

Computational Methods in Biology (Spring 2015)

Assignment 1 (due in class on Jan. 26)

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:

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

where C is the constant capacitance, g is the constant conductance and I_{ap} 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_∞). Finally, rewrite the solution as $V(t) = (V_0 - V_\infty)e^{-t/\tau} + V_\infty$ to find the time constant (τ).

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

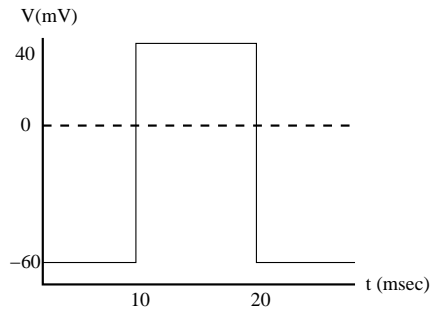
3. [10 points] The *Nernst-Planck* equation describes the flux of ions across a membrane from outside ("o") to inside ("i"). In one dimension (perpendicular to the membrane) it is

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

where J is the total ion flux, C is the concentration of the ion, and Φ 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. [15 points] This problem refers to the Hodgkin-Huxley model. Note that in this model the m_∞ and n_∞ functions increase from approximately 0 to approximately 1

as V increases from about -50 mV to voltages of 50 mV or greater, while h_∞ does the opposite. Also, the time constants for activation and inactivation all depend on V , but as an approximation $\tau_m = 0.5$ msec, $\tau_n = 5$ msec, and $\tau_h = 5$ 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} . (Hint: the ODEs for activation and inactivation are piecewise linear under the assumptions of the problem, and can be solved analytically.) 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} .