

580.439/639 Final Examination Solutions

Problem 1

Part a) The QA group binds in a region of the molecule that is designed to attract potassium ions, by having net negative charges surrounding the pore; the binding site for potassium has a strong negative dipole. Thus a positive charge promotes binding of the QA group in the pore. In addition, the normal membrane potential gradient should promote movement of positive charges into the cell. Since there is no QA inside the cell, the net “flux” of QA should therefore be into the cell if it is positively charged.

Part b) The normal activation gate of this channel is still present. The channel’s activation gate is closed at the cells’ resting potential.

Part c) S4 contains the gating charge for the activation gate. The mutation either causes the channel’s activation gate to be open always, or at least at the resting potential (in fact, it’s the latter).

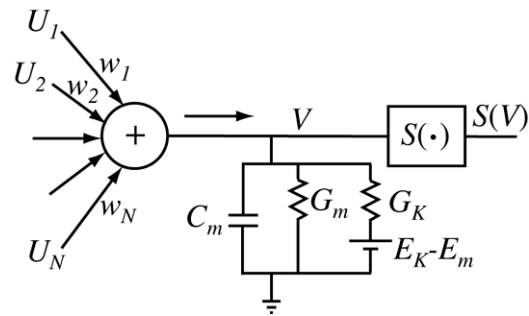
Problem 2

Part a) Strictly speaking the battery should be there to model the resting potential of the neuron. However, the model is linear, so the behavior of V does not change, except for an additive constant, if the battery is removed.

Part b) Low-pass filtering of the inputs, time delay of the inputs, non-linear interactions among the inputs (e.g. shunting inhibition).

Part c) The channel can be added by adding a conductance G_K in parallel to G_m as at right. A battery in series with G_K is necessary and is shown corrected for the missing resting potential at right. The conductance G_K is described by the usual HH model.

$$G_K = G_K^0 n^4 \quad \frac{dn}{dt} = \frac{n_\infty(V) - n}{\tau_n(V)}$$



except that both $n_\infty(V)$ and $\tau_n(V)$ need to be shifted along the V axis to correct for the definition of V as potential relative to rest. The differential equation for the model is now

$$C_m \frac{dV}{dt} = -G_m V - G_K (V - E_K + E_M) + \sum_{i=1}^N w_i U_i$$

Problem 3

Part a) A necessary assumption is that there is a fixed total amount Q of channel so that $Q = C + O + I$. Then the differential equations are as follows

$$\frac{dO}{dt} = k_1 C - (k_{-1} + k_2)O + k_{-2}I = k_1 Q - (k_1 + k_{-1} + k_2)O + (k_{-2} - k_1)I$$

$$\frac{dI}{dt} = k_2 O - k_{-2}I$$

In the first equation, $Q - O - I$ has been substituted for C .

Part b) In the steady state, $dO/dt=0$ and $dI/dt=0$ so

$$k_1 Q - (k_1 + k_{-1} + k_2)O + (k_{-2} - k_1)I = 0$$

$$k_2 O - k_{-2}I = 0$$

Solving these for the variables:

$$O = \frac{k_1}{k_1 + k_{-1} + k_2 + (k_1 - k_{-2})k_2/k_{-2}} Q = \frac{k_1}{k_1 + k_{-1} + k_1 k_2/k_{-2}} Q$$

$$I = \frac{k_2}{k_{-2}} O = \frac{k_1 k_2/k_{-2}}{k_1 + k_{-1} + k_1 k_2/k_{-2}} Q$$

$$C = \frac{k_{-1}}{k_1 + k_{-1} + k_1 k_2/k_{-2}} Q$$

Because k_1 and k_{-1} are voltage-dependent, the steady-state value of I in the equations above will be voltage dependent. This can be seen more clearly by rewriting the above as follows:

$$I = \frac{1}{1 + \left(1 + \frac{k_{-1}}{k_1}\right) \frac{k_2}{k_{-2}}} Q \quad (**)$$

Of course the voltage dependence of k_{-1} and k_1 could cancel in the ratio above. However, consideration of a barrier model for the C to O transition shows that the voltage terms enter the rate constants in such a way that they do not cancel.

