Resting membrane potential & action potential

TEXTBOOK OF MEDICAL PHYSIOLOGY

GUYTON & HALL 13TH EDITION

UNIT II CHAPTER 5

Pages 61-73

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Objectives

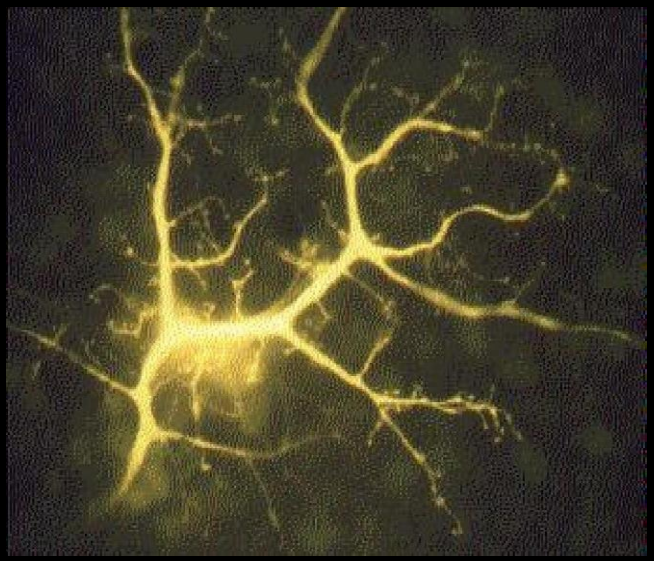
At the end of these lectures the student should be able to

- Explain why some membranes are excitable.
- Describe the electrochemical basis of RMP.
- Describe the mechanism of generation and propagation of AP.
- Describe conduction along nerve fibers, role of myelination and how nerve fibers are classified.

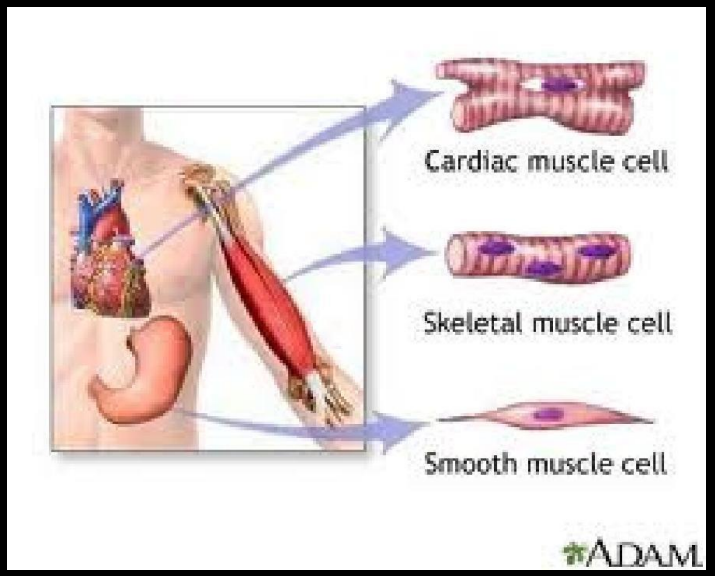
Excitable Tissues

- Tissues which are capable of generation and transmission of electrochemical impulses along the membrane

Nerve

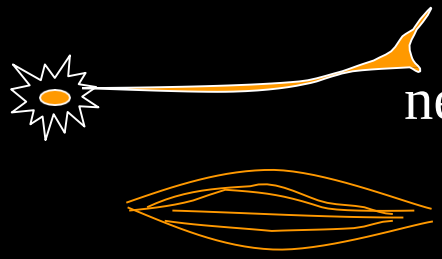


Muscles



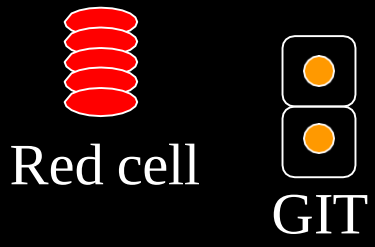
Excitable tissues

excitable



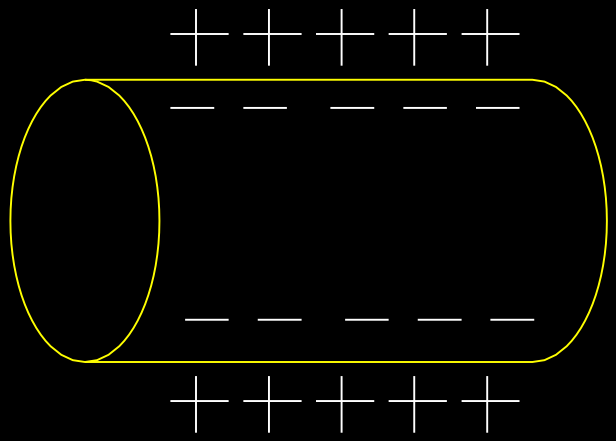
- Nerve
- Muscle
  - Skeletal
  - Cardiac
  - Smooth

Non-excitable



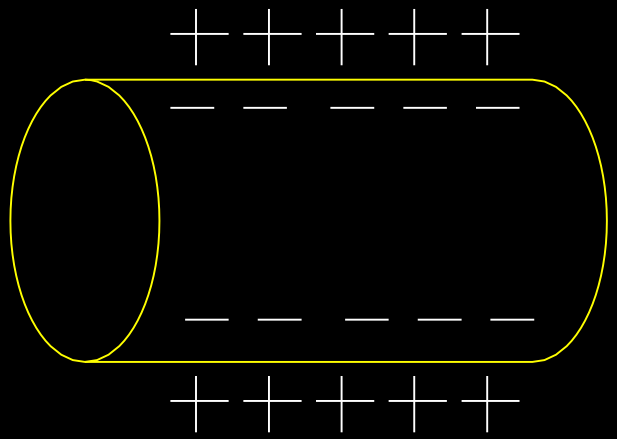
- RBC
- Intestinal cells
- Fibroblasts
- Adipocytes

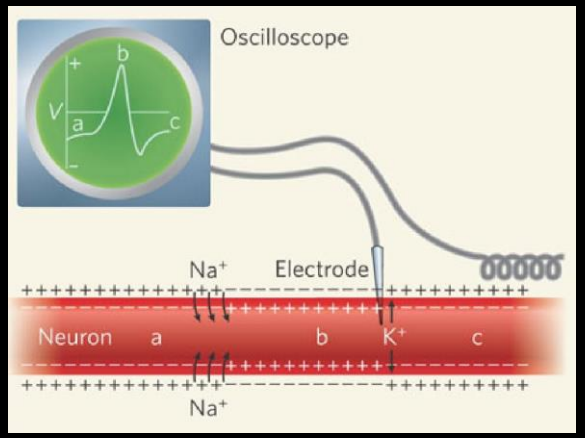
Membrane potential



- A potential difference exists across all cell membranes
- This is called
  - Resting Membrane Potential (RMP)

Membrane potential





– Inside is negative with respect to the outside
– This is measured using microelectrodes and oscilloscope (**VOLTMETER)**
– This is about -70 to -90 mV

Excitable tissues

excitable

- Excitable tissues have more negative RMP
  (- 70 mV to - 90 mV)

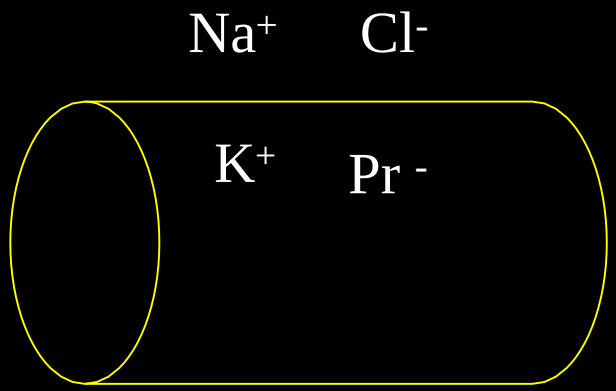
Non-excitable

- Non-excitable tissues have less negative RMP
  -53 mV epithelial cells
  -8.4 mV RBC
  -20 to -30 mV fibroblasts
  -58 mV adipocytes

