Nerve Action Potential :3

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Learning Objectives

1. **Role of Calcium ions**
2. **Initiation of action potential**
3. **Propagation of Action potential**
4. **Nerve and Muscle impulse**
5. **Direction of Propagation**
6. **All or Nothing Principle**
7. **Safety Factor for propagation**

Learning Objectives

8. Applied Physiology
    - Anesthetics
    - Membrane Stabilizers
9. Re-establishment of Na^+ K^+ ionic gradient
10. Heat production in Nerve fiber
11. Saltatory conduction

Calcium Ions

- **Membranes of almost all cells of the body**
- **Have Ca^{2+} pump**
- **Similar to Na^{+} pump**

Calcium ions serves →

- **Along with or Instead of Na^+**
- **In some cells**
- **To cause most of action potential**

Calcium pump ➔

- **Like**
- **Sodium (Na^+) pump**
- **Pumps Ca^{2+} ions**

Calcium pump → Ca^{2+}

- From the interior
- To the exterior of the cell membrane
- Or
- To endoplasmic reticulum (ER)

Calcium ions gradient ➔

- **Of 10,000 folds due to it**
- **Internal cell concentration of calcium ions of**
- **10^{-7} molar**
- **External concentration of 10^{-3} molar**

Voltage gated Ca^{2+} Channels

- Slightly permeable to Na^{+} ions also
- When channels open ➔ Both Ca^{2+} and Na^{+} ions
- Flow exterior of the fiber

Ca^{2+}-Na^{+} Channels → Slow channels

- **Slow to activation**
- **Require →10-20 times a long for activation**
- **As the → Sodium channels → Fast channels**

Ca^{2+} channels → Numerous

- Cardiac muscle
- Smooth muscle

Some types of Smooth Muscle

- Fast sodium channels
- Hardly present

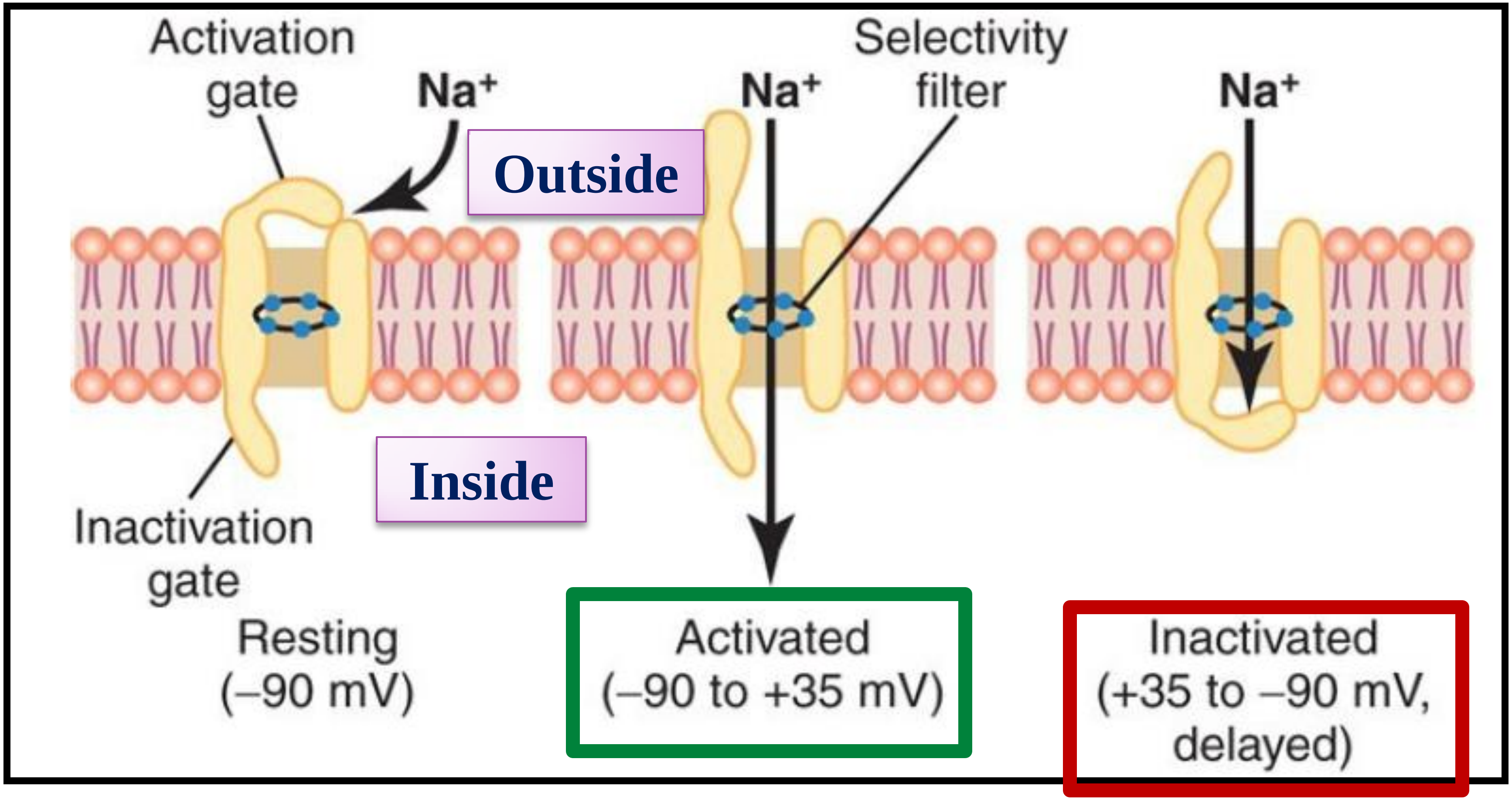
Some types of Smooth Muscle

- **Action potential caused → Entirely by**
- **Activation of the slow calcium channels**

Ca^{2+} ion Concentration in ECF → Effect

- **On the voltage level**
- **At which the Na^{+} channels become activated**
- **In Neurons → - 70mV to - 50mV**
- **In Nerve fiber → - 90mV to + 35mV**

Voltage-Gated Sodium Channel



Mechanism : Ca^{2+} affect the Na^{+} channel

- Ca^{2+} ions bind ➔
- To the exterior surfaces of
- The Na^{+} channel protein molecules

Mechanism : Ca^{2+} affect the Na^{+} channel

- **Positive charges of Ca^{2+} ions**
- **In turn**
- **Alter the electrical state of the channel protein itself**

Mechanism : Ca^{2+} affect the Na^{+} channel

- **Altering the voltage level required**
- **To open ➔ The sodium gate**

Deficit of Calcium Ions (Hypocalcaemia)

- Na^+ channels become activated (Opened)
- By very little increase
- Of the membrane potential
- From normal very negative level

Deficit of Calcium Ions (Hypocalcaemia)

- **Nerve fiber → Highly excitable**
- **Discharging → Repetitively**
- **Without provocation**
- **Rather than remaining in resting state**