Part c) Again, there is a fixed total amount of channel, so

$$\frac{dO}{dt} = \alpha C - (\beta + \gamma)O + \delta O_I = \alpha Q - (\alpha + \beta + \gamma)O - (\alpha - \delta)O_I - \alpha C_I$$

$$\frac{dO_I}{dt} = \gamma O - (\beta + \delta)O_I + \alpha C_I$$

$$\frac{dC_I}{dt} = \gamma C - (\alpha + \delta)C_I + \beta O_I = \gamma Q - \gamma O - (\alpha + \delta + \gamma)C_I - (\gamma - \beta)O_I$$

Part d) Add the second and third equations above to compute $d(O_I + C_I)/dt$:

$$\begin{aligned} \frac{dO_I}{dt} + \frac{dC_I}{dt} &= \gamma O - (\beta + \delta)O_I + \alpha C_I + \gamma Q - \gamma O - (\alpha + \delta + \gamma)C_I - (\gamma - \beta)O_I \\ &= \gamma Q - (\gamma + \delta)O_I - (\delta + \gamma)C_I \end{aligned}$$

Setting this to zero gives

$$\frac{d(O_I + C_I)}{dt} = 0 \quad \Rightarrow \quad (O_I + C_I) = \frac{\gamma Q}{\gamma + \delta} \quad (***)$$

Part e) Equation (**) is voltage-dependent as argued above. So if Eqn. (***) is to show the same voltage dependence as Eqn. (**), then either γ or δ or both must be voltage-dependent.

To make the steady-state inactivation behavior of the two models the same, it is necessary to make

$$\frac{\gamma Q}{\gamma + \delta} = \frac{Q}{1 + \delta/\gamma} = \frac{Q}{1 + \left(1 + \frac{k_{-1}}{k_1}\right) \frac{k_{-2}}{k_2}}$$

Clearly there is not a unique way to do this. From a barrier model of the system, it is clear that the voltage dependence should be in both γ and δ . That is, if one rate constant for a barrier is voltage-dependent, the reverse rate constant must also be so, except in unusual circumstances. Thus a useful way to relate the two systems might be as follows:

$$\delta = (k_1 + k_{-1})k_{-2} \quad \text{and} \quad \gamma = k_1 k_2$$

This makes γ , the forward inactivation rate for the HH model, equal to the product of the forward rates in the original model. The interpretation of δ is less clear.

Problem 4

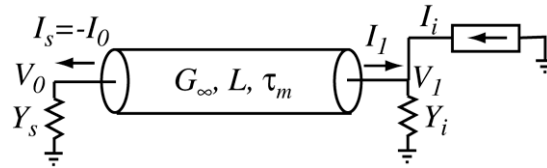
Part a) The easy way is to use transfer impedances. The transfer impedance K_{is} is $K_{is} = V_s/I_i$. But $V_s = I_s/Y_s$ from Ohm's law at the soma. Eliminating V_s between these equations give

$$B_{is} = \frac{I_s}{I_i} = \frac{V_s Y_s}{I_i} = \frac{K_{is} I_i Y_s}{I_i} = K_{is} Y_s$$

Then there's the hard way. Using one of the two-port equations derived in class:

$$\begin{bmatrix} V_1 \\ I_1 \end{bmatrix} = \begin{bmatrix} \cosh(qL) & -\sinh(qL)/G_\infty q \\ -G_\infty q \sinh(qL) & \cosh(qL) \end{bmatrix} \begin{bmatrix} V_0 \\ I_0 \end{bmatrix}$$

for the cylinder model below, a redrawing of the one in the problem set,



the relationships between currents I_i and I_s can be written as below.

$$\begin{bmatrix} V_1 \\ -I_i + Y_i V_1 \end{bmatrix} = \begin{bmatrix} \cosh(qL) & -\sinh(qL)/G_\infty q \\ -G_\infty q \sinh(qL) & \cosh(qL) \end{bmatrix} \begin{bmatrix} I_s/Y_s \\ -I_s \end{bmatrix}$$

Eliminating V_1 between these two equations gives

$$B_{is} = \frac{I_s}{I_i} = \frac{Y_s}{(Y_s + Y_i) \cosh(qL) + \left(\frac{Y_i Y_s}{G_\infty q} + G_\infty q \right) \sinh(qL)}$$

which is exactly $K_{is} Y_s$.