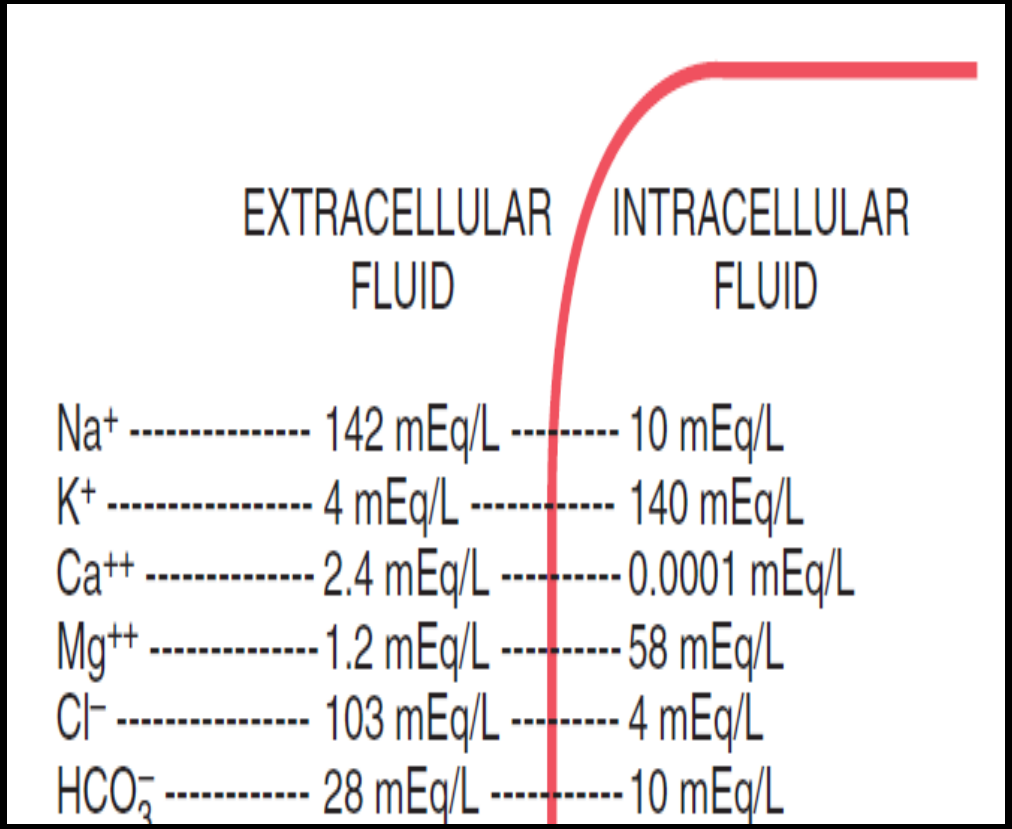
Resting Membrane Potential

- This depends on the following **factors**
  - Ionic distribution across the membrane
  - Membrane permeability
  - Other factors
    - Na^+/K^+ pump

Ionic distribution

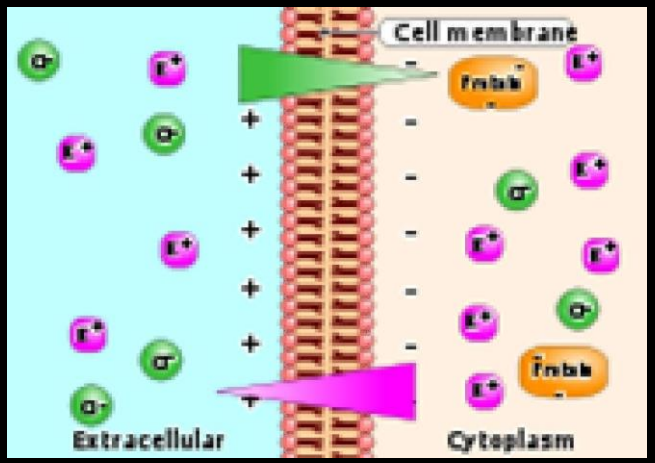


- Major ions
  - Extracellular ions
    - Na^+, Cl^-
  - Intracellular ions
    - K^+, Proteins



Gibbs Donnan Equilibrium

- When two solutions containing ions are separated by membrane that is permeable to some of the ions and not to others an electrochemical equilibrium is established



- Electrical and chemical energies on either side of the membrane are equal and opposite to each other

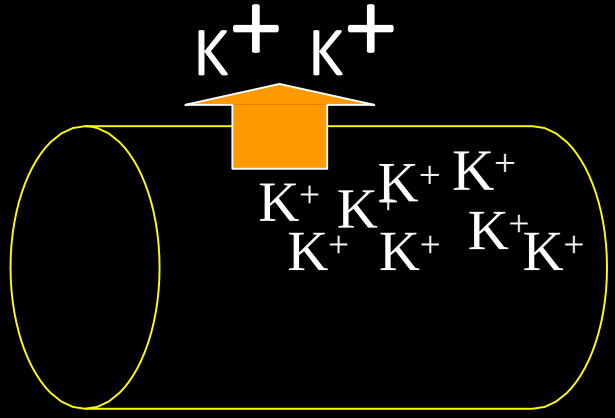
Electrochemical gradient

- At electrochemical equilibrium, there is an exact balance between two opposing forces:

- Chemical driving force = ratio of concentrations on 2 sides of membrane (concentration gradient)
  - The concentration gradient that causes K+ to move from inside to outside taking along positive charge and
- Electrical driving force = potential difference across membrane
  - opposing electrical gradient that increasingly tends to stop K+ from moving across the membrane

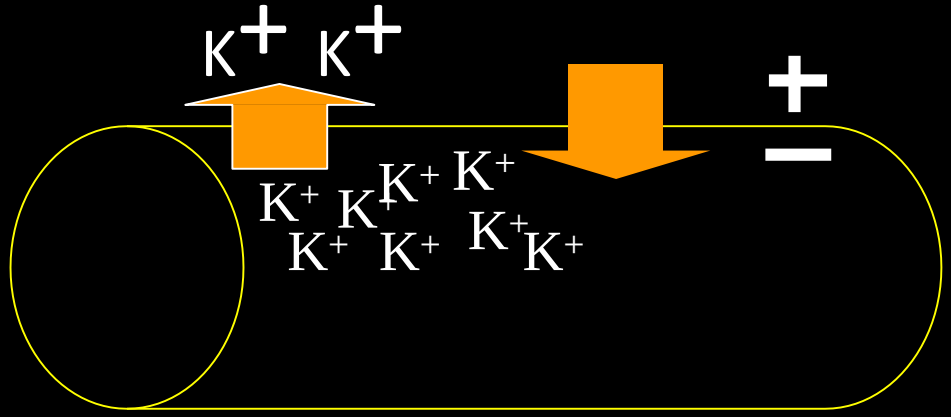
- Equilibrium: when chemical driving force is balanced by electrical driving force

Chemical driving force of Potassium



- Potassium concentration intracellular is more
- Membrane is freely permeable to K^+
- There is an efflux of K^+

Electrical driving force of Potassium



- Entry of positive ions in to the extracellular fluid creates positivity outside and negativity inside
- Outside positivity resists efflux of K^+ (since K^+ is a positive ion)
- At a certain voltage an equilibrium is reached and K^+ efflux stops

Nernst potential (Equilibrium potential)

- The potential level across the membrane that will exactly prevent net diffusion of an ion

- Nernst equation determines this potential

$$\text{EMF (millivolts)} = -\frac{61}{z} \times \log \frac{\text{Concentration inside}}{\text{Concentration outside}}$$

where *EMF* is electromotive force and *z* is the electrical charge of the ion (e.g., +1 for K^+).

