

# Resting membrane potential & action potential

TEXTBOOK OF MEDICAL PHYSIOLOGY

GUYTON & HALL 13<sup>TH</sup> EDITION

UNIT II CHAPTER 5

Pages 61-73



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# Objectives

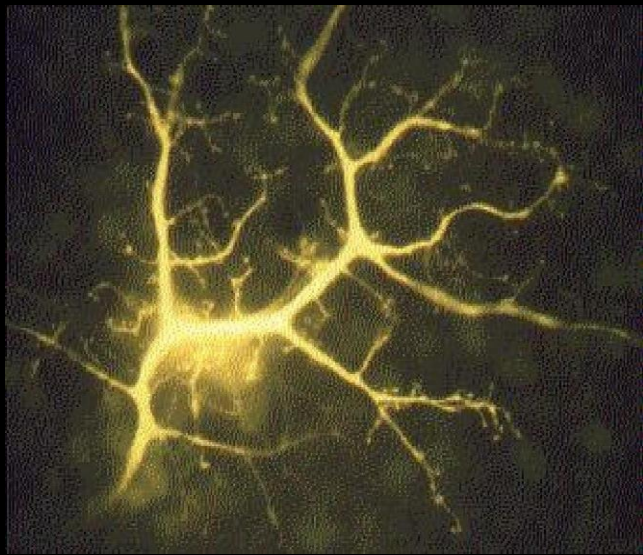
**At the end of these lectures the student should be able to**

- 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.

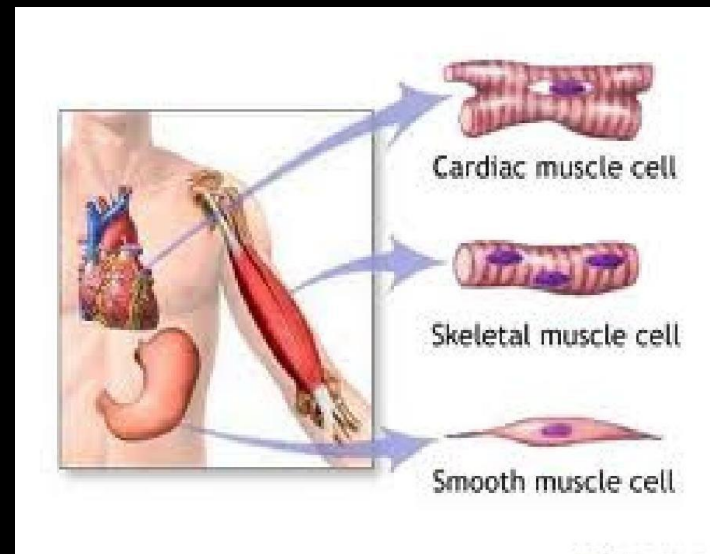
# Excitable Tissues

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

Nerve



Muscles



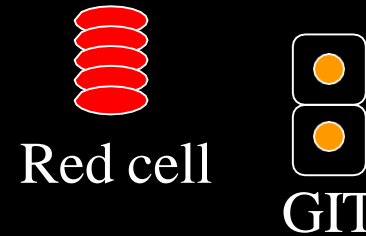
# Excitable tissues

excitable



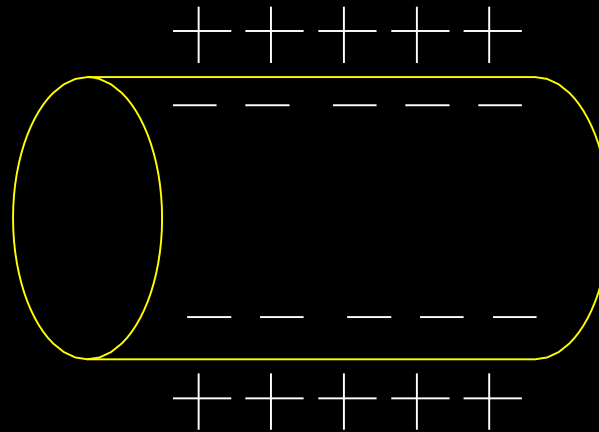
- Nerve
- Muscle
  - Skeletal
  - Cardiac
  - Smooth

Non-excitable



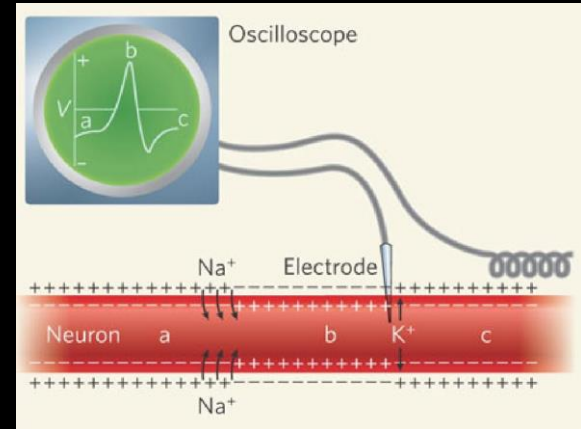
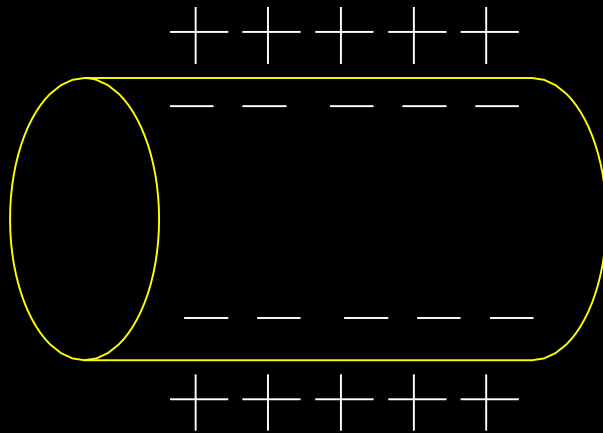
- RBC
- Intestinal cells
- Fibroblasts
- Adipocytes

# 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**

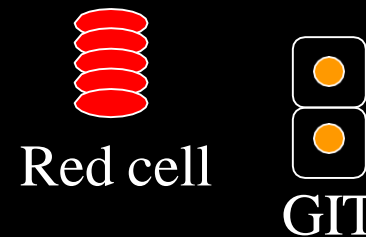
# Excitable tissues

excitable



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

Non-excitable



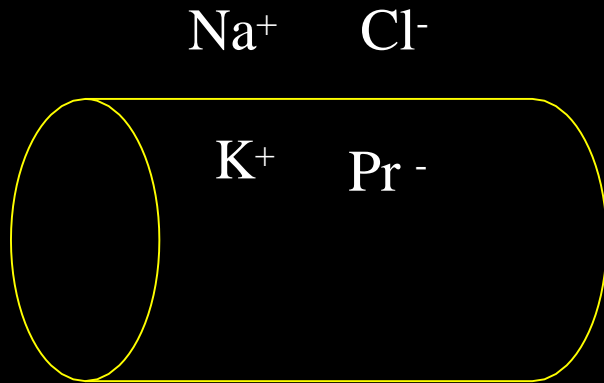
- Non-excitable tissues have less negative RMP
  - 53 mV epithelial cells
  - 8.4 mV RBC
  - 20 to -30 mV fibroblasts
  - 58 mV adipocytes

