Structure and Function Relationship in Nerve Cells & Membrane Potential

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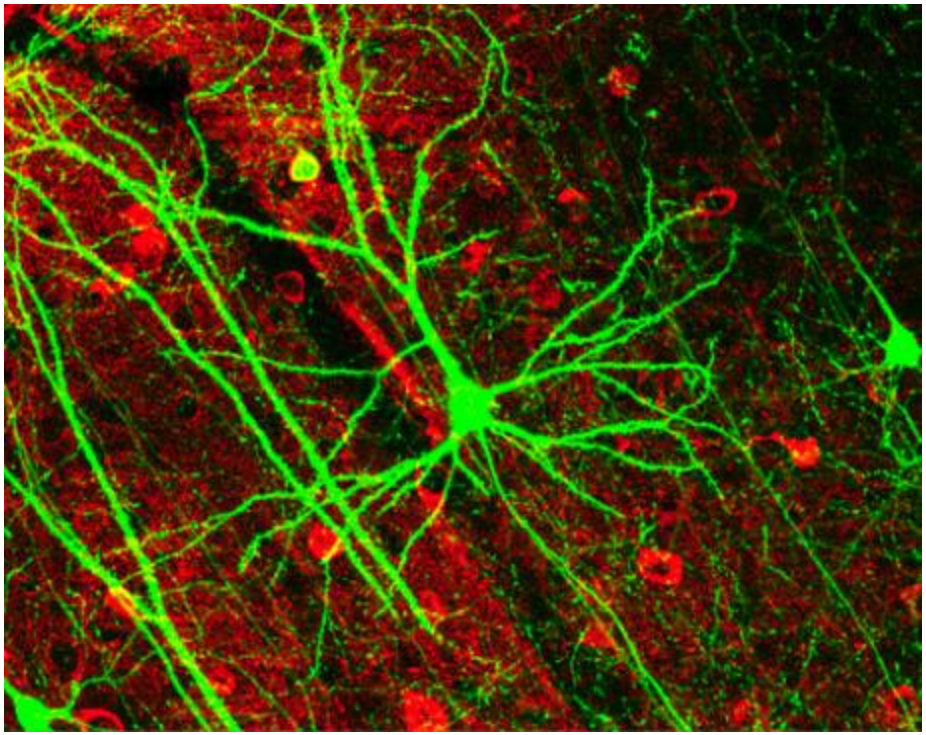
Nervous System Cells

- Glia
  - Not specialized for information transfer
  - Support neurons
- Neurons (Nerve Cells)
  - Receive, process, and transmit information

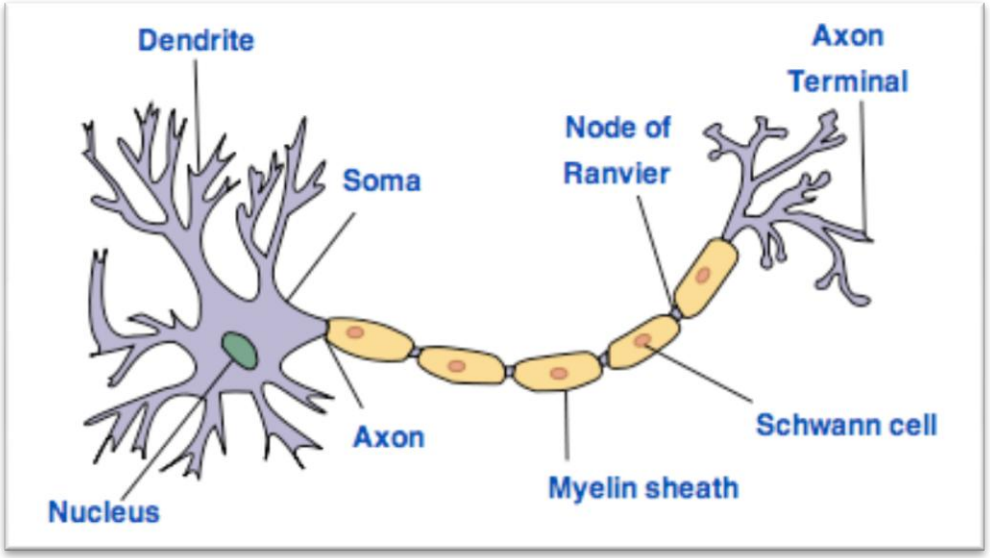
Neurons

- Neuron Doctrine
  - The neuron is the functional unit of the nervous system
- Specialized cell type
  - have very diverse in structure and function



Neuron: Structure/Function

- designed to receive, process, and transmit information
  - Dendrites: receive information from other neurons
  - Soma: "cell body," contains necessary cellular machinery, signals integrated prior to axon hillock
  - Axon: transmits information to other cells (neurons, muscles, glands)
- Information travels in one direction
  - Dendrite → soma → axon



How do neurons work?

- Function
  - Receive, process, and transmit information
  - Conduct unidirectional information transfer
- Signals
  - Chemical
  - Electrical

Membrane Potential

Because of motion of positive and negative ions in the body, electric current generated by living tissues.

What are these electrical signals?

- receptor potentials
- synaptic potentials
- action potentials

Why are these electrical signals important?

These signals are all produced by temporary changes in the current flow into and out of cell that drives the electrical potential across the cell membrane away from its resting value.

The resting membrane potential

The electrical membrane potential across the membrane in the absence of signaling activity.

Two type of ions channels in the membrane

- Non gated channels: always open, important in maintaining the resting membrane potential
- Gated channels: open/close (when the membrane is at rest, most gated channels are closed)

Learning Objectives

- How transient electrical signals are generated
- Discuss how the nongated ion channels establish the resting potential.
- How the flux channels of ions through gated channels generates the action potential.
- Illustrate how the channels, along with other component important for nerve cell signaling
- Represented by an electrical equivalent circuit.

Membrane potential results from the seperation of charge across the cell membrane

- A nerve cell at rest has an excess of positive charges on the outside of the membrane and an excess of negative charges on inside.
- This charge separation brings about *electrical potential difference* across the membrane.
- The potential difference is called the resting membrane potential.

