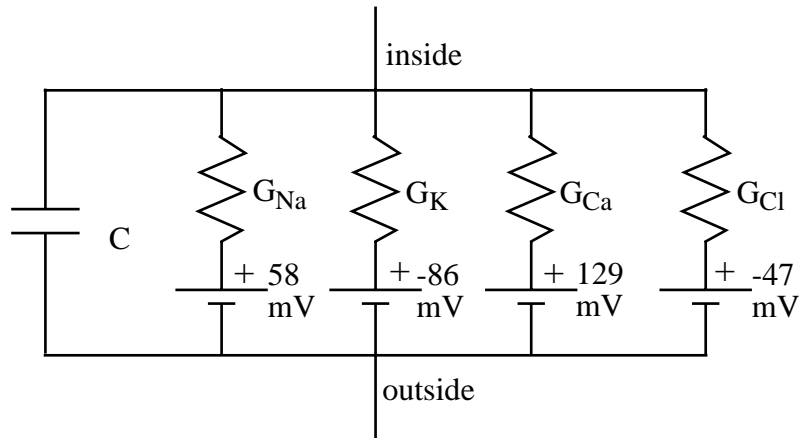# 580.439/639 Midterm Solutions  2001

## Problem 1

**Part a)**  The usual circuit is shown at right with four battery-resistor pairs, one for each ion. Batteries have values of the equilibrium potentials, computed from the table in the problem using the Nernst eqn:

$$E_i = \frac{RT}{z_i F} \ln \frac{C_{out}}{C_{in}}$$

**Part b)**  By changing the conductances, the circuit can range over the potentials spanned by the equilibrium potentials, -86 to 129 mV.

**Part c)**  In terms of conductivities, one can use the circuit at right for the channel, in which case its reversal potential is the potential at which the total current through the channel goes to zero, equal to the open circuit potential of the circuit, -62 mV.

One could also model the channel using the GHK formulation, in which case the total current through the channel would be:

$$I_{total} = I_{Na} + I_K = (const)\left[ \frac{Na_{in}e^{FV/RT} - Na_{out}}{\int_0^d e^{FV/RT}dx} + 5\frac{K_{in}e^{FV/RT} - K_{out}}{\int_0^d e^{FV/RT}dx} \right]$$
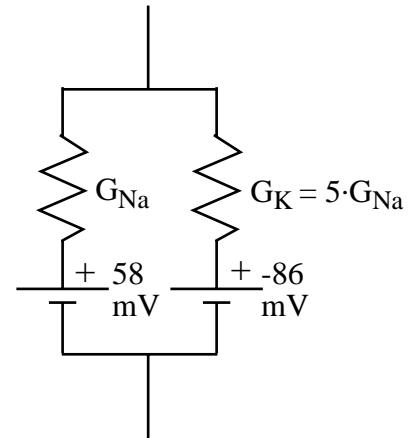
where each current is represented by a GHK current equation and the difference in permeabilities is represented by the factor of 5 in front of the potassium current. Setting $I_{total}$ to 0 gives the usual equation:

$$V = \frac{RT}{F}\ln\frac{5K_{out} + Na_{out}}{5K_{in} + Na_{in}}$$

from which the reversal potential can be computed as –37 mV.

**Part d)**  Increasing $G_{Cl}$ will pull the membrane from rest potential (–60 mV) toward $E_{Cl}$ (-47 mV), depolarizing the cell. Current will flow in the inward direction (consider $I_{Cl}$ in the circuit above when the membrane potential is –60). Chloride ions will flow out of the cell, opposite the direction of current flow, because they are negative.

**Part e)** At rest, the membrane must be dominated by Na or Ca conductance; K or Cl must take over during the action potential. Given the data mentioned, a resting Na seems more likely and a Cl-dependent action potential seems likely.

**Part f)** We presume that the cell is hyperpolarized by a Cl⁻ current during the action potential, meaning that chloride ions flow into the cell, so that charge is flowing out of the cell. If potassium currents are involved, potassium would flow out of the cell.

