BHARATHIDASAN UNIVERSITY

Program: M.Sc., Biomedical Science

Course Title: Neurobiology

membrane potential

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The Neuron at Rest

- Perception, action, thoughts, emotions all require active communication
  - between neurons and
  - between neurons and peripheral structures.

by using electrical signaling

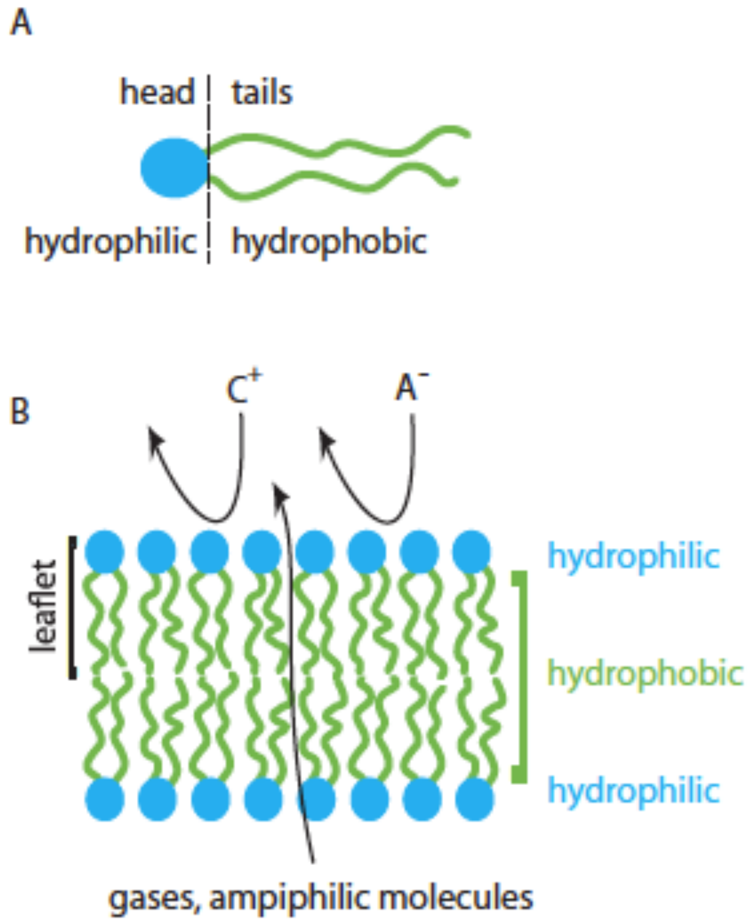
- There are two electrical properties
  1. Neurons at resting condition
  2. Neuron when firing an action potential