# Resting Membrane Potential

- This depends on the following **factors**
  - Ionic distribution across the membrane
  - Membrane permeability
  - Na<sup>+</sup>/K<sup>+</sup> ATPase pump



# Ionic distribution



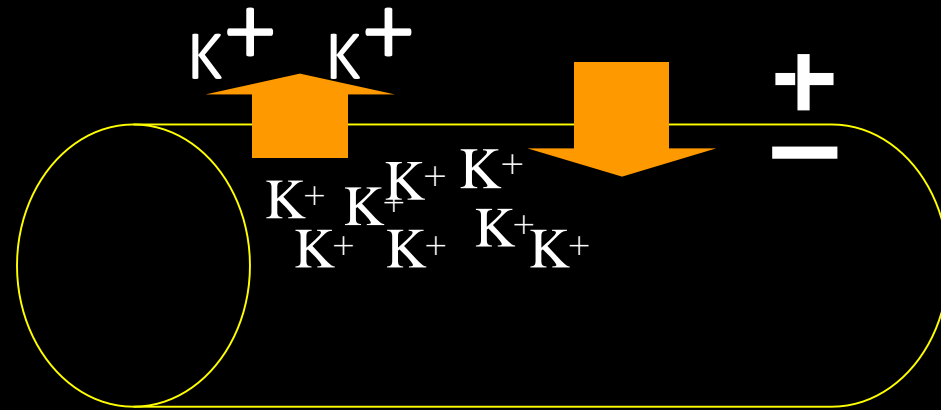
- Major ions
  - Extracellular ions
    - Na<sup>+</sup>, Cl<sup>-</sup>
  - Intracellular ions
    - K<sup>+</sup>, Proteins

	EXTRACELLULAR FLUID	INTRACELLULAR FLUID
Na <sup>+</sup>	142 mEq/L	10 mEq/L
K <sup>+</sup>	4 mEq/L	140 mEq/L
Ca <sup>++</sup>	2.4 mEq/L	0.0001 mEq/L
Mg <sup>++</sup>	1.2 mEq/L	58 mEq/L
Cl <sup>-</sup>	103 mEq/L	4 mEq/L
HCO <sub>3</sub> <sup>-</sup>	28 mEq/L	10 mEq/L

# Electrochemical gradient

- At electrochemical equilibrium, there is an exact balance between two opposing forces:
- **Electrical driving force** = potential difference across membrane
  - opposing electrical gradient that increasingly tends to stop the ion from moving across the membrane.
- **Chemical driving force** = ratio of concentrations on 2 sides of membrane (concentration gradient)
  - The concentration gradient that causes the ion to move from area of higher concentration to area of lower concentration.
- **Equilibrium:** when electrical driving force is balanced by chemical driving force

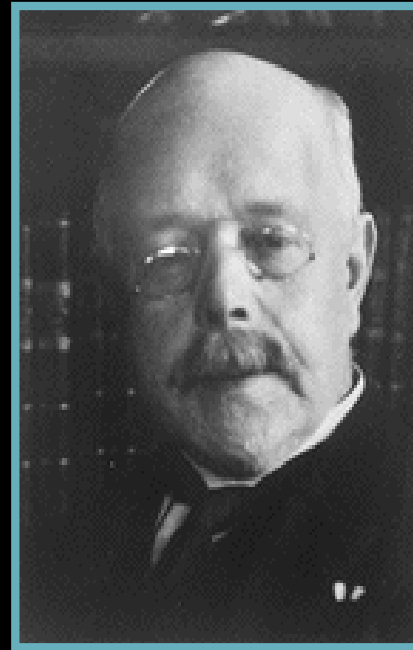
# Chemical & Electrical driving forces of Potassium ( $K^+$ )



- $K^+$  concentration intracellular is higher
- Membrane is freely permeable to  $K^+$
- There is an efflux of  $K^+$  to extracellular fluid
- Efflux of positive ions creates positivity outside and negativity inside
- Outside positivity resists efflux of  $K^+$  (since  $K^+$  is a positive ion)
- At a certain voltage, equilibrium is reached and  $K^+$  efflux stops

# The Nernst equation

Describes the balance of electrical and chemical forces across a cell membrane *membrane that will exactly prevent net diffusion of an ion*



Walther Hermann Nernst

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

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

# 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 <sup>+</sup>	14	140	+61
K <sup>+</sup>	140	4	-94
Cl <sup>-</sup>	4	103	-86
Ca <sup>2+</sup>	0.0001	2.4	+127
HCO <sub>3</sub> <sup>-</sup>	10	28	-27

(mmol/l)

# Goldman Equation

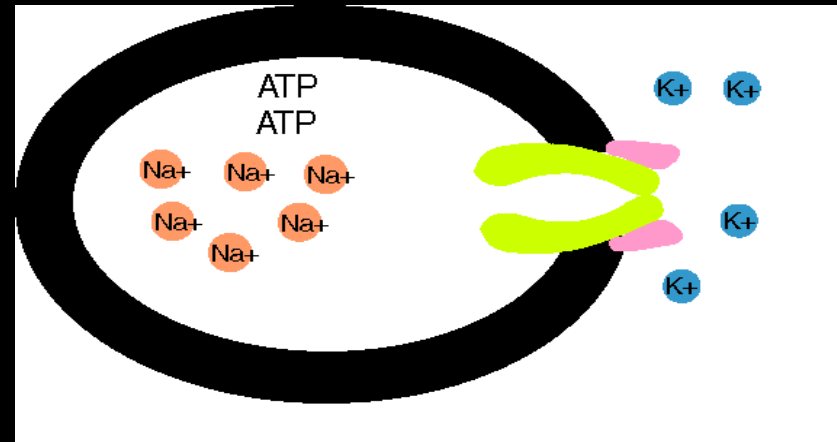
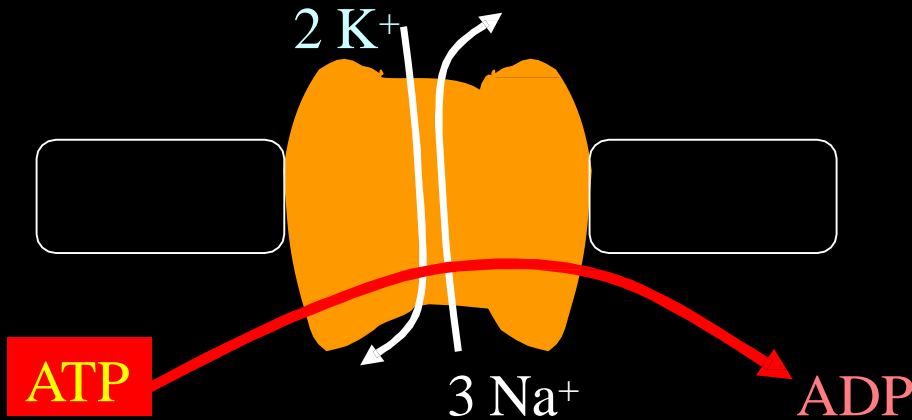
- When the membrane is permeable to **several ions**, the equilibrium potential that develops depends on:
  - Polarity of each ion
  - Membrane permeability
  - Ionic concentration
- This is calculated using Goldman Equation

