September 09, 2005 HST 131/ Neuro 200

Problem Set 1 – Ion Channels and Gating

(Answers)

$$E_x = \frac{RT}{zF} \ln \frac{[X_o]}{[X_i]}$$

1a.

Let RT/zF = 25.4 mV, assuming z=1 and T=22C. (Values for R and F can be found in the course guide, as well as this common assumption.)

Mammals

	Internal	External	Eq. Pot.	if T=37C
K^+	137	5	-84.1 mV	-88.4 mV
Na^+	9	140	+69.7 mV	+73.3 mV
Cl^-	8	115	-67.7 mV (since z=-1)	-71.1 mV
Ca^{2+}	.0001	1.8	+124.4 mV (since z=+2)	+130.8 mV

1b. Let RT/zF = 25.4 mV as above. Students may assume a lower temperature for seawater; this is acceptable.

Squid Giant Axon

	Internal	External	Eq. Pot.	if T=10C
K^+	380	15	-82.1 mV	-78.8 mV
Na^+	32	455	+67.4 mV	+64.7 mV
Cl^-	38	524	-66.6 mV (since z=-1)	-63.9 mV
Ca^{2+}	.001	9.3	+116.0 mV (since z=+2)	+111.3 mV

The Nernst potentials are similar because they depend on the ratio of the concentrations, which are themselves similar. Furthermore, they depend on the natural logarithm of the ratio, thus small changes in the ratio have little impact on the Nernst potential.

2a.

$$I_i = [X_o] z P_x \frac{V_m \frac{zF}{RT}}{1 - \exp(V_m \frac{zF}{RT})}$$ Amps = -3.44 nA.

Let external sodium = 0.140 moles, valence =+1, V=0.060 volts, RT/zF= 0.0254 volts, and permeability = 10^-7 amps/mole. Remember the sign!

I_O = +2.35 nA

2b.

At V= -60mV,

$$I_t = z\, P_{Cl}\, (V_m \frac{zF}{RT}) \left[\frac{[X_o] - [X_i]\exp(V_m \frac{zF}{RT})}{1 - \exp(V_m \frac{zF}{RT})} \right] \qquad (V_m \frac{zF}{RT}) = (\text{-}0.06\text{V}) \text{ x } (\text{-}39.37V^{-1}) = 2.36$$

For Cl $[Cl^-]_I$ = 8 mM, I_t = +0.74 nA(outward current; inward flux)

For $[Cl^-]_I$ = 25 mM, I_t = -3.69 nA (inward current; outward Cl flux)

Thus, the current reverses from outward (hyperpolarizing) to inward (depolarizing). Higher $[Cl^-]_I \Rightarrow$ more outward *flux* of Cl^-. Since z = -1, this means more inward *current* $\Rightarrow$ (outward current remains the same). Thus, there is more total current.

3.

Nernst Potential for an Ion:

The Nernst Potential for an ion is derived from a hypothetical situation where there is a concentration difference of that ion across the membrane, and the membrane is permeable to that ion species alone. The voltage at which the the chemical potential causing diffusion across the membrane is offset by the electrical potential across the membrane is known as the reversal potential (see question 4 for explanation that current continues to flow). Thus, the Nernst Potential is also the potential at which net ionic current for that ion switches from net inward flux to net outward flux.

Reversal Potential for a Single Channel:

This is the potential at which net ion flux through the channel is zero. If a single channel were permeable to only one species of ion, then the reversal potential for the channel would be equal to the Nernst Potential for that species of ion. In practice, however, channels tend to be more permeable to some types of ions than others. Thus, current through the channel will reverse at a potential which reflects the relative permeability to all ions capable of passing through the channel. For example, assume that the Nernst Potential is -80mV for potassium and +40mV for sodium. If a potassium channel is 10x more selective for potassium than sodium, then the reversal potential for the channel will be close to -80mV. If the channel is relatively nonselective between sodium and potassium, the reversal potential will be closer to 0 mV.

Resting Potential for the Cell:

Again, another level of complexity. The cell's resting potential is the potential at which the net ionic current into/out of the cell is zero. This is a balance between many different channel types. So, the net current through all channels open at rest is zero. Normally when we speak of resting potential, we mean the state of the cell between action potentials, so most voltage gated sodium channels are shut and the potassium channels mediating the after hyperpolarization are closed as well. The resting membrane potential consists of some potassium leak channels, and any other small conductances. Thus, resting potential is often near reversal for potassium (since this is the predominant conductance open at rest).