Neuron under resting conditions two features dominate

1. The resting membrane potential
2. Graded synaptic inputs (<u>Graded potentials)</u>

Membranes prevent the free diffusion of charged molecules

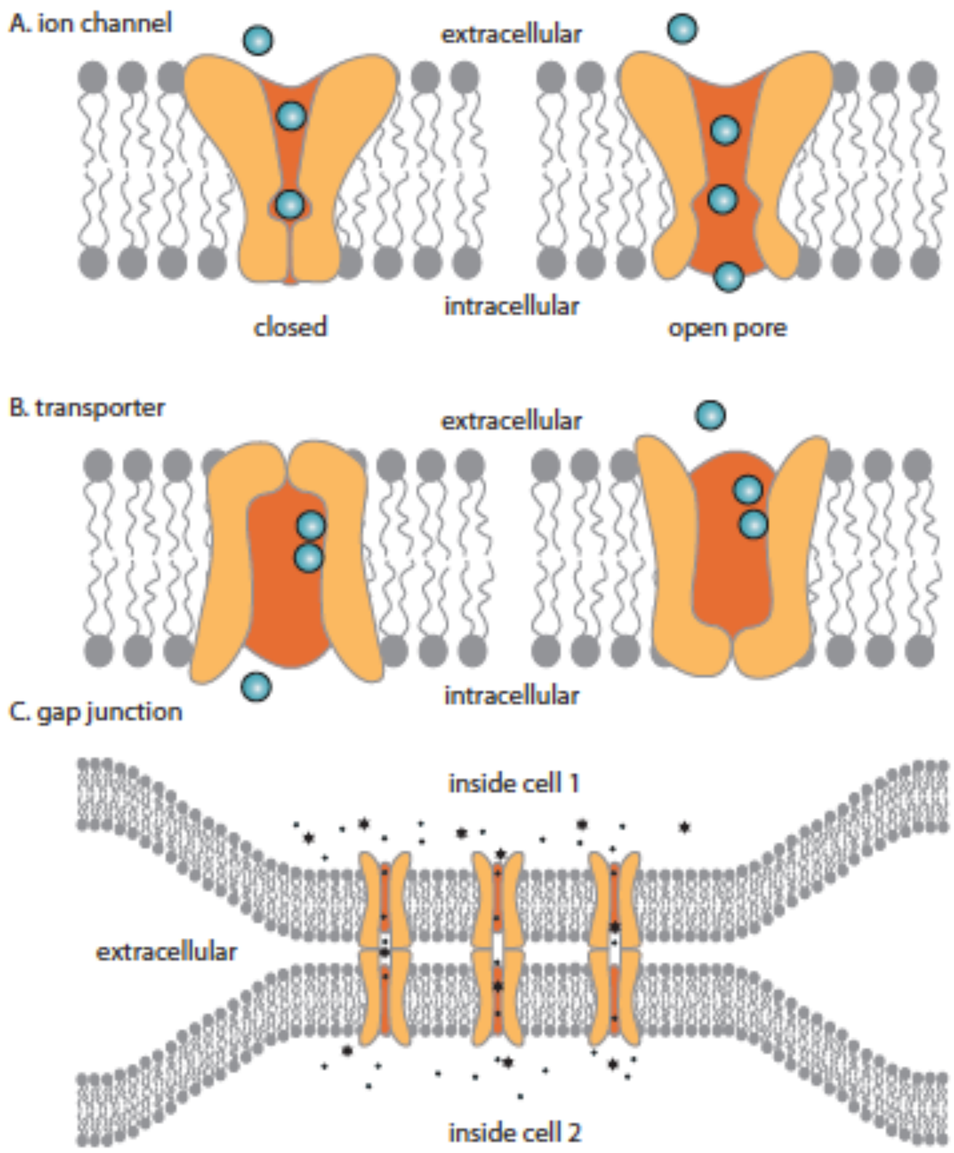
- plasma membranes: separate the inside of a cell, the intracellular compartment, from the outside or extracellular space.
- The plasma membrane's hydrophobicity prevents the free diffusion of both large and small charged molecules such as ions
- charged molecules cannot penetrate the tail region of the lipid bilayer which repel charged molecules and thus cannot cross the membrane



Ions do move across the membrane

- through several specialized routes that extend into both the extracellular and intracellular compartments.
- specialized routes are formed by membrane proteins ,
- multiple protein subunits complex that are anchored within the membrane and span the bilayer
- 3 types of transmembrane or membrane-spanning protein complexes

1. Ion channels (When appropriate conditions occur, ion channels switch from a closed conformation to an open conformation)
2. Transporters (Transporters exist in many varieties, including pumps and exchangers or carriers , and use energy)
3. Gap junctions (large pores between cells through which molecules below a certain size pass)



Mechanisms underlying the resting membrane potential

- All cells have a resting membrane potential that caused from an uneven distribution of charged molecules across the plasma membrane.
- Intracellular organic anions are not present extracellularly
    1. nucleic acids, (DNA, RNA, NTPs)
    2. two amino acids, (Aspartate and glutamate)
    3. Many proteins —
- are negatively charged molecules, or anions , and most of these do not leave the cell
- neuronal membrane at rest Na+, K+ (cations) and Cl- (anion) move across the membrane.
- Na+, K+ and Cl- differentially distributed across the membrane of a neuron

- K^+ more prevalent inside the cell and
- Na^+, Cl^- more prevalent outside the cell.
- at rest, each ionic species exists in steady state