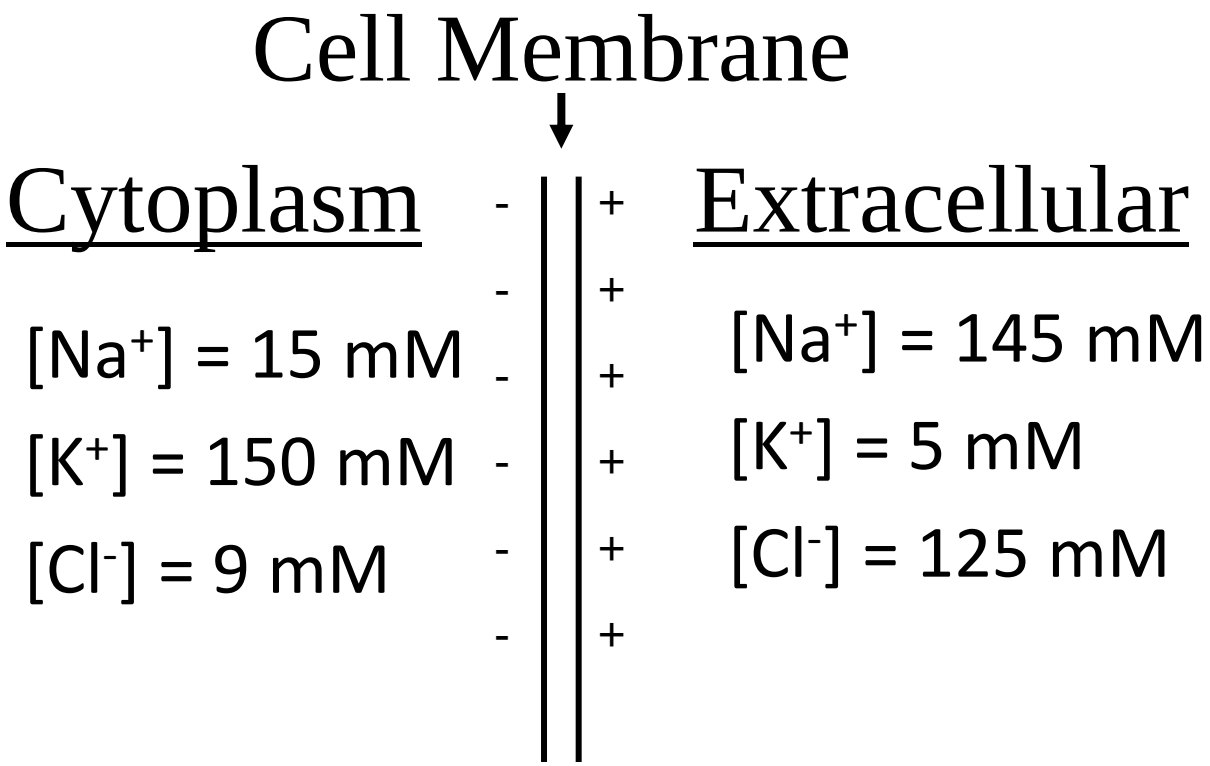
When the cell is at rest, the resting membrane potential applies only to the potential across the membrane.

- The more general term membrane potential refers to the electrical potential difference across the membrane at any moment in time.

- By convention, the potential outside the cell is randomly defined as zero, so membrane potential (V_m) is defined as

$$V_m = V_{in} - V_{out}$$

The resting membrane potential is determined by different types of non-gated ions channels



Nongated channels in glia cells are selective only for potassium.

- The membrane of glia cells have nongated channels.
- Most of nongated channels are selectively permeable to K^+ ion.
- In most of glia cells, membrane potential is about -75mV.

Nernst Equation

Calculates the equilibrium potential for each ion

$$E = -2{,}3 \frac{RT}{zF} log \frac{[C]_{outside}}{[C]_{inside}}$$

R = gas constant,

T = temperature in degrees Kelvin,

F = Faraday constant,

z = charge of the ion

Nongated channels in nerve cells are selective for several ion species

Nerve cells at rest, unlike glia cells, are permeable to Na^+ , K^+ and Cl^- ions.

The passive fluxes of Na^+ and K^+ through nongated channels are balanced by active pumping of Na^+/K^+ ions

- For the cell to have resting membrane potential, the charge separation across the membrane must be constant.
- Therefore, for the cell to achieve a resting state, the movement of K^+ out of the cell must balance the movement of Na^+ into the cell.

The charge separation across the membrane must be constant.

The balance provided by active pumping of Na^+/K^+ ions.

The action potential is generated by the opening of voltage-gated channels selective for Na^+ and K^+

- In nerve cell at rest
  - Na^+ influx through nongated channels is balanced by a steady efflux
  - so the membrane potential is constant.
- A transient depolarizing potential
  - causes some voltage-gated Na^+ channels to open.
- The resultant increase in membrane Na^+ permeability allows Na^+ influx to outstrip the K^+ efflux.

The action potential is generated by the opening of V-gated channels selective for Na^+ and K^+

A net influx of position charge flows through the membrane, and positive charges accumulate inside the cell, causing further depolarization.

Resting Membrane Potential

- *Goldman-Hodgkin-Katz Equation*
  - Takes into account all ionic species and calculates the membrane potential

$$E = \frac{RT}{F} \ln \frac{P_{Na}Na_o + P_K K_o + P_{Cl} Cl_i}{P_{Na}Na_i + P_K K_i + P_{Cl} Cl_o}$$

Permeability: $P_K : P_{Na} : P_{Cl} = 1 : 0.04 : 0.45$

Cl^- typically not pumped, so at equilibrium

K^+ dominates because the greatest conductance

Resting membrane potential usually very negative about -70 mV

E.g.

- **In nerve cell:**

  $pNa^+ / pK^+ = 0.06$ rest pot = -70mV

- **In muscle cell:**

  $pNa^+ / pK^+ = 0.01$ rest pot = -90mV

Electrical Signals-1

- Deviation in the membrane potential of the cell
  - Depolarization
    - Reduction of charge separation across membrane
    - Less negative membrane potential
  - Hyperpolarization
    - Increase in charge separation across membrane
    - More negative membrane potential
- Cause: Ion channels open/close
  - Large change in permeability of ions relative to each other
  - Changes in net separation of charge across cell membrane

Electrical Signals-2

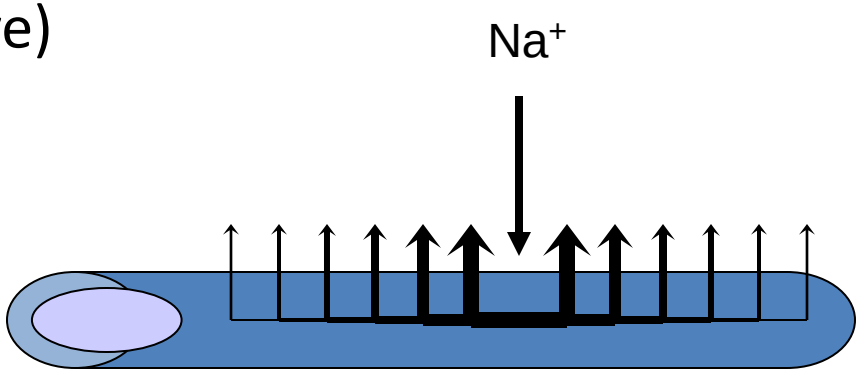
- Spread according to different mechanisms
  - Electrotonic conduction
    - Dendrites
  - Action Potential
    - Axons

