580.439/639 Midterm Solutions, 2010

Problem 1

The data in the figure are from AL Hodgkin and RD Keynes, *J. Physiol*. 128:61-88 (1955). A nice discussion of these data with an early interpretation of the result is in B Hille and W Schwarz, J. Gen. Physiol. 72:409-442 (1978).

Part a) Independence means that ions move independently through the membrane, so that there are no mechanisms that make one ion's transport dependent on other ions (except the shared membrane potential). Examples of non-independence are active transport, the saturation produced by the finite number of channels in the membrane and forced co-transport of ions by mechanisms like a Na-Ca exchanger or potassium chloride cotransporter.

Part b) Define side *A* to be outside and side *B* to be inside. Then the flux ratio equation can be written as

$$\frac{J_{in}}{J_{out}} = \left(\frac{C_{out}}{C_{in}} e^{-zF\Delta V/RT} \right)^n$$

$$\ln \frac{J_{in}}{J_{out}} = n \ln \frac{C_{out}}{C_{in}} - n \frac{\Delta V}{RT/zF}$$

$$\ln \frac{J_{in}}{J_{out}} = \frac{n \frac{RT}{zF} \ln \frac{C_{out}}{C_{in}} - n\Delta V}{RT/zF}$$

$$\ln \frac{J_{in}}{J_{out}} = n \frac{(E - \Delta V)}{RT/zF}$$

where $E = RT/zF \ln(C_{out}/C_{in})$ is the equilibrium potential of the ion of charge z. This function is in the form of the data shown in the problem. The flux ratio is 1 when $E=\Delta V$, which occurs at $\Delta V \sim$ -70 mV in the data shown. Thus E_K was -70 mV. The slope of the line between -110 mV and -40 mV is

$$\frac{\ln(58) - \ln(0.05)}{(-110 + 40)/26} = -2.6$$

Thus *n* is between 2 and 3. The flux is not consistent with independence.

Part c) Potassium ions move through channels like the Kcsa channel in single file of ~3, with 2 ions in the selectivity filter and a third in the center of the pore. A demonstration of this point is contained in the article by Hille and Schwarz quoted above.

Part d) Writing the expression for potassium conductance directly and using the fact that the net potassium current is $F(J_{out}-J_{in})$

$$G_K = \frac{F\left(J_{out} - J_{in}\right)}{\Delta V - E_K} = \frac{FJ_{out}\left(1 - J_{in}/J_{out}\right)}{\Delta V - E_K}$$

$$G_K = \frac{FJ_{out}\left(1 - e^{-nzF(\Delta V - E_K)/RT}\right)}{\Delta V - E_K}$$

For small deviation of ΔV from E_K

$$G_K \approx \frac{FJ_{out}\left(1 - (1 - nzF(\Delta V - E_K)/RT)\right)}{\Delta V - E_K} = \frac{FJ_{out} nzF(\Delta V - E_K)/RT}{\Delta V - E_K} = nz\frac{F^2}{RT}J_{out}$$

as requested (since z=1).

Problem 2

Part a) The model must give zero flux when KCl is at equilibrium, which requires

$$RT\ln K_o + FV_o + RT\ln Cl_o - FV_o = RT\ln K_i + FV_i + RT\ln Cl_i - FV_i$$

$$K_o Cl_o = K_i Cl_i$$

There are no terms involving membrane potential, because no net charge is transported. Thus *f(..)* should take the following form:

$$f(V, K_o, Cl_o, K_i, Cl_i) = F(V)(K_i Cl_i - K_o Cl_o)$$

None of the models considered in class have a concentration dependence in *F(V)*, but it is not impossible to conceive of one.

Part b) The flux must saturate at high concentrations. Thus *g(..)* must show the following limiting behaviors.

$$\lim_{K_i, Cl_i \to \infty} g(V, K_i, Cl_i, K_o, Cl_o) = (const)K_i Cl_i$$

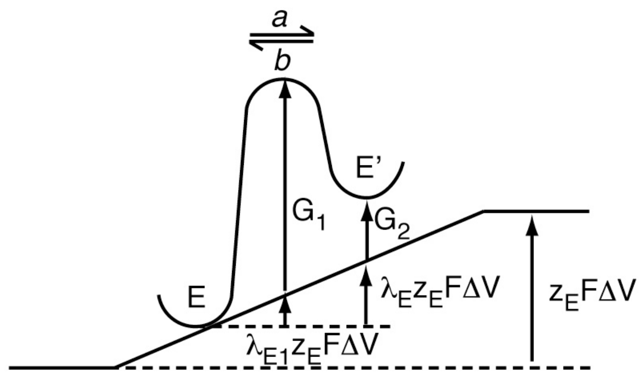
$$\lim_{K_o, Cl_o \to \infty} g(V, K_i, Cl_i, K_o, Cl_o) = (const)K_o Cl_o$$

In fact, the actual flux equation has a denominator that is the sum of terms like

$$p(1 + mK_i Cl_i)(1 + nK_o Cl_o)$$

where *p, m,* and *n* are constants, functions of the rate constants.