Calcium Ions falls 50% below normal

- Spontaneous discharge in peripheral nerves

Calcium Ions falls 50% below normal

- **Often causing muscle "Tetany"**
- **Lethal → Death**
- **Tetanic contraction of the respiratory muscles**

Propagation / Conduction of Action Potential

- **The nerve cell membrane is polarized at rest**
- **Positive charges lined up along the outside**
- **Negative charges lined up inside the membrane**

During Action potential

- **Polarity is abolished**
- **For a brief period**
- **It is reversed**

Nerve fiber is excited in its mid portion

- Positive charges of the membrane
- Ahead of and behind the action potential flow
- Into the area of negativity
- Represented by the action potential (Current sink)

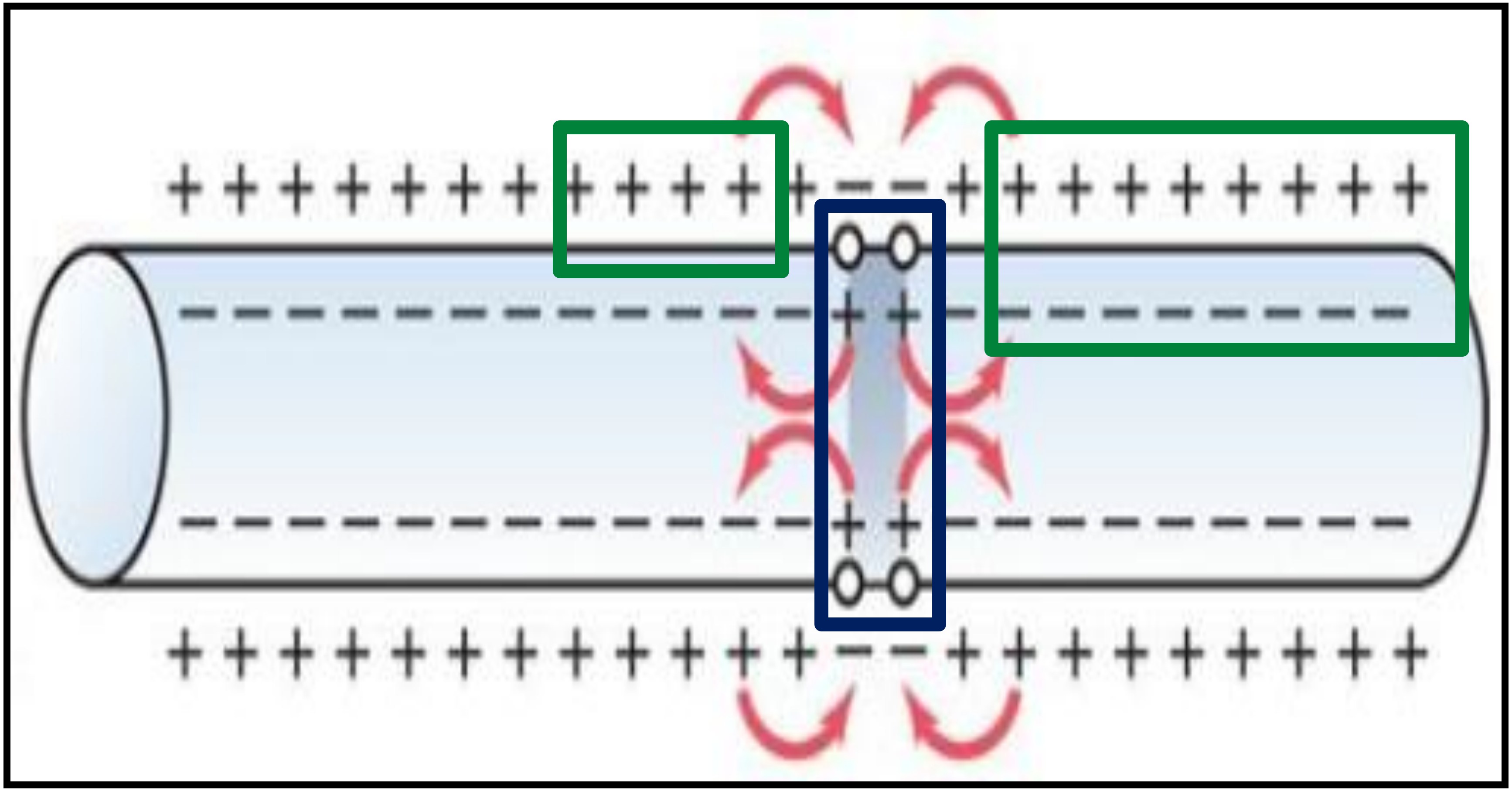
Nerve fiber is excited in its mid portion

- **Arrow → "Local circuit" of current flow**
- **Between**
- **The depolarized areas of the membrane**
- **Adjacent resting membrane areas**

Propagation / Conduction of Action Potential

- **Drawing off positive charges flow**
- **Decreases the polarity of the membrane**
- **Ahead of the action potential**

