BME 5742 Biosystems Modeling and Control

Lecture 32

Cell Electrical Activity: Ion Movement across Cell Membrane and Membrane Potential

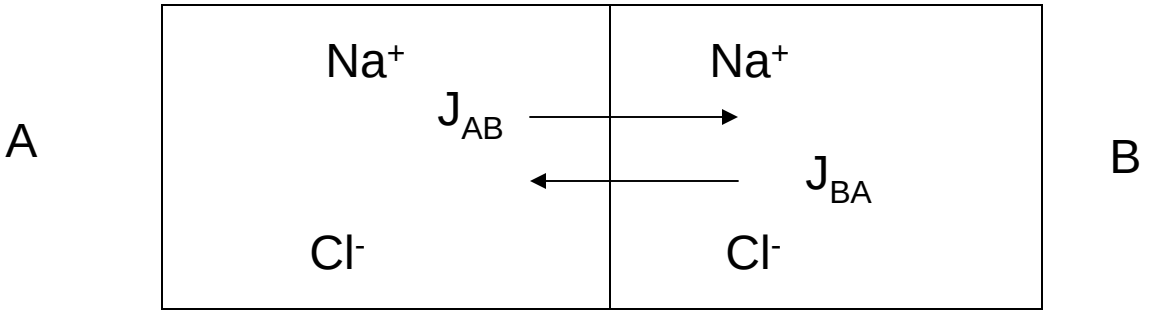
References

- Hoppensteadt-Peskin, Ch. 3
- Dr. Robert Farley's lecture notes "Ionic Equilibria and Resting Membrane Potentials", Core Principles System, HO-Phy-2 (USC Medical School), 8/2003
- Keener and Sneyd's "Mathematical Physiology", Ch. 2.

Introduction

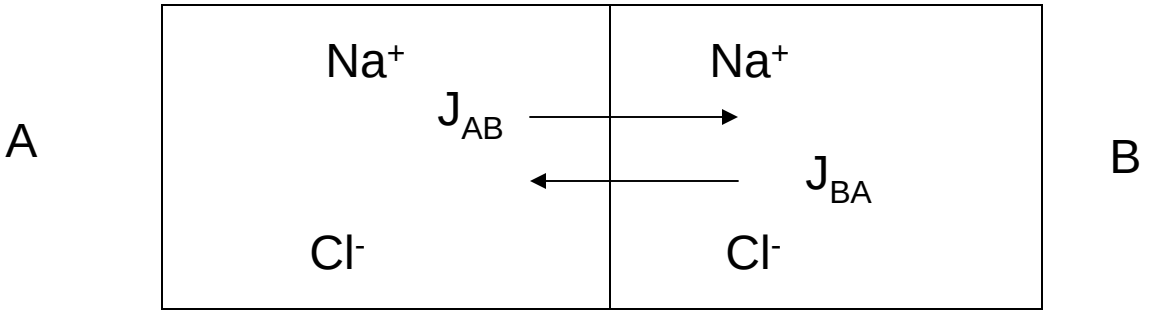
- Most animal cells have an electrical potential difference of 40-100 mV across their plasma membranes, with the cytoplasm at a negative potential relative to the ECF.
- This resting membrane potential is present both in excitable and non-excitable cells.
- Time-dependent changes in the resting potential of nerve and muscle cells may lead to action potentials → mechanism of communication between excitable cells.

Dissociation of Electrolytes in Aqueous Solution



When salt concentration is higher in one compartment than the other, there is a diffusion of ions from the compartment of higher concentration to the compartment of lower concentration.

Ions Diffusion Motion

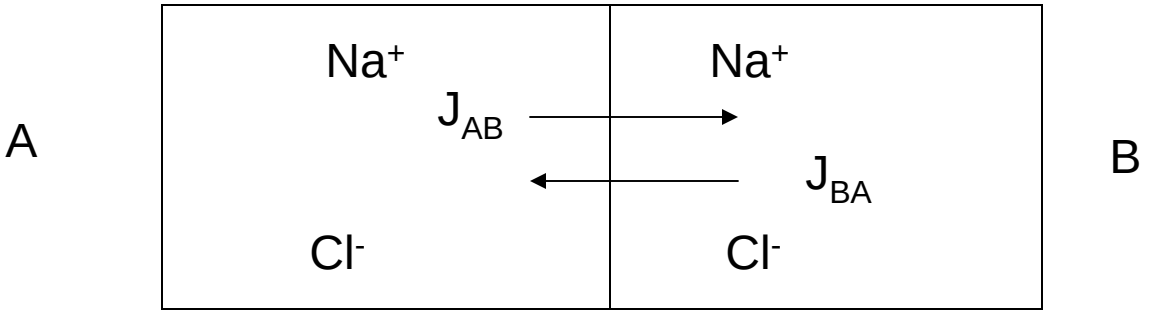


J_{AB} is the rate of diffusion of ions from A to B.

J_{BA} is the rate of diffusion of ions from B to A.