Part b) The answer is above.

Part c) Charge is the integral of current. With the assumptions in the problem statement:

$$Q_{\infty i} = \int_0^\infty I_i(t) dt \quad \text{and} \quad Q_{\infty s} = \int_0^\infty I_s(t) dt$$

The integrals extend to infinity because the duration of the current injection was not specified. Note that the integrals are just the Laplace transforms of the currents for $s=0$, where $e^{-st}=1$.

Part d) The charge gain is $C_{is} = Q_{\infty s} / Q_{\infty i}$. By definition the current $I_s(t)$ is the convolution of $I_i(t)$ and $B_{is}(t)$, which is the inverse transform of the current gain $\bar{B}_{is}(s)$. Define the signal $q_s(t)$ as the integral of $I_s(t)$ up to time t , so that $Q_{\infty s} = q_s(\infty)$.

$$q_s(t) = \int_0^t I_s(\xi) d\xi = \int_0^t B_{is}(\xi) * I_i(\xi) d\xi$$

(where “*” means convolution). The Laplace transform of $q_s(t)$ is $\bar{q}_s = \bar{B}_{is} \bar{I}_i / s$, because the Laplace transform of the convolution of two waveforms is the product of the transforms and because the time-integral is equivalent to dividing by s . The final value theorem allows $Q_{\infty s}$ to be computed as follows

$$Q_{\infty s} = \lim_{s \rightarrow 0} s \bar{q}_s(s) = \bar{B}_{is}(0) \bar{I}_i(0) = \bar{B}_{is}(0) Q_{\infty i}$$

Thus the charge gain $C_{is} = Q_{\infty s} / Q_{\infty i} = \bar{B}_{is}(0)$.

A simpler argument would be to say that, by definition, $\bar{I}_s(s) = \bar{B}_{is}(s) \bar{I}_i(s)$, so that the D.C. values are $\bar{I}_s(0) = \bar{B}_{is}(0) \bar{I}_i(0)$. From part c, this can be rewritten as $Q_{\infty s} = \bar{B}_{is}(0) Q_{\infty i}$ which is the desired result.

Problem 5

Part a) The constants are as follows:

$$c = \sum_{j=1}^N w_{ij} \quad \text{and} \quad d = bN$$

Clearly all neurons are identical only if c , the sum of the excitatory weights, is the same for all neurons. This doesn't mean the weights have to have the same values, only that their sum be fixed across neurons.

Part b) At the equilibrium point with $d=0$, $X = (a + cX)^2$. Solving this quadratic equation gives

$$X = \frac{1 - 2ac}{2c^2} \left[1 \pm \sqrt{1 - \frac{4a^2c^2}{(1 - 2ac)^2}} \right]$$

For $a=0$, there are two solutions: $X=0$, $X=1/c^2$. As a increases, the two solutions remain until $4a^2c^2 / (1 - 2ac)^2 = 1$ (at $a=1/4c$), at which point there is only one solution. For $a > 1/4c$, the solutions are complex and are not relevant.

The behavior of the equilibrium points is clarified by looking at a graphical solution of the equilibrium-point equation for a particular example. The figure below shows a plot of X (red) versus $(a+cX)^2$ for three values of a . The latter are parabolas, with minimum value of 0 when $X = -a/c$. For $a=0$ and $a=1/4$ the parabola intersects the red line