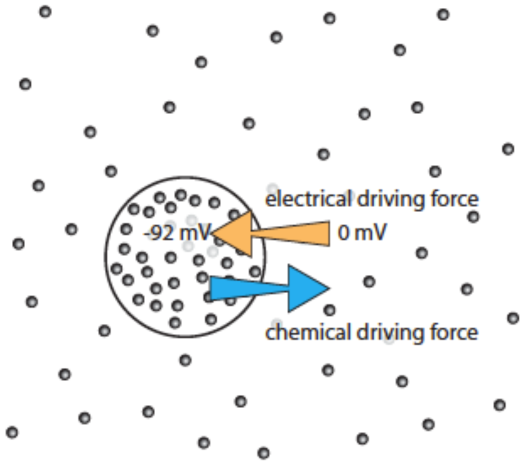
(Steady state means with the same number of ions leaving the cell as entering it)

- Consider how just one ionic species, K^+ , reaches electrochemical equilibrium.
- In a mammalian neuron cytoplasm contains 155 mM of K+ than ECF (5 mM).
- So there is a concentration gradient of K+ between

cytoplasm and ECF, due to concentration gradient

K try to diffuse out to maintain equilibrium this is

called chemical driving force.



- At the same time, cytoplasm is in negative, this negative forces attract K^+ inward called electrical driving force.
- Chemical and electrical driving forces oppose one another.
- At steady state,

chemical driving forces of K = electrical driving forces of K, BUT opposite.

One can calculate the voltage ie electrical potential exerted between cytoplasm and ECF.

Electrical potential (E_x) is chemical and electrical forces on ionic species, x,

which was empirically expressed as Nernst equation

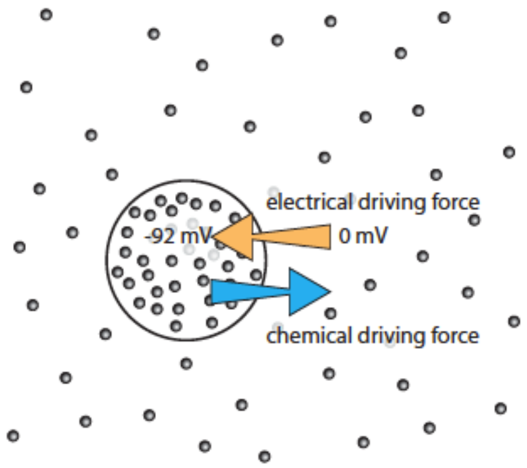
$E_x = -\frac{RT}{z\,F} ln \frac{[ion]_i}{[ion]_o}$ where R is gas constant, T absolute temp, F, the faraday

- E_x = 62*z* log$\frac{[X]_o}{[X]_i}$
- where $[X]_o$ and $[X]_i$ are the extracellular and cytosolic concentrations of the ionic species
- 62 is simplified constants
- z refers to the valence of the ionic species
- Nernst equation for potassium ions: E_x = 62*(+1)* log$\frac{5mM}{155mM}$

    1. 62 is simplified constants
    2. valence of the K+ species is +1
    3. $[X]_o$ ECF conc of K+ is 5mM
    4. $[X]_I$ cytosolic conc of K+ is 155mM

E_x = 62X 1X[0.69 – 2.19] $\Longrightarrow 62X1X(-1.49) \Longrightarrow$

E_x = -92mV , electrical potential of K+ is -92mV



- Net driving forces (electrical +chemical) is difference between calculated Nernst potential and actual cell potential.
- Driving force = E_x - V_m

When Nernst potential equals the actual cell potential, the driving force is zero. ie $E_x = V_m$ is called reverse potential

If the cytoplasm become more +tive, K will leave the cell. Depolarization

If the cytoplasm become more –tive K will enter the cell. Hyperpolarization

- In the cell 3 ionic species — K, Cl, and Na
- Nernst potential for these 3 ions are
- For Cl- $E_{\mathcal{Cl}} = 62*(-1)*\log\frac{100mM}{7mM}$ = -71mV

- For Na+ $E_{\mathcal{Na}} = 62*(+1)*\log\frac{145mM}{12mM}$ = 67mV

- If we add all $E_{Cl}+E_{Na}+E_K$ = -92+67+(-71) = -96mV but actual neuronal memb potential is -72mV.