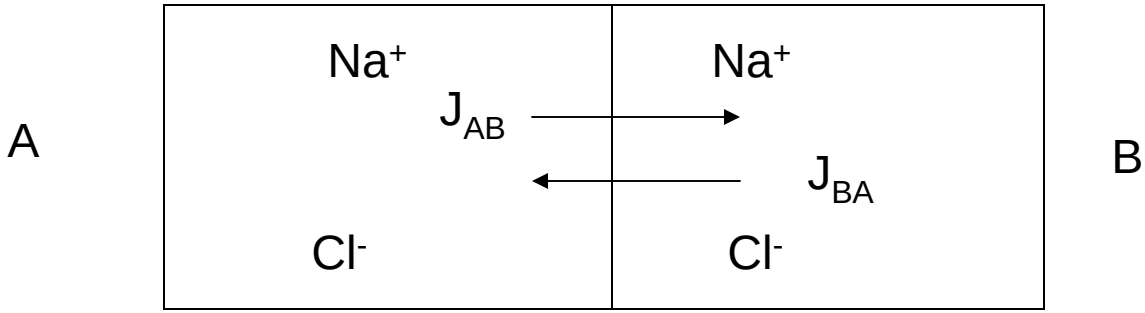
These rates are proportional to the concentration difference.

Under Concentration Equality:



$J_{AB} = J_{BA}$ although unidirectional fluxes of each ion will occur in both directions between B and A, at equal rates. There is no net movement.

Electrical Force Influence



Because ions are electrically charged they will also experience a force if a voltage difference between A and B exists. For example, if $V_A > V_B$ then Na^+ ions move from A to B, and Cl^- ions move from B to A, at a velocity proportional to the voltage difference, until electrochemical equilibrium is established.

Electrochemical Equilibrium

- Concentration differences and voltage differences are two interdependent driving forces.
- In a typical electrochemical equilibrium, there is a steady-state concentration difference, counter-balanced by a voltage difference (created by the moving charged ions themselves).

Nernst Equilibrium Potential -1

$$v_i - v_o = \frac{KT}{zq} \ln\left(\frac{[S]_o}{[S]_i}\right)$$

This is one of the most important equations in Electrophysiology. It describes how a difference in ionic concentration between two compartments can result in a potential difference between the two compartments.

Voltage is v, “i” and “o” stand for intracellular and extracellular (“outside” the cell), S is substance’s name.

Nernst Equilibrium Potential -2

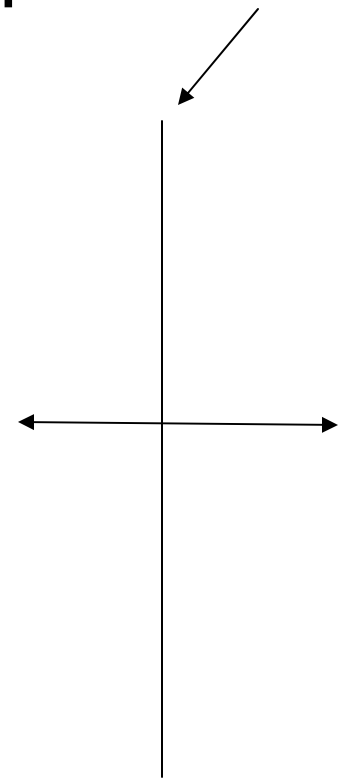
$$v_i - v_o = \frac{KT}{zq} \ln\left(\frac{[S]_o}{[S]_i}\right)$$

Each ion carries z elementary (positive) charges.

Ion's charge is zq, where q is the charge of a proton.

For Na^+ and K^+ we have z = +1, and for Cl^- we have z = -1.

Cell membrane permeable to S but not to S’



Inside

Outside

S

S

$[S]_i = [S']_i$

$[S]_o = [S']_o$

Voltage v_i

Voltage v_o

Nernst Equilibrium Potential -3

$$v_i - v_o = \frac{KT}{zq} \ln\left(\frac{[S]_o}{[S]_i}\right)$$

Assume that the solutions on each side of the membrane are initially electrically neutral.

Each ion S is balanced by another ion S’, with an opposite charge.

Now, let us assume that membrane is permeable to S but not to S’ – what happens?

Nernst Equilibrium Potential -4

$$v_i - v_o = \frac{KT}{zq} \ln\left(\frac{[S]_o}{[S]_i}\right)$$

Now, let us assume that membrane is permeable to S but not to S' – what happens?

Say, that S flows (by diffusion) from inside to outside. Because S' cannot go through membrane, there is a charge buildup across the membrane. This charge imbalance sets an electric field that opposes the diffusion motion.

Nernst Equilibrium Potential -5

$$v_i - v_o = \frac{KT}{zq} \ln\left(\frac{[S]_o}{[S]_i}\right)$$

The above relationship can be shown to satisfy the equation and boundary conditions of a motion equation that include both effects – diffusion and electrical field, acting on substance S.

Nernst Equilibrium Potential -6

$$E_S = v_i - v_o = \frac{KT}{zq}\ln\left(\frac{[S]_o}{[S]_i}\right)$$

Example: (Squid's axon)

ICF concentrations: Na^+: 50, K^+: 397, Cl^-: 40 mM.

