

## 580.439/639 Midterm Solutions 2014

### Problem 1

**Part a)** At equilibrium the sum of the electrochemical potentials of the two transported molecules must be zero. Assuming there is no contribution to free energy from terms other than concentration and electrical potential:

$$RT \ln H_{out} + FV_{out} + RT \ln X_{out} = RT \ln H_{in} + FV_{in} + RT \ln X_{in}$$

$$F(V_{in} - V_{out}) = RT \ln \frac{H_{out} X_{out}}{H_{in} X_{in}}$$

In a flux equation, this condition should appear as a difference in thermodynamic driving forces.

$$J_{in} = (\text{other terms}) \left[ H_{out} X_{out} - H_{in} X_{in} e^{F(V_{in} - V_{out})/RT} \right]$$

**Part b)** Equilibrium requires that the electrochemical potential of the three species are equal.

$$\mu_A = G_A + RT \ln A + z_A F V_A = \mu_B = \dots \text{ for } B = \mu_C = \dots \text{ for } C ,$$

where  $G_A$ ,  $G_B$ , and  $G_C$  are effects other than concentration and electrical potentials (as represented in a barrier diagram).

In steady state the flow of the reaction is such that the concentrations  $A$ ,  $B$ , and  $C$  are constant. If something maintains  $A$  and  $C$  (e.g. the usual assumption at the boundary of a membrane that there is a large pool of substance), then the fluxes must be equal, i.e.

$$J_{A \rightarrow B} = k_1 A - k_{-1} B = J_{B \rightarrow C} = k_2 B - k_{-2} C .$$

If there is a fixed total amount of  $A$ ,  $B$ , and  $C$  then fluxes must be zero at steady state (equilibrium).

### Problem 2

**Part a)** The three state variables are  $m$  the gating variable for the calcium channels,  $Ca$  the calcium concentration in the pool near the channels, and  $CaCh$  the inactivated calcium channels. The following would be sufficient.

$$\frac{dm}{dt} = \frac{m_{\infty}(V) - m}{\tau_m(V)}$$

$$\frac{dCa}{dt} = \frac{1}{Vol} \left( -\frac{I_{Ca}}{2F} - P Ca \right) \quad \text{where} \quad I_{Ca} = \bar{G}_{Ca} m F(Ca, V)$$

$$\frac{dCaCh}{dt} = k_1 \cdot Ca \cdot Ch - k_{-1} \cdot CaCh$$

$F(Ca, V)$  is whatever current-voltage relationship is assumed for the open  $Ca$  channels, the GHK equation or a linear equation or some other. There could be additional terms in the  $dCa/dt$  equation modeling the geometry of the  $Ca$  space, but for this simple model, they are not necessary.

**Part b)** This is just substitution for  $V$  fixed at  $V_{Cl}$ , using the condition that  $d(\ )/dt = 0$ .

$$m_{ss} = m_{\infty}(V), \quad Ca_{ss} = -\frac{\bar{G}_{Ca} m_{ss} F(Ca, V_{Cl})}{2FP}, \quad CaCh_{ss} = \frac{k_1 Ca T}{k_1 Ca + k_{-1}}$$

**Part c)** Question (1): The purple trace is at the resting potential and the Ca channels are not open or are minimally open, so no Ca current is seen during the conditioning pulse. Remember this is an L-type Ca channel, which is a high-threshold version. For the green curve there is substantial current, as shown in the response to the conditioning pulse, but no inactivation. This suggests that there is no calcium current there. +70 mV is high enough that the current through the channel is likely to be leakage of potassium.

Question (2): apparently  $CaCh$  is staying high between the pulses, i.e. the time constant of decay of  $CaCh$  is such that it does not decay much from the end of the conditioning to the beginning of the test. This could be for one of two reasons: first, the time constant of  $CaCh$  itself could be long or second, the time constant for  $Ca$  could be long, keeping  $Ca$  elevated between the pulses and holding  $CaCh$  elevated, regardless of its time constant. Without further data, one cannot tell.

### Problem 3

**Part a)** The differential equations are unique only to the extent of a multiplier, which can be a constant or a function of the state variables, as long as it doesn't go to zero and thereby affect the nullclines. The simplest systems consistent with the hint and the nullclines are

$$\begin{aligned} \frac{dX}{dt} &= -Y + a - X(X-1)(X+1) \\ \frac{dY}{dt} &= -\phi(Y - bX - a) \end{aligned}$$

Note the hint is ambiguous regarding whether  $\phi$  multiplies only  $Y$  or the whole r.h.s. of the differential equation.

**Part b)** The Jacobian is

$$J = \begin{bmatrix} -3X^2 + 1 & -1 \\ b\phi & -\phi \end{bmatrix} \text{ at the equilibrium point: } J = \begin{bmatrix} 1 & -1 \\ b\phi & -\phi \end{bmatrix},$$

so the characteristic equation is

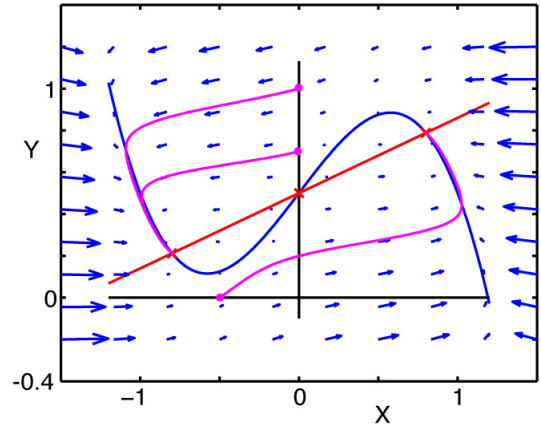
$$\begin{aligned} (\lambda - 1)(\lambda + \phi) + b\phi &= 0 \\ \lambda^2 + (\phi - 1)\lambda - (1 - b)\phi &= 0 \end{aligned}$$

with solutions

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

The value under the radical is larger than 1 (since  $b < 1$  and  $\phi > 0$ ), so the resulting eigenvalues are a pair with positive and negative values. Thus the equilibrium point at  $X=0$  is a saddle. The solution is slightly messier if  $\phi$  doesn't multiply  $b$ .

**Part c)** The low-temperature limit cycle would have to crawl along the nullclines, but in doing so it would have to pass the two equilibrium points at  $\pm 0.8$ . Because these are stable, they would capture any such trajectory. The example at right shows a phase plane for  $\phi=0.2$ . The magenta curves are trajectories that show the low-temperature behavior, including nullcline-crawling. They are captured by the stable equilibrium points as expected.



**Part d)** The modified Jacobian is

$$J = \begin{bmatrix} 3X^2 - 1 & 1 \\ b\phi & -\phi \end{bmatrix} \text{ at the equilibrium point: } J = \begin{bmatrix} -1 & 1 \\ b\phi & -\phi \end{bmatrix}$$

and the eigenvalues are

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

The value under the radical is positive, real, and less than one (as long as  $\phi > 0$  and  $0 < b < 1$ ), so the eigenvalues are real and negative and the equilibrium point is stable. It turns out that the equilibrium points at  $\pm 0.8$  are saddles in this case.