Electrotonic Conduction-1

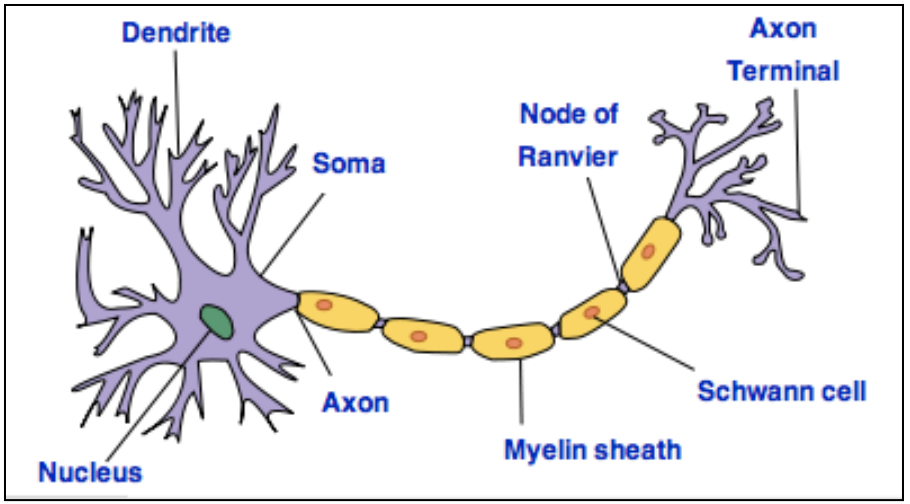
The passive spread of voltage changes along the neuron is called "***electrotonic***" conduction. Electrotonic conduction is important in the propagation of action potential.

Electrotonic Conduction-2

- Na^+ channels opened
  - Na^+ flows into cell
  - Membrane potential shifts toward Na^+ equilibrium potential (positive)
  - Depolarization



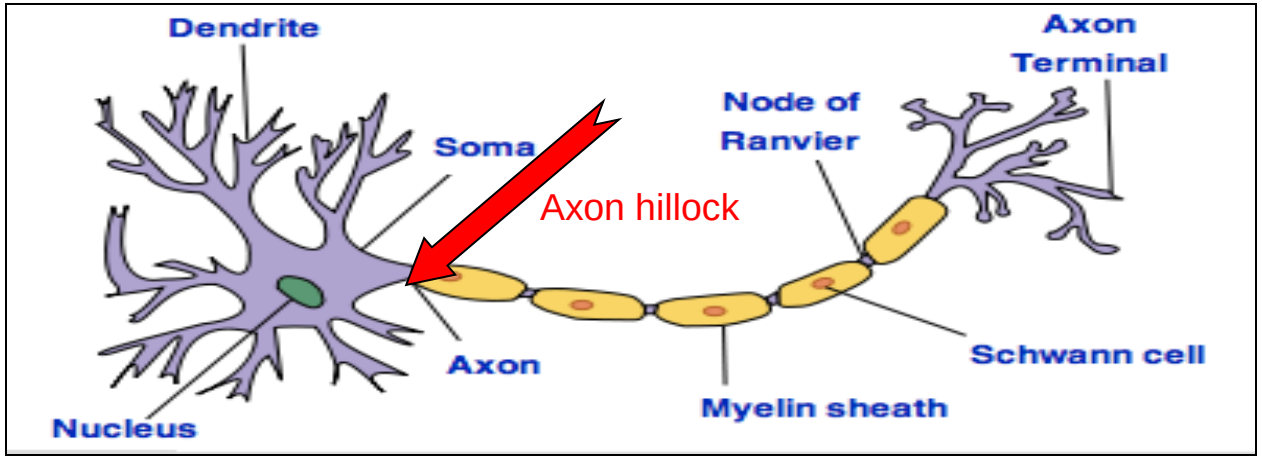
Information Processing



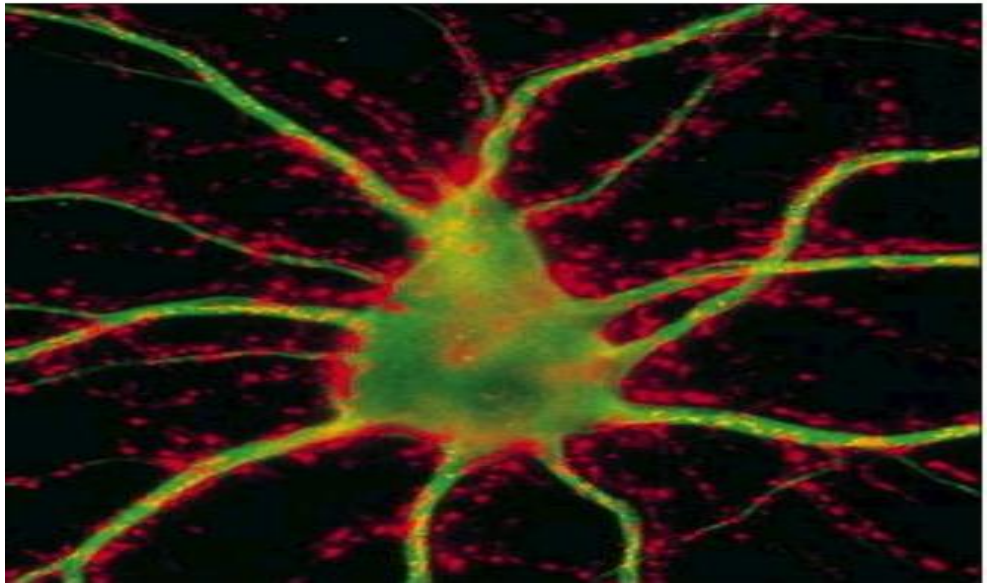
- A single neuron receives inputs from many other neurons
  - Input locations
    - Dendrites – principle site
    - Soma – low occurance

Transmitting Information

- Signal inputs do not always elicit an output signal
  - Change in membrane potential must exceed the threshold potential for an action potential to be produced
  - Mylenated axons
    - Axon hillock = trigger zone for axon potential
  - Unmyelenated axons
    - Action potentials can be triggered anywhere along axon