EMF (millivolts)

$$= -61 \times \log \frac{C_{Na^+}_i P_{Na^+} + C_{K^+}_i P_{K^+} + C_{Cl^-}_o P_{Cl^-}}{C_{Na^+}_o P_{Na^+} + C_{K^+}_o P_{K^+} + C_{Cl^-}_i P_{Cl^-}}$$

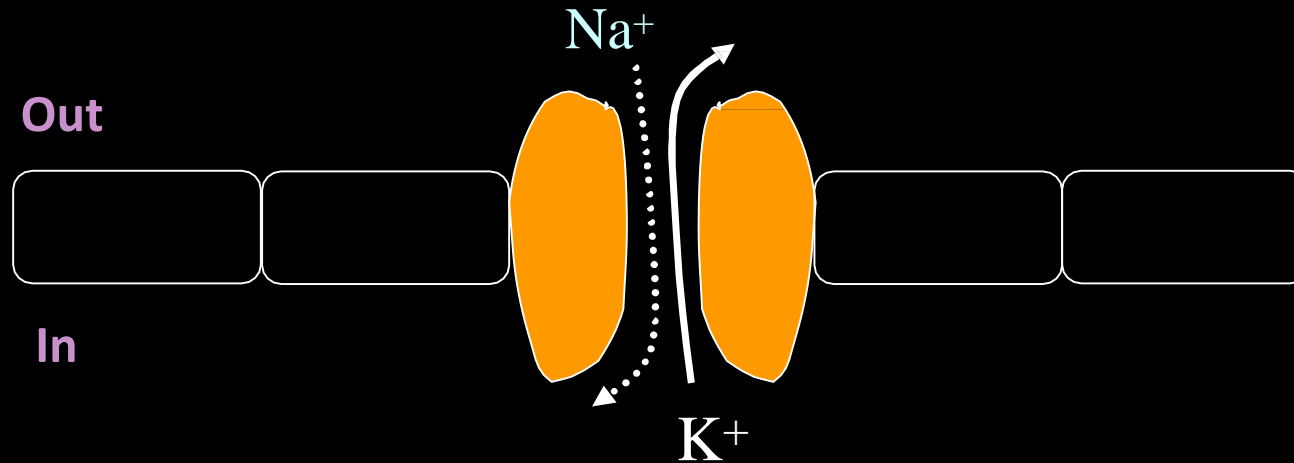
Using this value in the **Goldman equation** gives a potential inside the membrane of **-86 mV**

# Na<sup>+</sup>/K<sup>+</sup> ATPase pump



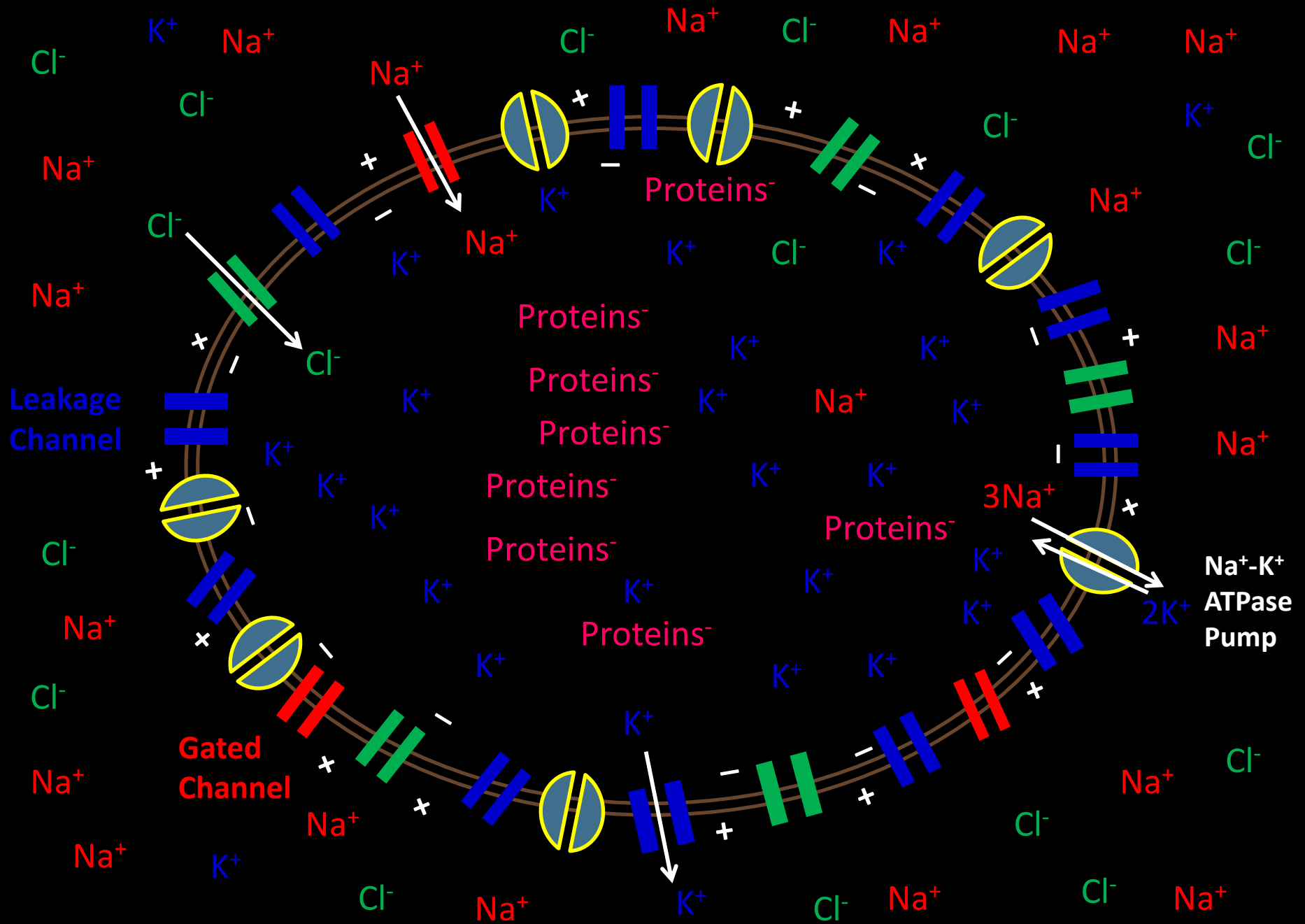
- Active transport system for Na<sup>+</sup>/K<sup>+</sup> exchange using energy
- It is an electrogenic pump since 3 Na<sup>+</sup> efflux are coupled with 2 K<sup>+</sup> influx
- Net effect of causing negative charge inside the membrane (-4mV)

# Ionic channels



- **Leaky channels** ( $\text{K}^+/\text{Na}^+$  leak channels)
  - More permeable to  $\text{K}^+$
  - Allow **free** flow of ions
- In the resting state
  - $\text{K}^+$  permeability is 100 times more than that of  $\text{Na}^+$

