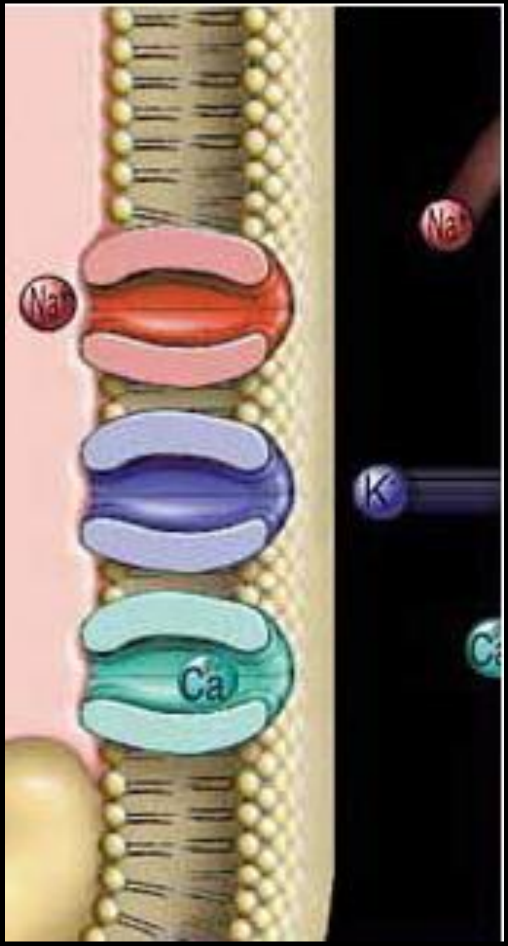



# Resting membrane potential & action potential

TEXTBOOK OF MEDICAL PHYSIOLOGY

GUYTON & HALL 13TH EDITION

UNIT II CHAPTER 5

Pages 61-73

Dr. Mohammed Alotaibi

# Objectives

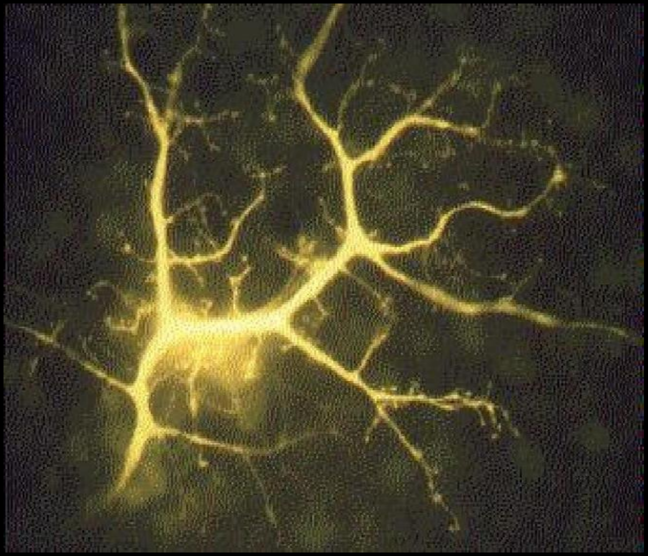
**At the end of these lectures the student should be able to**

- 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.

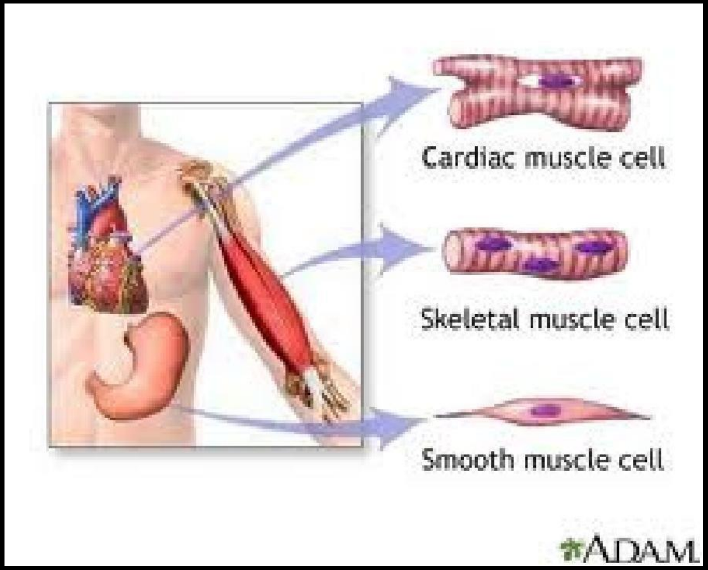
# Excitable Tissues

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

Nerve



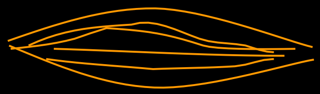
Muscles



# Excitable tissues

excitable

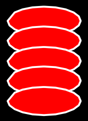
neuron



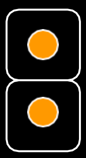
muscle

- Nerve
- Muscle
  - Skeletal
  - Cardiac
  - Smooth

Non-excitable



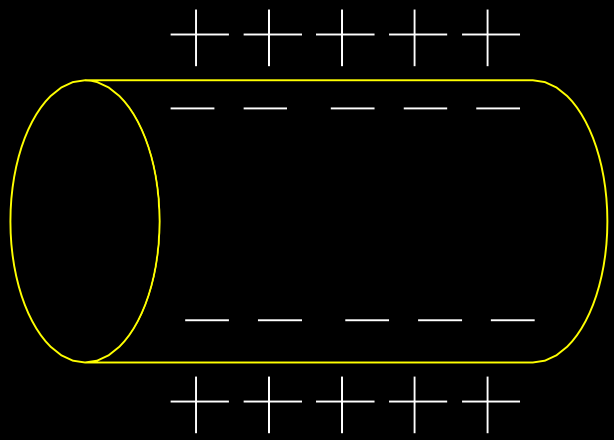
Red cell



GIT

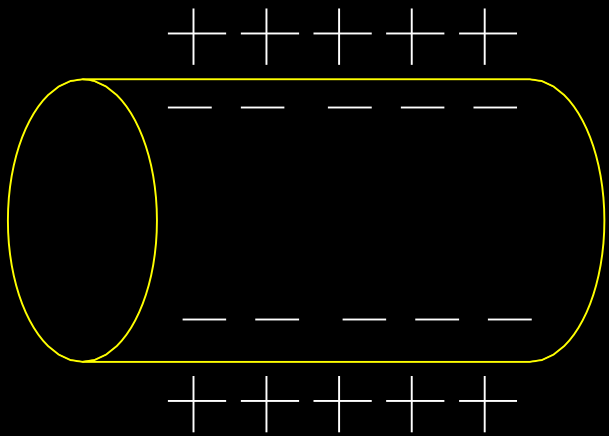
- RBC
- Intestinal cells
- Fibroblasts
- Adipocytes

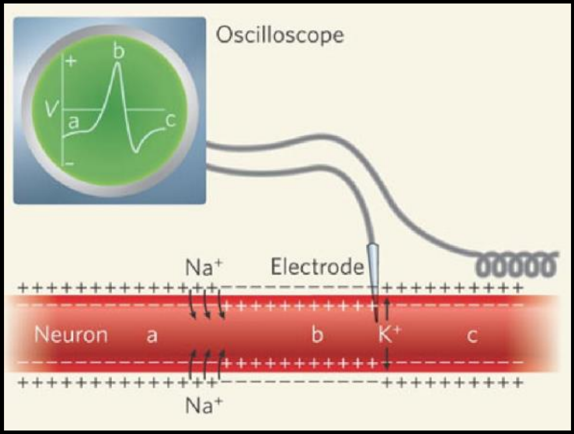
# Membrane potential




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

# Membrane potential

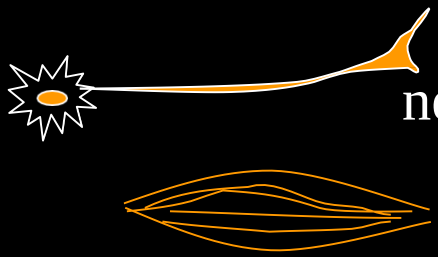





– Inside is negative with respect to the outside
– This is measured using microelectrodes and oscilloscope (**VOLTMETER)**
– This is about -70 to -90 mV

