Neurodynamics - Fall 2019

BENG 260 / BGGN 260 / PHYS 279

Homework 1: Due October 11

In this homework assignment we will study the membrane dynamics and steady-states associated with the Goldman-Hodgkin-Katz (GHK) nonlinear expression for membrane conductance, and other models of ion transport through membranes.

Background

Consider a biophysical membrane of a neuron under the following assumptions (Hille 2001):

1. *The membrane is a homogeneous substance.*
2. *The electrical field is constant: the transmembrane potential varies linearly across the membrane.*
3. *The ions access the membrane instantaneously from the intra- and extracellular solutions.*
4. *The movement of ions is affected by both concentration and voltage differences.*
5. *The permeant ions do not interact.*

Under these assumptions one can derive the current density carried by a single ionic species S traveling along a single axis perpendicular to the membrane as a function of membrane voltage. This is referred to as the *GHK current density equation*. The *Nernst reversal potential* can subsequently be derived. With this, we obtain:

$$J_S = z_S^2 \, P_S \, V_m \, \frac{[S]_i - [S]_o \, e^{-z_S V_m / V_t}}{1 - e^{-z_S V_m / V_t}} \qquad\qquad E_S = \frac{V_t}{z_S} \, \ln \frac{[S]_o}{[S]_i}$$

where J_S is the current, E_S is the reversal potential, V_m is the voltage across the membrane, $V_t = \frac{kT}{q} = \frac{RT}{F}$ is the thermal voltage, z_S is the valence of the ion S, P_S is the permeability of S, and $[S]_i$ and $[S]_o$ are the intracellular and extracellular concentrations of the ion.

For the K^+ channel type with $z_K = +1$ the current equation and reversal potential reduce to:

$$J_K = P_K \, V_m \, \frac{[K]_i - [K]_o \, e^{-V_m / V_t}}{1 - e^{-V_m / V_t}} \qquad\qquad E_K = V_t \, \ln \frac{[K]_o}{[K]_i}$$

Since the GHK equation is complex it is usually approximated as a linear equation as follows:

$$J'_K = g_K \, (V_m - E_K) \qquad\qquad g_K = P_K \, \frac{[K]_o [K]_i}{[K]_o - [K]_i} \, \ln \frac{[K]_o}{[K]_i}$$

where g_K is the K^+ conductance. The conductance is directly related to the permeability as shown above.

Similar expressions hold for Na^+ and Cl^-, with $z_{Na} = +1$ and $z_{Cl} = -1$.

Values to Use

$V_t = 26.7\ mV$ (thermal voltage at body temperature)

$C_m = 1\ \mu F/cm^2$ (standard membrane capacitance)

S	$g_S\ (mS/cm^2)$	$[S]_o\ (\mu M)^\dagger$	$[S]_i\ (\mu M)^\dagger$
Na^+	13.0	140	11
K^+	5.0	6	145
Cl^-	0.15	111	5

Computational Lab Problems

1. *Linear and nonlinear current approximations* [20 points].

   Plot J_K and J'_K as a function of V_m ranging between $-150\ mV$ and $+150\ mV$. Compare the two currents. Repeat for Na^+ and Cl^-. How good is the approximation? How are the ions different?

   For the case when $V_m \gg V_t$, what is a good approximation of J_K? And when $V_m \ll -V_t$? Compare both approximations with the GHK equation results by plotting.

2. *The resting potential* [30 points].

   (a) Consider a membrane permeable to K^+, Na^+, and Cl^-, with GHK currents for each ion species as a function of the membrane voltage. The resting potential, denoted V_r, is the membrane voltage observed when the current flux across the membrane is in dynamic equilibrium (or steady-state). Explain the difference between dynamic equilibrium and equilibrium. Derive the *GHK voltage equation* for the resting potential V_r by balancing the net current to zero. Your answer should include the concentration and permeabilities of all three ion types.
   Hint: First convert J_{Cl} so that it has the same denominator as J_{Na} and J_K

   (b) What is the value of the resting potential of this cell?

   (c) Repeat (a) using the linear approximation of the current density equations to derive:

$$V_r = \frac{g_{Na}\ E_{Na} + g_K\ E_K + g_{Cl}\ E_{Cl}}{g_{Na} + g_K + g_{Cl}}$$

   (d) What is the resting potential of this cell using the linear approximation?

3. *GHK membrane dynamics* [25 points].

   Plot the dynamics (time course over one second) of the membrane voltage V_m, where initially Na^+, K^+ and Cl^- are active for 250 ms, then the K^+ and Cl^- conductances are deactivated ($g_K = g_{Cl} = 0$) for 250 ms while Na^+ remains active, and finally the Na^+ conductance is deactivated ($g_{Na} = 0$) for 500 ms while K^+ and Cl^- are active. The membrane dynamics are given by:

$$C_m \frac{dV_m}{dt} = -J_{Na} - J_K - J_{Cl}$$

   The initial conditions are V_m at the resting potential calculated in (2a). Compare your result for the GHK conductance models versus the approximation with linear conductances. How good is the approximation? Comment on the role of each of the individual ionic currents in determining the membrane potential.