Action Potential

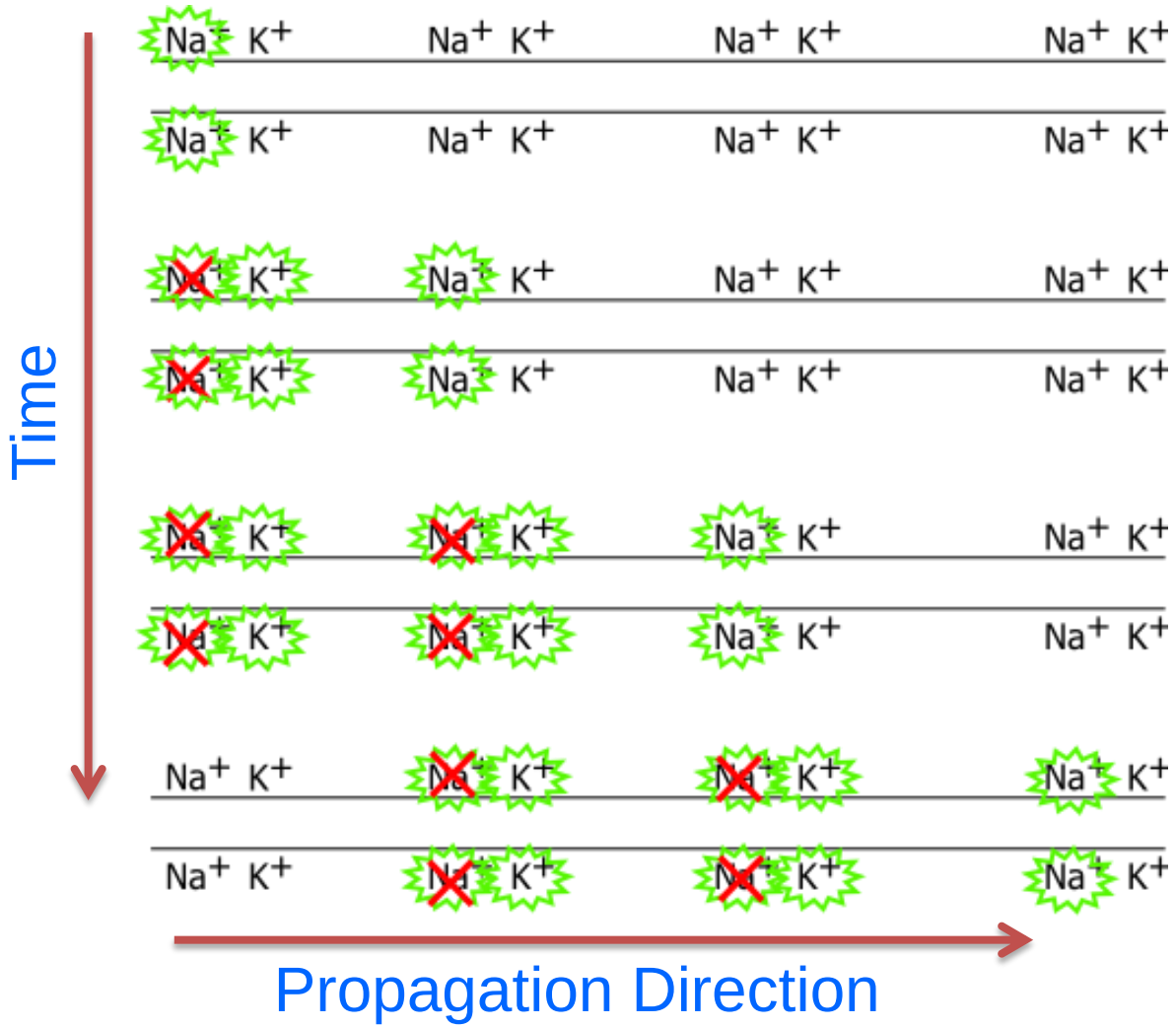


Action potential is

- seen in axon hillock.
- normally propagates from the axon hillock along the axon.
- works ‘All-or-none’ principle.

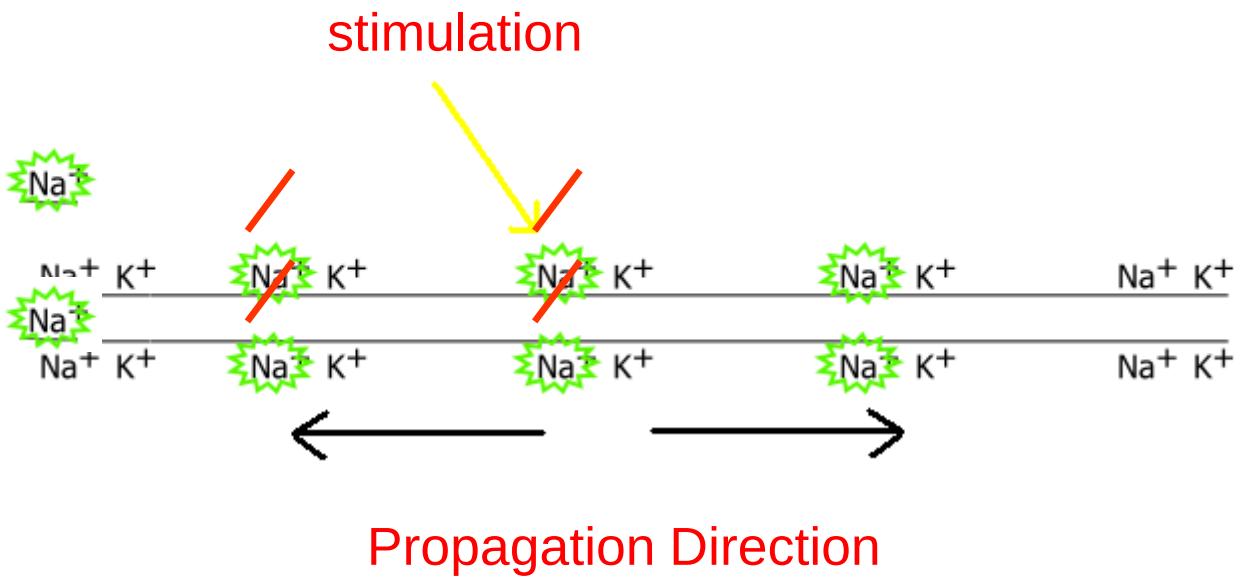
* *axon hillock:* The initial segment of the axon.

- Action potential normally propagates from the axon hillock along the axon.



