580.439/639 Final Exam, Solutions

Problem 1

Part a) For the usual circuit, a parallel capacitor and battery/resistor with a current I injected, Kirchoff's current law gives, for $t > 0$.

$$C\frac{dV}{dt} = I - G_m(V - E_{rest}) \ ,$$
$$\text{with initial value} \quad V(0) = E_{rest} \ .$$

The solution takes the form

$$V = A + Be^{-t/\tau} \qquad \text{where } \tau = C / G_m \ .$$

To make the solution solve the differential equation, $A=I/G_m+E_{rest}$. To match the initial condition, $B=-I/G_m$. Thus the final solution is

$$V = E_{rest} + \frac{I}{G_m}(1 - e^{-t/\tau}) \ .$$

Part b) Now there are two battery/resistors in parallel with the capacitor, one the resting membrane conductance G_m/E_{rest} and the second a voltage-gated channel G_{ch}/E_{ch}. The differential equation for the membrane is now (again using KCL):

$$C\frac{dV}{dt} = I - G_m(V - E_{rest}) - G_{ch}(V - E_{ch}) \ .$$

The steady-state solution, where dV/dt=0 is

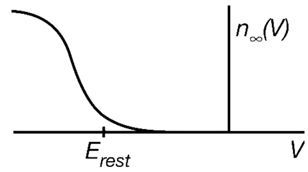
$$V = \frac{I + G_m E_{rest} + G_{ch}E_{ch}}{G_m + G_{ch}} \ .$$

Parts c) – g) There are two things to notice about the solid lines, both interpreted in terms of the last equation above:

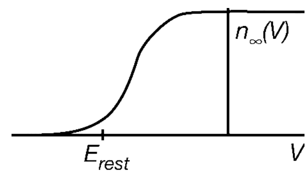
1. The potential prior to onset of the current (I=0). If this differs from E_{rest} then the channel has a non-zero conductance near the rest potential. The polarity of the difference provides information about the ion passed by the channel. If the deviation is positive (depolarization) the channel must be Na^+, Ca^{++}, or a mixed-cation channel like the H-channel. If the deviation is negative, the channel must be K^+ or possibly Cl^-, if E_{Cl} is sufficiently negative. The solutions below use Na^+ and K^+.

2. The final potential, after the transients have died away. This provides a hint about the steady-state conductance of the channel with depolarization or hyperpolarization, and thus provides a constraint on the $n_\infty(V)$ function for the channel.

Part c) The ion could be K^+. The channel has non-zero conductance at rest and increases its conductance as the membrane hyperpolarizes. Note this is a little ambiguous, because the conductance increase itself decreases the effect of I, but we assume that the effect of the $G_{ch}E_{ch}$ term is larger. A possible $n_\infty(V)$ function is shown at right.



Part d) The ion could be K^+, the n_∞ function is non-zero at rest and decreases to zero as the membrane potential hyperpolarizes.



Part e) The channel is off at rest, but could be a Na^+ channel that turns on with depolarization, part d) shifted to positive potentials.

Part f) The ion could be Na^+, as in part e), but the channel is on at rest, same n_∞ as part d).

Part g) The ion could be Na^+, with an n_∞ function as in part c). This could be an H-channel, for example.

Problem 2

Part a) The integral of force through distance is energy, so the work done to move the charges apart is

$$\Delta U = \int_{r_0}^{\infty} \frac{\alpha q^+ q^-}{r^2} dr = \frac{\alpha q^+ q^-}{r_0} \quad .$$

The negative of this is the contribution of work to the free energy of the charge when located at r_0.

Part b) For the K^+ in the selectivity filter, there are four charges at separation $a/\sqrt{2}$, so

$$\Delta U = -\frac{4\alpha q^+ q^-}{a/\sqrt{2}} \ ,$$

where q^+ is the charge on the K^+ ion and q^- is the charge on the fixed sites in the channel.

