

# Neurodynamics - Fall 2017

BENG 260 / BGGN 260 / PHYS 279

## Homework 1: Due October 13

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:

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

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:

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

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

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

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

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

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

$S$	$g_S \text{ (mS/cm}^2\text{)}$	$[S]_o \text{ (}\mu\text{M)}^\dagger$	$[S]_i \text{ (}\mu\text{M)}^\dagger$
$\text{Na}^+$	12.0	145	10
$\text{K}^+$	4.0	5	140
$\text{Cl}^-$	0.1	110	4

## 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  $-150 \text{ mV}$  and  $+150 \text{ mV}$ . Compare the two currents. Repeat for  $\text{Na}^+$  and  $\text{Cl}^-$ . 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  $\text{K}^+$ ,  $\text{Na}^+$ , and  $\text{Cl}^-$ , 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  $J_{\text{Cl}}$  so that it has the same denominator as  $J_{\text{Na}}$  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:

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

- (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  $\text{Na}^+$ ,  $\text{K}^+$  and  $\text{Cl}^-$  are active for 250 ms, then the  $\text{K}^+$  and  $\text{Cl}^-$  conductances are deactivated ( $g_K = g_{\text{Cl}} = 0$ ) for 250 ms while  $\text{Na}^+$  remains active, and finally the  $\text{Na}^+$  conductance is deactivated ( $g_{\text{Na}} = 0$ ) for 500 ms while  $\text{K}^+$  and  $\text{Cl}^-$  are active. The membrane dynamics are given by:

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

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  $q = C_m \cdot V_m$ . During an action potential,  $V_m$  typically changes from -70 mV to +35 mV.

- Considering a membrane capacitance of  $1.3 \mu\text{F}/\text{cm}^2$ , what is the change in charge necessary to cause the voltage change during an action potential?
- If the cell is represented by a sphere of radius  $r = 3 \mu\text{m}$  and is only permeable to  $\text{Na}^+$  and  $\text{K}^+$  ions, how many ions of each species enter (during depolarization phase; spike) and leave (during repolarization phase) the cell? *Note:  $\text{Na}^+/\text{K}^+$ -ATPase pumps have much slower turnover rates ( $\approx 500/\text{s}$ ) than  $\text{Na}^+$  and  $\text{K}^+$  ion channels ( $\geq 1 \text{ M/s}$ ).*
- Based on the intracellular concentrations presented in the table, what can be inferred about the impact of ion movement across the cell membrane during an action potential on the steady-state concentrations of  $\text{Na}^+$  and  $\text{K}^+$  in the cell?

### 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 ( $1.9 \times 10^{-5} \frac{\text{cm}^2}{\text{s}}$  for  $\text{Na}^+$ , and  $1.3 \times 10^{-5} \frac{\text{cm}^2}{\text{s}}$  for  $\text{K}^+$ ),  $r$  is the radius of the channel ( $5 \times 10^{-8} \text{cm}$ ), and  $F$  is the *Faraday constant* ( $9.649 \times 10^4 \text{C/mol}$ ).

- 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.

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

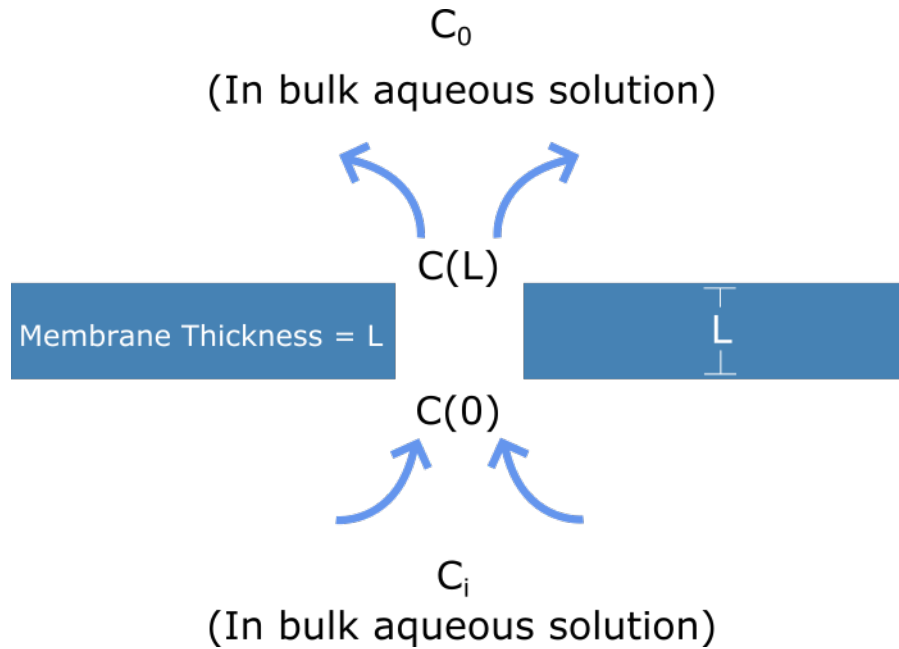


Figure 1: Concentrations in the bulk and near the ion channel openings

### 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`.