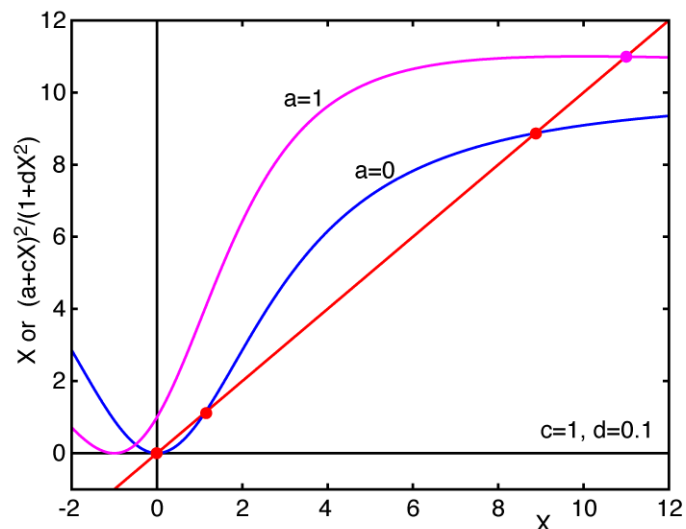
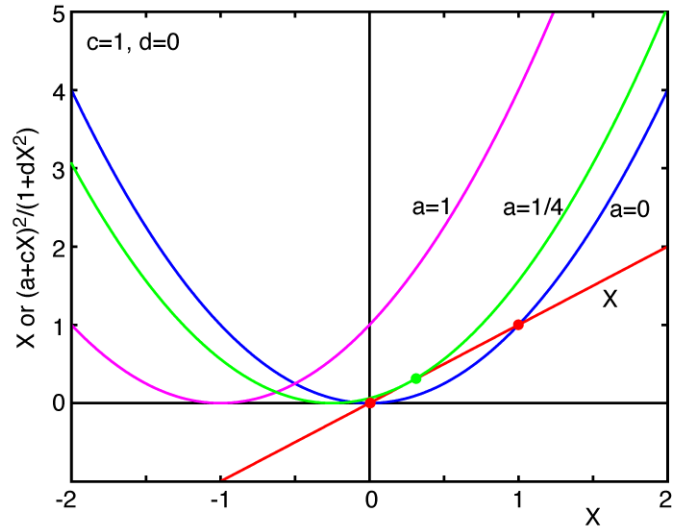
at two or one equilibrium point (the filled circles). As a increases, the parabola slides to the right and eventually, as shown above, there is no equilibrium point. The green parabola is the case of $a=1/4c$ where the parabola is tangent to the line.

Thus the equal-response system has equilibrium points when $0 \leq a \leq 1/4c$.

Part c) Now the equilibrium point condition is as follows (using the suggested example, magenta curve in the plot below right):

$$X = \frac{(a + cX)^2}{1 + dX^2} = \frac{(1 + X)^2}{1 + 0.1X^2}$$

At $X=0$, the r.h.s. of this equation is 1, so the r.h.s. is larger than the l.h.s. As $X \rightarrow \infty$, the r.h.s. goes to an asymptote of $c^2/d=10$, so the r.h.s. is smaller than the l.h.s. for $X > 10$. Given this reversal of the sign of the difference between the two sides, there must be a zero (an equilibrium point) in between (the functions are continuous). The equilibrium points produced by the divisive normalization are shown at right near $X=10$. The new equilibrium point can coexist with one or two equilibrium points near the origin, as for the blue curve at right, for $a=0$.



Note that as long as $d > 0$, this argument holds; only a very small amount of divisive normalization is necessary to produce an equilibrium point. Of course, the smaller d is, the larger the value of X at the equilibrium point and the further it takes the network from its operating range.

Part d) This is a one-dimensional system, so the Jacobian is a scalar constant equal to the derivative of the r.h.s. of the differential equation w.r.t. the state variable X . That is,

$$J = \frac{d}{dX} \left[-X + \frac{(a + cX)^2}{1 + dX^2} \right]_{X=X_0}$$

where X_0 is the equilibrium point. If $J < 0$ the system is stable, otherwise it is unstable. Thus the stability reduces to the slope of the function $-X + (a + cX)^2 / (1 + dX^2)$ at its equilibrium points. From the graphs in part b) it is evident that for a small enough to produce two equilibrium points near the origin, the value of the function $-X + (a + cX)^2 / (1 + dX^2)$ will be positive to the left of the first equilibrium point, negative between the equilibrium points, and then positive again. Thus the first equilibrium point will be stable and the second one will not be stable. Such a system will be unstable (and $X \rightarrow \infty$) if it is moved beyond the unstable equilibrium point. In the case of the system with divisive gain control in part c), the slope can be seen to be negative at the equilibrium point, if there is only one (magenta curve). With three equilibrium points (blue curve) they are stable, unstable, and stable, respectively from left to right.

Thus the system is stable at the equilibrium point near $X=0$ for small a (blue curve). If a is subsequently increased to larger than $\approx 1/4c$, the system will switch to the second stable point near $X=10$ (magenta curve) and will then be stable there, regardless of the value of a .