Propagation / Conduction of Action Potential

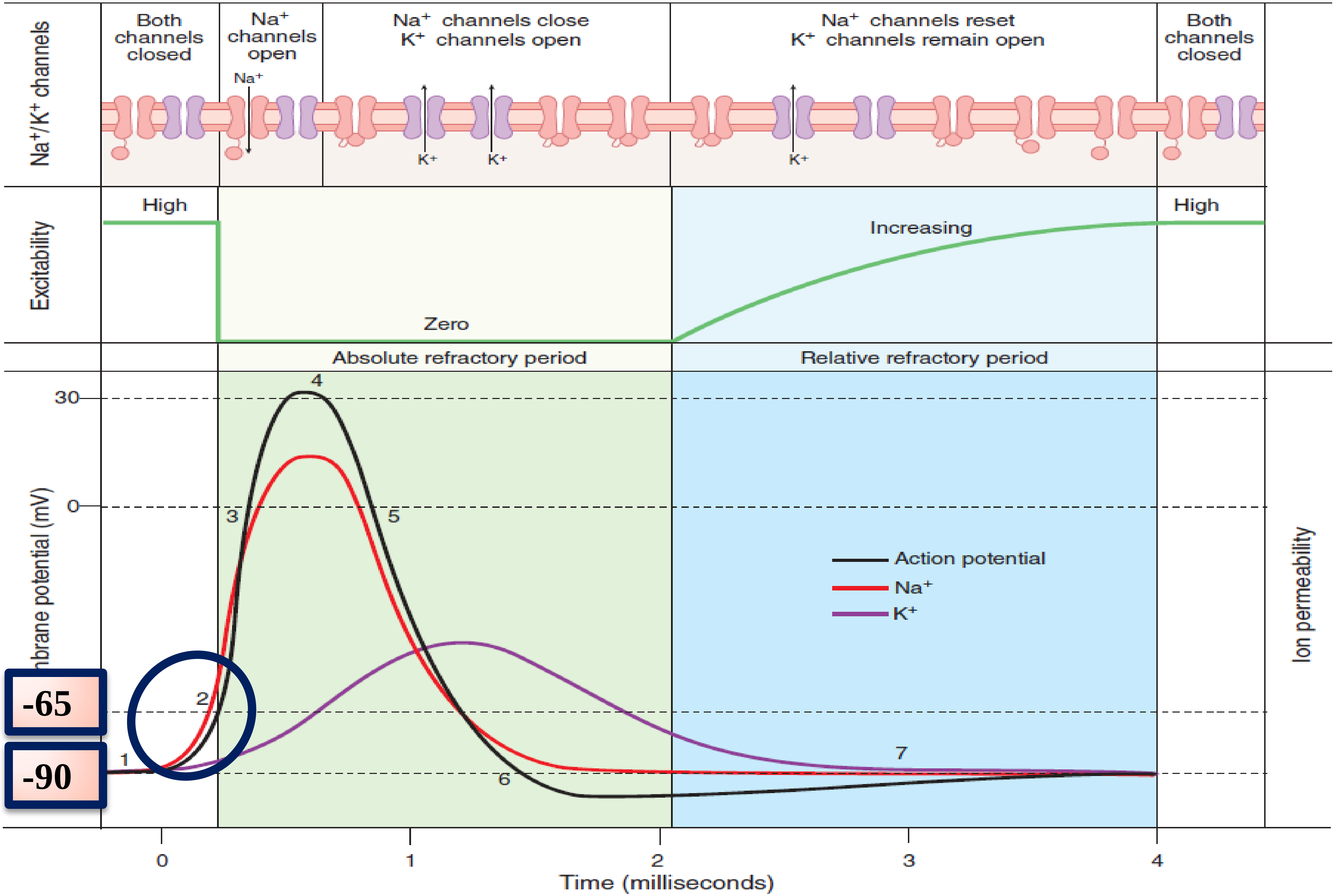


Local response

- **Subthreshold stimulus**
- **Do not produce an action potential**
- **Do have effect on the membrane potential**

Threshold for initiation of Action potential

- Level of
- - 65 mV
- Threshold for stimulation


Na+/K+ channels
Both channels closed
Na+ channels open
Na+
Na+ channels close
K+ channels open
K+
K+
Na+ channels reset
K+ channels remain open
K+
Both channels closed
Excitability
High
Zero
Increasing
High
Absolute refractory period
Relative refractory period
30
0
4
3
5
2
1
6
7
Action potential
Na+
K+
Ion permeability
-65
-90
0
1
2
3
4
Time (milliseconds)

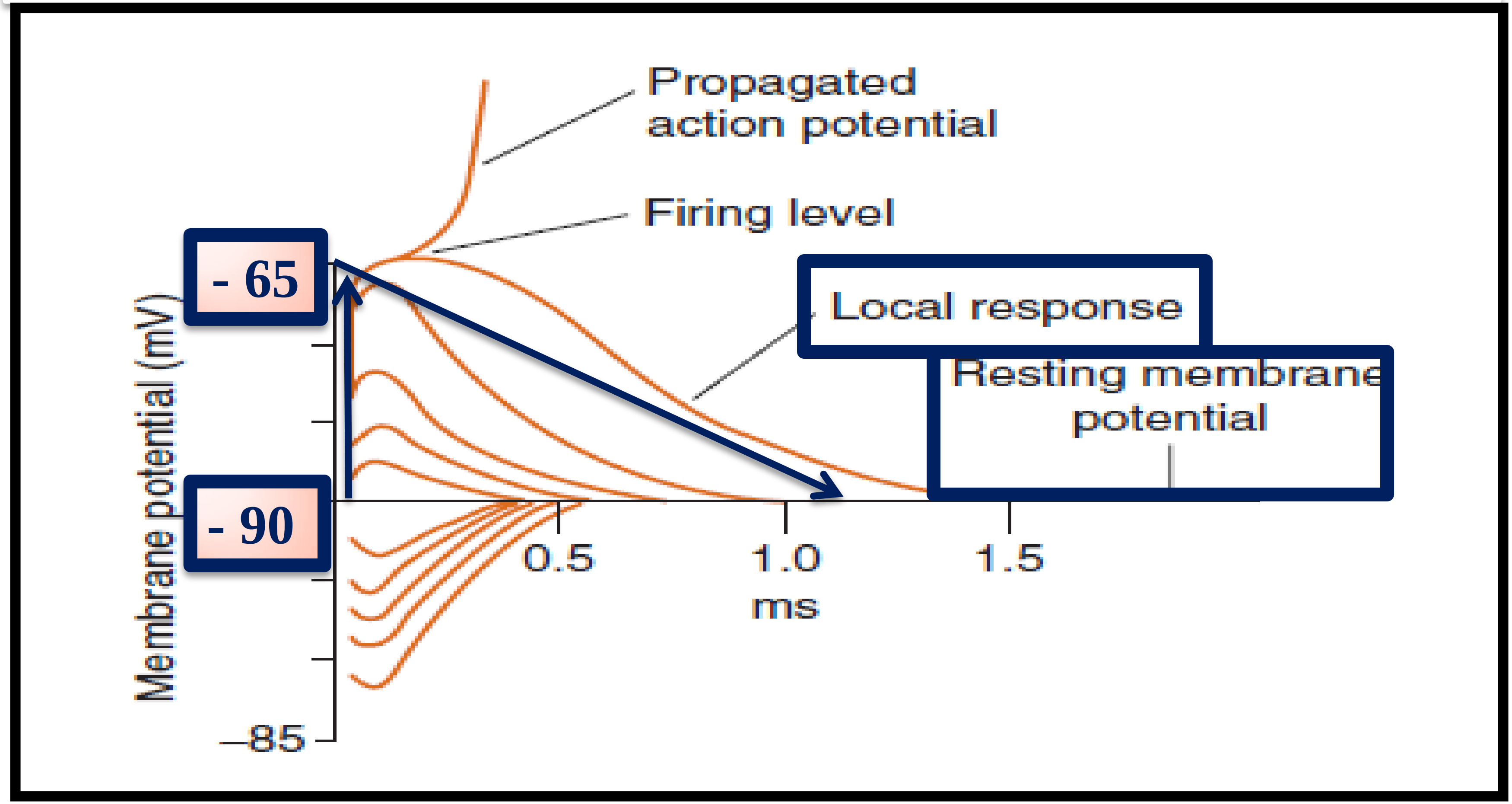
Local response

- Placing → Recording electrodes
- Within
- The few millimeters of → A stimulating electrodes
- Apply Subthreshold stimulus of fixed duration

Local response

- **Such currents**
- **Leads to ➔**
- **Localize depolarizing potential change**
- **Rises sharply**
- **Decays exponentially with time**

Local response



Local response

- **Magnitude of this response to Subthreshold Stimulus**
- **Drops off rapidly**
- **As the distance between the**
- **Stimulating and recording electrodes is increased**