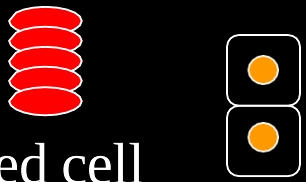
# Excitable tissues

excitable




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

Non-excitable

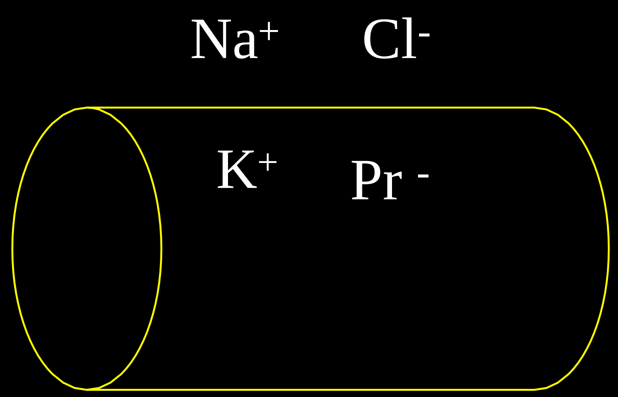


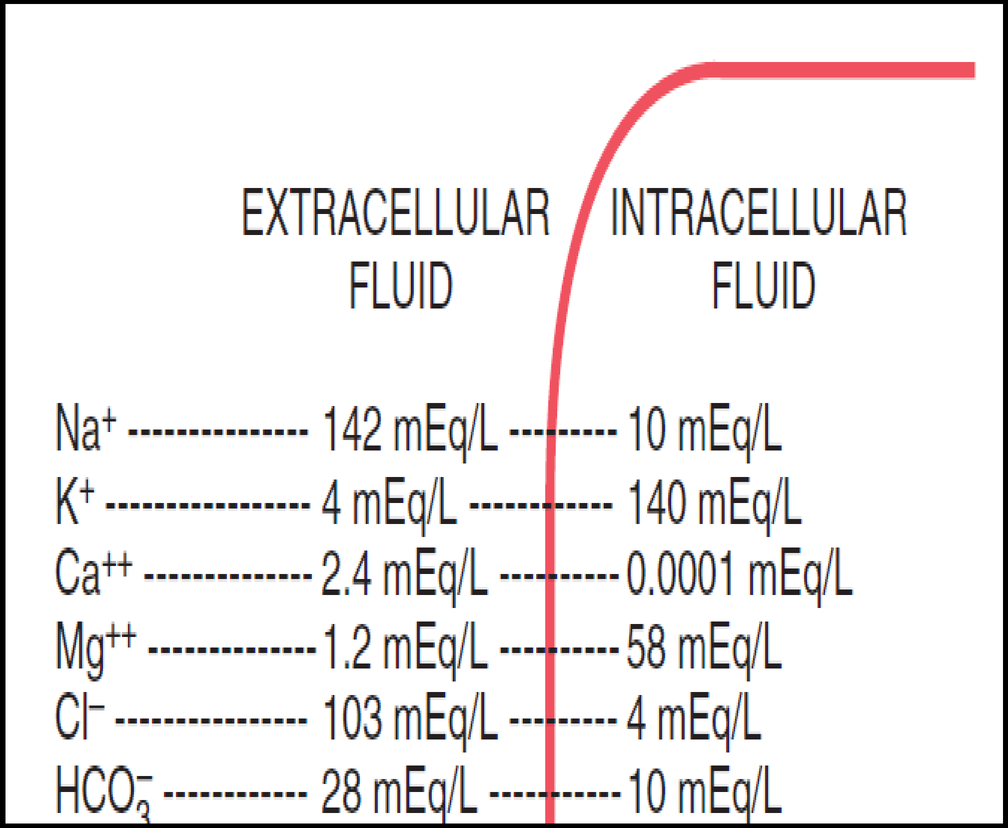

- Non-excitable tissues have less negative RMP
-53 mV epithelial cells
-8.4 mV RBC
-20 to -30 mV fibroblasts
-58 mV adipocytes

# Resting Membrane Potential

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

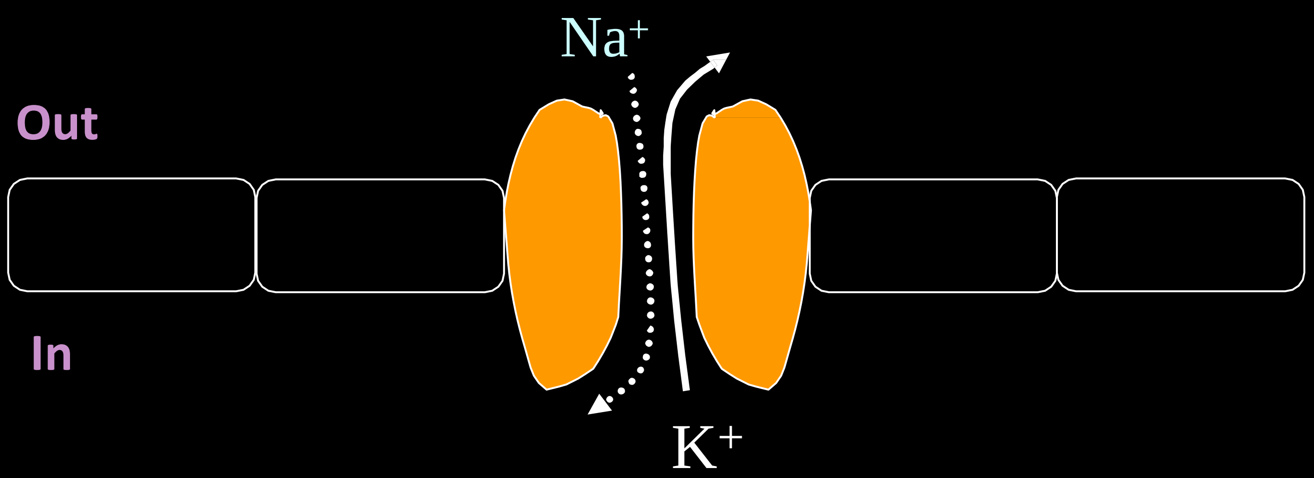
# Ionic distribution




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

# Ionic channels

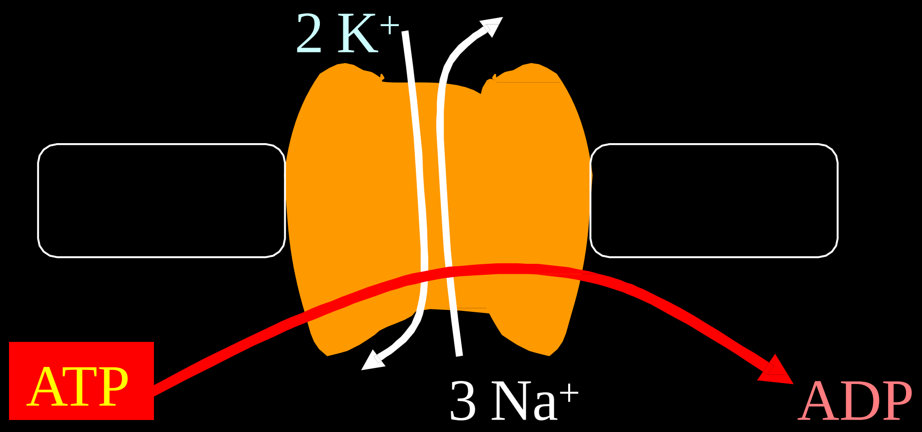


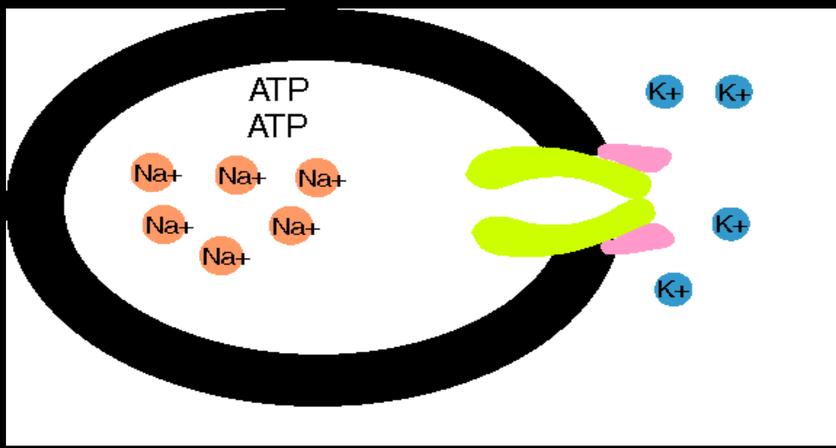

- Leaky channels (K+/Na+ leak channels)
  - – More permeable to K
  - – Allows free flow of ions

