MgC - k_c Mg \cdot C = k_o T - (k_o + k_c Mg)C = \frac{\frac{k_o T}{k_o + k_c Mg} - C}{\frac{1}{k_o + k_c Mg}}$$

This is a first-order differential equation like a HH equation. Notice, however, that the usual HH parameters are functions of the concentration of  $Mg^{++}$  as well as membrane potential (through the rates).

$$f_{\infty} = \frac{k_o}{k_o + k_c Mg} \quad \tau_f = \frac{1}{k_o + k_c Mg}$$

For the glutamate gate, the differential equation for  $ON_2$  is

$$g = \frac{ON_2}{T} \quad \text{and} \quad \frac{dON_2}{dt} = k_1 C \cdot N^2 - k_{-1} ON_2 = k_1 N^2 (T - ON_2) - k_{-1} ON_2 = k_1 N^2 T - (k_1 N^2 - k_{-1}) ON_2 .$$

This also can be put in the form of a HH equation.

$$\frac{dON_2}{dt} = \frac{g_{C\infty} - CN_2}{\tau_{CN_2}}$$

where

$$g_{C\infty} = \frac{k_1 N^2 T}{k_1 N^2 - k_{-1}} \quad \text{and} \quad \tau_{CN_2} = \frac{1}{k_1 N^2 - k_{-1}}$$