All three could be the same if:
-channel is perfectly selective to one ion
-cell has only that one sort of channel

4. At the reversal potential for a channel:

First, let's assume the channel only conducts one species of ion. The reversal potential is the potential at which inward current equals outward current. Thus, there are still ions flowing in and out of the cell, so ion flow does not cease. The two currents merely offset one another and the potential does not change.

Next, making the situation more complicated, the channel may be permeable to more than one type of ion. The reversal potential for the channel will be the point at which the *net* ion flux is zero. Assuming the Nernst Potentials for the ions are different (as is the case for common cations such as potassium and sodium), this means the reversal potential could be different from the Nernst potential for either channel. So, for a cation channel that does not distinguish between potassium and sodium, the reversal potential may be about zero, even though potassium (-80mV) and sodium (+40mV) may have different Nernst potentials. So there could be a net flux of sodium in and potassium out at zero millivolts. Again, we conclude that ion flow does not cease at the reversal potential.

5. Concentration change with an action potential.

Use Mammalian Concentrations

Area of a sphere $A = 4\pi r^2$; if r = 11.5μm then A= 1661.9μm^2
Since capacitance is ~ 1μF/cm^2, C_m= 16.62 pF
5a. Charge $Q = CV$; if ΔV = 115mV then Q = 1.91 pC.
5b. Moles Q/zF; z=1 and F=96485 coul/mol so Δmol = 1.98x 10^{-17} mol Na^+
5c. Mole Fraction
Volume of a sphere $v = \frac{4}{3}\pi r^3$; volume =6370.6μm^3 = 6.37 pL
Total sodium = concentration x volume = 9 mM x 6.37 pL= 5.73 x 10^{-14} mol
Fractional change = (Sodium change)/(Total Sodium) = 1.98x10^-17/5.73x10^-14.
This is about =0.00034553.
Intracellular Na^+ will rise by about 1.98x10^-17 mol/6.37x10^-12 liter, or about 3.11 μM, which is negligible.

5d. Volume of extracellular space: For the difference of volumes between spheres of r = 11.5 μm and r= 11.6 μm:
6538.3 μm^3 – 6370.6μm^3 = 167.6 μm^3 or 168 fl.
Moles of Potassium: Δ K_O =1.98x 10^{-17} mol K^+
Extracellular K^+ will rise by about 116 μM, which may be significant, particularly if the cell were to fire multiple action potentials in rapid succession.

6.

6a. Since the reversal potential is -35mV, we know that the internal concentration is less than the external concentration. The osmotic pressure for chloride to come into the cell (since it is higher on the outside) is only offset by the negative potential at reversal (-35mV). Thus, when we change the potential to 0 mV, more chloride is diffusing into the cell (higher outside concentration) than into the cell (lower internal concentration. This is a net inward flux of negative ions, which is the same current as a net outward flux of positive ions. Thus, current is "outward" which chloride ion flux is "inward". Conveniently, "outward" current is by convention positive, and the current stated in the equation (4.2 nA) is positive.

6b. The I(V) relation is approximated by a straight line. This is the same as an equivalent circuit with a battery to represent the reversal potential (Erev) and a resistor to represent the chloride channels. Ohm's Law tells us that the slope between current and voltage is resistance. We know two points on the line: current is zero at -35mV, and current is 4.2 nA at 0mV. Thus, change in voltage is: +35mV and change in current is +4.2 nA. Equivalent resistance is: (35x10^-3 V)/(4.2x10^-9A) = 8.3 MOhms. Equivalent conductance is the inverse of equivalent resistance, so G= 1/R = 1/(8.3x10^6) = 0.00000012 Siemens = 0.12 uSiemens = 120 nS.

6c. The time constant, tau, is simply the product of R (Ohms) and C (F). R = 8.3x10^6 Ohms. C = 16.62x10^-12 F. Thus, tau = 137.9x10^-6 seconds or 137.9μs.

Simulation Questions (Require IV.exe, IVVG.exe, and lvrt.dll):

7a. The steady state current passes inward current at a more hyperpolarized potentials, and its slope is less negative.

7b. This would represent halving the charge in the S4 voltage sensor. A larger gating charge would provide the cell with a channel that is more sensitive to potential changes, over a shorter range of voltages.

7c. The channel opens at a more positive voltage, resulting in less outward current until higher potentials are reached. This could result in a cell that is more excitable given that much less K current can flow to counteract the depolarizing Na current, and thus neurons would reach action potential threshold faster.

7d. Inward current through potassium channels occurs when the cell is hyperpolarized (sufficiently negative potentials) that membrane voltage is below potassium reversal potential. This rarely occurs *in vivo*, since it is potassium currents that tend to return the cell to rest following an action potential.