- $V_m = 62 * \log \frac{[(1)*(5)+(0.04)*(145)+(0.45)*(7)]}{[(1)*(155)+(0.04)*(12)+(0.45)*(100)]} = 62 * \log \frac{[5+6+3]}{[155+0+45]}$

- V_m = -72mV

- permeabilities of potassium, chloride and sodium ions are:
- P_K =1. 00
- P_{Cl} = 0.45
- P_{Na} = 0.04

Different Cl transport mechanisms produce different distributions of Cl-

- The distribution of chloride ions is actively determined by transporters that shuttle chloride ions across the membrane. Two types of chloride transporters exist:
- A sodium / potassium /chloride carrier, NKCC , transports Cl- into the cell.
- A potassium /chloride carrier, KCC , transports Cl- out of the cell.

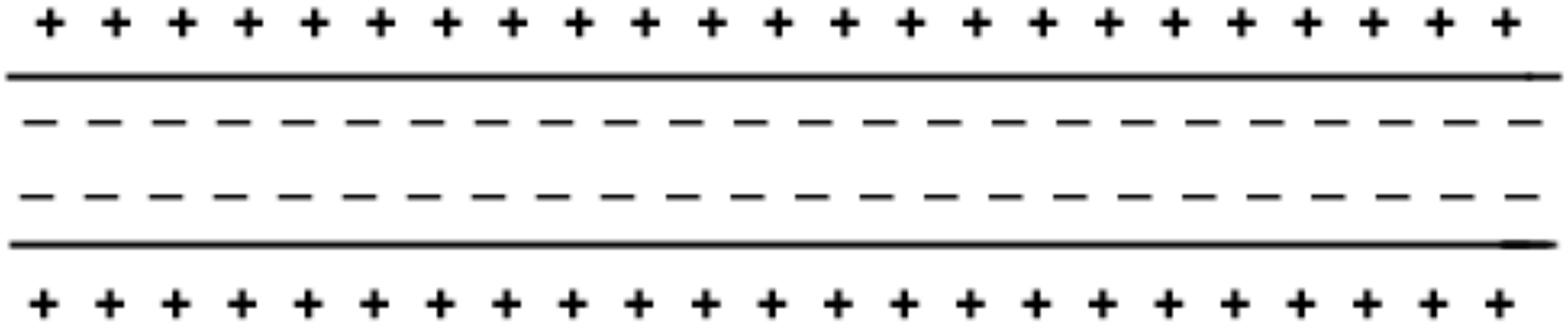
active transport

- Neurons use active transport to prevent redistribution of sodium and potassium ions
- Na + /K + ATPase is a pump, a type of ion transporter that requires

the hydrolysis of one ATP molecule in order to pump three sodium ions out and twopotassium ions in

How Do Neurons Operate?