ECF concentrations: Na^+: 437, K^+: 20, Cl^-: 556 mM.

Resulting Nernst potentials for each ion (at 27^0C):

Na^+: 56, K^+: -77, Cl^-: -68 mV.

Nernst Equilibrium Potential -7

$$E_S = v_i - v_o = \frac{KT}{zq}\ln\left(\frac{[S]_o}{[S]_i}\right)$$

Example: (human cells)

Resulting room temperature Nernst potentials E for each ion :

Na^+: 62, K^+: -89, Cl^-: -81 mV.

The overall measured membrane potential is around -85mV. It varies in different cell types, and by temperature

Nernst Equilibrium Potential -8

$$E_S = v_i - v_o = \frac{KT}{zq}\ln\left(\frac{[S]_o}{[S]_i}\right)$$

In reality, voltage differences across cell membranes arise because ions move across the membrane at different rates.

Mobility of ions is inversely proportional to their size. In addition, there are various carrier-mediated membrane transport mechanisms that strongly affect the speed of motion of each ion.

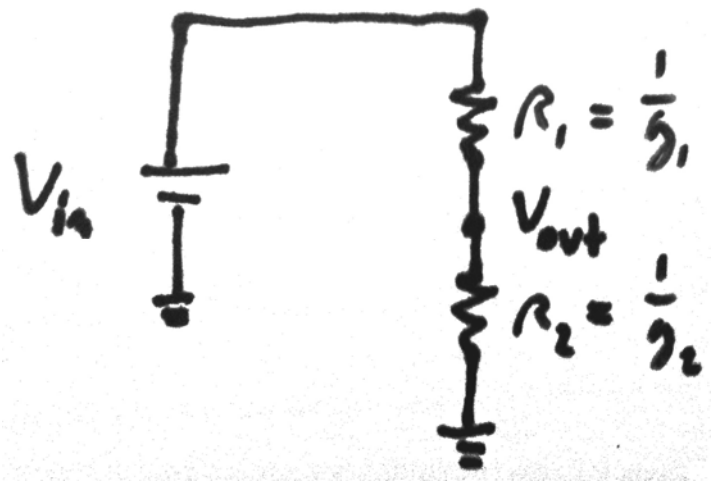
Overall Cell Membrane Potential

$$v = v_i - v_o =$$

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

- For each ion S we have a membrane conductance g_S, determined by the transport protein embedded in the cell membrane.
- Overall voltage is a weighted sum of the E_S potentials, weighted according to relative conductances.

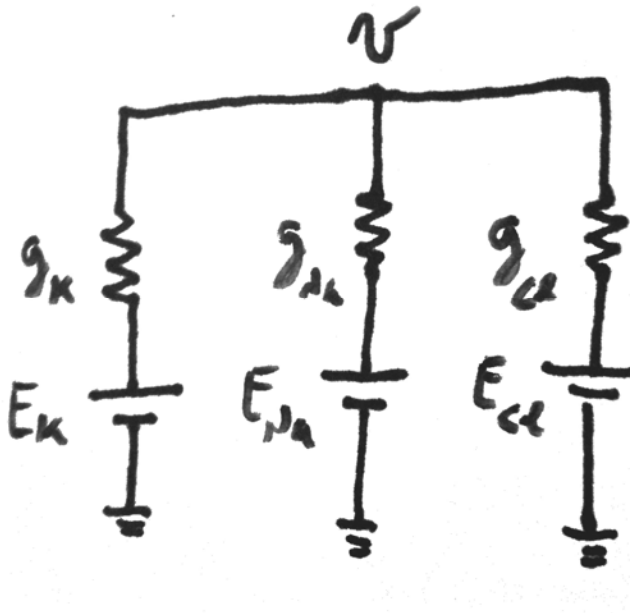
Recall Voltage Division



$$V_{out} = V_{in} \frac{R_2}{R_1 + R_2} = V_{in} \frac{g_2^{-1}}{g_1^{-1} + g_2^{-1}}$$

$$= V_{in} \frac{g_1}{g_1 + g_2}$$

Cell Membrane Potential Explained



Superposition

$$E_K \neq 0, E_{Na} = 0, E_{Cl} = 0 \Rightarrow$$

$$\Rightarrow v = E_K \frac{R_{Na} \parallel R_{Cl}}{R_K + R_{Na} \parallel R_{Cl}} = E_K \frac{g_{Na}^{-1} + g_{Cl}^{-1}}{g_K^{-1} + g_{Na}^{-1} + g_{Cl}^{-1}}$$

Cell Membrane Potential Examples

$$v = v_i - v_o =$$

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

- Typical conductance ratio for K^+,Na^+ and Cl^- is 0.7: 0.07: 0.23. Then v comes out to be very close to E_K. (True in most mammal cells)
- If, for instance, g_{Na} jumps to 0.9 when more sodium channels open up, then v moves more towards E_{Na}.