Homework Problems

4. *Concentration changes during action potentials* [25 points].

   The lipid bilayer of the cell acts as a capacitor and the charge stored across the biological membrane can be described by $q = C_m V_m$. During an action potential, V_m typically changes from -70 mV to +35 mV.

   (a) Considering a membrane capacitance of 1.1 μF/cm^2 and a spherical cell of radius $r = 3\mu m$, what is the change in charge necessary to cause the voltage change during an action potential?

   (b) If the cell is only permeable to Na^+ and K^+ ions, how many ions of each species enter (during depolarization phase; spike) and leave (during repolarization phase) the cell?

   (c) Given the number of ions from part (b) and that Na^+/K^+-ATPase pumps have much slower turnover rates ($\approx 500/\text{s}$) than Na^+ and K^+ ion channels (≥ 1 M/s), what is the maximum firing rate based on how quickly the ions can replenish?

5. *Saturating ionic currents* [Bonus Problem: 15 points].

   Refer to Fig. 1.

   So far in this homework we have been dealing with GHK currents across the ion channel. Now let's assume that due to point source diffusion (treating the ion channel opening as a source) the concentrations in the bulk aqueous solution are different than the concentrations right at the openings of the ion channels. The relationship between concentrations in the bulk and near the ion channel openings are given as follows:

$$C(0) = C_i - \frac{I}{2\pi D r z_s F}$$
$$C(L) = C_0 + \frac{I}{2\pi D r z_s F}$$

   where I is the current through a single channel, D is the diffusion coefficient ($1.9 * 10^{-5} \frac{cm^2}{s}$for Na^+, and $1.3 * 10^{-5} \frac{cm^2}{s}$ for K^+), r is the radius of the channel ($4.5 * 10^{-8} cm$), and F is the *Faraday constant* ($9.649 * 10^4 C/mol$).

   (a) Substitute the above two expressions for concentration, into the GHK current density equation, to derive an expression for current density J that saturates at high values of membrane voltage. Use the relation

$$I = J/n$$

   where n is the density of ion channels.

   (b) From your expression in part (4a), find expressions for the saturating values of J for $V_m \gg 0$, $V_m \ll 0$

   (c) For sodium and potassium, plot your expression in (5a) against membrane voltage, and compare with your plots for the GHK current density (from Problem 1). Vary your value of n; what effect does this have?

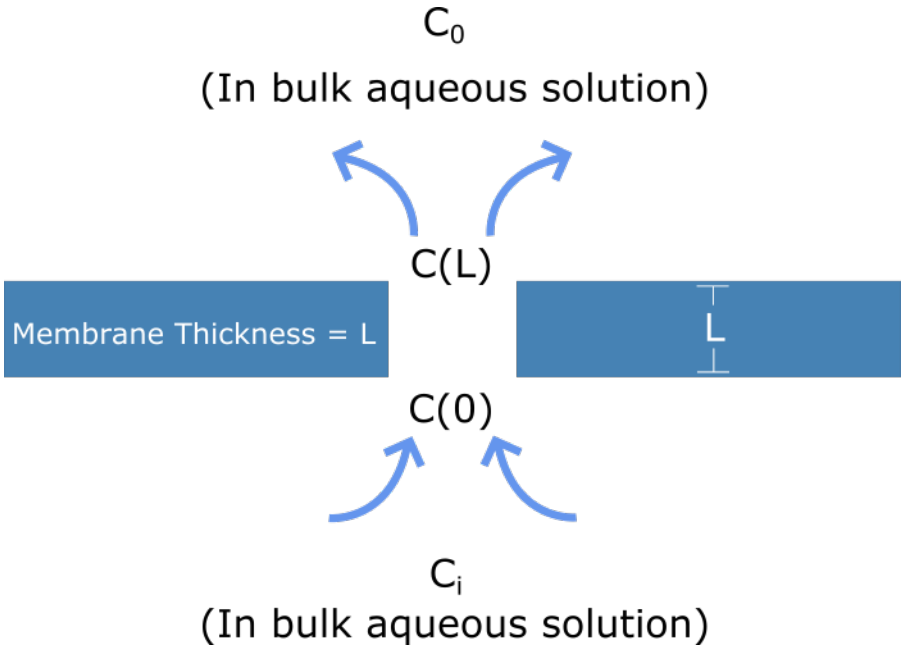

Figure 1: Concentrations in the bulk and near the ion channel openings

Submission Guidelines

Solutions without work or explanations where applicable will receive no credit. Submit a single .zip file containing solutions, plots, and Matlab/Python code to both computational lab and homework problems by 3:00pm of due date on TritonEd.

The submission file should follow the naming scheme `LastFirst_A12345678_HW1.zip`.