Electrical potentials

- **Anodal current produce**
- **A hyperpolarizing potential change**
- **Similar change**
- **Known as Electrical potentials**

Firing level

- **As the strength of the current → Increased**
- **The response is → Greater**
- **Due to the increasing strength in addition of the**
- **Local response of the membrane → Firing level**

Firing level → - 65mV

- At 25 mV of depolarization
- Potential of - 65mV (- 90mV + 25mV = - 65 mV)
- The firing level (Threshold potential)
- An action potential occurs

Propagation / Conduction of Action Potential

- **Electronic depolarization**
- ***Initiates*** **➔ A local response**
- **When firing level is reached ➔**
- ***Propagated response occurs***

Initiation and Regulation of Action Potential

- **Spatial distribution of ion channels**
- **Along the axon**
- **Key role**

Voltage gated Na^{+} Channels

- **Highly concentrated in →**
- **The Nodes of the ranvier**
- **Initial segment in → Myelinated neurons**

Spatial Distribution of Na^+ Channels

- **Number of**
- **Na^+ channels per square micrometer**
- **Of membrane**
- **Myelinated mammalian neurons**

Spatial Distribution of Na^+ Channels

- 50-70 ➔ Cell body
- 350-500 ➔ In Initial segment
- < 25 on the Surface of the myelin
- 2000-12,000 at the Node of Ranvier
- 20-75 at the Axon terminals

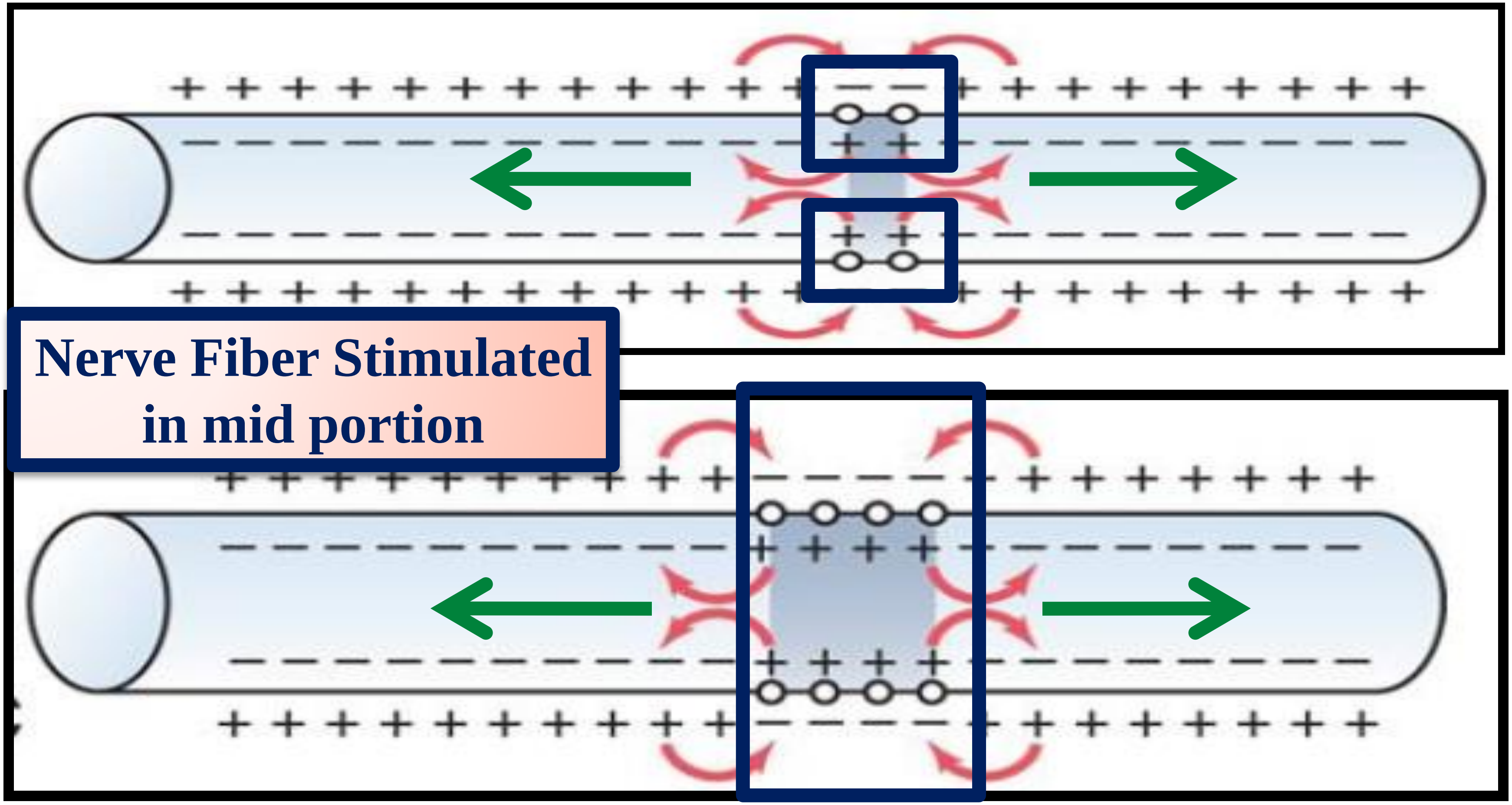
In Unmyelinated Neurons: Na^+ Channels

- **Number of Na^+ channels per square micrometer**
- **Of membrane axons of Unmyelinated neurons**
- **110**

Initiation and Regulation of Action potential

- **Positive electrical charges are carried by**
- **Inward diffusing Sodium (Na^+) ions**
- **Through depolarized membrane several millimeters**
- **In both the direction along the core of the axon**