Propagation of the Action Potential

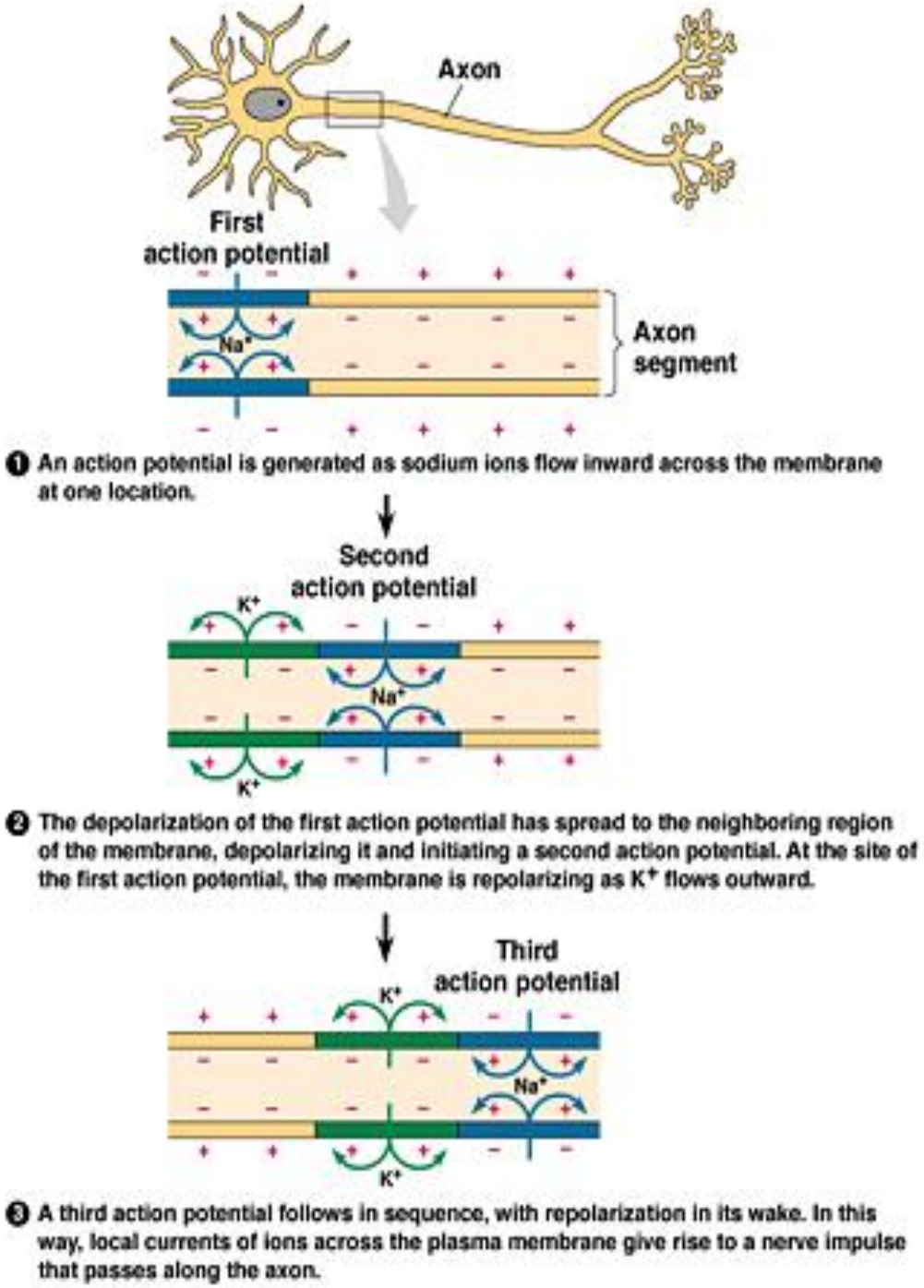
If excitation is initiated artificially somewhere along the axon, propagation then takes place in *both* directions from the stimulus site.



Propagation of The Action Potential Steps

An action potential is generated in any region.

- As a response, voltage-gated Na^+ channels are opened.
- This local depolarization then spreads electrotonically along the axon.
- The voltage-sensitive channels in the new (next) location will go through the same sequence previously described regenerating the action potential.
- Subsequent portions of the axons are depolarized in the same manner.
- Strong depolarization in one area results in depolarization above the threshold in neighboring areas.



❶ An action potential is generated as sodium ions flow inward across the membrane at one location.

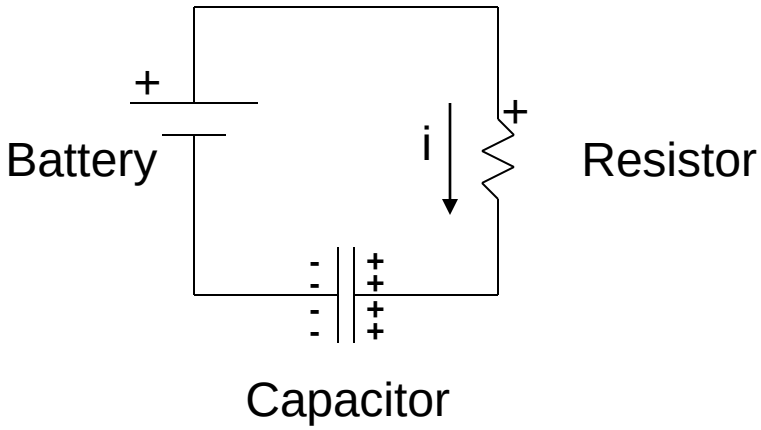
❷ The depolarization of the first action potential has spread to the neighboring region of the membrane, depolarizing it and initiating a second action potential. At the site of the first action potential, the membrane is repolarizing as K^+ flows outward.

❸ A third action potential follows in sequence, with repolarization in its wake. In this way, local currents of ions across the plasma membrane give rise to a nerve impulse that passes along the axon.