Nernst potential (Equilibrium potential)

- The potential level across the membrane that will exactly prevent net diffusion of an ion

Ion	Intracellular	Extracellular	Nernst potential
Na^+	14	142	+61
K^+	140	4	-94
Cl^-	4	103	-86
Ca^{2+}	0.0001	2.4	+134
HCO_3^-	10	28	-27

(mmol/l)

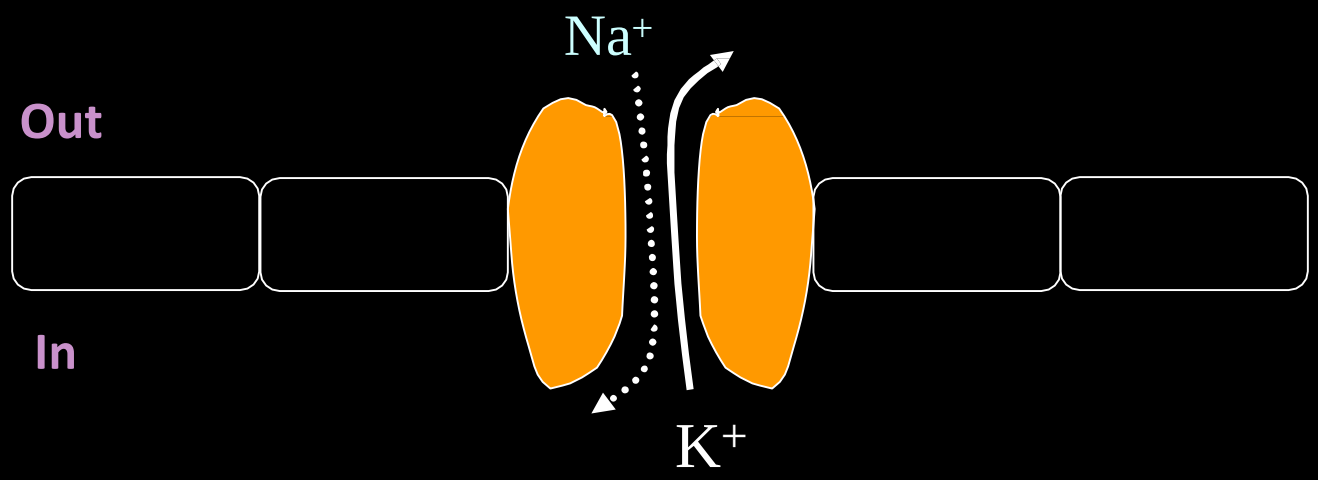
Goldman Equation

- When the membrane is permeable to several ions the equilibrium potential that develops depends on
  - Polarity of each ion
  - Membrane permeability
  - Ionic concentration
- This is calculated using Goldman Equation

$$\text{EMF (millivolts)} = -61 \times \log \frac{C_{Na_i^+} P_{Na^+} + C_{K_i^+} P_{K^+} + C_{Cl_o^-} P_{Cl^-}}{C_{Na_o^+} P_{Na^+} + C_{K_o^+} P_{K^+} + C_{Cl_i^-} P_{Cl^-}}$$

Using this value in the **Goldman equation** gives a potential inside the membrane of **–86 mV.**

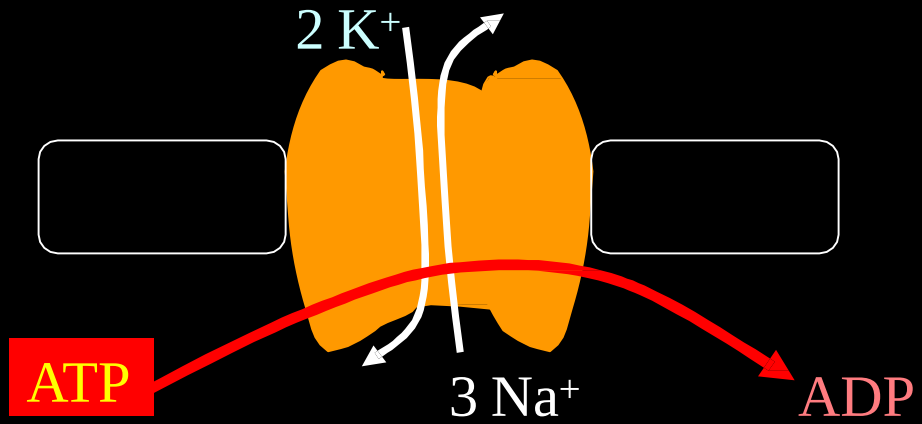
Ionic channels

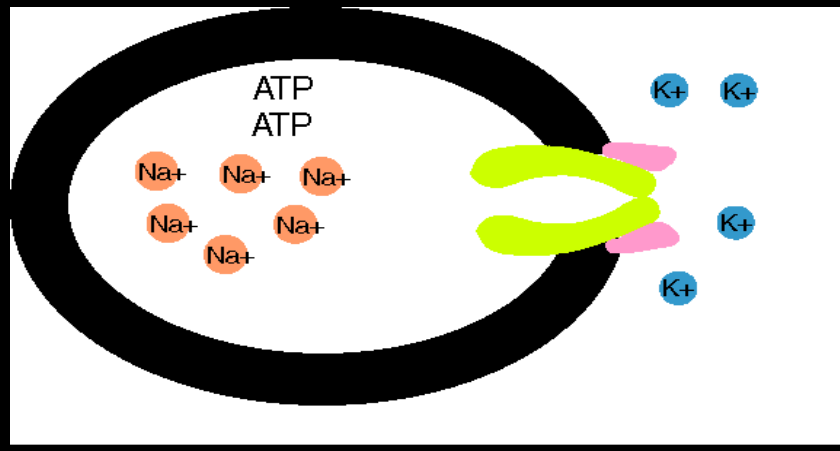


- Leaky channels (K+/Na+ leak channels)
  - More permeable to K
  - Allows free flow of ions
- In the resting state

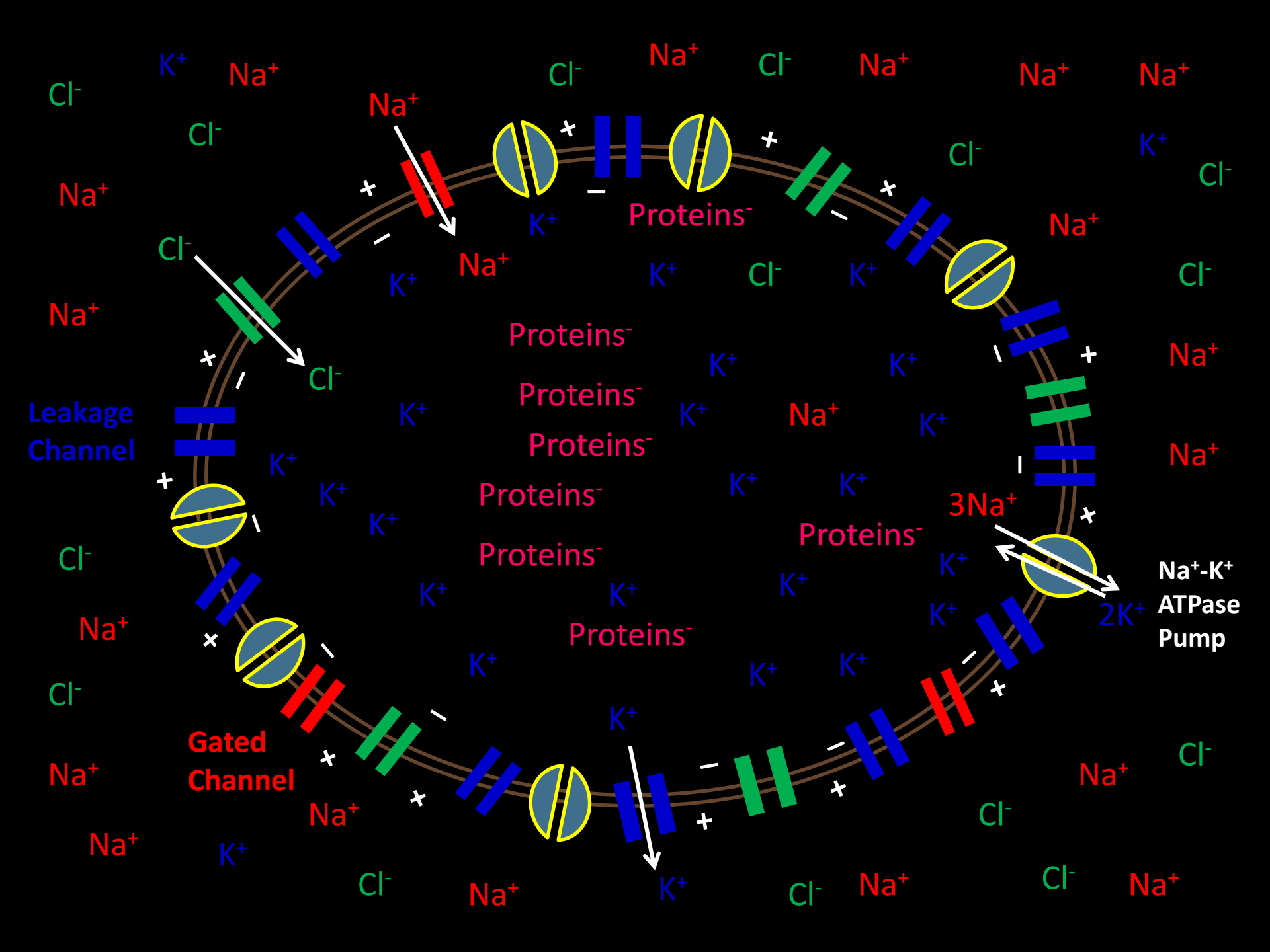
  K+ permeability is 100 times more than that of Na+