Initiation and Regulation of Action potential



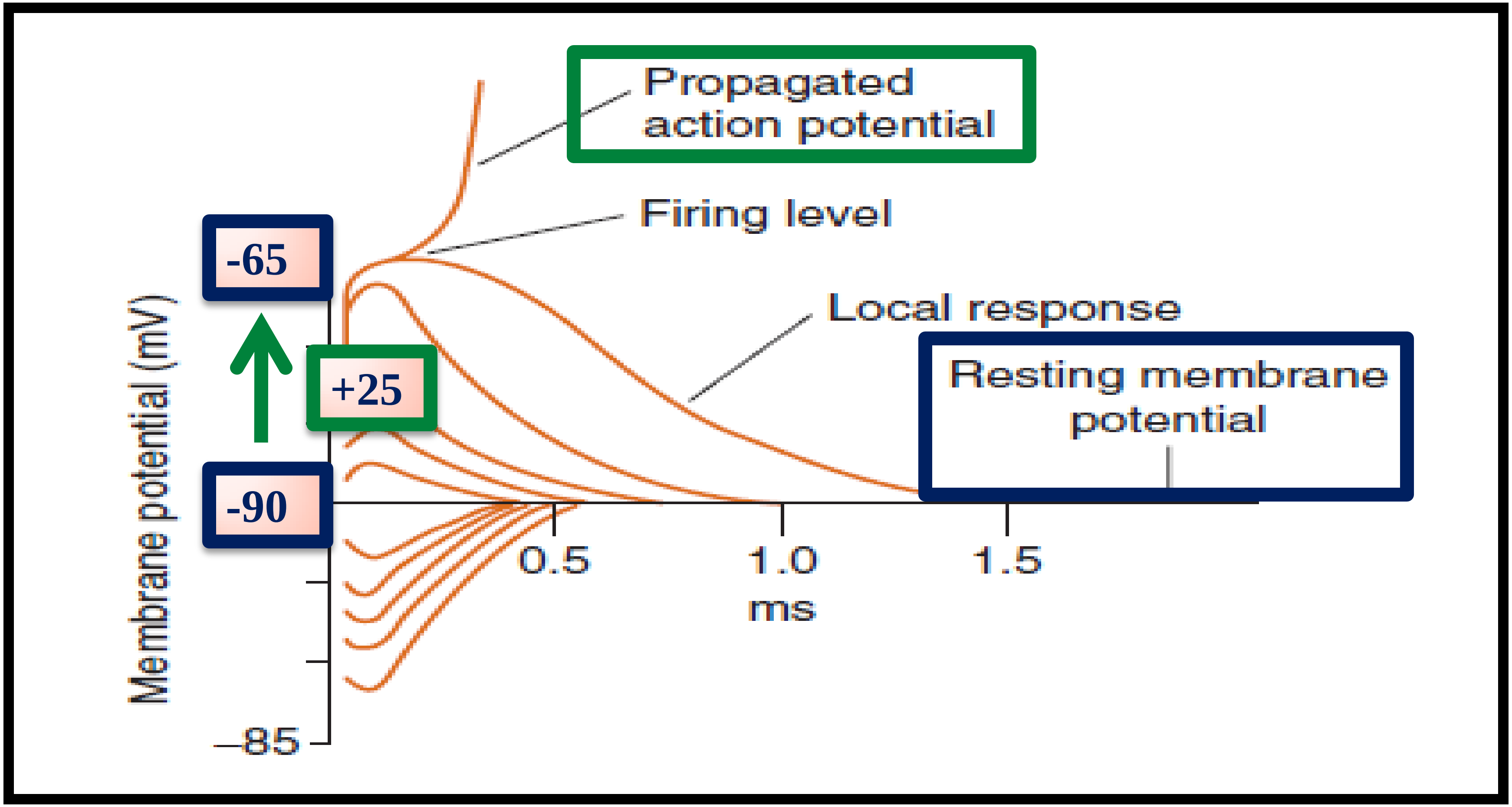
Initiation of Action Potential

- **Positive charges increase the voltage**
- **For distance of 1 to 3 mm**
- **Inside → The large myelinated fiber**

Initiation of Action Potential

- **Voltage increased**
- **To above threshold voltage (- 65mV)value**
- **For → Initiating action potential**

Initiation of Action Potential



The Sodium channels in new areas

- **Immediately open**
- **Explosive action potential → Spread**

New depolarized areas produces

- **Still more → Local circuits of Current flow**
- **Progressively more and more depolarization**
- **Along the membrane**

Depolarization process travels →

- **Along**
- **The entire length of the fiber**

Nerve or Muscle Impulse

- **Transmission of the depolarization process**
- **Along**
- **The nerve or muscle fiber**
- **Is called → Nerve or Muscle Impulse**

Direction of propagation

- **No single direction of propagation**
- **Action potential travels in all directions**

Direction of propagation

- **Away from the stimulus**
- **Along all the branches of a nerve fiber**
- **Until entire membrane is depolarized**

All-or-Nothing Principle

- **Once action potential elicited**
- **At any point on the membrane of a normal fiber**

All-or-Nothing Principle

- **Depolarization process travels**
- **Over the entire membrane**
- **If conditions are right**

All-or-Nothing Principle

- Or it might not travel at all
- If conditions are Not right
- Known as All-or-nothing principle

“Safety factor” for propagation

- Occasionally
- Action potential reaches
- A point on the membrane at which it

“Safety factor” for propagation

- Dose not generate
- Sufficient voltage
- To stimulate the next area of the membrane

“Safety factor” for propagation

- **When this occurs**
- **The spread of depolarization ➔ Stops**

"Safety factor" for propagation

- **Continued propagation of an impulse to occur**
- **The ratio of**
- **Action potential to Threshold for excitation**

“Safety factor” for propagation

- Must at all time be greater than 1(>1)
- >1 requirement is called
- “Safety factor” for propagation

Applied Physiology: Local Anesthetics

- **Ester-linked :**
- **Cocaine**
- **Procaine**
- **Tetracaine**

Applied Physiology: Local Anesthetics

- **Amide-linked:**
- **Lidocaine**
- **Bupivacaine**

Applied Physiology: Local Anesthetics

- **Aromatic group:**
- **Drug's hydrophobic characteristics**

Applied Physiology: Local Anesthetics

- **Amide group:**
- **Latency to onset of action**
- **And potency**

Applied Physiology: Anesthetics

- **Local or regional anesthesia is used to**
- **Block the conduction of action potential**
- **In Sensory and Motor nerve fibers**

Applied Physiology: Anesthetics

- **Act directly**
- **On**
- **The Activation gates of the sodium channels**

Applied Physiology: Anesthetics

- Make difficult for the gates to open
- Reducing
- The membrane excitability

Applied Physiology: Anesthetics

- **Gradually**
- **Increase the threshold**
- **For electrical excitability of the nerve**

Applied Physiology: Anesthetics

- **So Low that → Ratio of**
- **Action potential strength**
- **To excitability threshold (Safety factor)**
- **Is reduced below 1.0**

"Safety factor" for propagation

- Ratio
- Action potential to
- Threshold for excitation

>1
For
Continued
propagation

Applied Physiology: Anesthetics

- **Nerve impulses**
- **Fail to pass through**
- **The anaesthetized nerves**

Applied Physiology:
Membrane Stabilizers

- **Membrane-stabilizing factors**

- **Decrease ➔ The excitability**

Applied Physiology: Stabilizers

- **A High extracellular fluid (ECF)**
- **Calcium (Ca^{2+}) ion concentration ➔**
- **Hypercalcaemia**
- **Normal ECF [Ca^{2+}] = 9 to 11mg/dl**

Applied Physiology: Stabilizers

- **High ECF [Ca^{2+}]**
- **Decrease the membrane permeability to Na^{+} ions**
- **Reduce excitability**
- **Ca^{2+} ions called → Stabilizers**

