580.439/639 Solutions to Homework #1

Problem 1

Part a) At equilibrium, the electrochemical potentials of molecules in the A and B states will be equal, so

$$\mu_{al}^A = \mu_{al}^B$$

or

$$\mu_{al}^{0A} + RT \ln C_{al}^A + FV^A = \mu_{al}^{0B} + RT \ln C_{al}^B + FV^B$$

Note that $z_{al} = +1$ and that it has been assumed that the chemical interactions of alamethecin with the lipid cause $\mu_{al}^{0A} \neq \mu_{al}^{0B}$. Solving for the concentration ratio gives

$$RT \ln \frac{C_{al}^B}{C_{al}^A} = \mu_{al}^{0A} - \mu_{al}^{0B} + F(V^A - V^B)$$

Using the fact that $\Delta V = V^B - V^A$ and exponentiating gives

$$\frac{C_{al}^B}{C_{al}^A} = \exp\left[\frac{\mu_{al}^{0A} - \mu_{al}^{0B} - F \Delta V}{RT} \right] \tag{1}$$

Part b) There are two reactions at equilibrium:

where C is the density of channels in the membrane. At equilibrium,

$$\frac{C^B}{C^A} = K_{AB} \qquad \text{and} \qquad \frac{C^C}{\left(C^B\right)^2} = K_2 \tag{2}$$

in addition, the total amount of alamethecin is fixed, so that

$$C^A + C^B + 2C^C = Q \tag{3}$$

Substituting Eqns. 2 into Eqn. 3 to eliminate C^B and C^C gives

$$C^A + K_{AB}C^A + 2K_2\left(K_{AB}C^A\right)^2 = Q$$

or

$$\left(C^A\right)^2 + \frac{(1 + K_{AB})}{2K_2 K_{AB}^2} C^A - \frac{1}{2K_2 K_{AB}^2} Q = 0$$

which can be solved using the quadratic formula giving

$$C^A = \frac{1 + K_{AB}}{4 K_2 K_{AB}^2} \left[\sqrt{1 + \frac{8 K_2 K_{AB}^2 Q}{(1 + K_{AB})^2}} - 1 \right] \tag{4}$$

The concentrations of B and C then follow from Eqns. 2:

$$C^B = K_{AB} C^A \quad \text{and} \quad C^C = K_2 \left(K_{AB} C^A \right)^2$$

Part c) Assume that $K_{AB} \gg 1$; then Eqn. 4 simplifies to

$$C^A \approx \frac{1}{4 K_2 K_{AB}} \left[\sqrt{1 + 8 K_2 Q} - 1 \right]$$

If $K_2 Q \ll 1$, then $\sqrt{1 + 8 K_2 Q} \approx 1 + 4 K_2 Q$ and

$$\boxed{C^A \approx \frac{Q}{K_{AB}} \quad \text{so that} \quad C^B \approx Q \quad \text{and} \quad C^C \approx K_2 Q^2}$$

This result makes sense, because the assumptions mean that both equilibria are strongly pushed in the direction of B; most of the alamethecin is in the B state as a result, and then the concentrations of A and C follow directly from Eqns. 2. In this situation, C^C depends only on K_2 and Q, neither of which is voltage-dependent, so the conductance of the membrane should be constant.

Now assume that $K_{AB} \ll 1$; then Eqn. 4 simplifies as

$$C^A = \frac{1}{4 K_2 K_{AB}^2} \left[\sqrt{1 + 8 K_2 K_{AB}^2 Q} - 1 \right]$$

Once again, the radical simplifies as $\sqrt{1 + 8 K_2 K_{AB}^2 Q} \approx 1 + 4 K_2 K_{AB}^2 Q$ so that

$$\boxed{C^A = Q \quad \text{and} \quad C^B = K_{AB} Q \quad \text{and} \quad C^C = K_2 (K_{AB} Q)^2}$$

In this case, almost all the alamethecin is in the A state and now C^B and C^C depend on K_{AB} which is voltage dependent (Eqn. 1), so the membrane conductance is voltage dependent.

Problem 2

Part a) The equilibrium potentials are given in the table below, calculated using the Nernst equation. The directions of active transport are also given; these are the opposite of the passive fluxes.

Ion	perilymph	endolymph	E_i	A.T. direction
Na^+	145 mM	2 mM	111 mV	out of endo
K^+	5	157	-90	into endo
Ca^{++}	1	0.02	51	into endo
Cl^-	120	132	2.5	out of endo

HCO3⁻	20	31	11	out of endo
urea	5	5	--	equilibrium

Part b) The electrochemical gradient for sodium must exceed that for potassium plus twice that of chloride, so that the net change in electrochemical potential is negative each time a transport step is taken. Assuming the transport goes directly from perilymph to endolymph

$$\sum_{i=Na,K,2Cl} n_i \mu_{i\,endo} - n_i \mu_{i\,peri} \le 0$$

$$\sum_{i=Na,K,2Cl} n_i RT \ln \frac{C_{i,endo}}{C_{i,peri}} + n_i z_i F(V_{endo} - V_{peri}) \le 0$$

$$26\ln\frac{2}{145} + 26\ln\frac{157}{5} + 2\cdot 26\ln\frac{132}{120} + (1+1-2)\cdot 90 = -16.6 \text{ mV}.$$

The n_i terms give the stoichiometry of the transport (1 or Na and K and 2 for Cl). The equation was divided by F at the third line above. Note that the electrical charges cancel, i.e. the net transport is neutral, so the transporter works only against the concentration gradients. The net change in electrochemical potential is negative, so the transporter will work under these conditions.