## Problem 2

**Part a)** The net fluxes from $A$ to $B$ ($J_{AB}$) and from $B$ to $C$ ($J_{BC}$) are given by

$$J_{AB} = (const)\, A \cdot X_f\, e^{-(G_1 + zFV/4)/RT} - (const)\, B\, e^{-(G_1 - G^* - zFV/4)/RT} \quad \text{and}$$

$$J_{BC} = (const)\, B\, e^{-(G_2 - G^* + zFV/4)/RT} - (const)\, C \cdot X_f\, e^{-(G_2 - zFV/4)/RT}$$

where $X_f$ is the concentration of free channel. Taking advantage of the fact that there is a fixed total amount of channel $X = X_f + B$, and setting the fluxes equal to zero gives

$$0 = A \cdot (X - B) e^{-(G_1 + zFV/4)/RT} - B\, e^{-(G_1 - G^* - zFV/4)/RT} \quad \text{and}$$

$$0 = B\, e^{-(G_2 - G^* + zFV/4)/RT} - C \cdot (X - B) e^{-(G_2 - zFV/4)/RT}$$

Solving for $B$, the concentration of ion bound to the channel gives the equilibrium concentrations of $B$ in terms of the other parameters of the system:

$$B = \frac{A \cdot X\, e^{-(G_1 + zFV/4)/RT}}{A\, e^{-(G_1 + zFV/4)/RT} + e^{-(G_1 - G^* - zFV/4)/RT}} = \frac{A \cdot X}{A + e^{(G^* + zFV/2)/RT}} \quad \text{and}$$

$$B = \frac{C \cdot X\, e^{-(G_2 - zFV/4)/RT}}{C\, e^{-(G_2 - zFV/4)/RT} + e^{-(G_2 - G^* + zFV/4)/RT}} = \frac{C \cdot X}{C + e^{(G^* - zFV/2)/RT}} \tag{*}$$

These equations can be related to the usual equilibrium formulation by rearrangement. For the $A - B$ equilibrium, some rearrangement of the first part of Eqn. (*) gives

$$RT \ln A + RT \ln(X - B) = G^* + RT \ln B + zFV$$

which says that the free energy of $A$ plus the free energy of unbound channel (*X-B*), due to concentration, is equal to the free energy of $B$ due to concentration plus $G^* + zFV$, its free energy from being in the channel.

**Part b)** Using the definition of equilibrium above (zero flux), having zero flux over both barriers requires that the two parts of Eqn. (*) be satisfied simultaneously. Setting them equal (equal values of $B$) gives

$$\frac{A \cdot X}{A + e^{(G^* + zFV/2)/RT}} = \frac{C \cdot X}{C + e^{(G^* - zFV/2)/RT}} \quad \text{or} \quad \frac{A}{C} = e^{zFV/RT} \quad \text{or} \quad V = \frac{RT}{zF} \ln \frac{A}{C}$$

which is the Nernst equation relating the concentrations in solution outside the membrane ($A$ and $C$) to the membrane potential $V$. In other words, if $A$ and $C$ are at equilibrium in the usual thermodynamic sense, then it is possible for $B$ to be in equilibrium with both.

**Part c)** If the system is at steady state, then $J_{AB} = J_{BC}$ in order that $dB/dt = 0$. Thus if $A$ and $B$ are in equilibrium in the sense that $J_{AB} = 0$, then the steady state requires that $B$ and $C$ also be at equilibrium. Note that this implies that $B$ cannot come to equilibrium with either $A$ or $C$ unless $A$ and $C$ are at equilibrium with each other.

**Part d)** The flux equation derived for this two-barrier system in class is as follows:

$$J = (const) \cdot$$

$$e^{G*/RT} e^{-(G_1+G_2)/RT} e^{-zFV/2RT} \frac{A - C e^{zFV/RT}}{e^{G*/RT}\left[e^{-(G_1-zFV/4)RT} + e^{-(G_2+zFV/4)/RT}\right] + \left[e^{-(G_1+zFV/4)RT}A + e^{-(G_2-zFV/4)/RT}C\right]}$$

The assumption of indepenence ( sufficiently low concentrations $A$ and $C$) allows the second term in the denominator to be ignored; the assumption that one barrier is larger than the other (e.g. exp(-$G_1/RT$)<<exp(-$G_2/RT$)), allows the remaining terms in the denominator to be simplified, giving:

$$J = (const)e^{-G_1/RT} e^{-zFV/4RT}\left[A - C e^{zFV/RT}\right] \quad \text{for } G_1 > G_2$$

$$J = (const)e^{-G_2/RT} e^{-zF3V/4RT}\left[A - C e^{zFV/RT}\right] \quad \text{for } G_2 > G_1$$