- In the resting state

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

# Na+/K+ pump



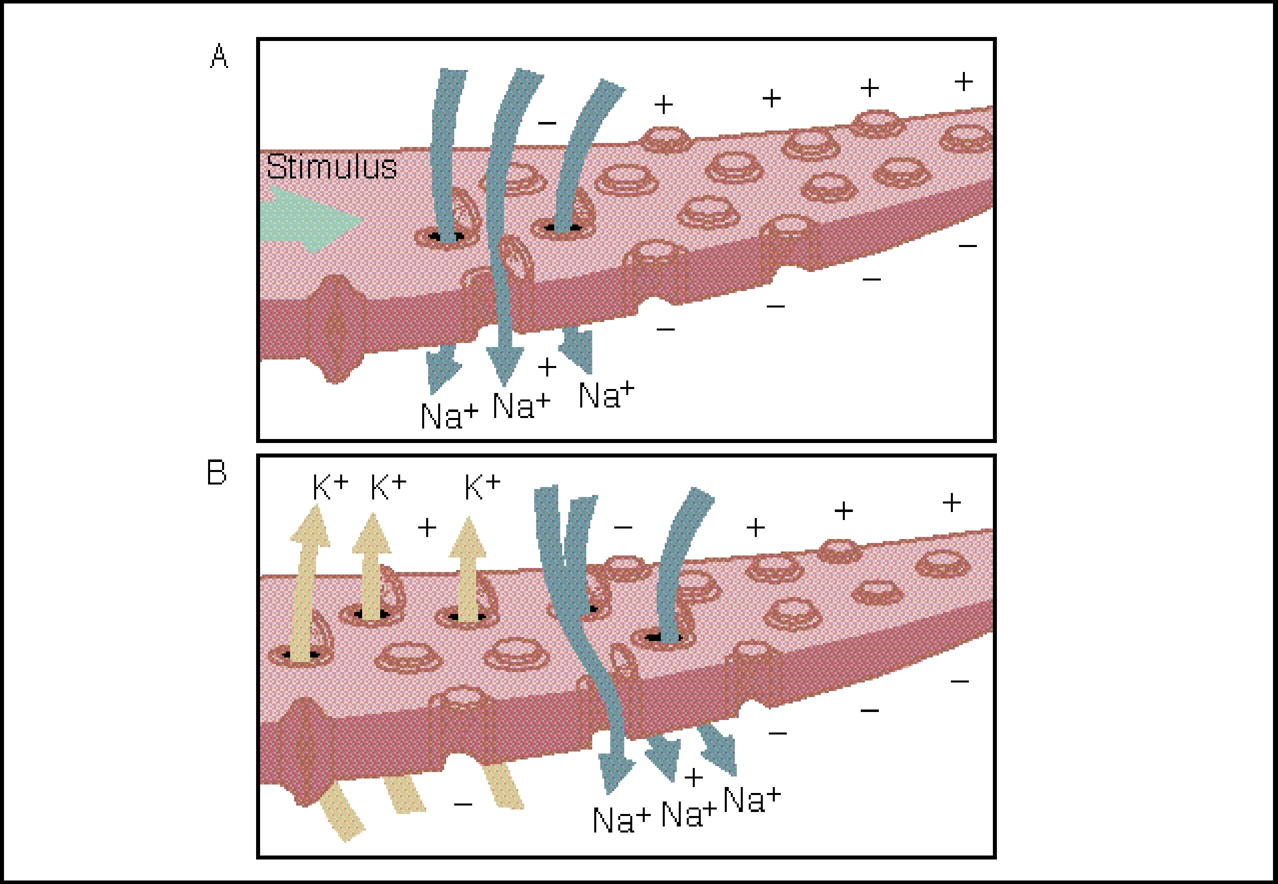




- Active transport system for Na+-K+ exchange using energy
- It is an electrogenic pump since 3 Na+ efflux coupled with 2 K+ influx
- Net effect of causing negative charge inside the membrane

# 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

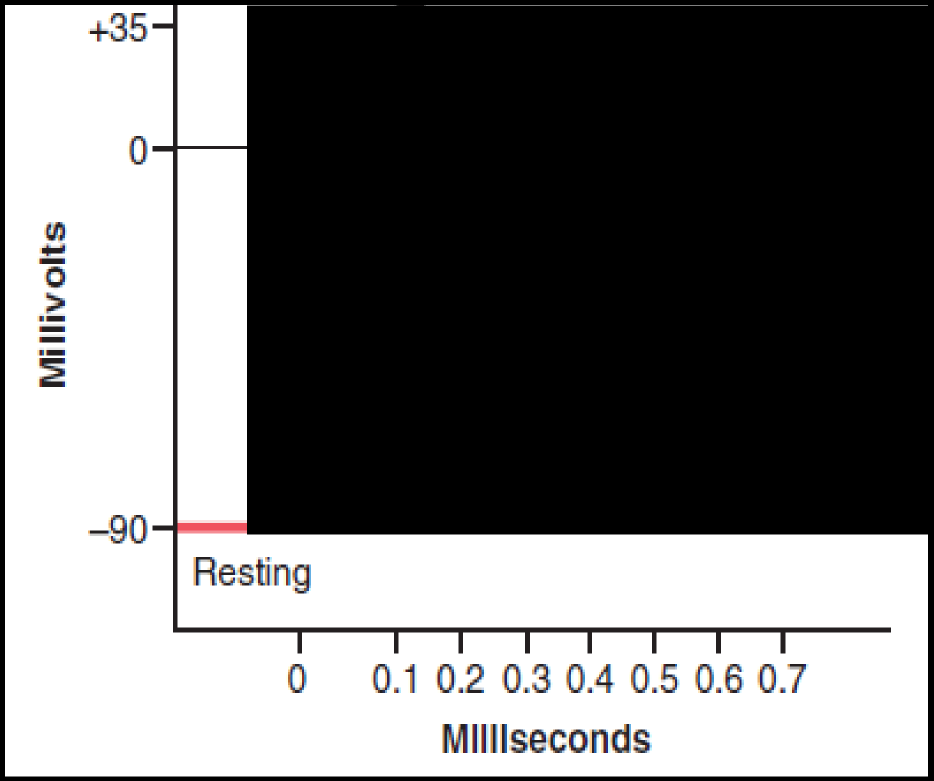
Nerve signals are transmitted by ***action potentials***, *which* are rapid changes in the membrane potential that spread rapidly along the nerve fiber membrane to produce physiological effects **such as:**

- 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:

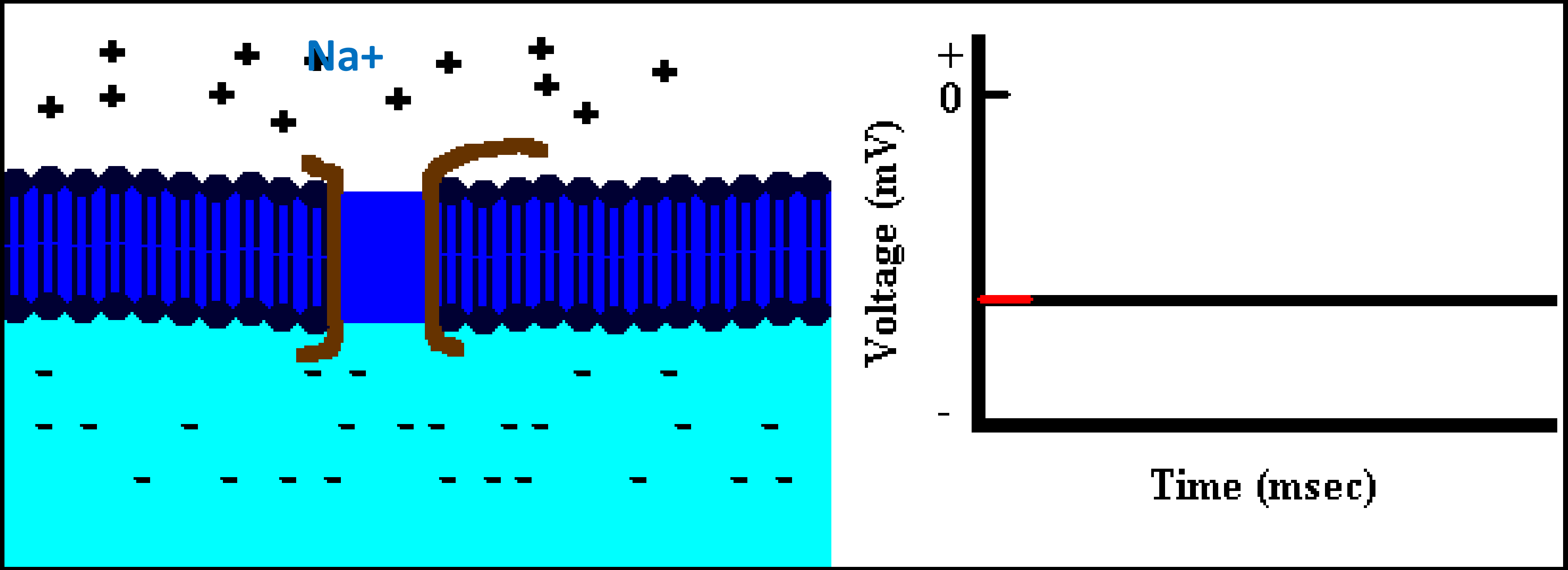
**Resting Stage.** It is the resting membrane potential before the action potential begins. The membrane is "polarized".




