580.439/639 Midterm Solutions, 2013

Problem 1

If all states in the system are at equilibrium, the free energy of ions in those states should be the same. Thus

$$RT\, ln\, S_1 = G^* + \lambda zFV + RT\, ln\, S^* = zFV + RT\, ln\, S_2$$

expresses the condition for equilibrium. S_1, S^*, and S_2 are the concentrations of ion in the three sites. λ is the fraction of the membrane potential that appears at the G^* site in the channel.

For steady state, the fluxes over the two barriers must be the same in order that $dS^*/dt = 0$. Thus a steady state requires

$$J_1 = k_1 S_1 Ch - k_{-1} S^* = J_2 = k_2 S^* - k_{-2} S_2 Ch$$

where J_1 and J_2 are fluxes across the two barriers the k_i are rate constants defined in the usual way, and Ch is the concentration of free channel (it would have been OK to make the independence assumption, so that the effects of fixed total channel could be ignored). The rate constants, of course, are functions of the barrier heights as

$$k_1 = \alpha e^{-(G_1+\lambda_1 zFV)/RT} \qquad k_{-1} = \beta e^{-(G_1+\lambda_1 zFV - G^* - \lambda zFV)/RT}$$
$$k_2 = \beta e^{-(G_2+\lambda_2 zFV - G^* - \lambda zFV)/RT} \qquad k_{-2} = \alpha e^{-(G_2+\lambda_2 zFV - zFV)/RT}$$

where α and β are constants reflecting the 1st vs 2nd order reactions involved and the λ

Problem 2

Part a) Three equations are needed:

$$C\frac{dV}{dt} = I_{ext} - G_K n(V - E_K) - G_H h(V - E_H) - G_{leak}(V - E_{leak})$$
$$\frac{dn}{dt} = \frac{n_\infty(V) - n}{\tau_n(V)}$$
$$\frac{dh}{dt} = \frac{h_\infty(V) - h}{\tau_h(V)}$$

Part b) The resting potential is an equilibrium point, so $d\vec{X}/dt\big|_{\bar{V}} = 0$, where $\vec{X}$ is the state vector of the system. At the equilibrium point $n = n_\infty(\bar{V})\ and\ h = h_\infty(\bar{V})$, so the following equation must be solved for $\bar{V}$, the equilibrium potential with an applied current I_{ext}.

$$I_{ext} = G_K n_\infty(\bar{V})(\bar{V} - E_K) - G_H h_\infty(\bar{V})(\bar{V} - E_H) - G_{leak}(\bar{V} - E_{leak}) \qquad (*)$$

Part c) The condition for the equilibrium point with I_{ext}=0 and ignoring G_{leak} is

$$0 = G_{KH}\left[n_\infty(\bar{V})(\bar{V}-E_K)+h_\infty(\bar{V})(\bar{V}-E_H)\right]$$

where G_{KH} is the common value of G_K and G_H. Note that at $\bar{V}$ =-60 mV, $n_\infty(\bar{V}) = h_\infty(\bar{V})$= 0.5 and $(\bar{V}-E_K)$ = $-(\bar{V}-E_H)$= 30 mV, so the above equation is satisfied. Thus -60 is the equilibrium potential.

Including G_{leak} in the calculation adds a negative value of the current in Eqn. (*). Thus the H current (which is negative at -60) must be smaller and the K current (which is positive) must be larger to compensate. Thus adding G_{leak} makes $\bar{V}$ more positive.

Part d) The time constant is the product of membrane capacitance C and membrane resistance at rest:

$$\tau = \frac{C}{G_{KH}\left[n_\infty(V)+h_\infty(V)\right]+G_{leak}}$$

Part e) The only part of τ that is voltage dependent is the term $\left[n_\infty(V)+h_\infty(V)\right]$. Writing it out gives

$$\begin{aligned}\left[n_\infty(V)+h_\infty(V)\right] &= \frac{1}{1+e^{-(V+60)/k}}+\frac{1}{1+e^{(V+60)/k}}\\ &= \frac{1+e^{(V+60)/k}+1+e^{-(V+60)/k}}{\left(1+e^{-(V+60)/k}\right)\left(1+e^{(V+60)/k}\right)} = 1\end{aligned}$$

This result depends on the two HH functions having thresholds at the same potential, -60 mV and having the same width k of their gating.

Problem 3

Part a) The Jacobian at the equilibrium point is given by the usual matrix of partial derivatives.

$$J = \left.\begin{bmatrix} \partial F_x/\partial x & \partial F_x/\partial y \\ \partial F_y/\partial x & \partial F_y/\partial y \end{bmatrix}\right|_{eq.pt.} = \begin{bmatrix} a & -1 \\ 1 & a \end{bmatrix}$$

The eigenvalues are $a \pm j$, so the origin is a spiral which is stable if $a<0$ and unstable if $a>0$. This is a Hopf bifurcation at $a=0$, because the real part of the complex eigenvalues change sign.

Part b) The most direct solution is to use the transformations $x = r\cos\Theta$ and $y = r\sin\Theta$. Differentiating these give

$$\frac{dx}{dt} = \frac{dr}{dt} cos\Theta - r\, sin\Theta \frac{d\Theta}{dt}$$
$$\frac{dy}{dt} = \frac{dr}{dt} sin\Theta + r\, cos\Theta \frac{d\Theta}{dt}$$

Substituting the transformations into the original differential equations gives

$$\frac{dx}{dt} = a\, r\, cos\Theta - r\, sin\Theta - r\, cos\Theta\, r^2$$
$$\frac{dy}{dt} = r\, cos\Theta + a\, r\, sin\Theta - r\, sin\Theta\; r^2$$

Equating terms in sinΘ and cosΘ in the two sets of equations above gives the result requested in the test problem.

This transformation can also be done by differentiating the transformation in the form given in the test problem. Skipping some steps, this goes as follows:

$$\frac{dr^2}{dt} = 2r\frac{dr}{dt} = 2x\frac{dx}{dt} + 2y\frac{dy}{dt} = 2a(x^2 + y^2) - 2(x^2 + y^2)^2$$
$$\frac{dr}{dt} = ar - r^3$$

and

$$\frac{d\Theta}{dt} = \frac{d\, tan^{-1}(x/y)}{dx}\frac{dx}{dt} + \frac{d\, tan^{-1}(x/y)}{dy}\frac{dy}{dt}$$

which eventually leads to $d\Theta/dt = 1$.

Part c) From the radial form of the differential equations, solutions must encircle the origin in the counterclockwise direction because of the constant value of the phase derivative. From the equation for r when a>0, it is clear that r increases for $r<a^{1/2}$ and decreases for $r>a^{1/2}$. Thus the radius approaches a value of $a^{1/2}$ regardless of the initial condition and is stable at that value, in a limit cycle.

Part d) If $a<0$, then dr/dt<0 for all values of r (remember that $r>0$) and all trajectories will lead to the origin.