The difference in rectification behavior derives from the difference in the membrane potential dependence of the exponents. Multiplying the exponentials through makes this clearer:

$$J_{G_1>G_2} = (const)e^{-G_1/RT}\left[Ae^{-zFV/4RT} - C e^{zF3V/4RT}\right]$$

$$J_{G_1>G_2} = (const)e^{-G_2/RT}\left[Ae^{-zF3V/4RT} - C e^{zFV/4RT}\right]$$

Notice that, for $G_1>G_2$, the dependence on $V$ of the *inward* flux ($Ae^{-zFV/4RT}$, from $A$ to $C$) is weaker than that of the *outward* flux ($-Ce^{zF3V/4RT}$), by a factor of 3 ($V/4$ versus $3V/4$). The opposite holds for $G_2>G_1$. The result is rectification, plotted at right (assuming $A=C$). You can get an intuitive feel for rectification by considering what happens to the barrier diagrams at extreme values of $V$.
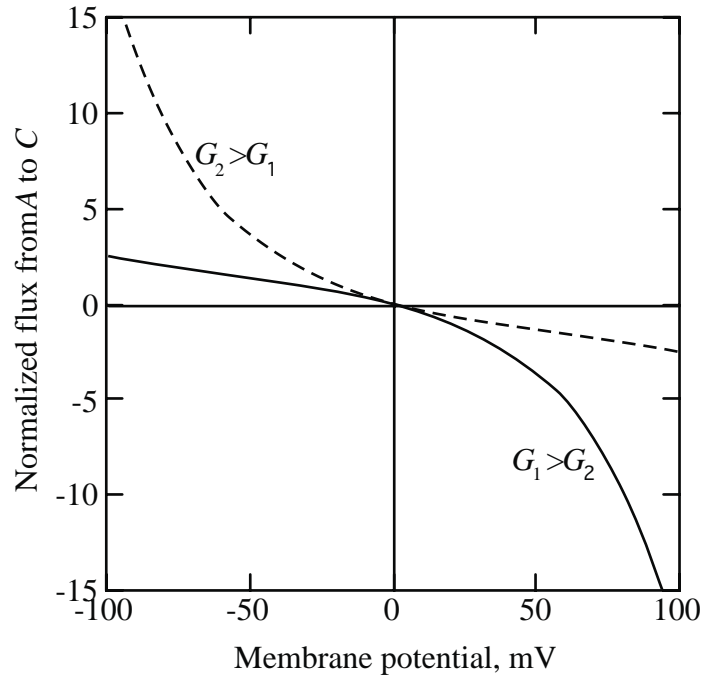
## Problem 3

a) Can't tell. There could be a limit cycle around the stable equilibrium point, but the conditions of the Poincaré-Bendixson (PB) theorem don't hold. Usually, one would expect *S* to be attracting.

b) There is a limit cycle around the unstable equilibrium point, from the PB theorem.

c) Can't tell without knowing what the manifolds of the saddle node do. The PB theorem is hard to apply here, but there could be limit cycles around *S* or *U* or all three equilibrium points, from index theory.

d) Can't tell. Although the saddle's stable manifolds rule out a limit cycle around all three equilibrium points, there could be a limit cycle around either of the *S*s, depending on what the saddle node's unstable manifolds do. Both of them could terminate in *S*s (no limit cycles) or one of them could terminate in a limit cycle (examples of both were given in class and in the notes).

e) No limit cycle. There cannot be a limit cycle around either *S*, because any such limit cycle would have to cross a manifold of the saddle. A limit cycle around all three equilibrium points can also be excluded by considering where the stable manifolds of the saddle have to originate. Given the structure drawn, they have to originate at infinity because there is no other possibility. They cannot originate in the *S*s, which are stable; the possibility of one of them originating in an unstable periodic orbit is excluded because there is then no choice for the other one except infinity, which makes such an orbit impossible.

a)

b)

c)

d)

e)