**Depolarization Stage.**

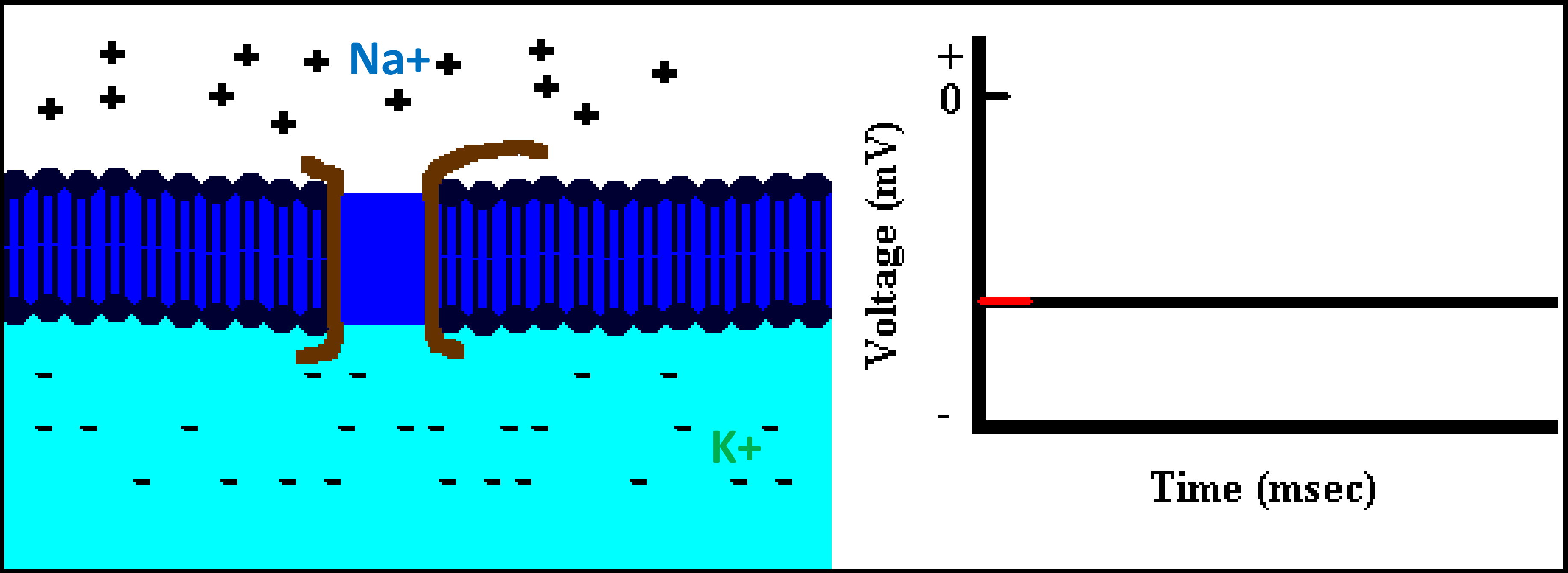
**Repolarization Stage.**

# 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



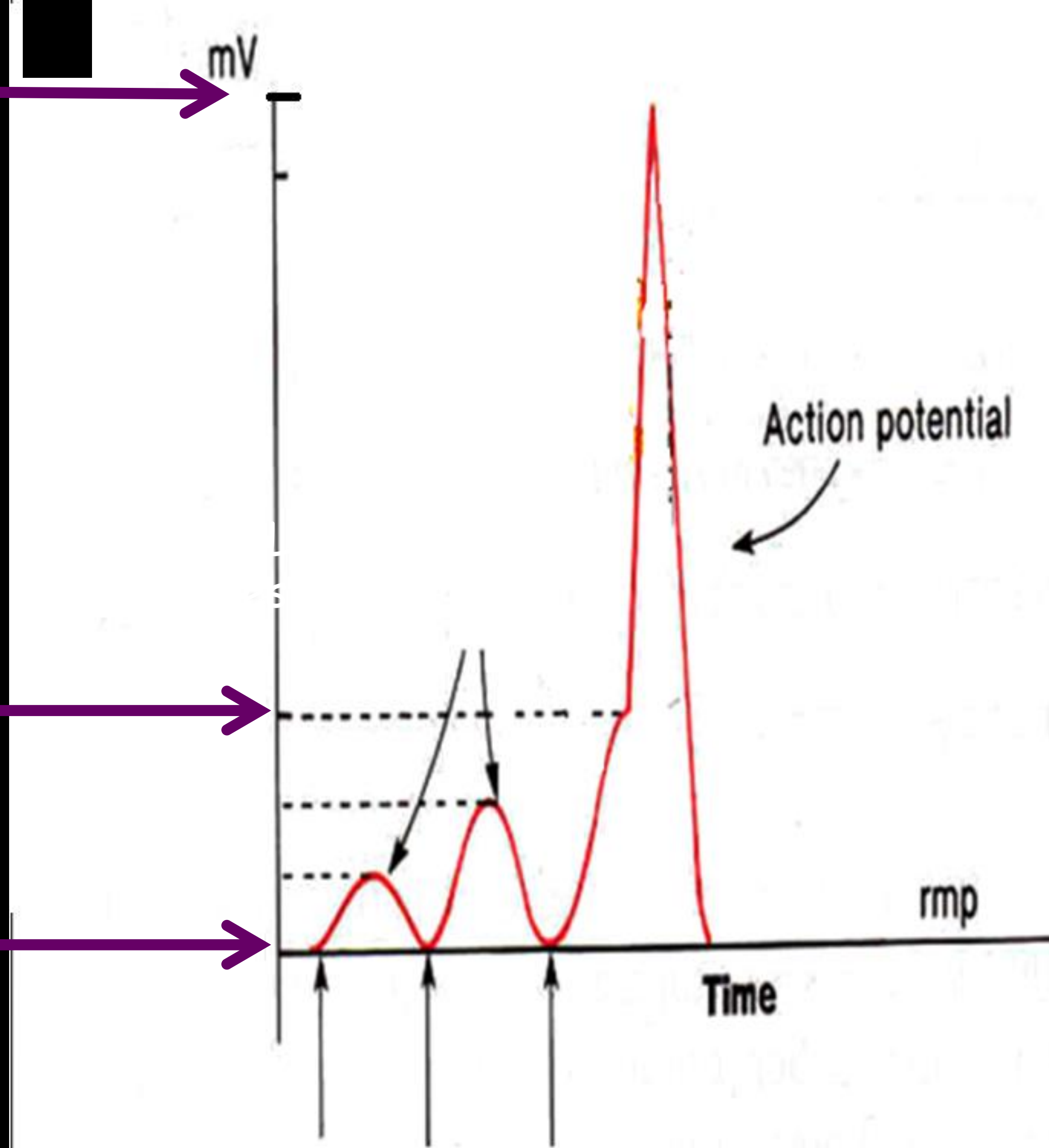

**Repolarization:** $Na^+$ channels begin to close and the $K^+$ channels open. Rapid diffusion of $K^+$ ions to the exterior re-establishes the normal negative resting membrane potential.

Reversal Potential
= + 35 mV

Threhold
Potential ( Firing Level )
= -50 to -65 mV

RMP= -90 mV

Q : What opens the voltage-gated channels ? Opened by a stimulus strong enough to depolarize them to threshold




Increasing Stimulation

**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.

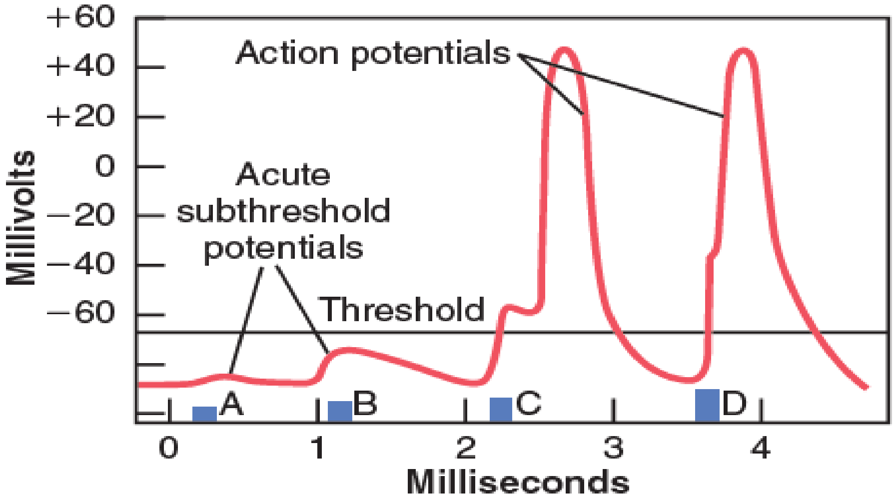



**Figure 5-18.** Effect of stimuli of increasing voltages to elicit an action potential. Note development of acute subthreshold potentials when the stimuli are below the threshold value required for eliciting an action potential.

**<u>All-or-nothing principle:</u>**

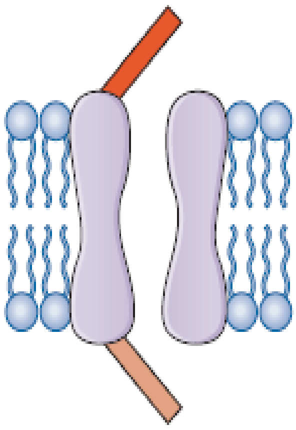
Once threshold value for excitation is reached a full AP is produced, its intensity can not be increased by increasing stimulus intensity.