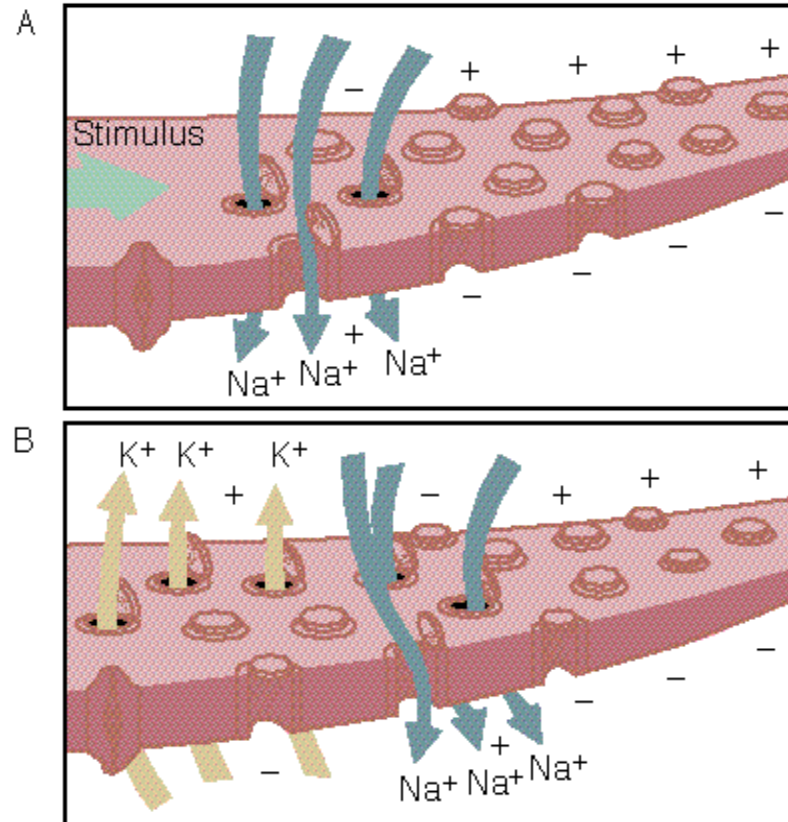




# Factors contributing to RMP

- One of the main factors is  $K^+$  efflux (Nernst Potential:  $-94\text{mV}$ )
- Contribution of  $Na^+$  influx is little (Nernst Potential:  $+61\text{mV}$ )
- $Na^+/K^+$  pump creates additional degree of negativity inside the membrane ( $-4\text{mV}$ )
- 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

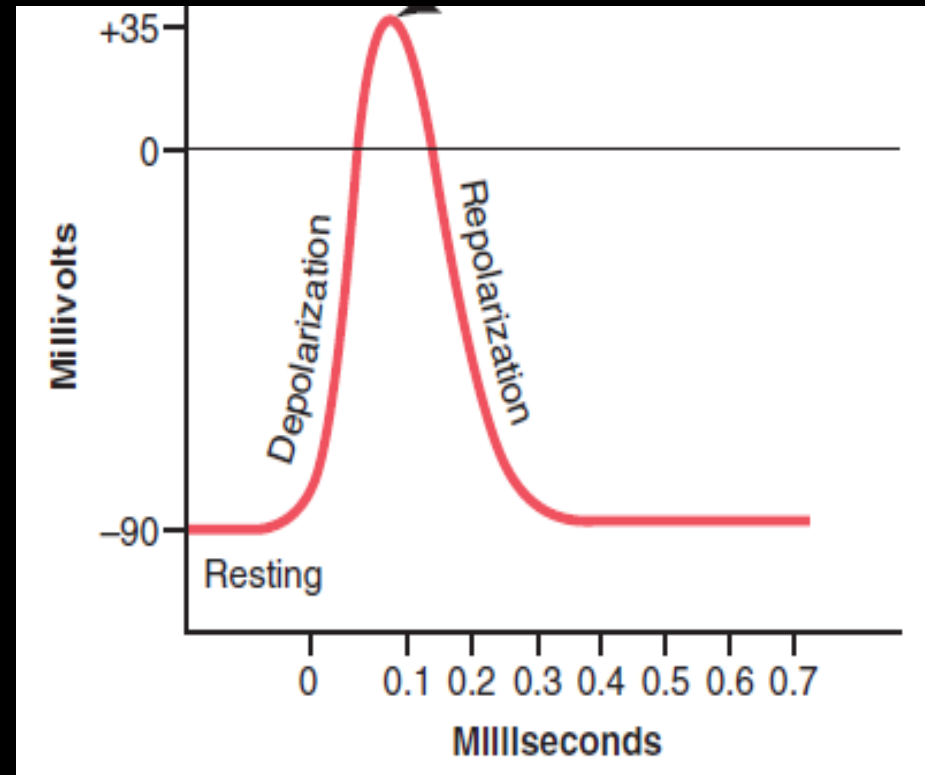
Each action potential begins with a sudden change from the normal resting **negative** membrane potential to a **positive** potential and ends with an almost equally rapid change back to the **negative** potential.

## Stages of the action potential:

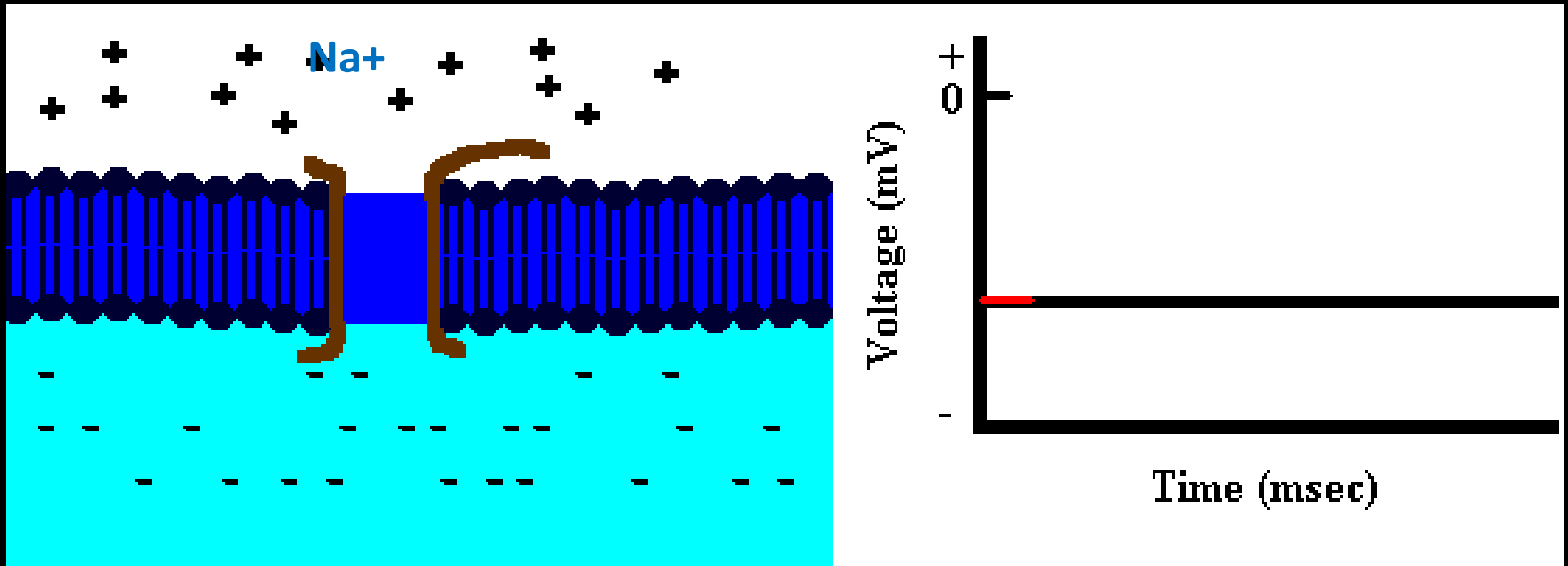
**Resting Stage.** It is the resting membrane potential before the action potential begins. The membrane is “polarized”.