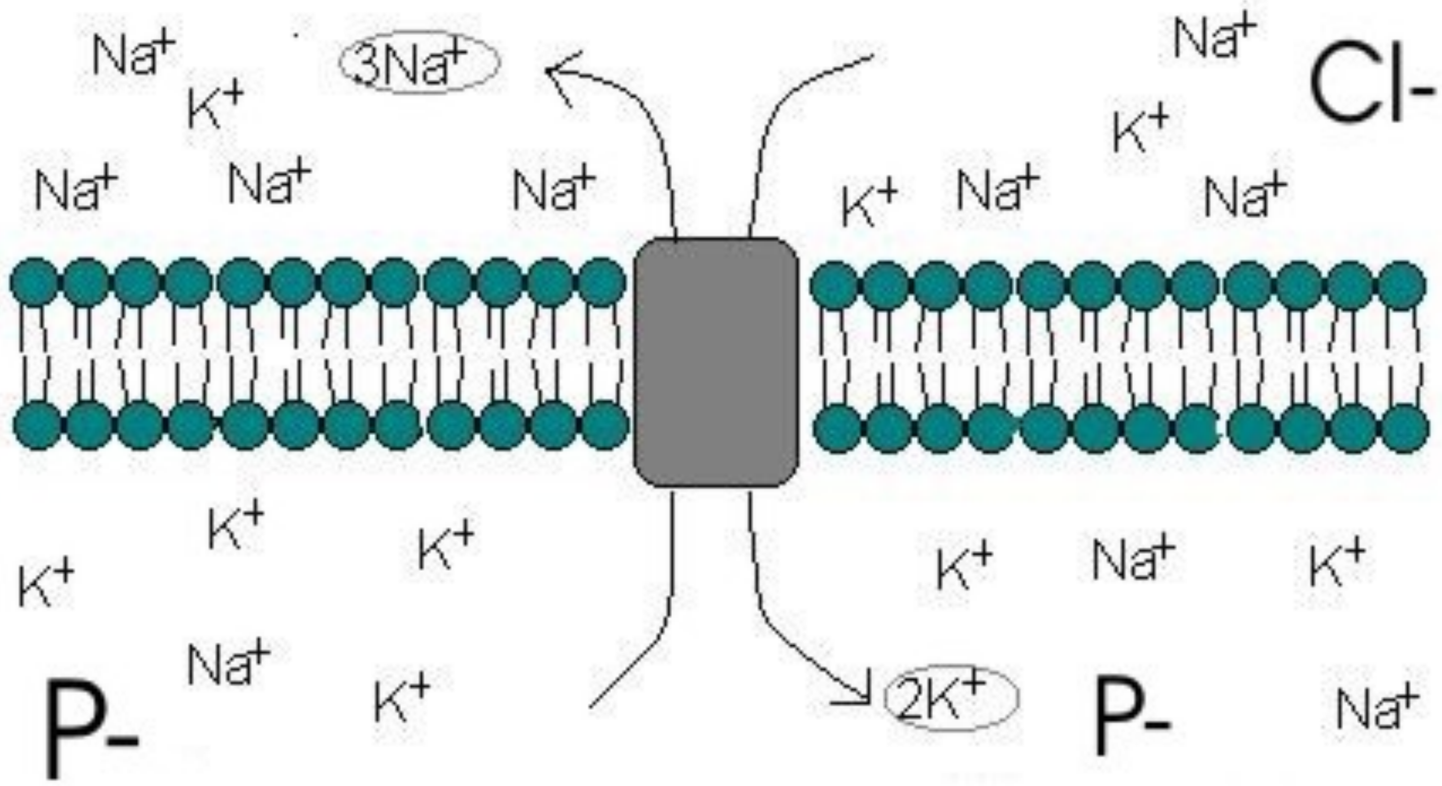
- Neuron at Rest → Resting Potential
  - Occurs when the neuron is at rest.
  - A condition where the *outside* of the membrane is *positively(+)* charged compared to the inside which is *negatively(-)* charged.
  - Neuron is said to be ***polarized.***
  - Neuron has a voltage difference of -70 mV



Section of an axon during the resting potential.

How is resting potential maintained?

Ion Distribution



How is resting potential maintained?

- At rest, the sodium gates are closed.
- Membrane is 50 times more permeable to K^+ ions causing them to "leak" out.
- This causes outside of membrane to have an abundance of + charges compared to inside. The inside of the membrane is negative compared to the outside. This is helped by the (-) proteins etc.
- The "sodium-potassium" pump pulls 2 K^+ ions in for 3 Na^+ ions sent out. This further creates a charge difference!!

Action Potential

The mechanism by which neurons send impulses.
They are comprised of electrical signals generated at the soma and moving along the axon toward the end opposite the soma (motor neurons)

Action potentials occur in two stages:

- Depolarization
- Repolarization

Depolarization in an action potential

- When the neuron is excited past its "Threshold" the following events occur:
  - Sodium ions (Na^+) rush into the axon.
  - This neutralizes the negative ions inside.
  - The inside of the axon becomes temporarily (+) while the outside becomes temporarily (-). The reversal of charge is known as *"depolarization"*
  - Nearby Sodium (Na^+) channels open to continue the depolarization.

Repolarization

- This is the restoring of the (+) charge on the outside of the axon and (-) on the inside.
  - Potassium gates open and potassium floods out.
    - This generates positive charge on the outside of membrane.
  - Sodium Channels Close (no + charges can get inside)
  - The Sodium/Potassium pump rapidly moves Sodium out of the cell.
    - Further creates the (+) charge outside with a (-) charge inside.