Na+/K+ pump





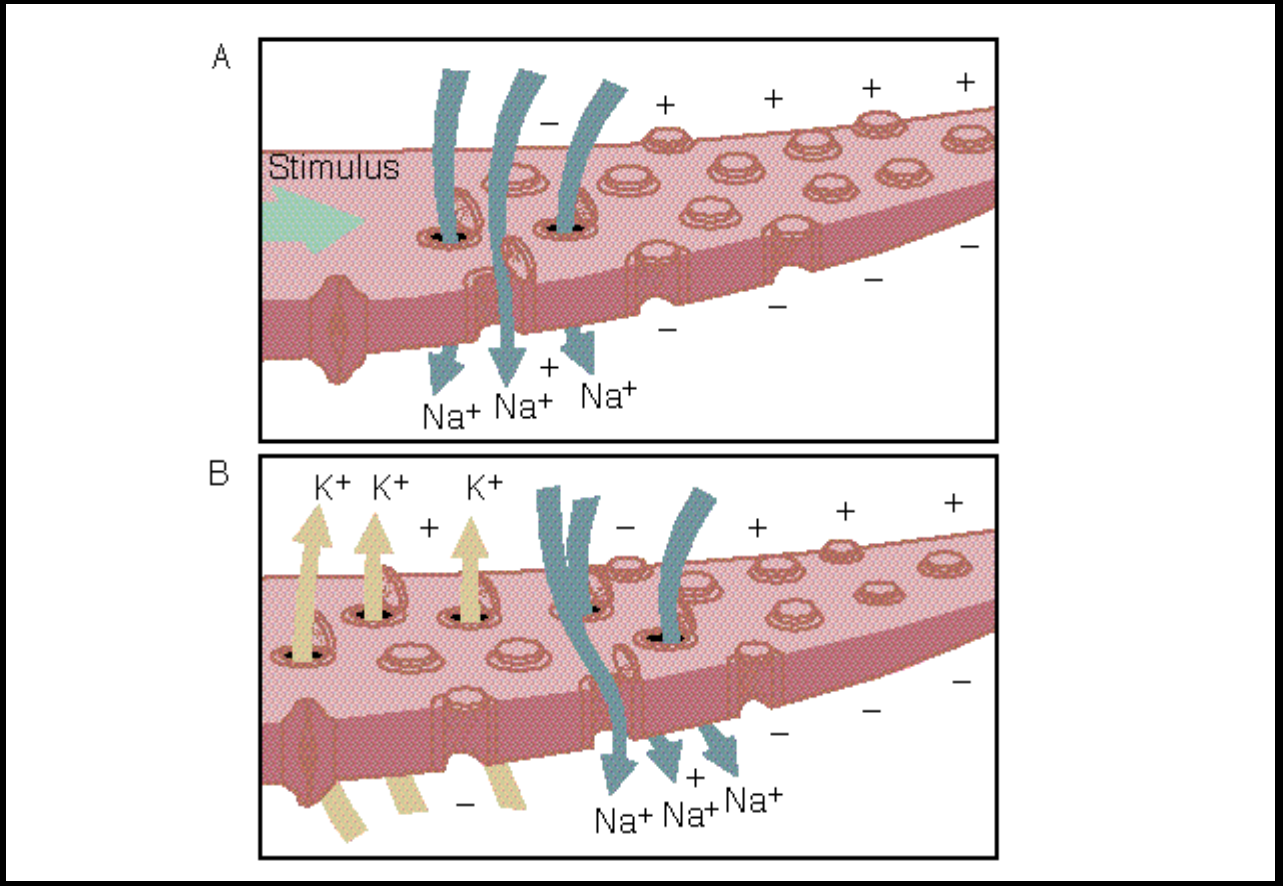
- Active transport system for Na+-K+ exchange using energy
- It is an electrogenic pump since 3 Na+ efflux coupled with 2 K+ influx
- Net effect of causing negative charge inside the membrane


Leakage Channel
Gated Channel
Na+-K+ ATPase Pump
3Na+
2K+
Proteins-
Proteins-
Proteins-
Proteins-
Proteins-
Proteins-

Factors contributing to RMP

- One of the main factors is K+ efflux (Nernst Potential: -94mV)
- Contribution of Na+ influx is little (Nernst Potential:+61mV)
- Na+/K+ pump creates additional degree of negativity inside the membrane (-4mV)
- Negatively charged protein ions remaining inside the membrane contributes to the negativity
- Net result: -70 to -90 mV inside

Neuron Action Potentials



The action potential

Nerve signals are transmitted by ***action potentials***, *which* are rapid changes in the membrane potential that spread rapidly along the nerve fiber membrane to produce physiological effects **such as:**

- Transmission of impulse along nerve fibres
- Release of neurotransmitters
- Muscle contraction
- Activation or inhibition of glandular secretion

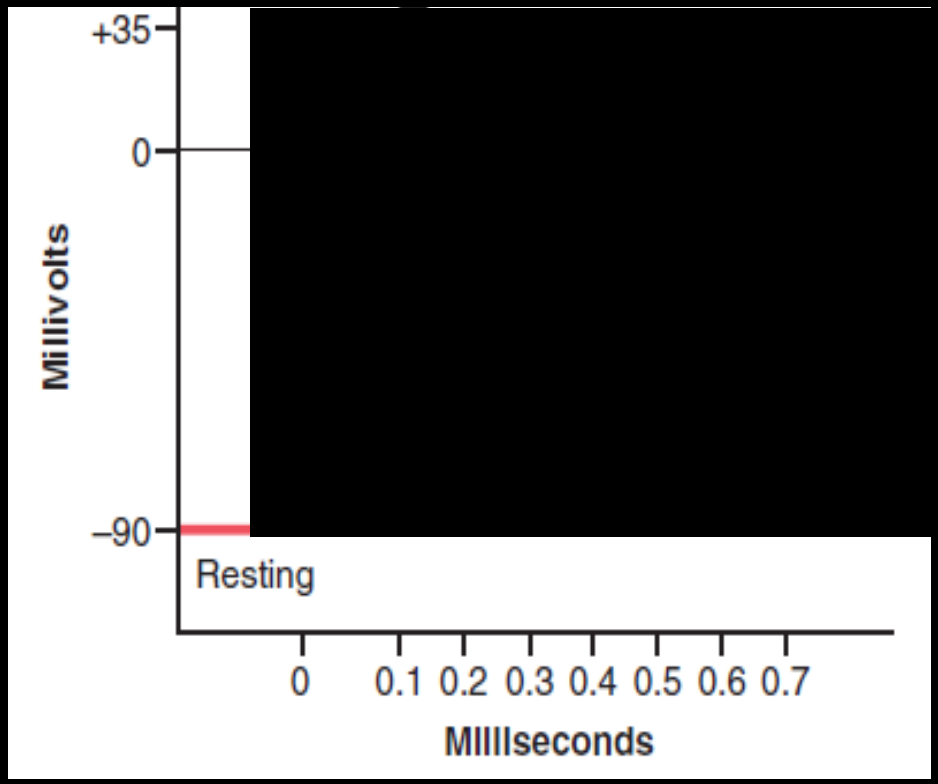
Each action potential begins with a **sudden change** from the normal resting negative membrane potential to a positive potential and ends with an almost equally rapid change back to the negative potential.