Types of transport channels through the nerve membrane:

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

# Voltage gated $Na^+$ channels

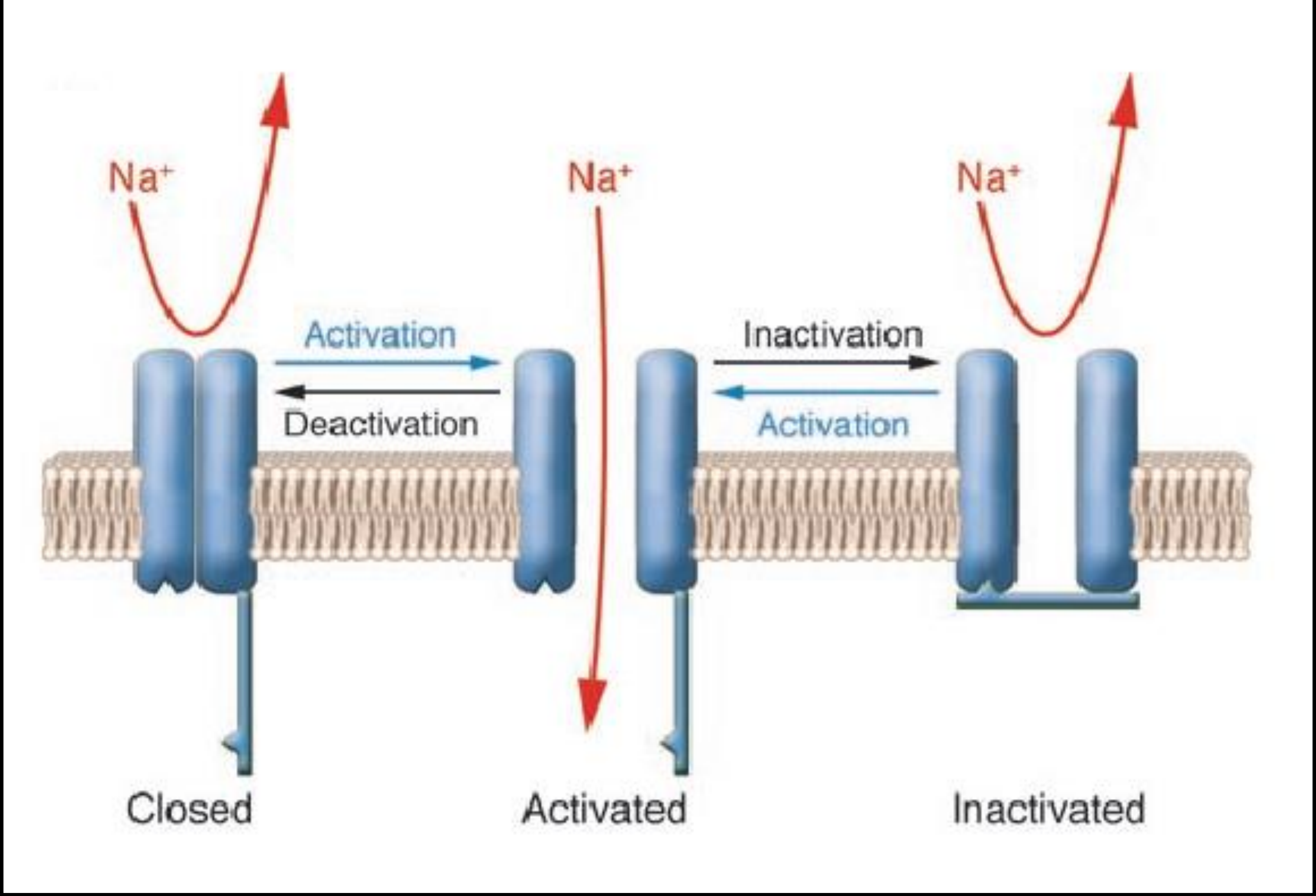
At rest, the activation gate is closed and the inactivation gate is open. During the upstroke of the action potential, both gates are open and $Na^+$ flows into the cell down its electrochemical potential gradient. During repolarization, the activation gate remains open but the inactivation gate is closed.




local anesthetic **lidocaine** blocks this channel

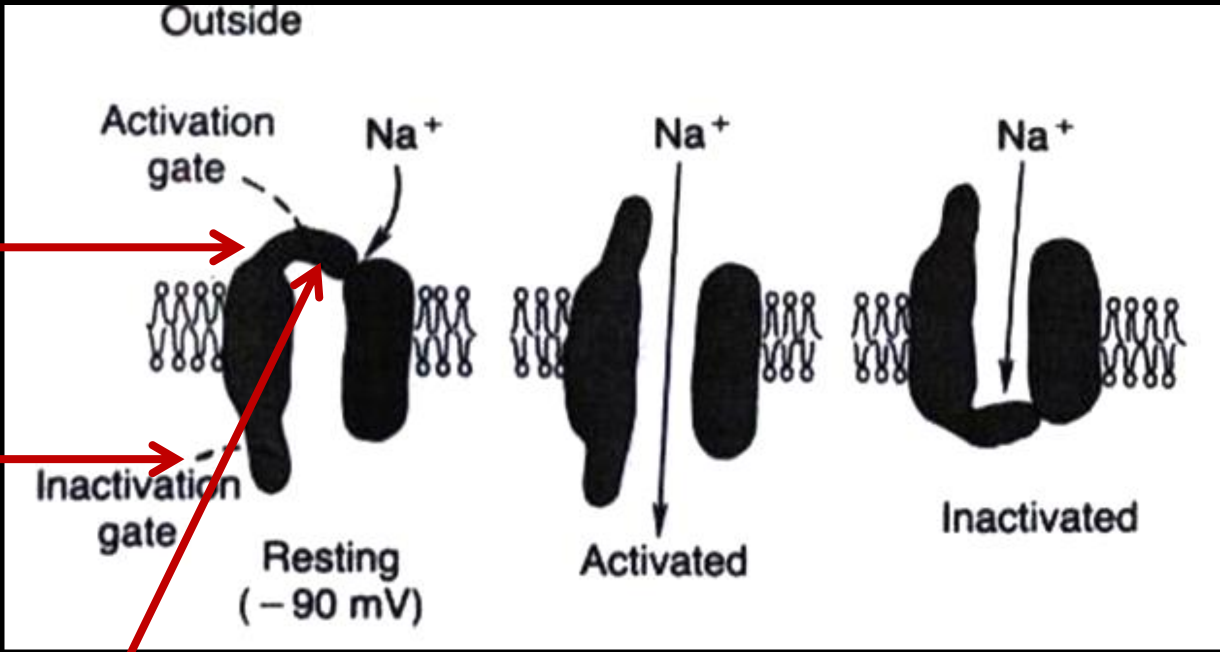
Cannot elicit new AP

# Activation-Inactivation-Deactivation



# The Na+ Voltage-Gated Channel (1)

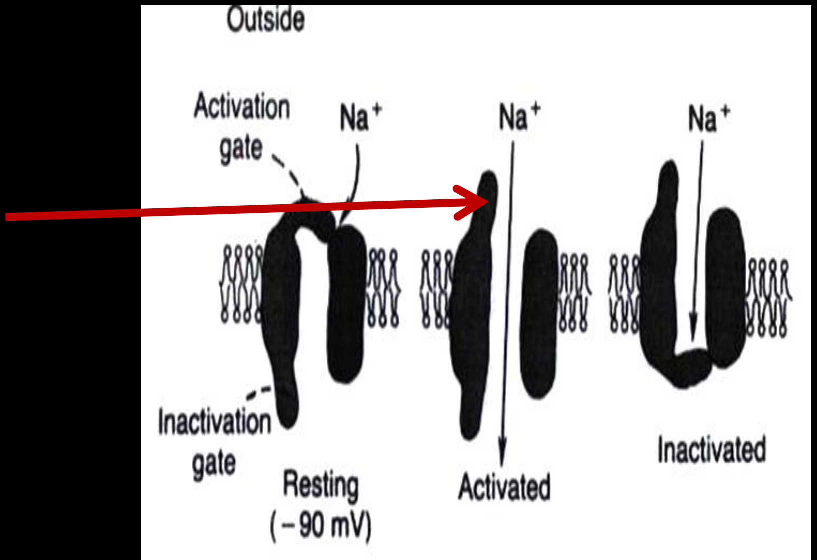
- Has 2 gates : one on the outer side of the membrane and is called the activation gate ,
- and another one on the inner side of membrane called the inactivation gate .
- And this channel has 3 states :




- (1) Resting state : in the resting cell when the MP = RMP = -70 to -90 mV , →
- the activation gate is closed
- this prevents entry of Na+ to the interior of the cell through this gate.