Modeling Neurons

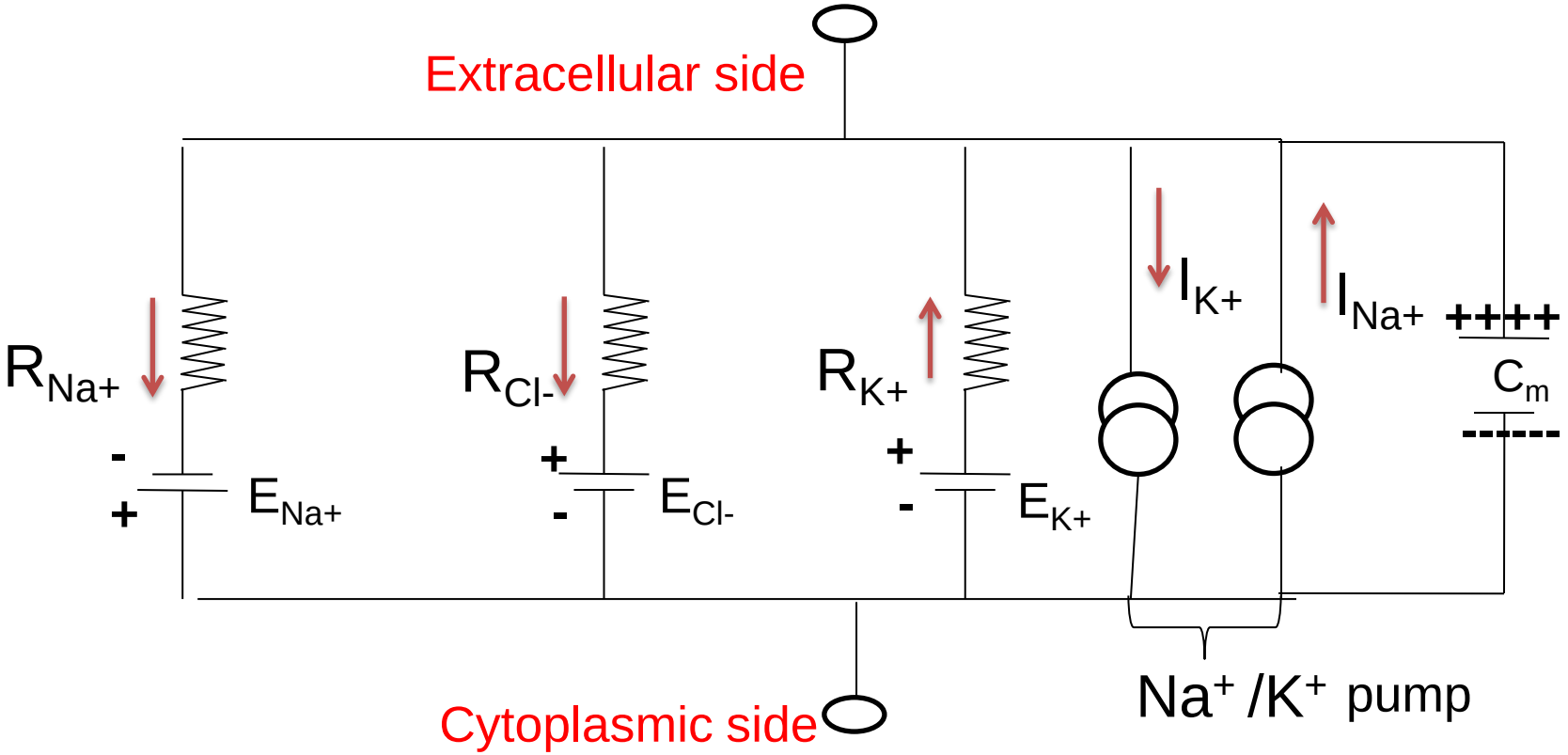
The current flow in a neuron can be modeled by an electrical equivalent circuit.

- Neurons are electrically active
- Model as an electrical circuit
  - Battery :Current (I) generator, Na^+/K^+ pump
  - Resistor: Leak channels for Na^+, K^+, Cl^- ions.
  - Capacitor: Lipid bilayer
  - Generators: Ions currents (inward or outward) from leak channels.



Neuron modeled as an electrical circuit

If we consider a neuronal membrane **at the rest**;



Ionic Gradients as Batteries

- Concentration of ions differ between inside the neuron and outside the neuron

- Ion channels permeate the membrane
  - Selective for passage of certain ions
  - Vary in their permeability
  - Always open to some degree = “leaky”

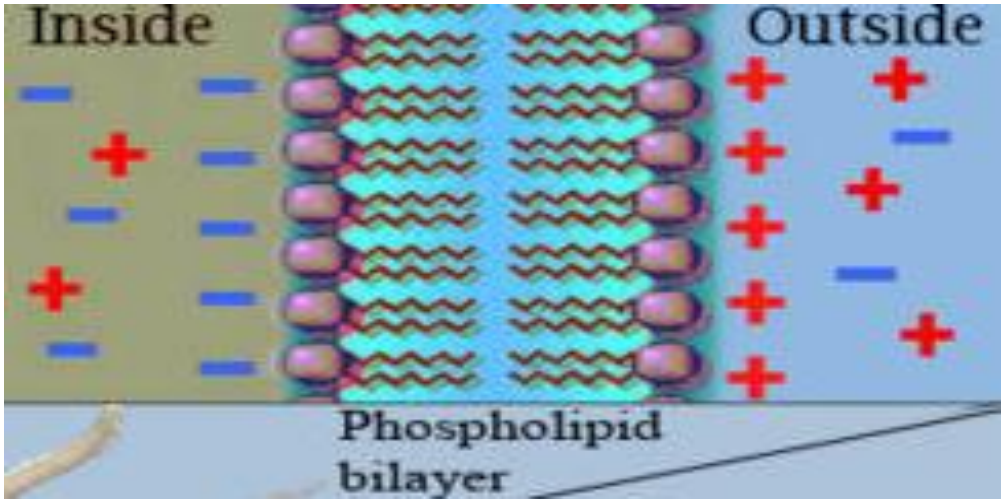
- Net Result: each ionic gradient acts as a battery
  - Battery
    - Source of electric potential
    - An electromotive force generated by differences in chemical potentials

Ion Channels as Resistors

- Resistor
  - Device that impedes current flow
    - Generates resistance (R)
- Ion channels vary in their permeability
  - "Leaky"
    - Always permeable to some degree
  - Permeability is proportional to conductivity
- Leak channels
  - conductance relationship g
    - Conductance (g) = 1/R

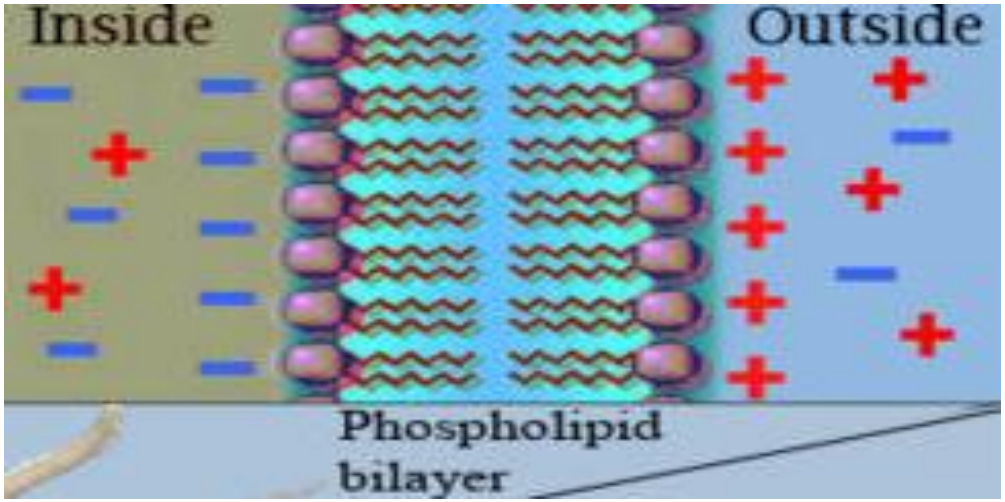
Membranes as Capacitors-1

- Capacitor
  - A simple capasitor consist of two metal plates separated by an insulated material.
  - Each plate is a conducter, at constant potential.
  - Potential difference between the plates is V.



