Harvard-MIT Division of Health Sciences and Technology
HST.131: Introduction to Neuroscience
Course Director: Dr. David Corey

HST 131/ Neuro 200

Problem Set 1 – Ion Channels and Gating
(due Monday, Sept 12, 2005)

You will need access to two simulation programs for this problem set: *IV.exe* and *IVVG.exe*. *IV.exe* will be useful to study IV plots, but is not necessary for this problem set. *IVVG.exe* will be used for questions 5 and 6. Lab View Run Time (lvrt.dll) must also be downloaded and stored in the same folder as IV.exe and IVVG.exe. Unfortunately, they don't run on Mac computers.

1. a.   The following are typical mammalian ion concentrations in mM. Calculate the Nernst potential for each ion species.

	Internal	External
K^+	137	5
Na^+	9	140
Cl^-	8	115
Ca^{2+}	0.0001	1.8

   b.   The following are ion concentrations in mM for the squid giant axon. Again, calculate the Nernst potential for each ion species. Although the ion concentrations for squid giant axons are quite different , you'll note that the Nernst potentials are remarkably similar. How can this be the case?

	Internal	External
K^+	380	15
Na^+	32	455
Cl^-	38	524
Ca^{2+}	0.001	9.3

2.   Use the GHK equations and the *mammalian* concentrations above, and assume a whole-cell permeability of 10^{-7} amps/M for each ion species.

   a. What is the inward and outward sodium current at +60 mV? (Show your work)

   b. What is the total chloride current at -60 mV?   Recalculate the total chloride current at -60mV with an internal Cl^- concentration of 25 mM. Does the current increase, decrease or stay the same? Explain.

3.   Explain the difference between the Nernst potential for an ion, the reversal potential for a single channel type, and the reversal potential ("resting potential") for a whole cell. When might all three be the same?

4.   At the reversal potential for a channel, does ion flow cease? Explain.

5.   In a typical action potential, the membrane potential of a neuron may go from –70 mV to +45 mV.
        a. Based on the expression V=Q/C, for a spherical neuron with a diameter of 23 μm and membrance capacitance of 1 μF/cm², how much charge (in coulombs) must move across the membrane to effect this potential change?
        b. How many moles of Na+ would this represent?
        c. What mole fraction of the total intracellular Na+ is this?
        d. Assume that the extracellular space around this neuron has a width of 0.1 micrometer, and that the amount of potassium that leaves the cell during an action potential is equal to the sodium that entered. How does the extracellular potassium concentration change?

6.   Suppose a neuron has only chloride channels. The intracellular and extracellular concentrations are such that the Nernst potential for chloride is -35 mV. If you experimentally change the membrane potential to 0 mV, you measure 4.2 nA flowing through the channels.

        a. Is this current flowing inward or outward? Is the chloride flux inward or outward?

        b. Approximating the I(V) relation with a straight line, what is the equivalent conductance of the cell membrane? What is the equivalent resistance?

        c. Using the capacitance you calculated in question 5a, calculate the time constant for the neuron.

The program **IVVG** is a good model for voltage-gated channels that don't inactivate; for them it represents the steady-state current as a function of voltage. It's not so good for sodium channels, which have *no* steady-state current after they've inactivated. However, you could think of the sodium channel plot as a *peak* I(V) relation--what you would observe after the channels have activated but before inactivation kicks in.
        Two main plots are shown, the I/V relationship and the P(V) function. Each ion species can be turned on or off individually, and is represented on the plots by a unique color. Ion concentrations, permeability, valence, gating charge, and gating midpoint can be adjusted for each ion species.

7.   Set all values to physiological values (Physiological Values button). Now turn on the Na+ channels.
        a. Observe the peak I(V) curve. If the Na+ gating charge ('s' value) is halved, how does this affect the peak I(V) curve?
        b. What physical change in the Na+ channel structure would this represent, and why would a cell want a larger or smaller gating charge for a channel?

        Reset to the physiological values. Turn the Na+ channels off and K+ channels on.
        c. Change the midpoint of the probability function ('midpt') from –50 mV to –25 mV. How does this affect the peak IV curve for K+? What advantage could this give a neuron?
        d. Reset to physiological values once again. Under what general conditions is there inward current through potassium channels?