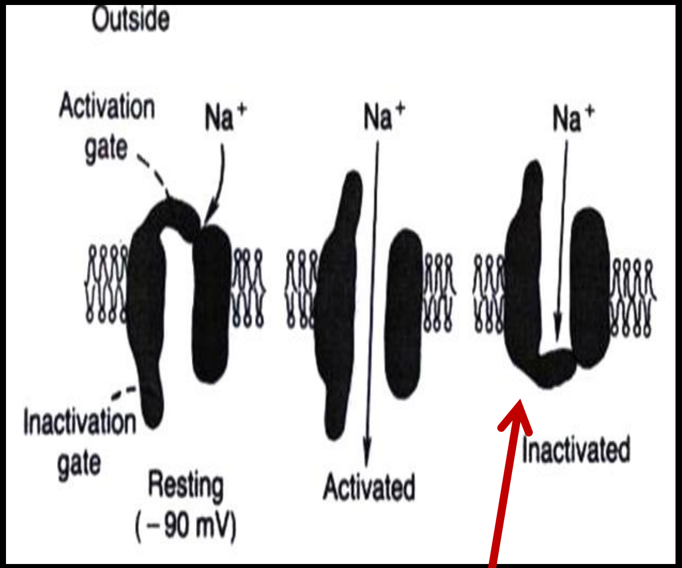
# Activated State of Sodium Channel

- (2) <u>Activated state :</u> when a Threshold Depolarizing Stimulus moves the MP from its resting value (-90 mV ) to its Threshold value (-65 to -55mV)
- → this opens the activation gate , and now the Na+ channel is said to be in the **Activated State**
- ( NB in this case BOTH the activation gate & inactivation gate are <u>open )</u> →
- permeability to Na+ becomes increased 500 to 5000 times → Na+ influx
- Na+ flows into the cell in large amounts ,



# Inactivated State of Sodium Channel

- (3) Inactivated state : A few milliseconds after the activation gate opens , the channel becomes inactivated :

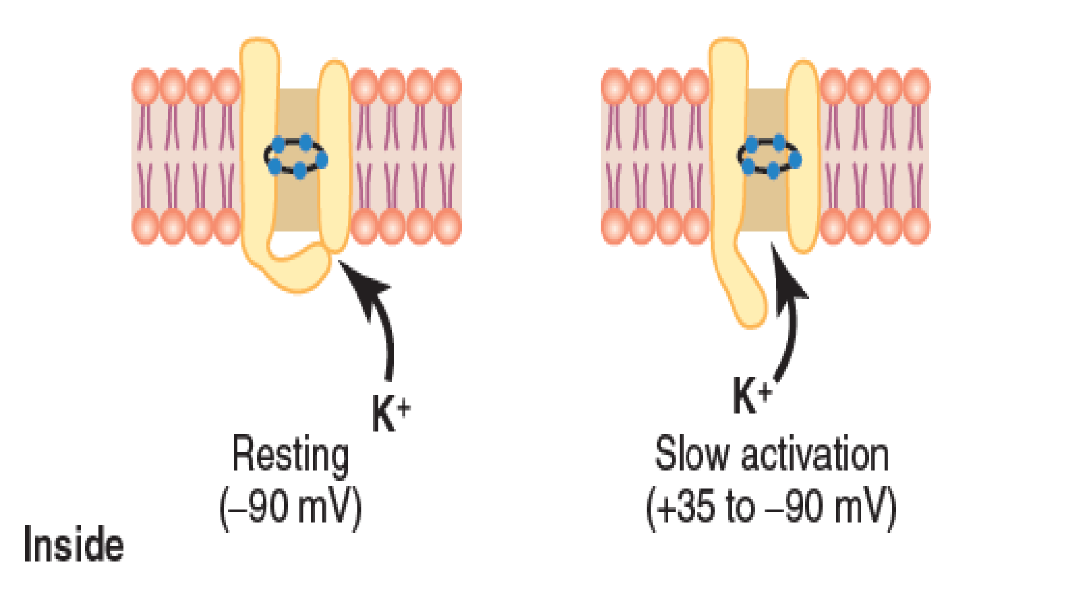



**At the peak of AP the inactivation gate will close**
**•the inactivation gate will not open by a second stimulus → & the cell becomes Refractory (ممانعة) to another stimulation .**
**•This goes on until the MP has gone back to its resting ( RMP) level ( -70 to -90mV).**

- → in this case , while the activation gate is still open , the inactivation gate is closed .

# Voltage gated $K^+$ channels

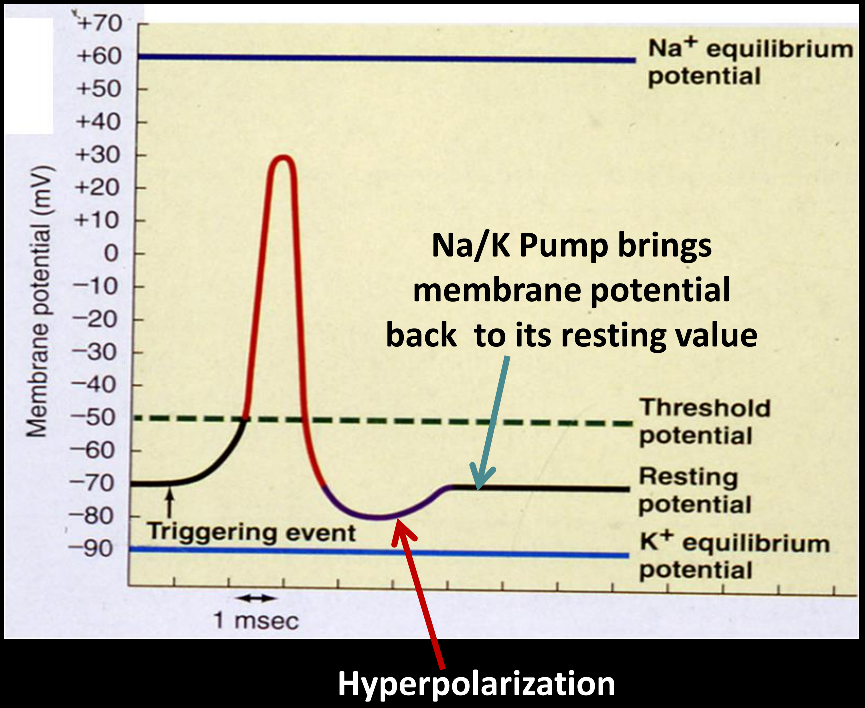
- Has one gate only .
- During the resting state, the gate of the potassium channel is closed and potassium ions are prevented from passing through this channel to the exterior.
- Shortly after depolarization, when the sodium channel begins to be inactivated, the potassium channel opens.