**Depolarization Stage.**

**Repolarization Stage.**

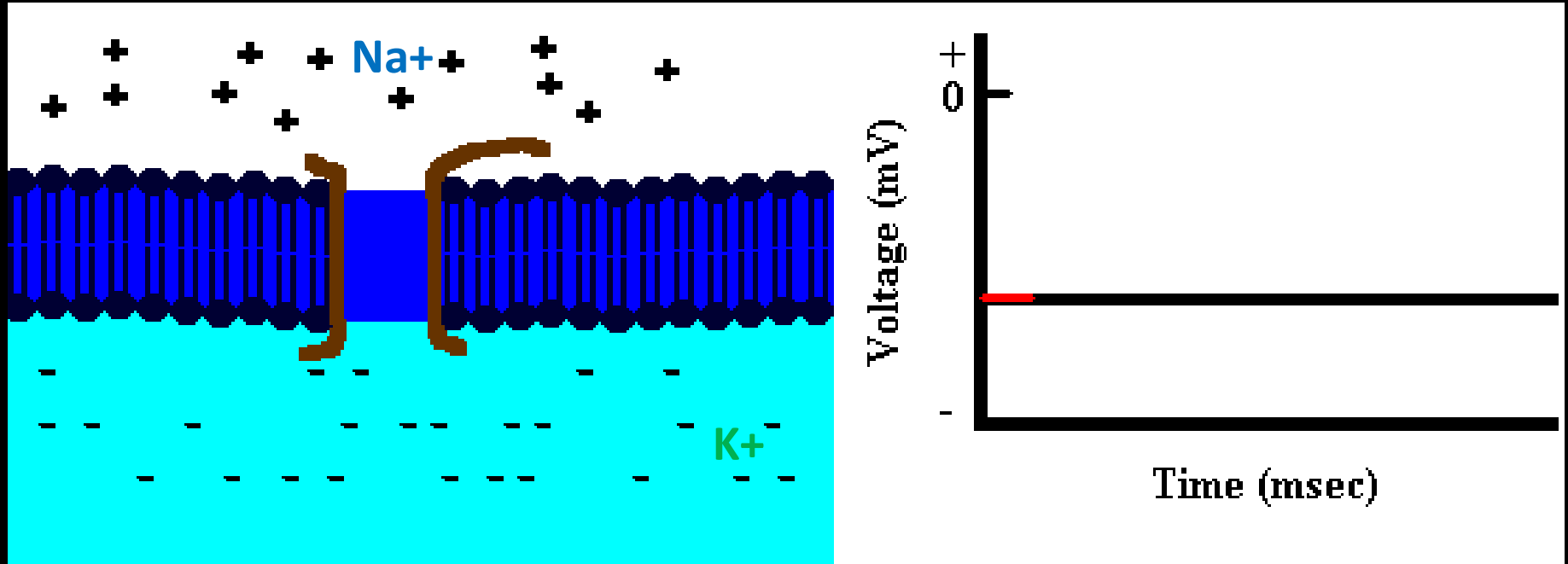


# Depolarization



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

# Repolarization



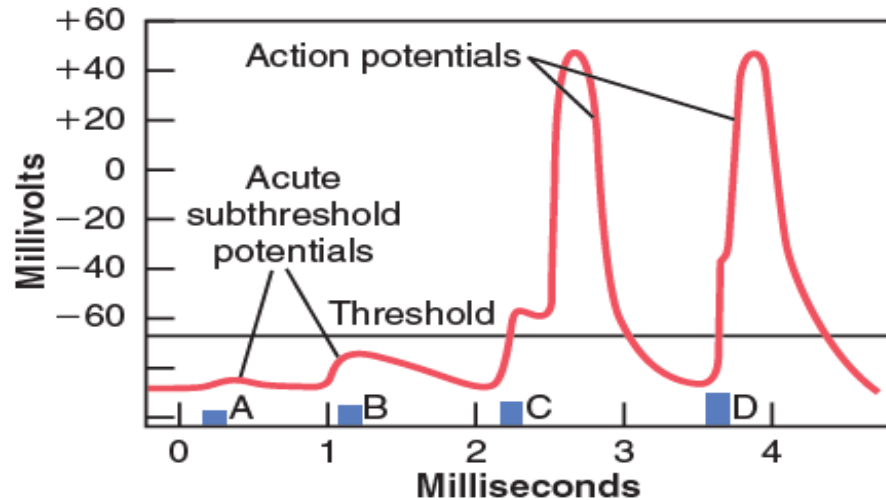
**Repolarization:**  $\text{Na}^+$  channels begin to close and the  $\text{K}^+$  channels open. Rapid diffusion of  $\text{K}^+$  ions to the exterior re-establishes the normal negative resting membrane potential.

## 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:

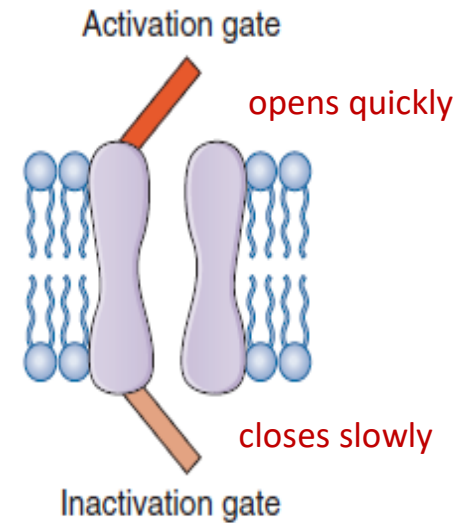
- **Voltage gated Na<sup>+</sup> channels**
- **Voltage gated K<sup>+</sup> channels**