Part c) Each transition can be described by a barrier like the one at right. The parameter λ_{E1} is needed to fully specify the rate constants. With this model, the rate constants are given by the following.



$$a = (const)\, e^{-(\lambda_{E1} z_E F \Delta V + G_1)/RT} \qquad \text{and}$$

$$b = (const)\, e^{-(\lambda_{E1} z_E F \Delta V + G_1 - \lambda_E z_E F \Delta V - G_2)/RT}$$

and similarly for c and d.

This does not change the answer to part a). You can show this by working out the full flux equation or by arguing that the charge transfer associated with the change of transporter state doesn't affect the equilibrium of KCl between the solutions. However this charge transfer might affect the membrane-potential dependence of the flux by making it smaller or larger.

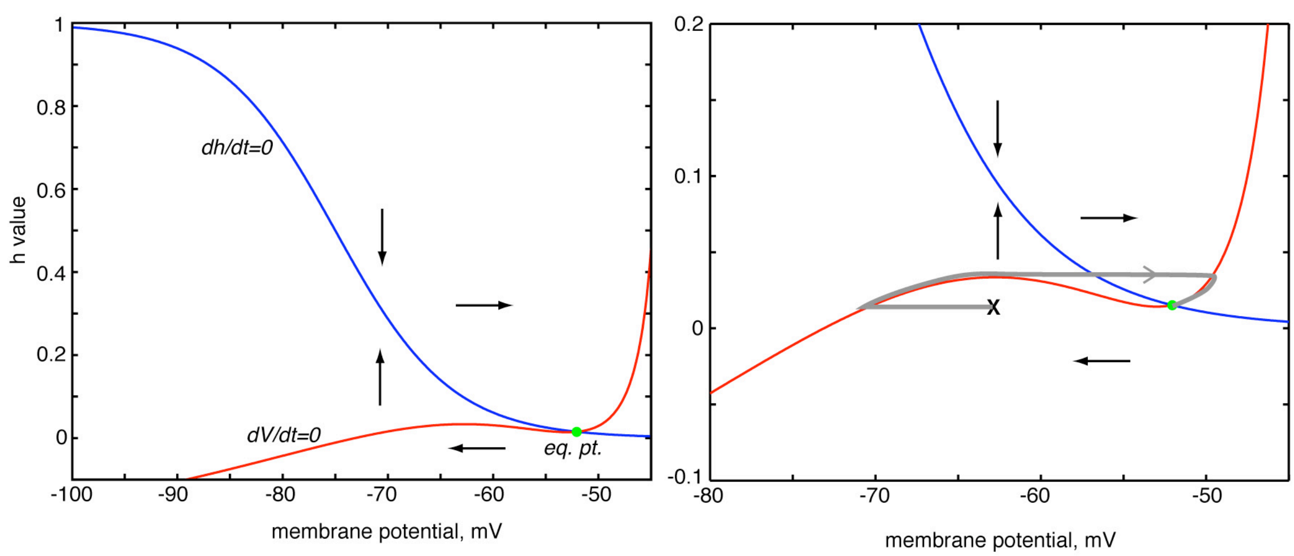
Problem 3

Part a)

$$C\frac{dV}{dt} = I - G_L(V - E_L) - G_{Na} m_\infty(V)(V - E_{Na}) - G_H h(V - E_H)$$

$$\frac{dh}{dt} = \frac{h_\infty - h}{\tau_H}$$

Part b) Because of the low-temperature assumption that trajectories along h are slower than those along V, the trajectory from X will look something like that drawn at right.



Part c) The Poincaré Bendixson Theorem applies because all trajectories are inward around the outside of the phase plane drawn at left below, and a contour around the unstable equilibrium point defines in inner boundary of a region with only inward-pointing trajectories. Because of the low temperature assumption, the limit cycle looks like the plot at right.