Membranes as Capacitors-2

- Plasma Membrane
  - Lipid bilayer acts like an insulator separating two conducting media:
  1. The external medium of the axon
  2. The internal medium of the axon .



Which properties of the membrane affect the speed of action potential propagation?

Speed of electrotonic conduction is determined by passive electrical properties of the cell:

1- The conductance of nongated ion channels
2- The membrane capacitance
3- The conductance of the cytoplasm

All these properties contribute ***synaptic integration***;

A nerve cell adds up all incoming signals and determines whether or not it will generate an action potential.

- The conduction velocity depends on the electric properties and the geometry of the axon.

- The conduction of action potential in the axon is achieved by local current flow (also called passive spread of depolarization)

How does the capacitance of membrane affect conductivity of action potential ?

The rate of change in the membrane potential determines the rate of information transfer within a neuron.

During signaling, the rate of change in the membrane potential is dependent on membrane capacitance.

Membrane capacitance prolongs the time course of electrical signals

When current flows into or out of a cell throught ion channels in the membrane;

The membrane potential always changes more slowly then the current.

Two types current :

1- ***Ionic current (I_i)*** : is carried by ions flowing throught ion channels

2- ***Capacitive current (I_c):*** is carried by ions that change the net charge stored on the membrane

The sum of these two components is total membrane current

$$I_m = I_c + I_i$$

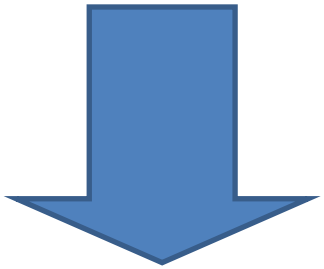
The potential across capacitor is proportional to the charge stored on the capacitor:

$$V = Q/C$$

The capacitance of the membrane reduces the role of the membrane potential changes.

The time constant of the membrane is important for integration of synaptic input.

The longer time constant means the longer duration of the synaptic potential.



When synaptic potentials overlap in time, they add together: Temporal summation

Temporal summation

The individual postsynaptic potentials that alone might be too small to trigger an action potentials can some to reach threshold.

If postsynaptic cell has a longer time constant;

- the synaptic potential lasts longer
- there is more chance for temporal summation

Membrane axoplasmic resistance affects the efficiency of signal conduction

$$R = \rho . \frac{l}{A}$$

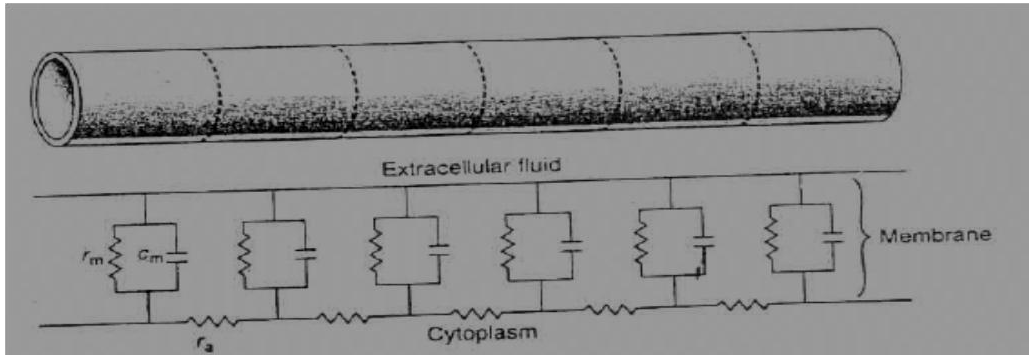
The cytoplasmic core of a dentrite has relatively small cross-sectional area and thus offers significant resistance to the flow of current.

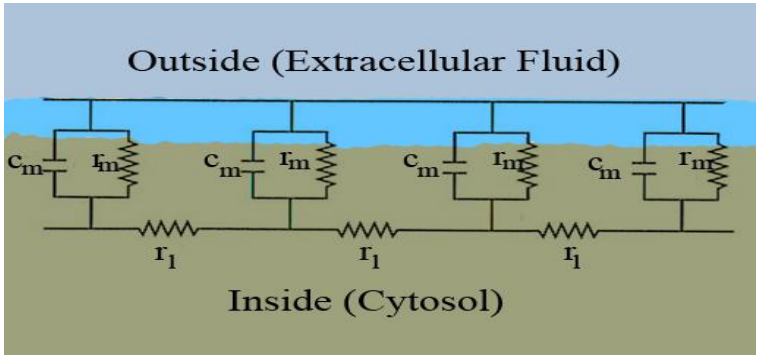
The longer length of the cytoplasmic core results in larger resistance to the flow of current.

- Larger axon=smaller axial resistance= larger current flow=shorter time to discharge the capasitor around axon= faster conduction velocity.
- Smaller neuron= smaller area= shorter time to change membrane potential=faster conduction velocity
- Smaller neuron= fewer channels and smaller area= greater resistance=smaller current flow a given membrane potential= longer time to dischange capacitor= slower conduction velocities.

Cable Equation

- To explain the effect of resistance, the dentrite can be thought as a series of membrane cylinders.





Each unit has its own membrane resistance (r_m) and capacitance due to electrostatic forces (C_m).

All circuits are connected by the axial resistors (r_a) (cytoplasmic resistance)

Lipid bilayer= great insulator properties and very thin= high capacitance

r_m: Membrane resistance
r_l : Longitudinal resistance
c_m: Capacitance due to electrostatic forces

Passive Electrical Properties

- Axial resistance (r_a)
  - Limits conduction velocity

    Ohm's Law: $\Delta V = I \times r_a$
  - $r_a = \rho/\pi a^2$

    ρ = resistance of cytoplasm

    a = cross-sectional area of process
  - Increases with decreasing axonal radius
  - Larger axon = smaller axial resistance = larger current flow = shorter time to discharge the capacitor around axon = faster conduction velocity

Increasing Conduction Velocity

- Myelination of axons
  - Wrapping of glial membranes around axons
  - Increases the functional thickness of the axonal membrane
    - 100x thickness increase
    - Decreases capacitance of the membrane

$$C = \frac{\varepsilon A}{d}$$

  - Same increase in axonal diameter by myelination produces larger decrease in $r_a C_m$
    - More effective increase of conduction velocity

Demyelination

- Loss of the myelin sheath that insulates axons
- Examples:
  - Multiple sclerosis
  - Acute disseminated encephalomyelitis
  - Alexander's Disease
  - Transverse myelitis
  - Chronic inflammatory demyelinating neuropathy
  - Central pontine myelinosis
  - Guillain-Barre Syndrome
- Result:
  - Impaired or lost conduction
  - Neuronal death
  - Symptoms vary widely and depend on the collection of neurons affected

If current is injected into the dentrite at one point, how will the membrane potential with distance?