Part c) If the transporter were electrogenic, one net positive charge per cycle, then the third line of the equation above would be

$$26\ln\frac{2}{145} + 26\ln\frac{157}{5} + 26\ln\frac{132}{120} + (1+1-1)\cdot 90 = 70.7 \text{ mV}.$$

and now the transporter would run the opposite direction.

Problem 3

Part a) In the steady state, the membrane potential must be steady in time; the membrane potential can only be steady if there is no net charge transfer through the membrane. If Na and K are the only permeant ions, then there will be no net charge transfer if

$$I_{Na} + I_K = 0 \tag{1}$$

The concentrations of Na and K must also be constant in steady state, which would seem to imply that $I_{Na} = I_K = 0$. However, we are ignoring this condition, as usual, by assuming that the membrane is bounded by effectively infinite pools of solution, or that there is some transport mechanism which maintains the concentrations with minimal charge transfer.

Part b) Substituting the current equation (* in the problem set) into Eqn. 1 gives

$$Fu_{Na}RT \frac{C_{Na}^2 e^{F\Delta V/RT} - C_{Na}^1}{\displaystyle\int_0^d e^{FV/RT}dx} \; + \; Fu_K RT \frac{C_K^2 e^{F\Delta V/RT} - C_K^1}{\displaystyle\int_0^d e^{FV/RT}dx} = 0 \tag{2}$$

where use has been made of the fact that $z_{Na} = z_K = +1$. Notice that the integrals in the denominators are identical and non-zero, and therefore can be canceled by multiplying both sides of the equation by the integral, giving

$$Fu_{Na}RT\left[C_{Na}^2\, e^{F\Delta V/RT} - C_{Na}^1\right] + Fu_k RT\left[C_k^2\, e^{F\Delta V/RT} - C_k^1\right] = 0 \qquad (3)$$

Canceling FRT and rearranging the equation above to isolate the terms involving ΔV gives

$$\left[u_{Na}\, C_{Na}^2 + u_k\, C_k^2\right] e^{F\Delta V/RT} = u_{Na}\, C_{Na}^1 + u_k\, C_k^1$$

from which the result in the problem set follows:

$$\Delta V = \frac{RT}{F}\ln\frac{u_K K_1 + u_{Na} Na_1}{u_K K_2 + u_{Na} Na_2} \qquad (4)$$

with the definitions $K_1 = C_K^1$, etc.

Note that no assumptions, other than that steady state (Eqn. 1) holds and that current flow in the membrane is described by the Nernst-Planck equation, were made in deriving Eqn. 4. Thus under the conditions of the steady state equation (1), it is not necessary to make the constant field assumption in order to derive a constant-field type voltage equation. This equation can be extended to a membrane permeant to any number of monovalent cations. However, if anions or divalent cations (Ca^{++}) are permeant, then the derivation above does not work because the integrals in the denominator of Eqn. 2 are not all the same.

Part c) Eqn. 4 is often used to define permeability ratios for two ions that are both permeant through a membrane. Eqn. 4 can be rearranged by dividing numerator and denominator of the ratio within the logarithm by u_K to give

$$\Delta V = \frac{RT}{F}\ln\frac{K_1 + \frac{u_{Na}}{u_K}Na_1}{K_2 + \frac{u_{Na}}{u_K}Na_2}$$

which can be solved for u_{Na}/u_K as

$$\frac{u_{Na}}{u_K} = \frac{K_1 - K_2\, e^{F\Delta V/RT}}{Na_2\, e^{F\Delta V/RT} - Na_1}$$

This equation then defines the relative permeability of a membrane for two cations, in terms of the experimentally observed membrane potential ΔV when the membrane separates two solutions containing Na_1 and K_1 on one side and Na_2 and K_2 on the other.

Part d) With active transport, there are now four currents to worry about; the active Na^+ current, the passive Na^+ current, the active K^+ current and the passive K^+ current. In order that the Na^+ and K^+ concentrations be steady, there must be zero net transport of both ions, so that

$$I_K^a + I_K^p = 0 \qquad\qquad \text{and} \qquad\qquad I_{Na}^a + I_{Na}^p = 0 \qquad (5)$$

where the superscripts "a" and "p" refer to active and passive transport mechanisms, respectively. Eqns. 5 above also guarantee zero net charge transfer through the membrane (as long as only Na^+

and K$^+$ are permeable). The ion transporter forces $rI_K^a = -I_{Na}^a$, which is equivalent to saying that r Na$^+$ ions are transported one way for each K$^+$ ion transported the other way. Combining this property of the active transport currents with Eqn. 5 yields the following steady-state relationship for the passive currents:

$$I_{Na}^p + rI_K^p = 0$$

With this assumption, Eqns. 3 and 4 are changed to:

$$Fu_{Na}RT\left[C_{Na}^2\,e^{F\Delta V/RT} - C_{Na}^1\right] + Fru_k RT\left[C_k^2\,e^{F\Delta V/RT} - C_k^1\right] = 0 \qquad (3a)$$

and

$$\Delta V = \frac{RT}{F}\ln\frac{ru_K K_1 + u_{Na}Na_1}{ru_K K_2 + u_{Na}Na_2} \qquad (4a)$$

so that the only change produced by the more complete steady-state assumption is to modify the permeability ratio of the ions by the pumping ratio r of the active transport mechanism.