$K^+$ exits (Efflux) → Repolarization

## 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

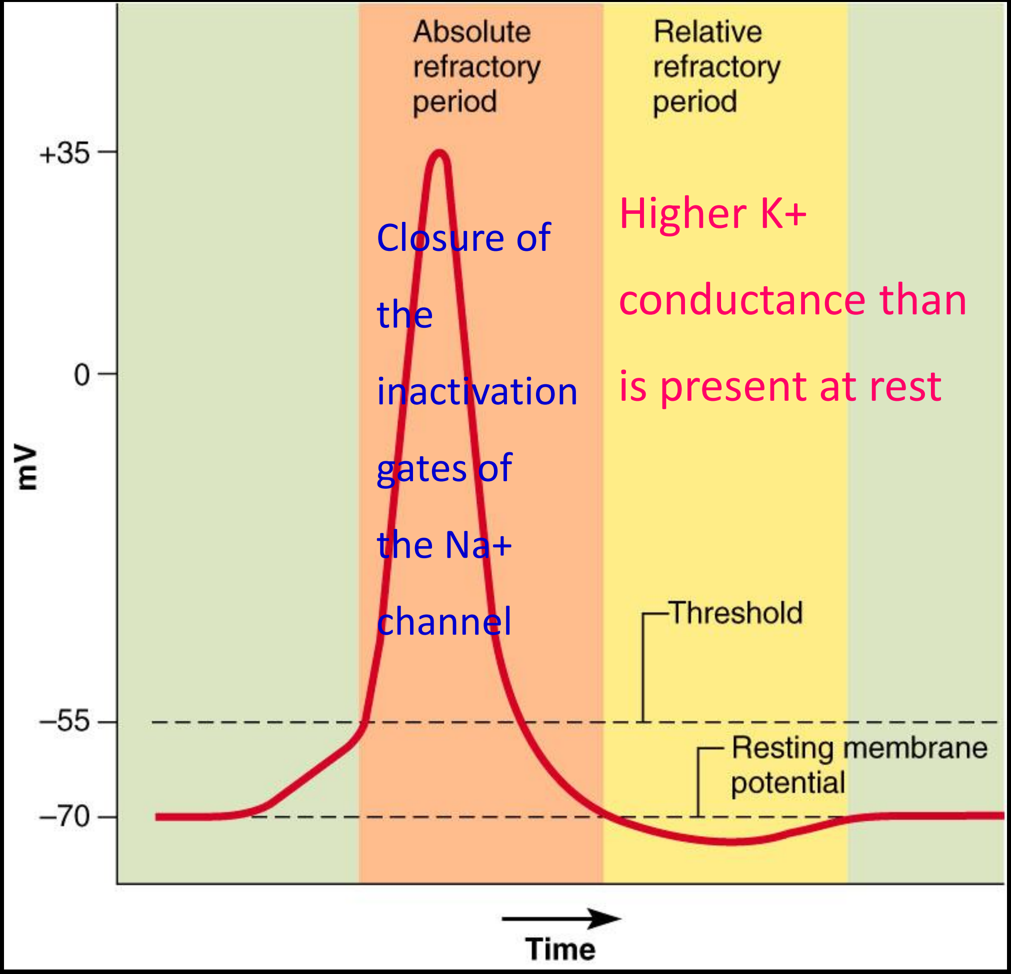
**Two stages**

- **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

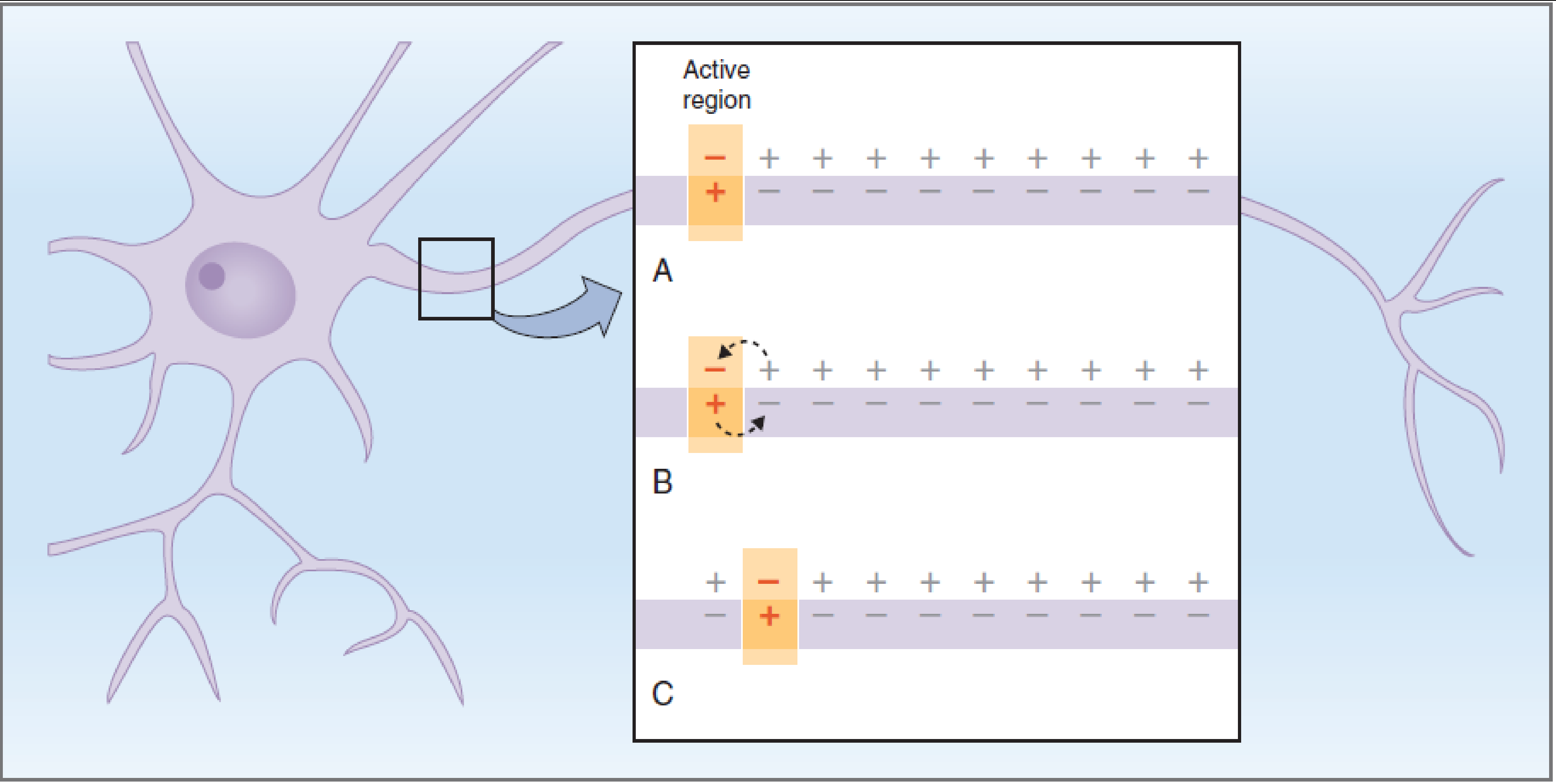



**Figure 1–15 Spread of depolarization down a nerve fiber by local currents. A,** The initial segment of the axon has fired an action potential, and the potential difference across the cell membrane has reversed to become inside positive. The adjacent area is inactive and remains at the resting membrane 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*

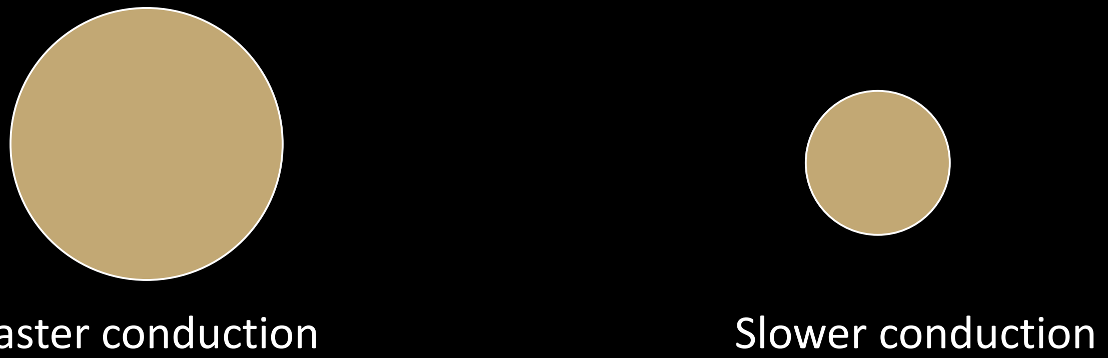
It is the speed at which action potentials are conducted (propagated) along a nerve or muscle fiber.

