

# Computational Methods in Biology (Spring 2009)

## Assignment 1 (due in class on Jan. 30)

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1. [10 points] (a) Determine the  $K^+$ ,  $Na^+$ , and  $Cl^-$  Nernst potentials (in mV) for the membrane of the squid giant axon using the following data. Here  $[K]_o$  means  $K^+$  concentration outside (in mM) and  $[K]_i$  means  $K^+$  concentration inside. Data:  $[K]_i = 430$ ,  $[Na]_i = 50$ ,  $[Cl]_i = 65$ ,  $[K]_o = 20$ ,  $[Na]_o = 440$ ,  $[Cl]_o = 560$ . Other parameters are temperature  $T = 20^\circ$  celsius (must convert to kelvin  $K$ ), Faraday's constant  $F = 9.648 \times 10^4$  C/mol, and gas constant  $R = 8.315$  J/(mol · K).

(b) Calculate the resting membrane potential given the following conductances:  $g_{Na} = 1\mu S$ ,  $g_K = 10\mu S$ , and  $g_{Cl} = 3\mu S$ .

2. [10 points] (a) Suppose that a membrane has non-voltage-dependent ion channels and the reversal or Nernst potential is  $V_{rev}$ . Also suppose that a current is being applied through an electrode. Then the voltage can be described by:

$$C \frac{dV}{dt} = -g(V - V_{rev}) + I_{app}$$

where  $C$  is the constant capacitance,  $g$  is the constant conductance and  $I_{app}$  is the constant applied current. If voltage is initially at  $V_0$ , find a solution to the differential equation. Also find the steady state solution ( $V_\infty$ ). Finally, rewrite the solution as  $V(t) = (V_0 - V_\infty)e^{-t/\tau} + V_\infty$  to find the time constant ( $\tau$ ).

(b) What are two ways in which the approach to equilibrium can be made slower?

3. [10 points] The *Nernst-Planck* equation describes the flux of ions across a membrane from outside ("o") to inside ("i"). In one dimension (perpendicular to the membrane) it is

$$J = -D \left( \frac{dC}{dx} + \frac{zCF}{RT} \frac{d\Phi}{dx} \right)$$

where  $J$  is the total ion flux,  $C$  is the concentration of the ion, and  $\Phi$  is the electrical potential. The first term on the right represents the ion concentration gradient, while the second term represents the electrical gradient. The *Nernst* equation is obtained by setting the flux to 0 (it is an equilibrium equation) and solving for  $V_{rev} = \Phi_i - \Phi_o$ . Set  $J = 0$  and integrate from outside to inside to derive the Nernst equation.

4. [10 points] This problem refers to the Hodgkin-Huxley model. Note that in this model the  $m_\infty$  and  $n_\infty$  functions increase from near 0 to near 1 as  $V$  increases from

about  $-50$  mV to voltages of  $50$  mV or greater, while  $h_\infty$  does the opposite. Also, the time constants for activation and inactivation all depend on  $V$ , but as an approximation  $\tau_m = 0.5$  msec,  $\tau_n = 4$  msec, and  $\tau_h = 4$  msec. Suppose that the membrane is voltage and space clamped, and that the voltage is pulsed as in the figure below.

(a) Sketch the driving force  $V - V_{rev}$  for  $K^+$  and for  $Na^+$ . Assume that  $V_K = -70$  mV and  $V_{Na} = 50$  mV.

(b) Sketch the activation variables ( $m$  and  $n$ ) and the inactivation variable  $h$  as well as the conductances  $g_K$  and  $g_{Na}$ . Indicate in the conductance sketches where activation is occurring, where deactivation is occurring, and (if applicable) where inactivation is occurring. Recall that the maximum conductance for  $g_K$  is  $\bar{g}_K$  and for  $g_{Na}$  is  $\bar{g}_{Na}$ .

(c) Sketch the  $K^+$  current  $I_K$  and the  $Na^+$  current  $I_{Na}$ .