Part c) This is mainly a problem of geometry. The distances from the center of the Na^+ to the four negative charges are $a/\sqrt{2}-\varepsilon$, $a/\sqrt{2}+\varepsilon$, and two at $\sqrt{a^2/2+\varepsilon^2}$. Thus the energy is

$$\Delta U=-\alpha q^+q^-\left[\frac{1}{a/\sqrt{2}-\varepsilon}+\frac{1}{a/\sqrt{2}+\varepsilon}+\frac{2}{\sqrt{a^2/2+\varepsilon^2}}\right].$$

Assming that $\varepsilon \ll a/\sqrt{2}$ allows the equation above to be approximated as follows:

$$\Delta U=-\frac{\alpha q^+q^-}{a/\sqrt{2}}\left[1+\frac{\sqrt{2}\varepsilon}{a}+1-\frac{\sqrt{2}\varepsilon}{a}+2\left(1-\frac{\varepsilon^2}{a^2}\right)\right]$$
$$=-\frac{4\alpha q^+q^-}{a/\sqrt{2}}\left(1-\frac{\varepsilon^2}{2a^2}\right).$$

which is a smaller ΔU than for the K^+ ion above. Thus the energy well for the charges in the two positions assumed is deeper for the K^+ ion, favoring K^+.

Part d) If the Na^+ ion is centered between the four negative charges ($\varepsilon=0$), its energy well will be the same as the K^+ ion, assuming that the charges are the same. Thus the minimum free energy for the Na^+ ion is at least as low as for the K^+ ion. Somehow, one has to argue that the K^+ ion induces the correct shape of the selectivity filter and the shape is different for Na^+ in a way that does not allow Na^+ to assume the same centered location (not known experimentally). Or, this model could be too simple.

Problem 3

Part a) The voltage gain rule derived in class can be applied here. For a finite cylinder with parameters L and G_∞ terminated with admittance Y_L and voltage clamped to V_0 at $\chi=0$, the potential V_1 at $\chi=L$ is given by

$$V_1=V_0\frac{1}{\cosh[qL]+\frac{Y_L}{qG_\infty}\sinh[qL]}.$$

In this case, $Y_L=0$, so

$$V_1=V_0\frac{1}{\cosh[qL]}.$$

For the same cable voltage clamped to V_1 at the other end, the same rule gives

$$V_0 = V_1 \frac{1}{\cosh[qL] + \frac{G_S + s\,C_S}{qG_\infty}\sinh[qL]} \ .$$

because Y_L is the soma input admittance in this case, $G_S + s\ C_S$.

Part b) At DC, q=1 and s=0 so that the two gains are given by

$$V_1 = V_0 \frac{1}{\cosh[L]} \quad \text{and} \quad V_0 = V_1 \frac{1}{\cosh[L] + \frac{G_S}{G_\infty}\sinh[L]} \ .$$

Clearly the gain V_0/V_1 is smaller than the opposite gain V_1/V_0 because the sinh term in the denominator is positive at DC.

Part c) If G_S/G_∞ is small (0.1) then the difference is the voltage gains is small, since for real arguments sinh(x)<cosh(x). Thus the difference demonstrated in **b** points the right direction, but is likely to be a small effect.

Transfer impedance is symmetric ($K_{01} = K_{10}$) so considering the problem in that way will not help.

Problem 4

Part a) The isoclines are as follows:

$$\frac{dV}{dt} = 0 \qquad R = V - \frac{V^3}{3} + I \ ,$$
$$\frac{dR}{dt} = 0 \qquad R = 1.25V + 1.5 \ .$$

These are plotted in the left figure below. There is one equilibrium point for I=0 at V=–1.5, R=-0.375. The Jacobian is given by

$$J = \begin{bmatrix} 10 - 10V^2 & -10 \\ 1 & -0.8 \end{bmatrix} .$$

At the equilibrium point,

$$J = \begin{bmatrix} \text{-12.5} & \text{-10} \\ 1 & \text{-0.8} \end{bmatrix} \quad \text{with eigenvalues -11.6 and -1.7} \ .$$

Thus the equilibrium point with I=0 is stable.

Part b) The phase plane for I=1.5 is plotted in the right figure below. Now the equilibrium point is at $V=0$, R=1.5 where the eigenvalues are 8.98, 0.22. Thus the equilibrium point is unstable. The Poincare-Bendixson theorem can be applied to show that a limit cycle exists by considering the region bounded by the dashed orange lines in the phase plane (the orange shaded region). Because the equilibrium point is unstable, there must be a circle around it (not necessarily the one drawn) across which all trajectories point away from the equilibrium point into the interior of the orange shaded region. Along the outside edges of the region, the trajectories must point in the general directions of the green arrows, from the isoclines. That is, above both isoclines the trajectories must be downward and to the left, etc. These trajectories also point into the interior of the orange shaded region, so it fits the conditions of the Poincare-Bendixon theorem. Because this region contains no equilibrium points, it must contain a limit cycle.