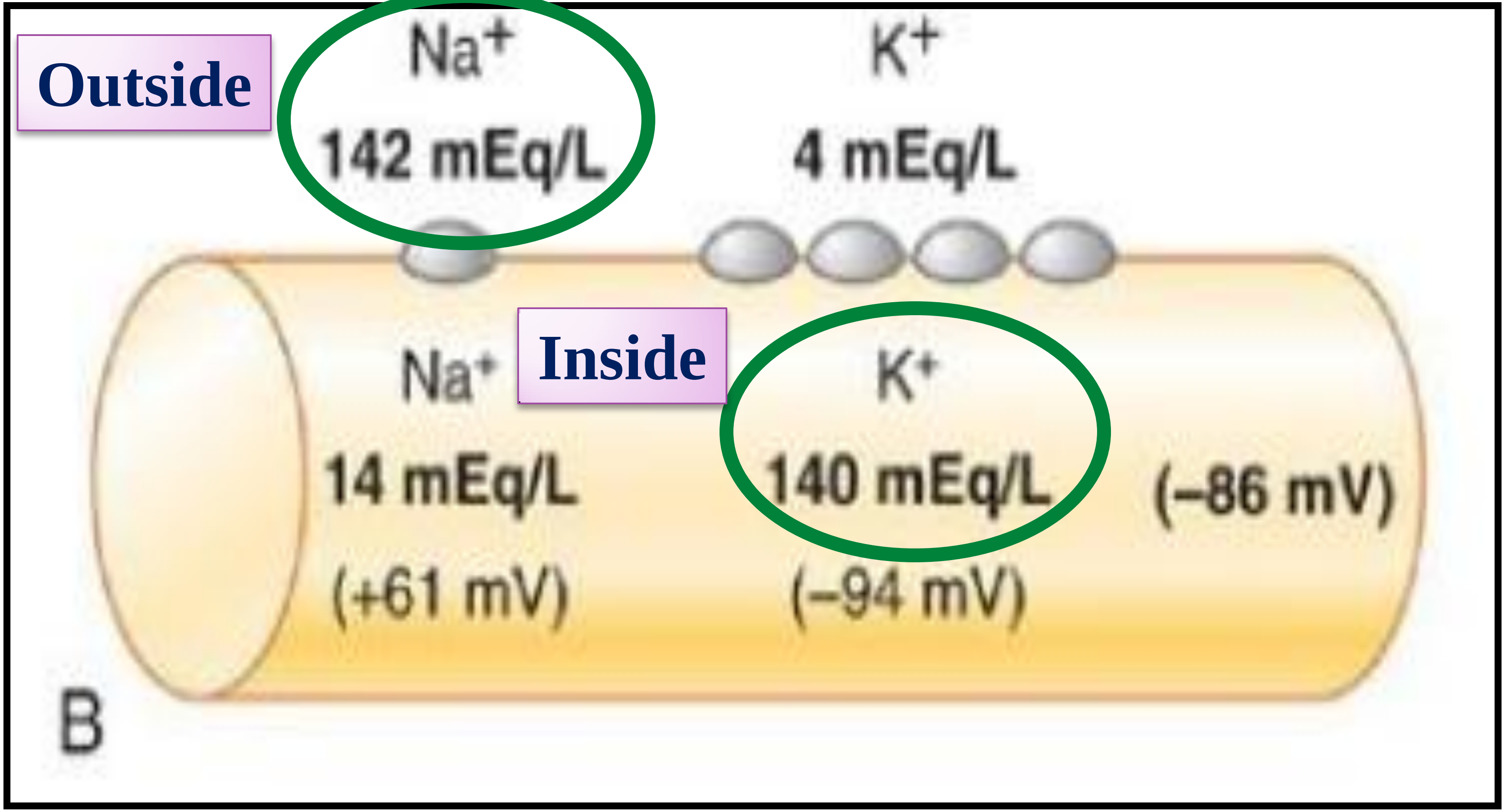
Role of Calcium Ions

- **$[Ca^{2+}]$ in ECF → Effect on the voltage level**
- **At which the Na^{+} channels become activated**
- **Hypocalcaemia →**
- **Nerve fiber → Highly excitable**

Re-establishing Na^+&K^+ Ionic Gradient

- **Concentration differences of Na^+ and K^+**
- **Between inside and outside of the membrane**
- **Diffusion of Na^+ ions to inside → Depolarization**
- **Diffusion of K^+ ions to outside → Repolarization**

Concentration differences of Na^+ and K^+



Re-establishing Na^+&K^+ Ionic Gradient

- **Action potential conduction ceases**
- **With time**
- **If Na^+ & K^+ concentration difference**
- **Not re-established**

Re-establishing Na^{+}& K^{+} Ionic Gradient

- **Re-establishing the gradient**
- **Achieved by Na^{+}-K^{+} pump**
- **Primary Active Transport**
- **This pump requiring the energy (ATP)**

Re-establishing Na^{+}&K^{+} Ionic Gradient

- **Process of Recharging the nerve fiber**
- ***Active metabolic one***
- **Use energy derived from ATP energy system of the cell (Mitochondria)**

Re-establishing Na^+&K^+ Ionic Gradient

- **Heat production**
- **Is measure of energy expenditure**
- **Heat production →Excess**
- **When Impulse frequency →Increases**

Na^+- K^+ ATPase pump

- Na^+-K^+ ATPase pump
- Degree of activity → Stimulated strongly
- When excess sodium ions accumulate
- Inside the cell membrane

Na^+- K^+ ATPase pump: Activity increase

- **Pumping activity of Na^+-K^+ pump increasing**
- **Approx in proportion to ICF =$[Na^+]^3$**
- **3rd power of intracellular Na^+ concentration**

Na^+ Concentration rises → 10-20mEq/L

- Na^+ concentration rises
- 10 to 20 mEq/L
- The pumping activity of Na^+-K^+ pump increases 8 folds