**Mechanisms that increase conduction velocity along a nerve:**

**1- Nerve diameter.**

The larger the diameter, the faster the transmission, **<u>Because:</u>**

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



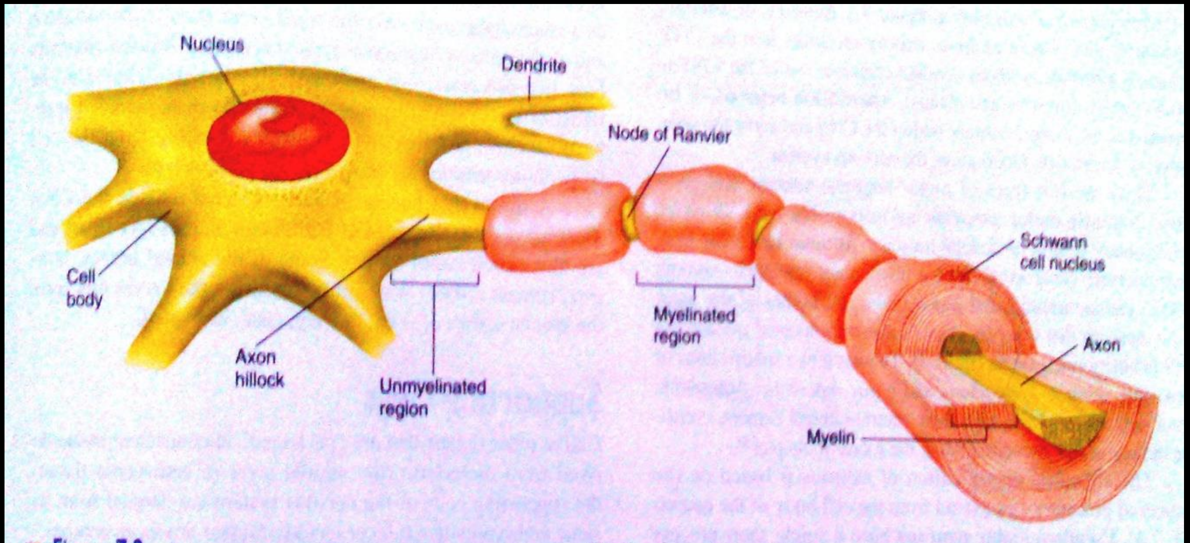



**Figure 7.2** **Parts of a neuron.** The axon of this neuron is wrapped by Schwann cells, which form a myelin sheath.

# *Conduction Velocity*

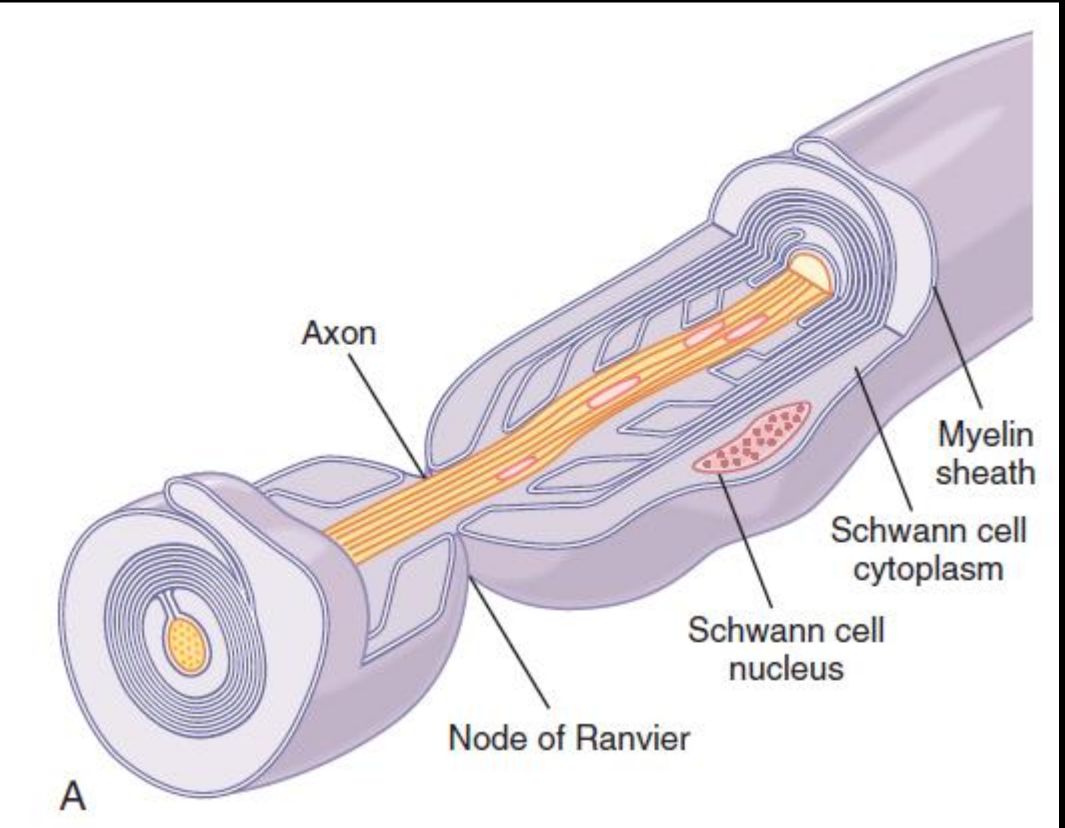
**Mechanisms that increase conduction velocity along a nerve:**

**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.



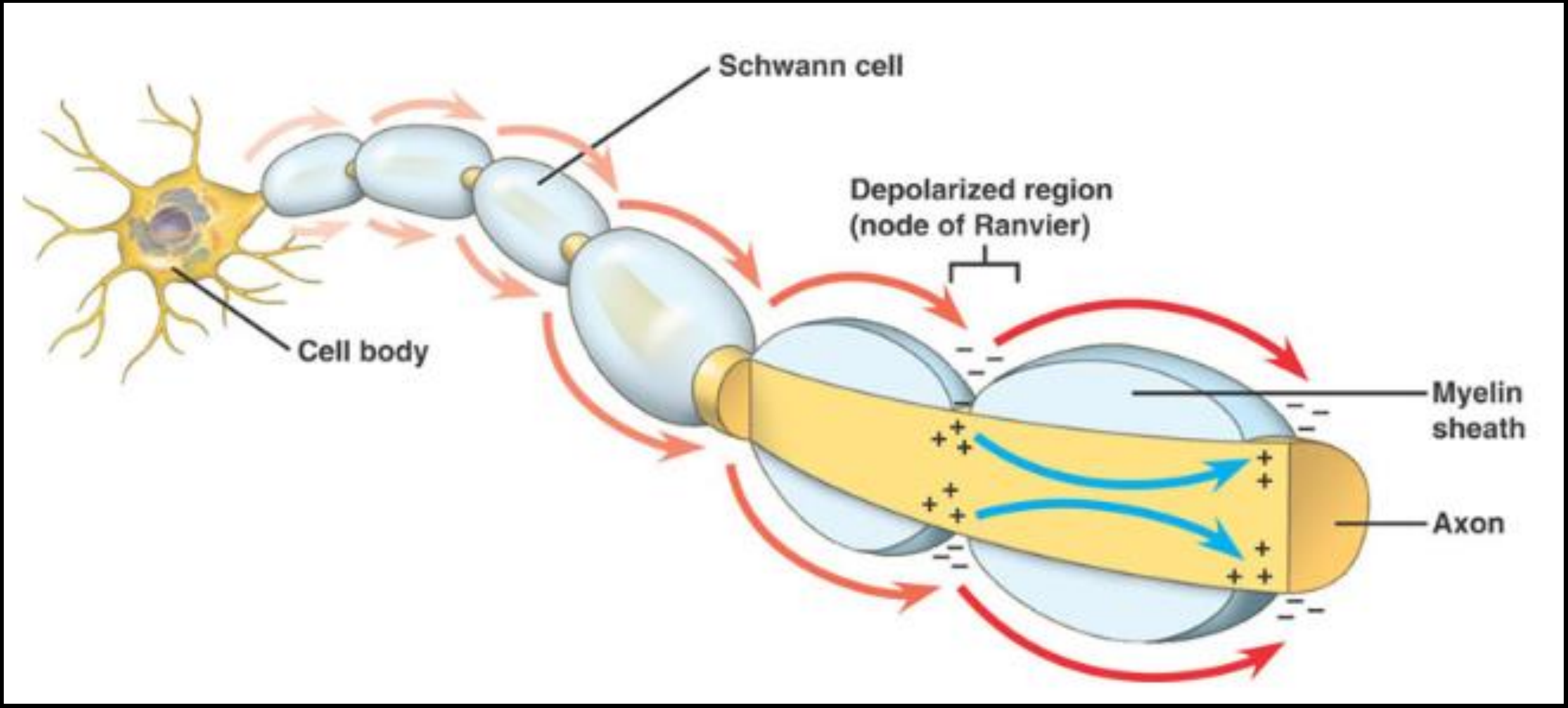
# Saltatory Conduction

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

**Value:-**

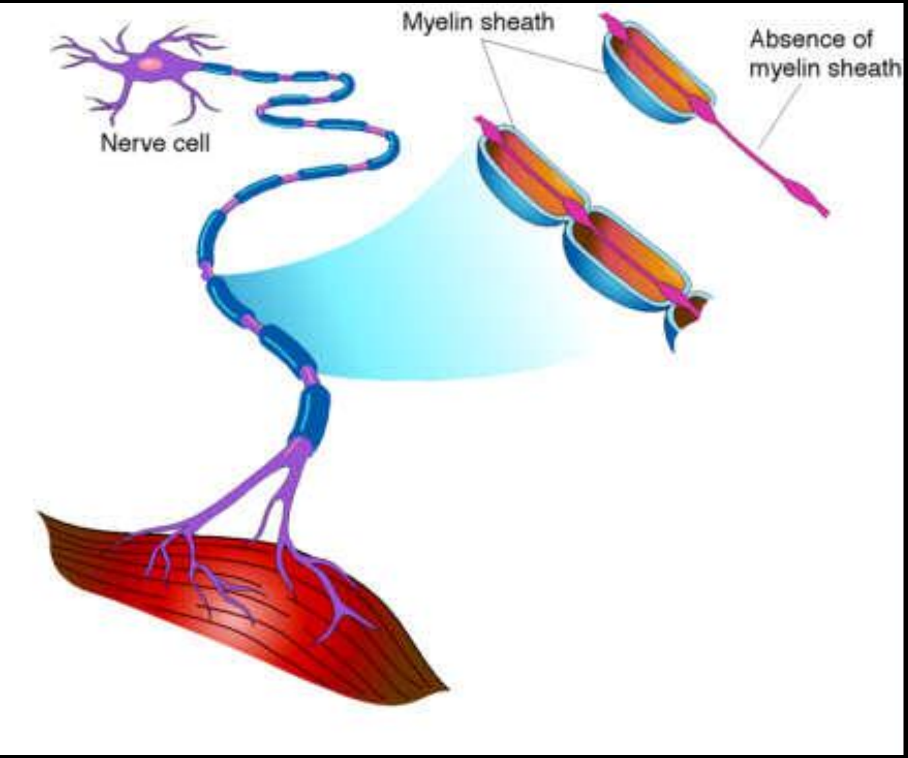
**1- Increases conduction velocity.**

**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