# Voltage gated Na<sup>+</sup> channels

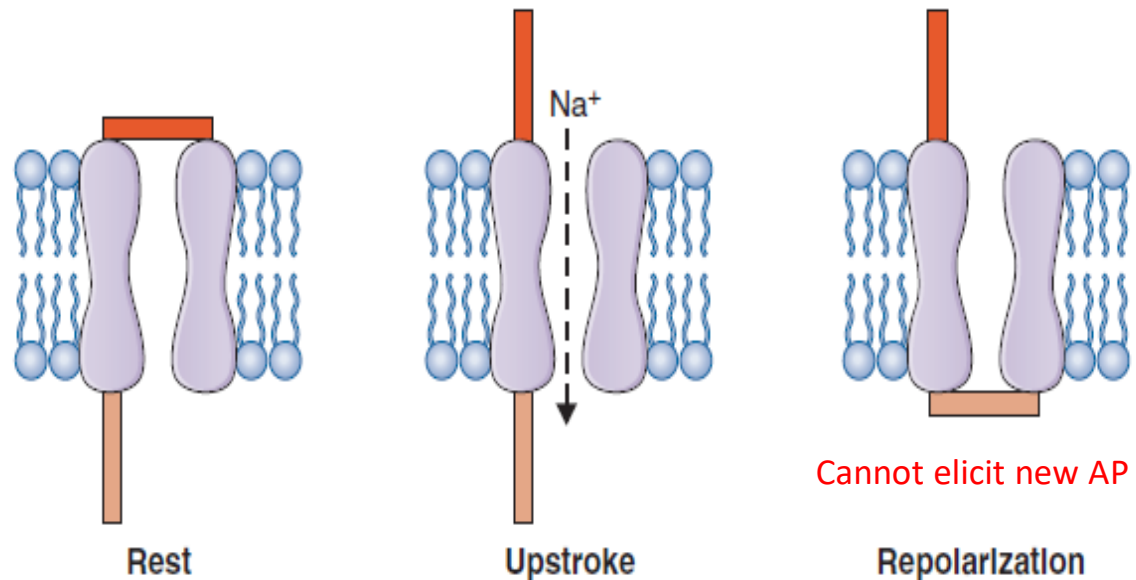
At rest, the activation gate is closed and the inactivation gate is open.

During the upstroke of the action potential, both gates are open and Na<sup>+</sup> 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

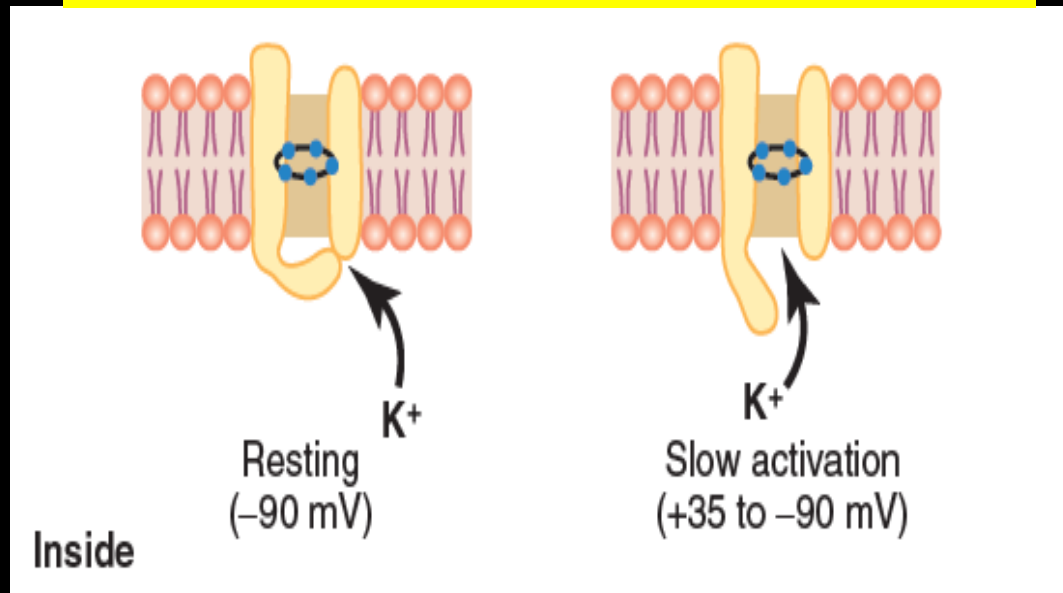


# Voltage gated $K^+$ channels

- 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.

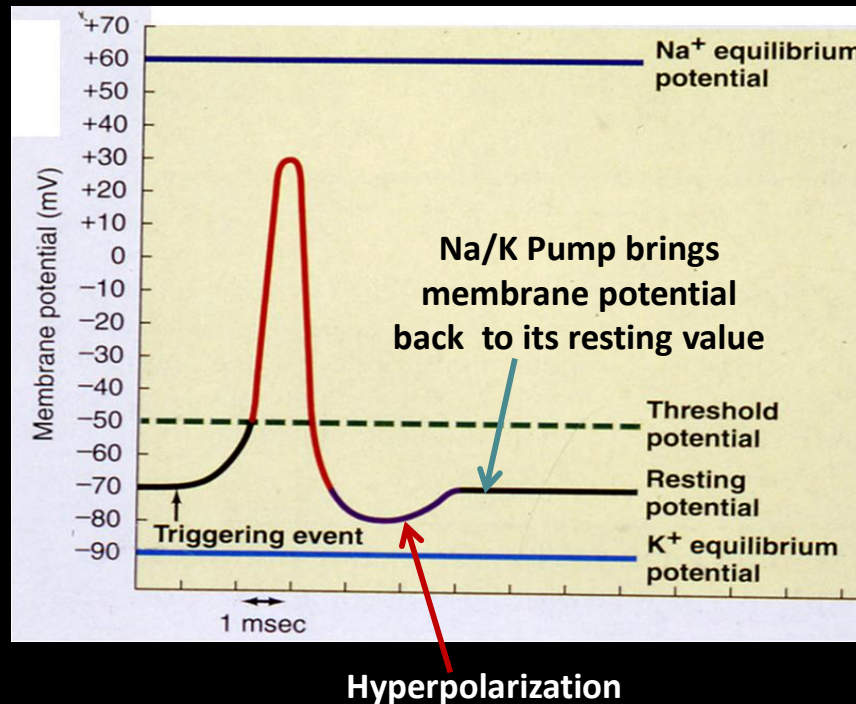
$K^+$  exits (Efflux)  $\rightarrow$  Repolarization