Stages of the action potential:

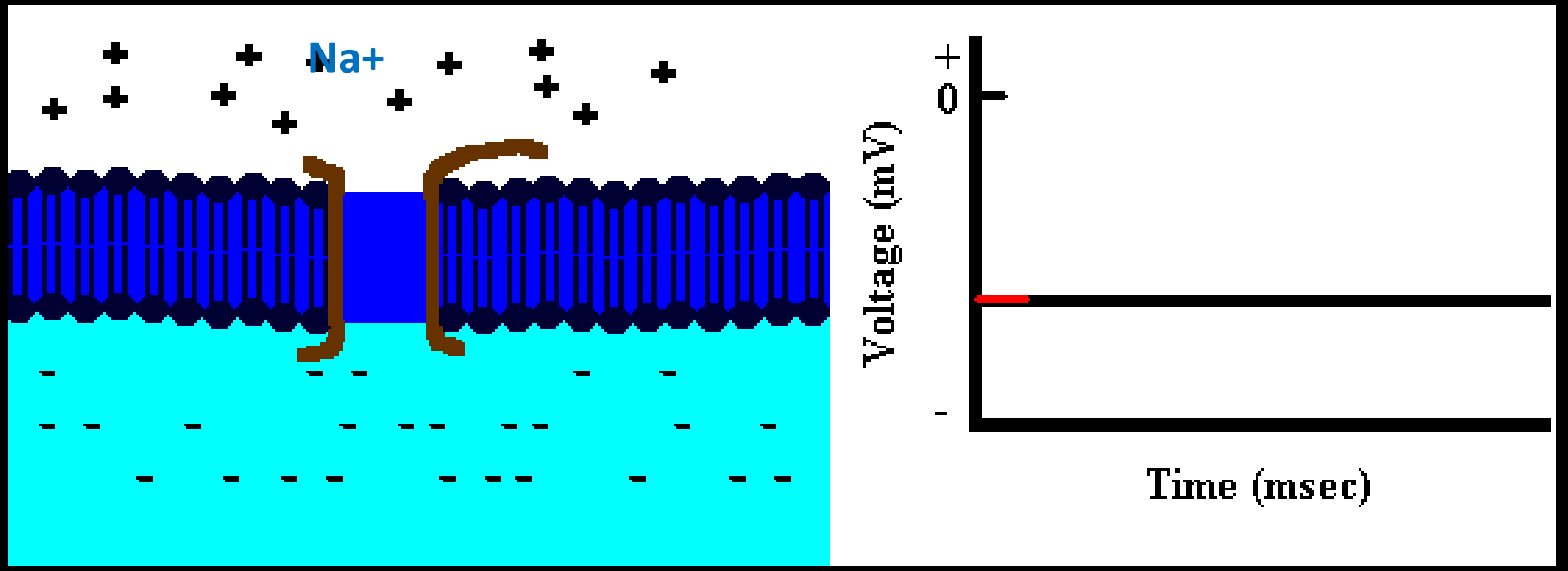
Resting Stage. It is the resting membrane potential before the action potential begins. The membrane is "polarized".

Depolarization Stage.

Repolarization Stage.

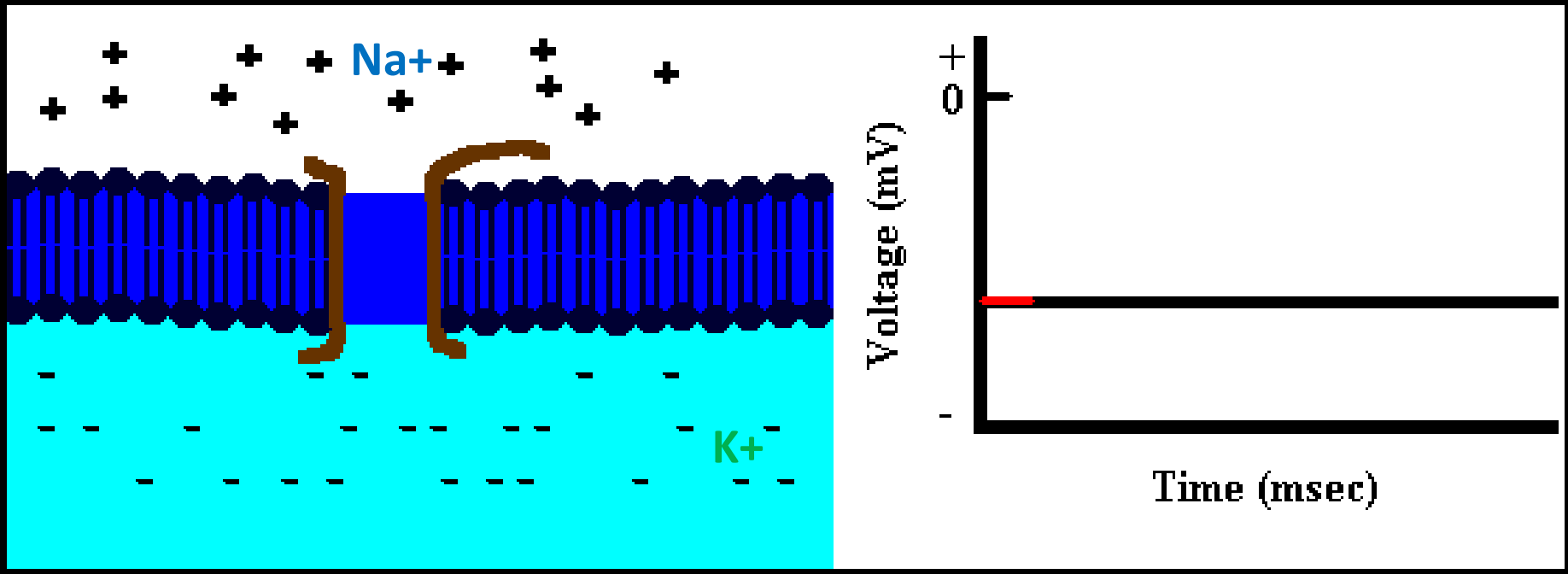


Depolarization



Depolarization: The membrane suddenly becomes permeable to Na^+ ions, allowing tremendous numbers of positively charged Na^+ to diffuse to the interior of the axon **(Upstroke).**

Repolarization



Repolarization: Na^+ channels begin to close and the K^+ channels open. Rapid diffusion of K^+ ions to the exterior re-establishes the normal negative resting membrane potential.

Threshold stimulus:
The membrane potential at which occurrence of the action potential is inevitable.

Acute subthreshold potential:
Stimulus that results only in local depolarisation (*acute local potentials*) when stimulus is below the threshold.

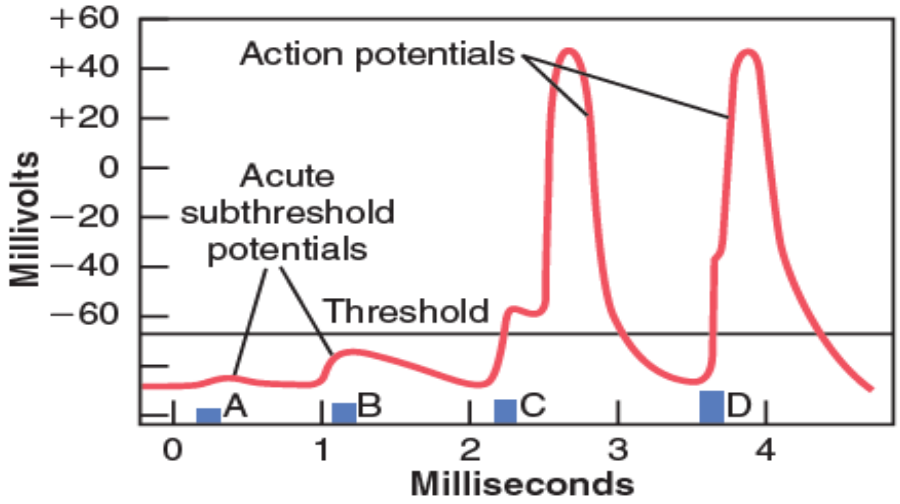


Figure 5-18. Effect of stimuli of increasing voltages to elicit an action potential. Note development of acute subthreshold potentials when the stimuli are below the threshold value required for eliciting an action potential.