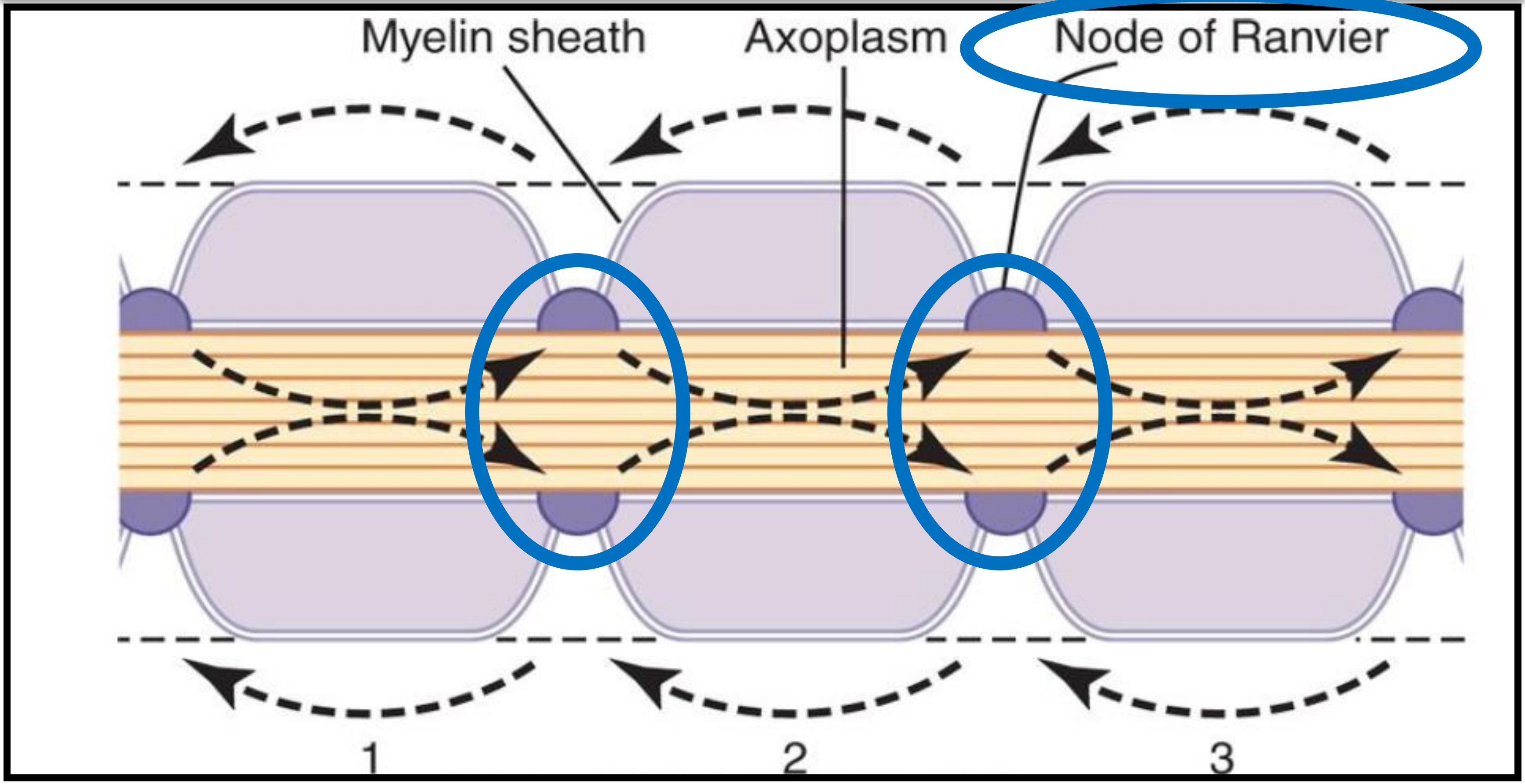
Saltatory Conduction

- **No ions can flow through the thick myelin sheaths**
- **Of myelinated nerve fibers**
- **Ions can *flow with ease through***
- **The *nodes of Ranvier***

Saltatory Conduction

- **Action potential can occur**
- **Only at the nodes Ranvier**
- **Action potentials are conducted from node to node**

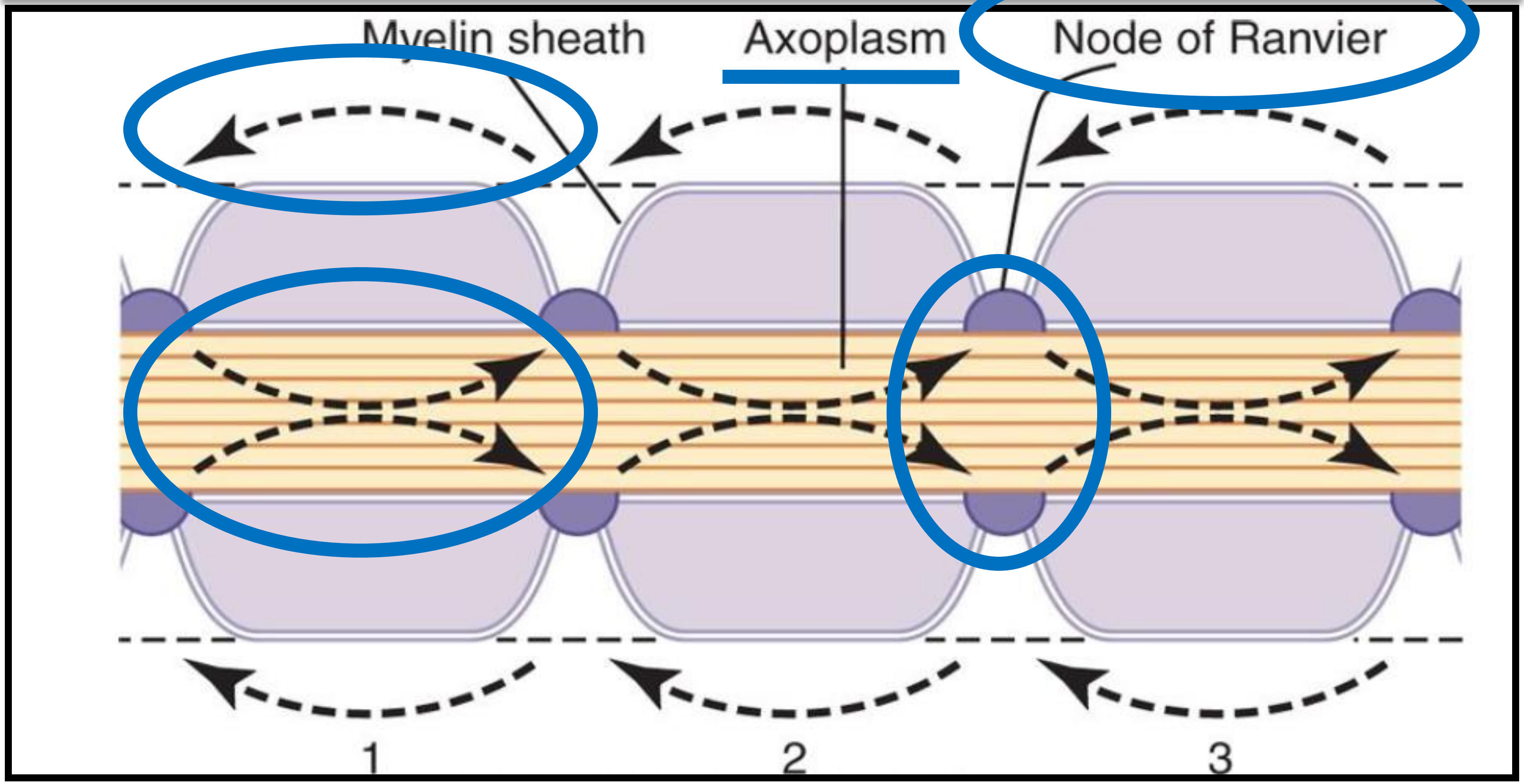
Saltatory Conduction



Saltatory Conduction

- **Electrical current flows through**
- **Surrounding ECF outside the myelin sheath**
- **As well as through the axoplasm inside the axon**
- **From node to node**