Tetraethylammonium (TEA) blocks this channel



## Hyperpolarization: Why?

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



# Refractory Periods

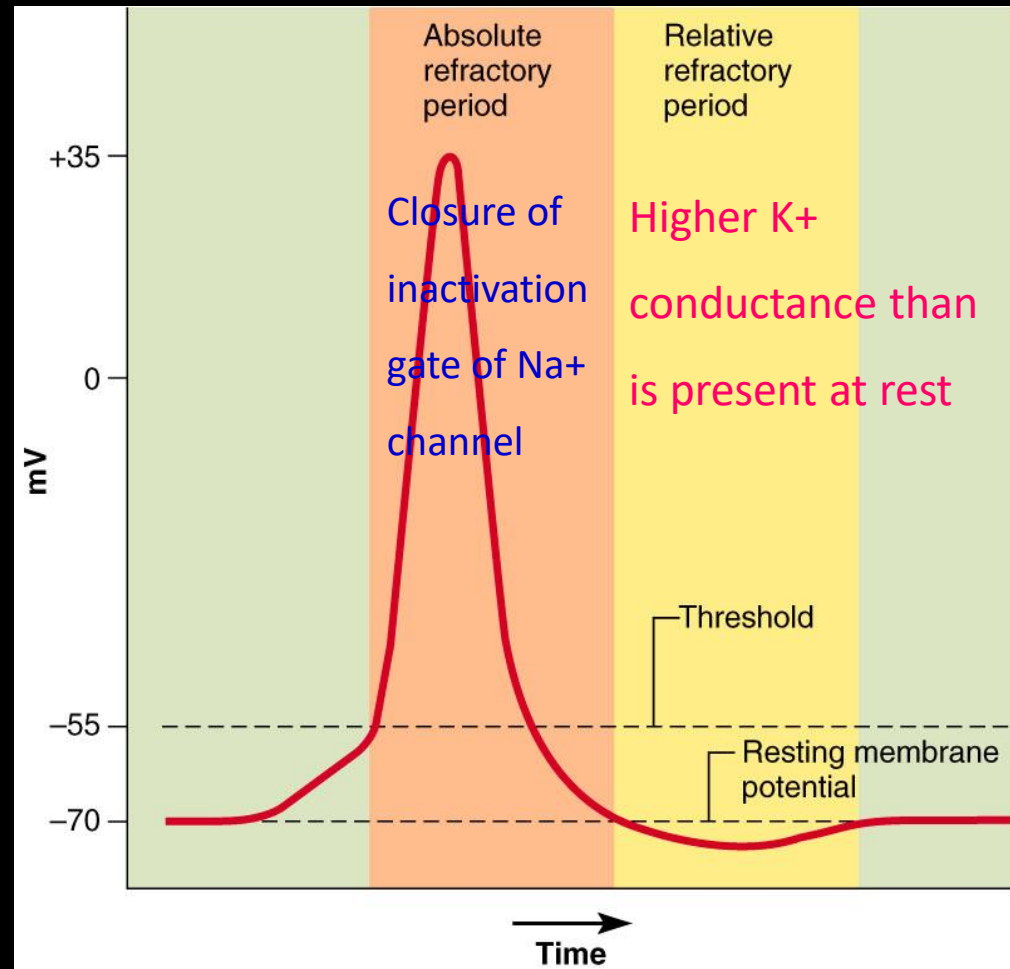
## Two stages

### ➤ **Absolute refractory period**

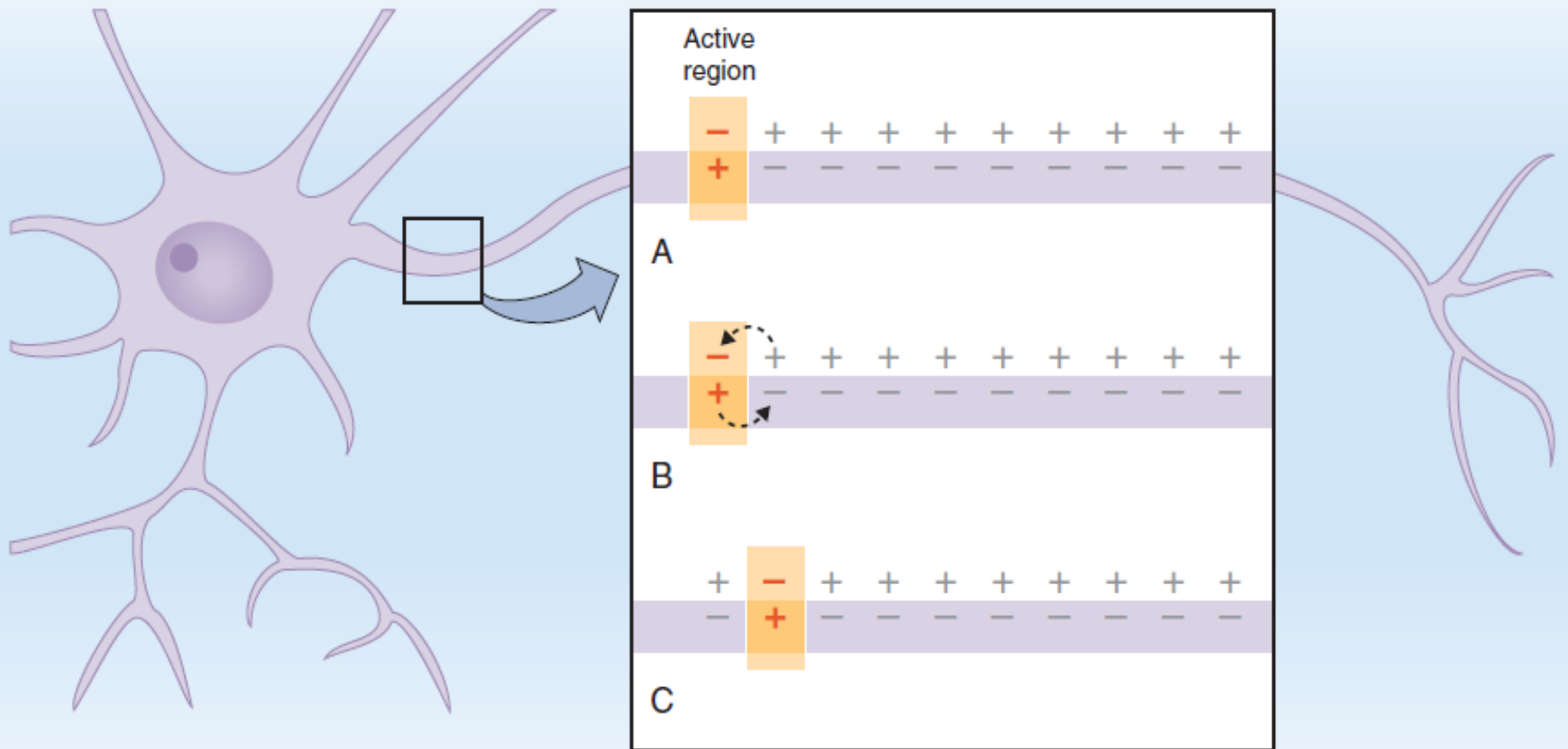
The period during which a second action potential cannot be elicited, even with a strong stimulus.

### ➤ **Relative refractory period**

Can trigger new action potential if stimulus is very strong.



# Propagation of 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.

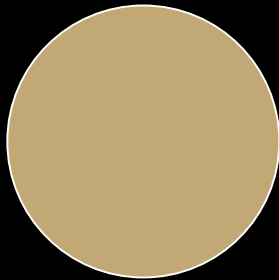
# Conduction Velocity

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

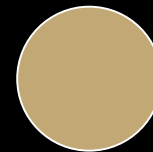
**Mechanisms that increase conduction velocity along a nerve:**

## 1- Nerve diameter.

- The larger the diameter, the faster the transmission, **Because:**
- Large fiber offers Less internal resistance ( $R_i$ ) to local current flow & more ions will flow (***Internal resistance is inversely proportional to the cross sectional area.***)



Faster conduction



Slower conduction

# Conduction Velocity

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

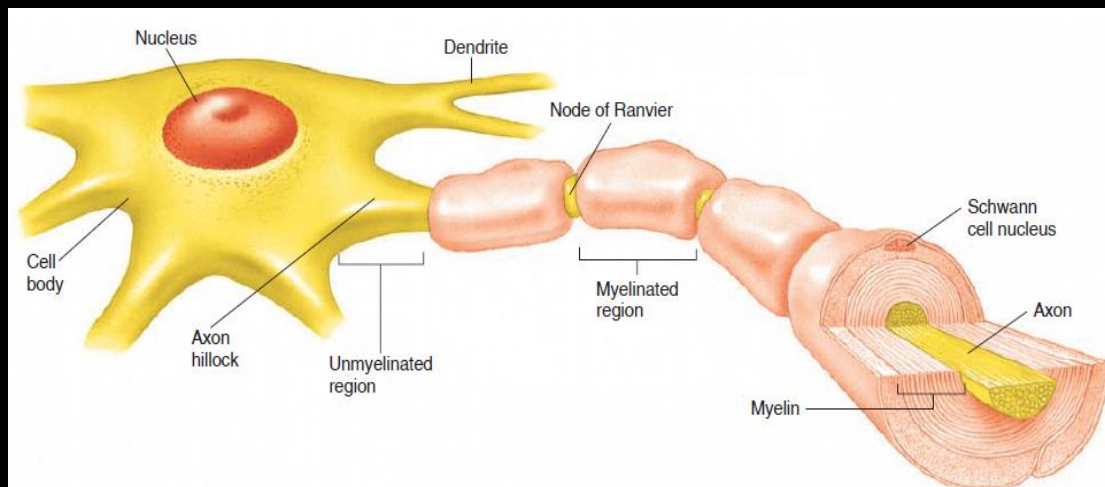
## 2- Myelination.