All-or-nothing principle:

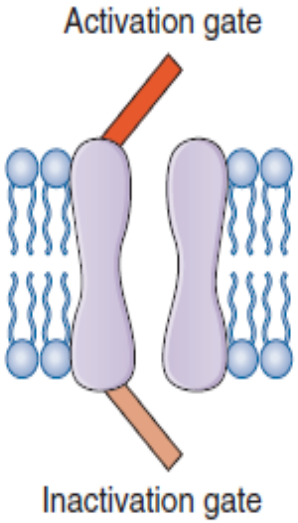
Once threshold value for excitation is reached a full AP is produced, its intensity can not be increased by increasing stimulus intensity.

Types of transport channels through the nerve membrane:

- **Voltage gated Na^+ channels**
- **Voltage gated K^+ channels**

Voltage gated Na^+ channels

At rest, the activation gate is closed and the inactivation gate is open. During the upstroke of the action potential, both gates are open and Na^+ flows into the cell down its electrochemical potential gradient. During repolarization, the activation gate remains open but the inactivation gate is closed.



local anesthetic **lidocaine** blocks this channel

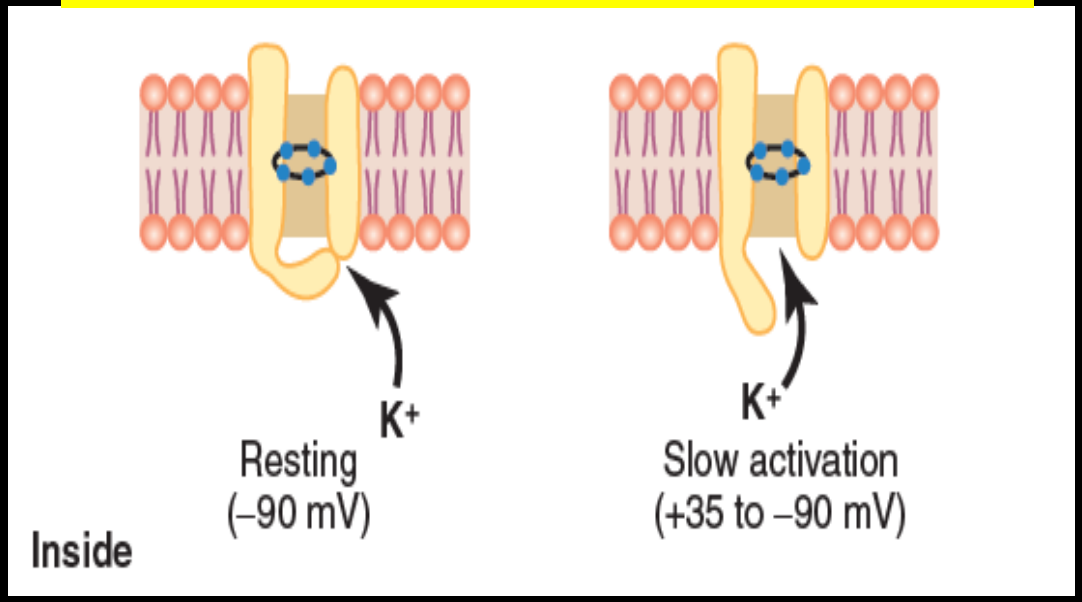
Cannot elicit new AP

Voltage gated K^+ channels

- Has one gate only .
- During the resting state, the gate of the potassium channel is closed and potassium ions are prevented from passing through this channel to the exterior.
- Shortly after depolarization, when the sodium channel begins to be inactivated, the potassium channel opens.

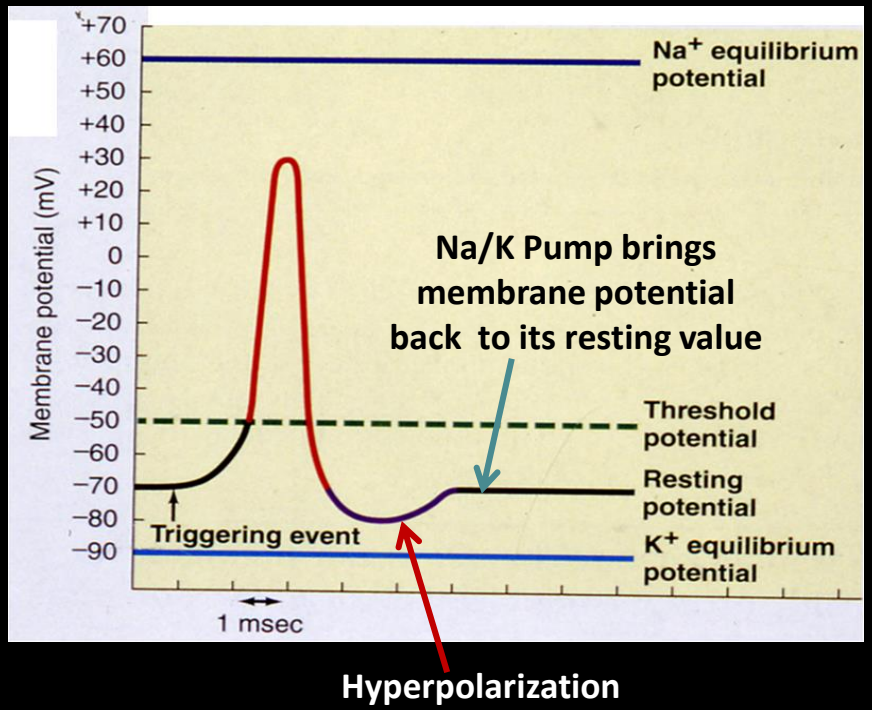
K^+ exits (Efflux) → Repolarization

Tetraethylammonium (TEA) blocks this channel



Hyperpolarization: **Why?**

- For a brief period following repolarization, the K^+ conductance is higher than at rest.
- **<u>Na^+-K^+ ATPase pump</u>** now starts to move Na^+ out & K^+ in against their concentration gradient.