For a dentrite of a uniform diameter, r_m is the same for equal lengths of membrane cylinder.

For each current pathway, the total axial resistance is cytoplasmic resistance between the site of injection and any point along the dentrite.

Since resistors are connected in serial, the total axial resistance will be

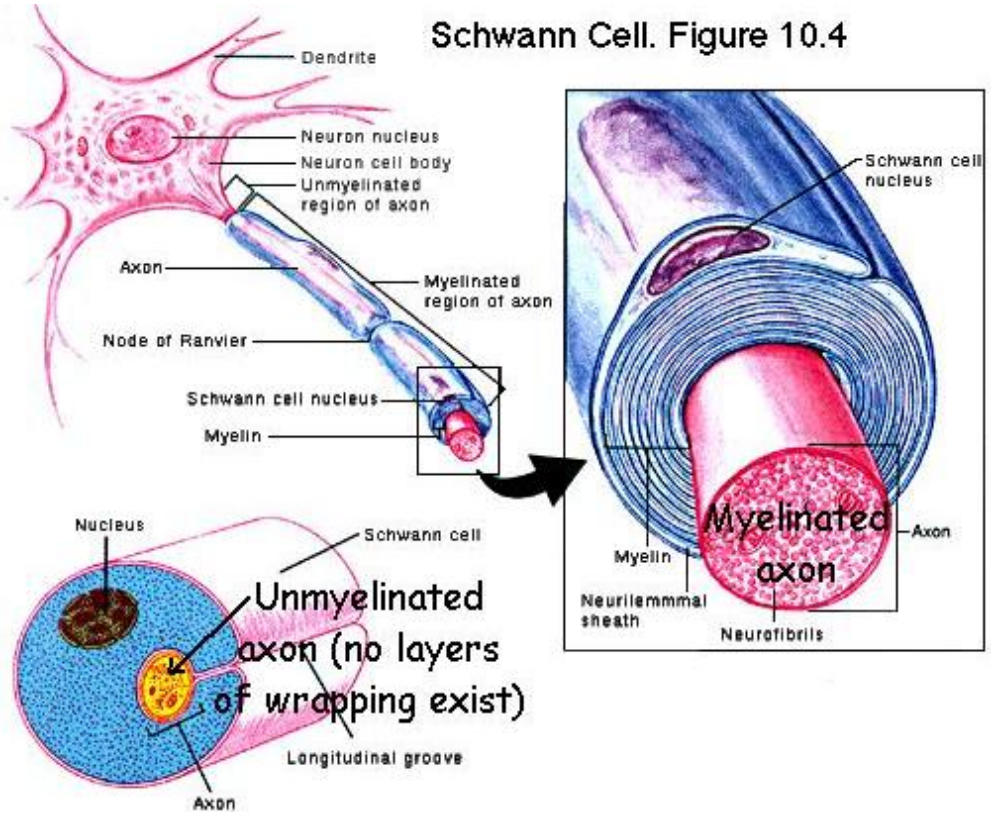
$$R_a = r_a.x \text{ (x : distance)}$$

To increase velocity of the membrane potential conductivity;

- $\Delta V = \Delta Q/C$
- If current is small; ΔQ will change slowly, the membrane potential will change slowly.
- If membrane capacitance is large; more charge will be deposited on the membrane to change membrane potential. The current must flow for a longer time.

Myelination-1

The wrapping of glial cell membranes around *an axon.*



The myelination increases tickness of axonal membrane 100 times.

Myelination-2

Myelination reduces C_m

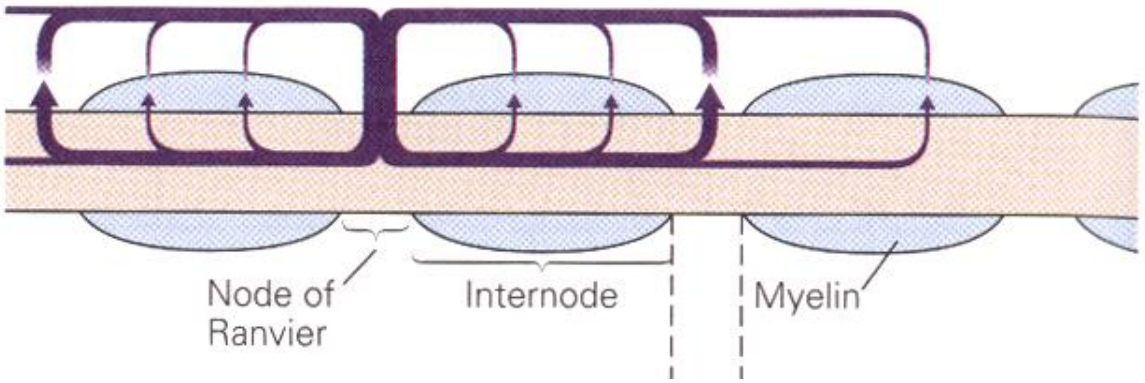
The conduction in myelinated axons is faster than the unmyelinated axons.

1- <u>The larger the diameter of the axon, the faster the rate of transmission</u>

2- <u>The conduction im myelinated axons is faster than the unmyelinated axons.</u>

The action potential propagates very fast along the myelinated regions (low capacitance), then potential spread slowly along nodes.

While the action potential propagates along the axon, it seems to jump quickly from node to node : ***Saltotory Conduction***



Action Potential Propagation

- Myelin decreases capacitance
  - Depolarization current moves quickly
  - Current flow not sufficient to discharge capacitance along entire length of axon
- Myelin sheath interrupted every 1-2 mm
  - Nodes of Ranvier
    - Increases capacitance
    - Depolarization current slows
    - High density of Na+ channels
- Saltatory Conduction
  - Action potential “hops” from one node of Ranvier to the next, down the axon
    - Fast in myelinated regions
    - Slow in bare membrane regions
- Ion flow restricted to nodes of Ranvier
  - Improves energy efficiency
    - High resistance of myelinated membrane reduces current leak
    - Less work by Na+/K+ pump