**Myelin** is a lipid *insulator* that makes it more difficult for charges to flow between ICF and ECF (**increases membrane resistance;  $R_m$** ).

-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.

The increased membrane resistance forces current to flow along the path of least resistance of the axon interior



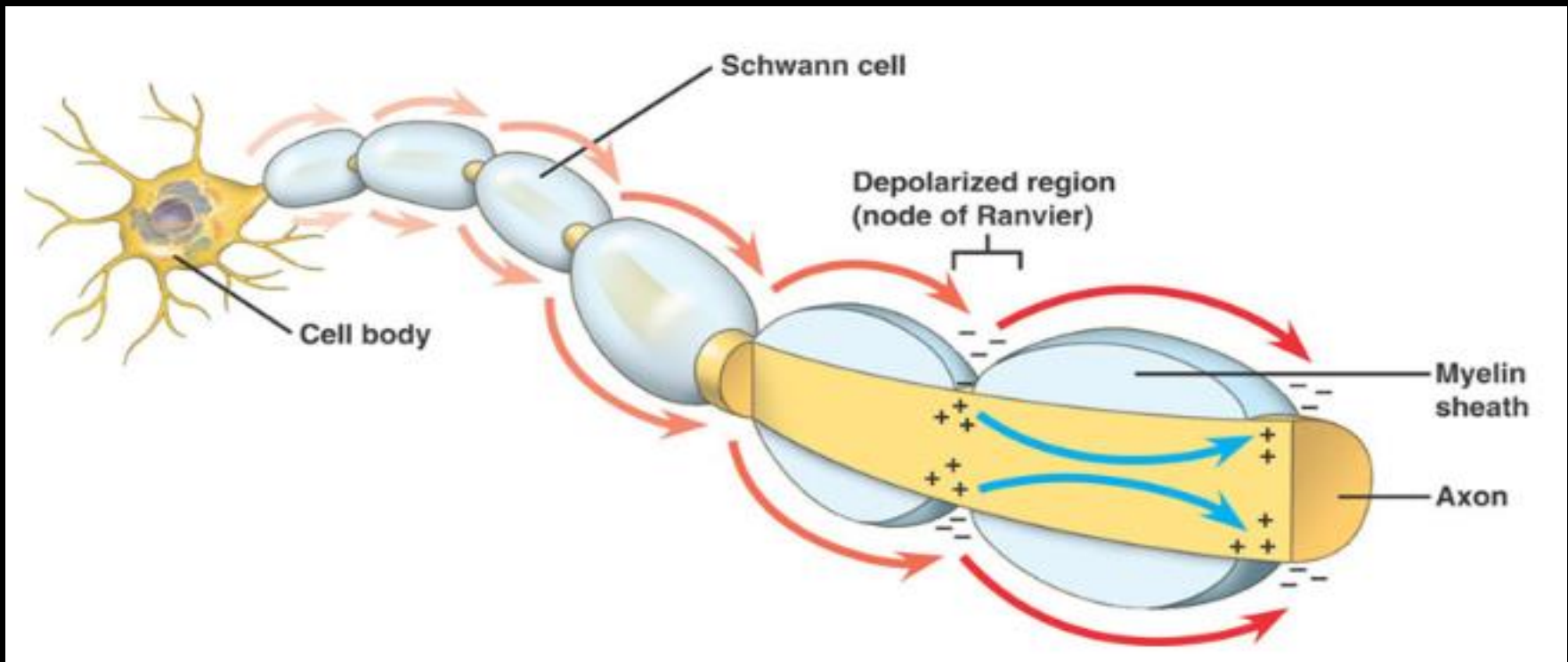


## Saltatory Conduction

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

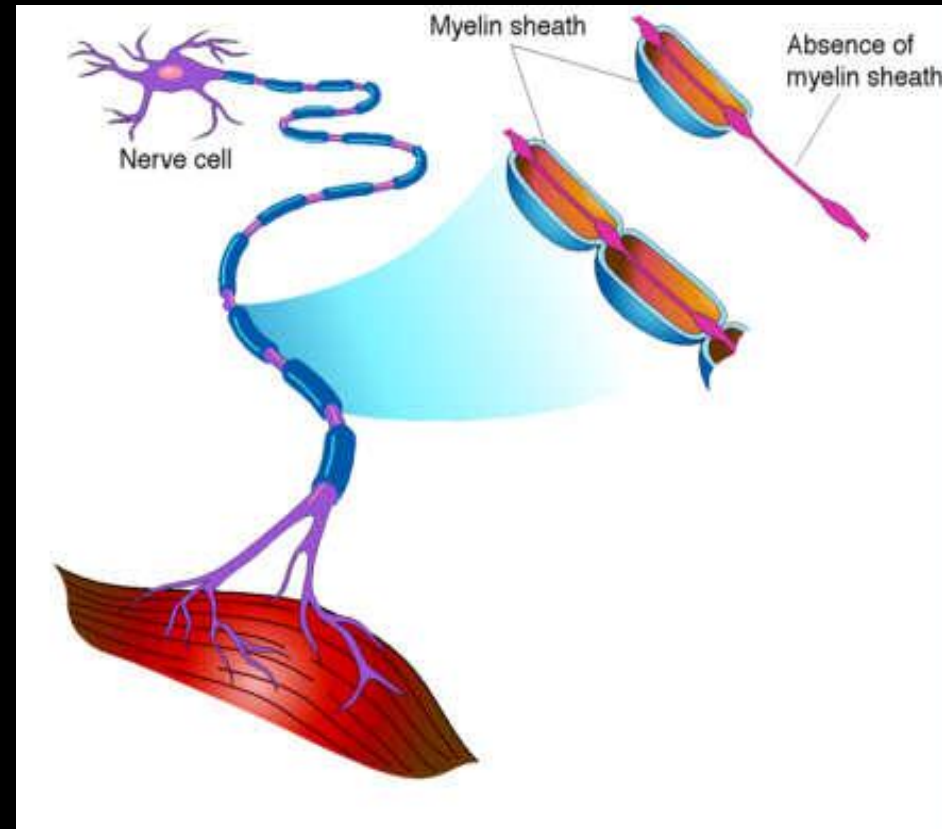
### Value:-

- 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.



Loss of myelin sheath around nerves causes a **decrease** in membrane resistance, which means that current “leaks out” across the membrane during conduction of local currents.

- The End