Refractory Periods

Two stages

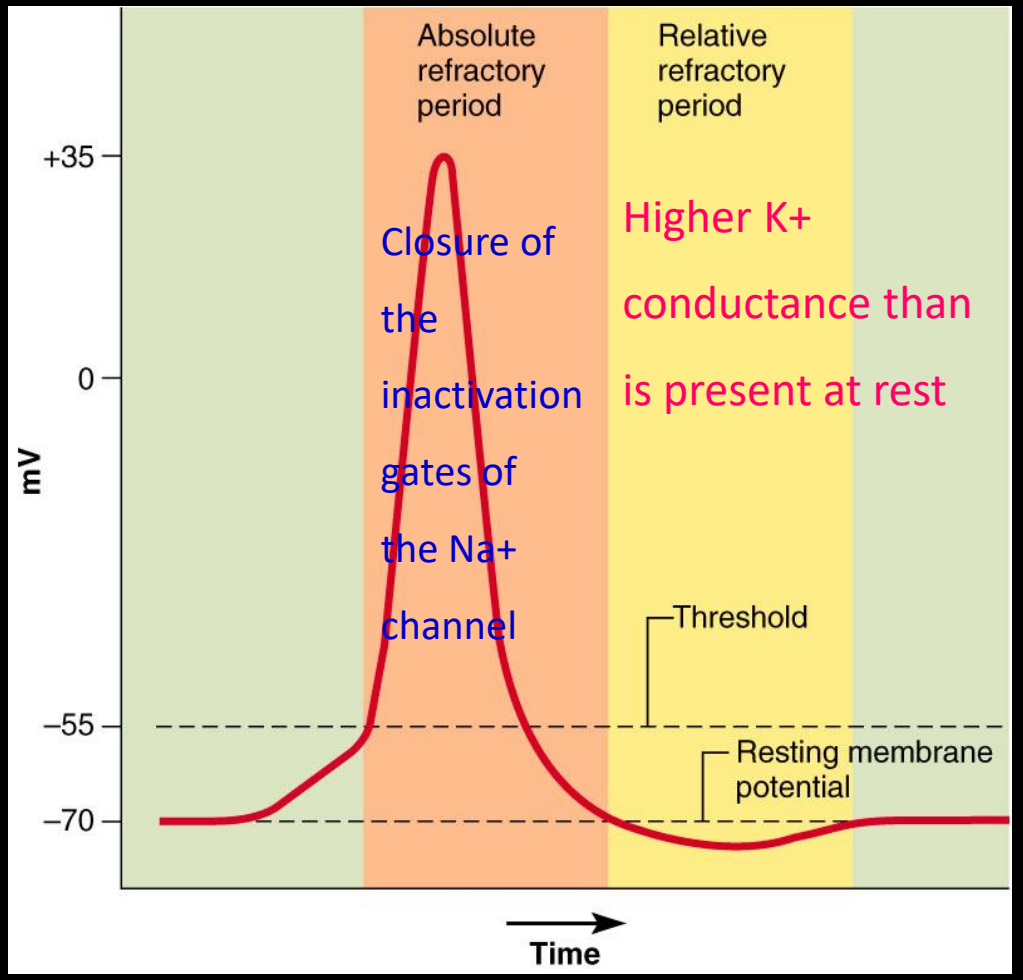
- **Absolute refractory period**

The period during which a second action potential

cannot be elicited, even with a strong stimulus.

- **Relative refractory period**

Can trigger new action potential if stimulus is very strong.



Propagation of the action potential

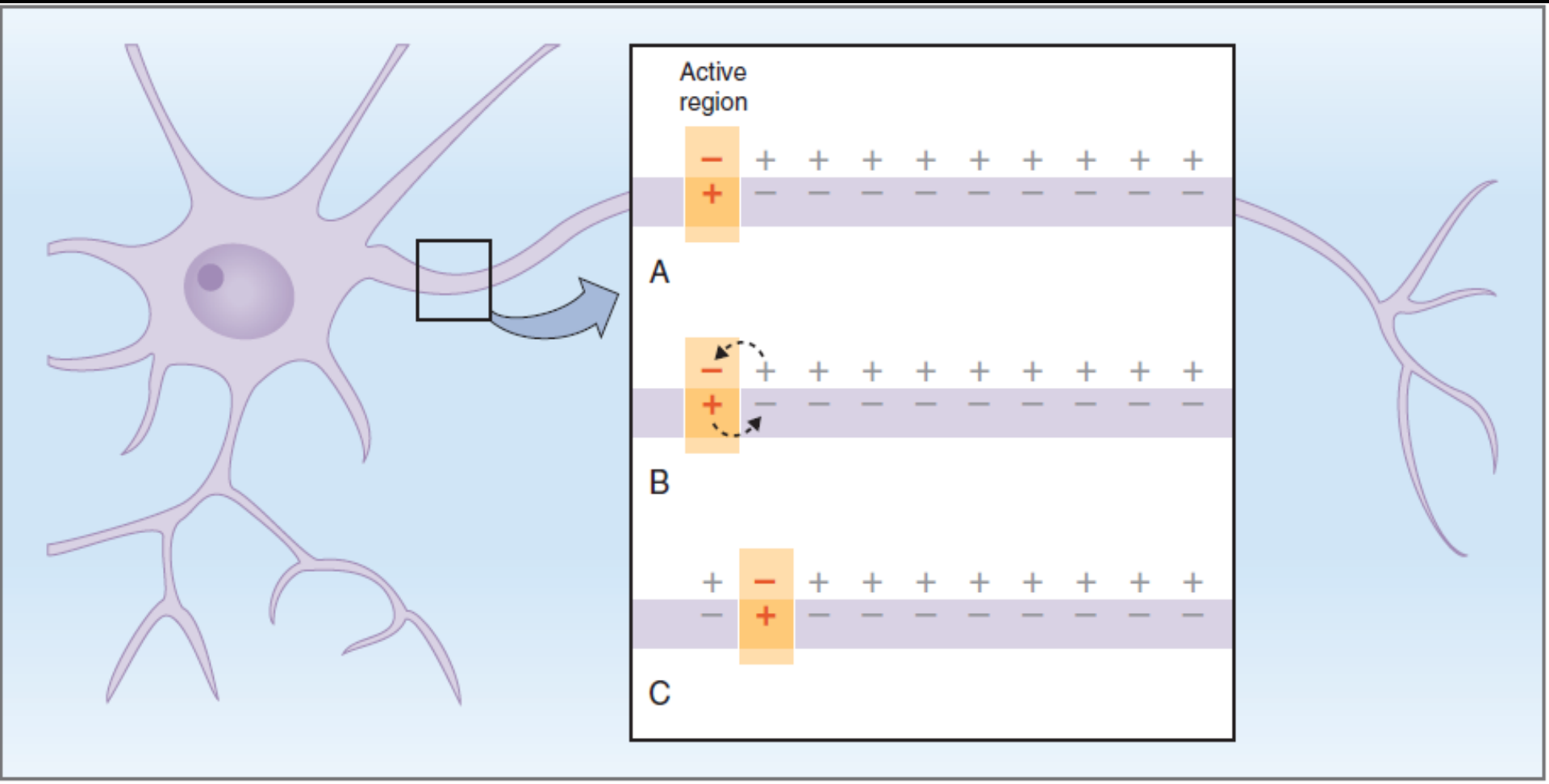


Figure 1–15 **Spread of depolarization down a nerve fiber by local currents.** **A**, The initial segment of the axon has fired an action potential, and the potential difference across the cell membrane has reversed to become inside positive. The adjacent area is inactive and remains at the resting membrane potential, inside negative. **B**, At the active site, positive charges inside the nerve flow to the adjacent inactive area. **C**, Local current flow causes the adjacent area to be depolarized to threshold and to fire action potentials; the original active region has repolarized back to the resting membrane potential.

Conduction Velocity

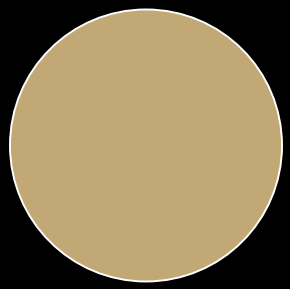
It is the speed at which action potentials are conducted (propagated) along a nerve or muscle fiber.

Mechanisms that increase conduction velocity along a nerve:

1- Nerve diameter.

The larger the diameter, the faster the transmission, **Because:**

-Large fiber offers Less resistance to local current flow & more ions will flow.



Faster conduction

Slower conduction

Conduction Velocity

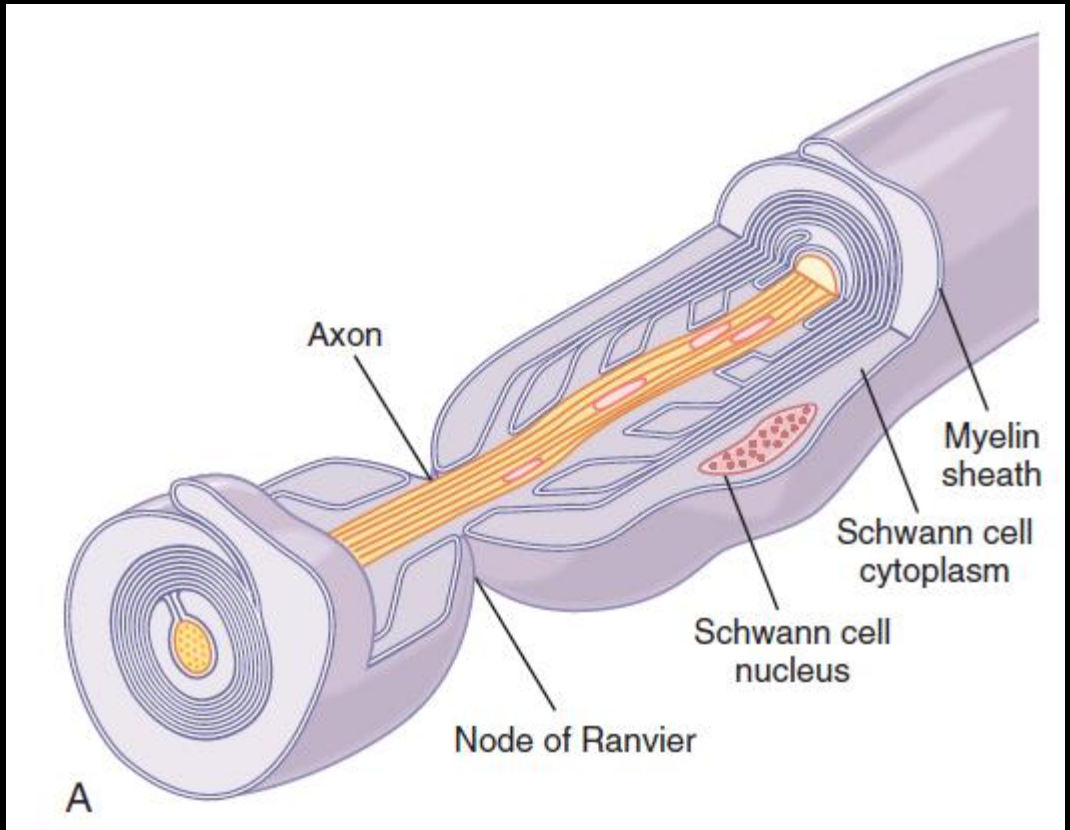
Mechanisms that increase conduction velocity along a nerve:

2- Myelination.

Myelin is an *insulator* that makes it more difficult for charges to flow between intracellular and extracellular fluids.

-The layers of Schwann cell membrane contain the lipid substance sphingomyelin which is excellent electrical insulator that decreases ion flow through the membrane.

- **Node of Ranvier:** small uninsulated area where ions can flow with ease.



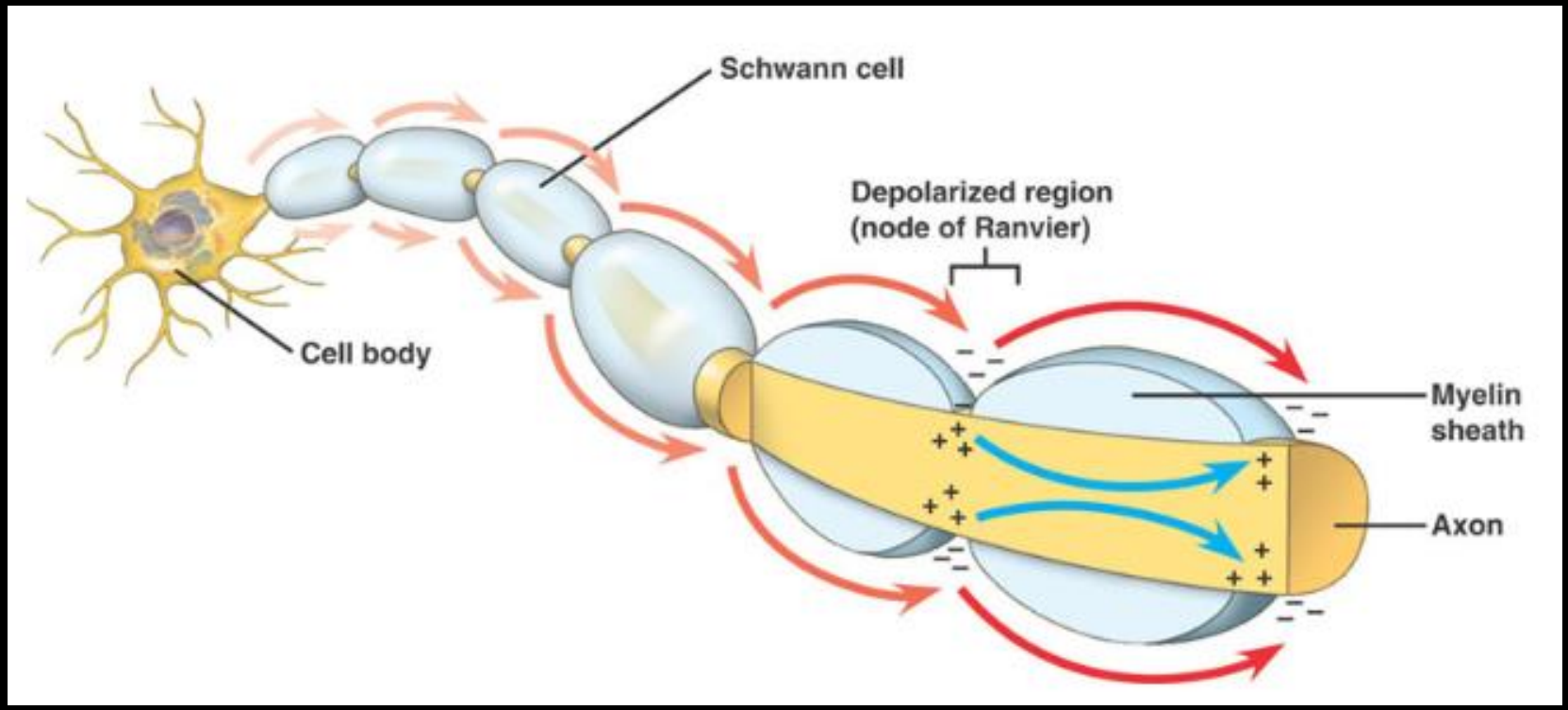
Saltatory Conduction

It is the jumping of action potentials from one node of ranvier to the next as they propagate along a myelinated fiber.

Value:-

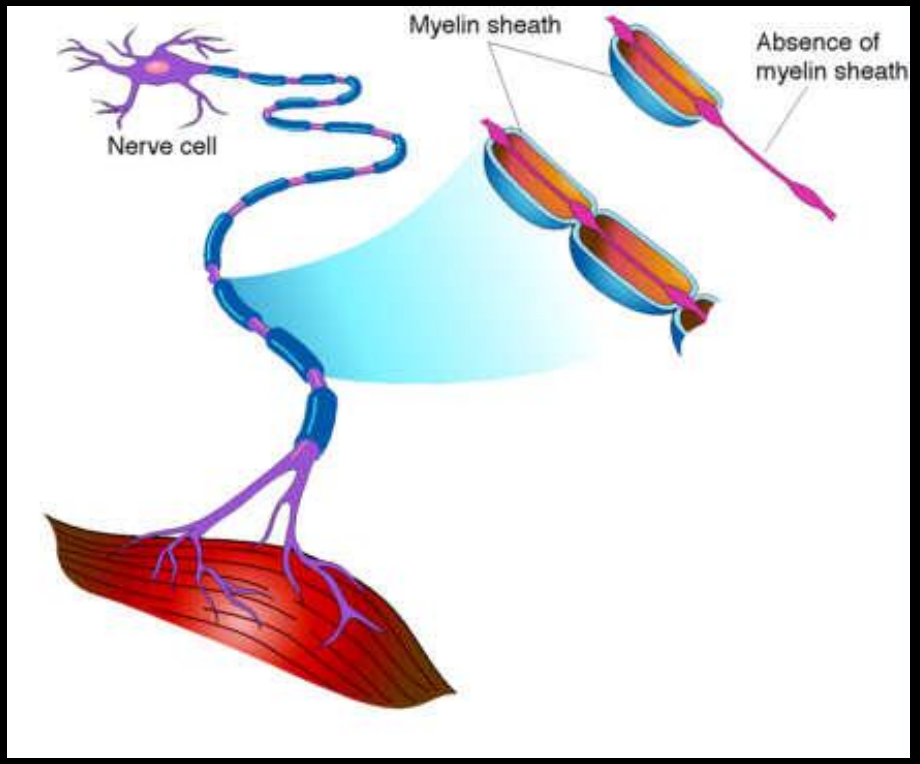
1- Increases conduction velocity.

2- Conserves energy for axon because only nodes depolarize.



What happens if myelination is lost?

- Multiple sclerosis
  - Autoimmune disease (Immune system attacks the myelin sheaths surrounding axons as well as the axons themselves).
  - Usually young adults
  - Blindness, problems controlling muscles
    - Ultimately paralysis
  - Scar tissues (scleroses) replaces some damaged cells.



- The End