Saltatory Conduction



Saltatory Conduction

- **Exciting the successive nodes**
- **One after another**
- **Thus, Nerve impulse jumps <u>down the fiber</u>**
- **Which is <u>the origin of the term </u>"Saltatory"**

Saltatory Conduction: Importance

- **Depolarization process**
- **Jump long intervals**
- **Along the axis of the nerve fiber**

Saltatory Conduction

- **Conduction of nerve impulse**
- **In myelinated nerve fiber is accomplished**
- **Almost entirely**
- **By ion conduction through the**
- **Voltage –gated sodium (Na^+) channels**

Saltatory Conduction

- **Conduction of nerve impulse**
- **Little contribution by**
- **Potassium (K^+) channel**

Saltatory Conduction: Importance

- Increases the velocity of nerve transmission
- In myelinated nerve fiber
- As much as 5- fold to 50-fold

Saltatory Conduction: Importance

- Saltatory conduction is rapid process
- Myelinated axon conduct up to 50-times faster
- Than fastest unmyelinated fibers

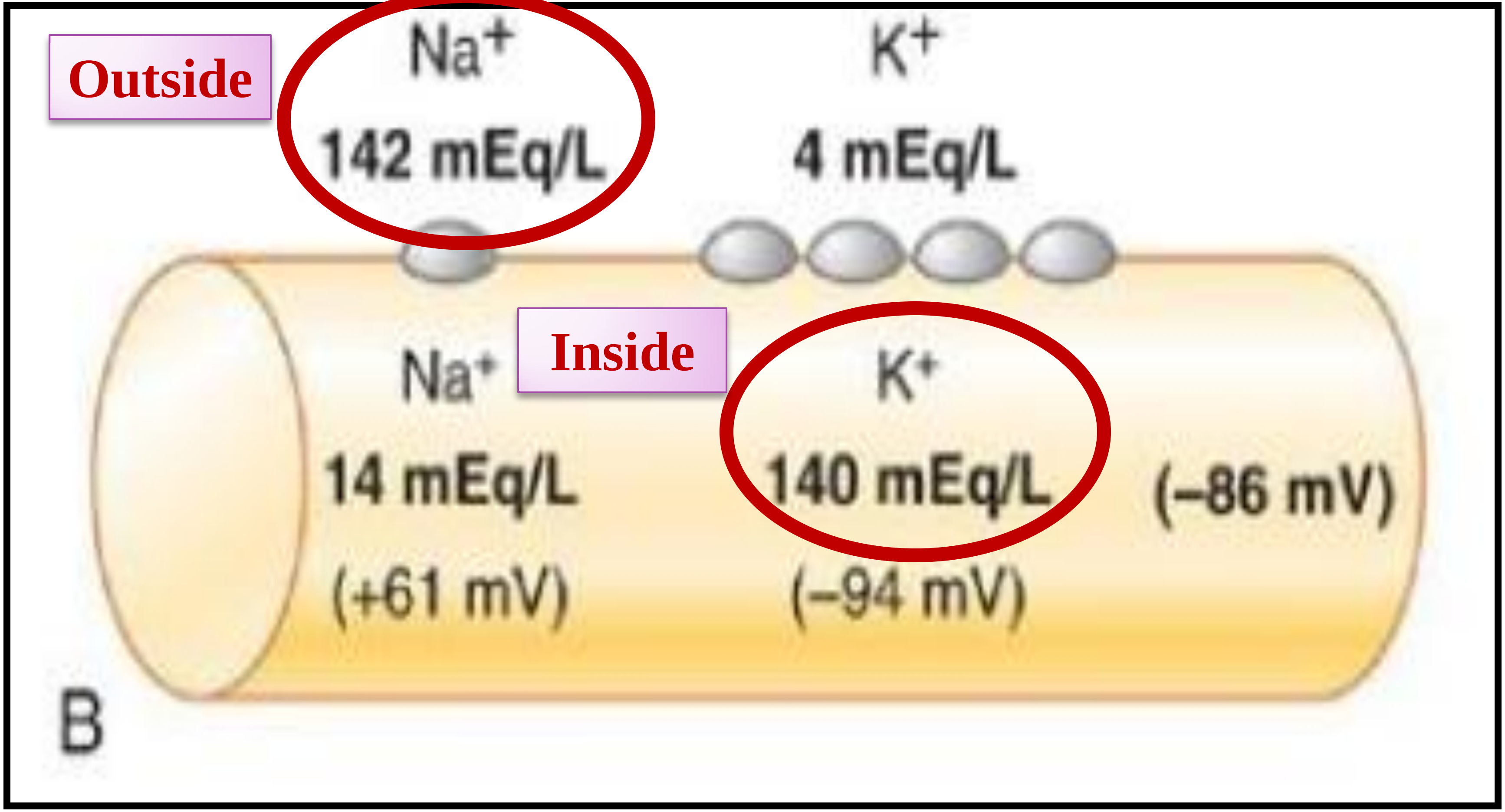
Saltatory Conduction: Importance

- Conserves the energy for the axon
- Because only the nodes depolarizes
- 100 times less the loss of ions need otherwise

Saltatory Conduction: Importance

- **Requiring little metabolism**
- **For reestablishing the Sodium (Na^+) and Potassium (K^+) concentration differences**
- **Across the membrane**
- **After a series of nerve impulses**

Concentration differences of Na^+ and K^+



Saltatory Conduction: Importance

- 50-fold decrease in membrane capacitance
- In large myelinated nerve fibers:
- Excellent insulation by myelin membrane

Saltatory Conduction: Importance

- Repolarization occur with little transfer of ions
- At the end of action potential
- When Sodium (Na^+) channels begin to close

Saltatory Conduction: Importance

- Repolarization occurs so rapidly
- That many of the Potassium (K^+) channels
- Have not yet open

Comparison

Local potential	Action potential
1. Nature of stimulus – Subthreshold	1. Nature of stimulus– Threshold or Suprathreshold
2. Type of potential change	2. Type of potential change
▫ Graded	▫ Fixed amplitude ▫ All or nothing principle

Comparison

Local potential	Action potential
2. Type of potential change ▫ May be positive Depolarization, Excitatory ▫ May be negative Hyperpolarization Inhibitory	2. Type of potential change ▫ Always positive ▫ Depolarization

Comparison

Local potential	Action potential
3. **Propagation –**	3. **Propagation –**
▫ Conducted over short distance with a reduction in magnitude of potential	▫ Conducted over the entire cell membrane

Comparison

Local potential	Action potential
4. **Summation** ▪ Can be summated	4. **Summation–** ▪ Can <u>not</u> be summated

Short notes: 4 Marks

- **Action potential in myelinated nerve fiber**
- **Saltatory conduction**
- **Action potential in a nerve**

Attend Your Roll Call

Short notes: 4 Marks

- **Action potential in myelinated nerve fiber**
- **Saltatory conduction**
- **Action potential in a nerve**