Nerve Action Potential and Properties of Nerve Fibers

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دكتوراه في علم وظائف الأعضاء السريري (بريطانيا)

عضوية الجمعية الأمريكية للفحوصات الكهربائية للمخ و الأعصاب و العضلات (الولايات المتحدة الأمريكية)

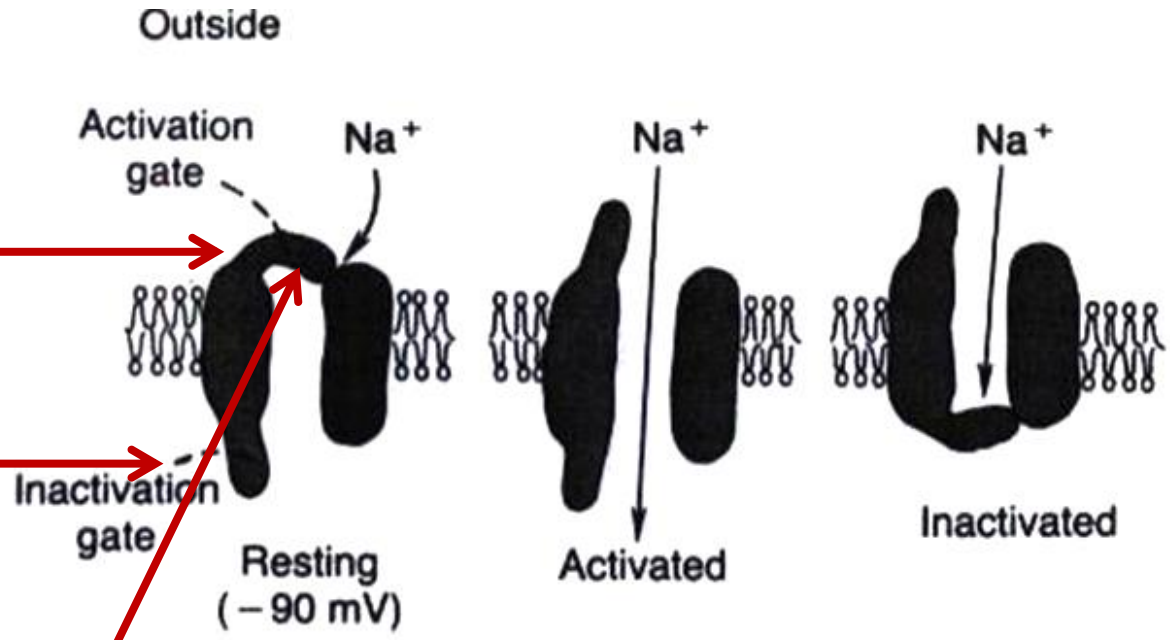
إستشاري تخطيط المخ و الأعصاب (الهيئة السعودية للتخصصات الطبية)

عضو الأتحاد العالمي لمكافحة و علاج الصرع

عضو الأتحاد العالمي للعلوم العصبية

The Voltage-Gated Na+ 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 : وهذه القناة لها ثلاثة حالات



- (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.

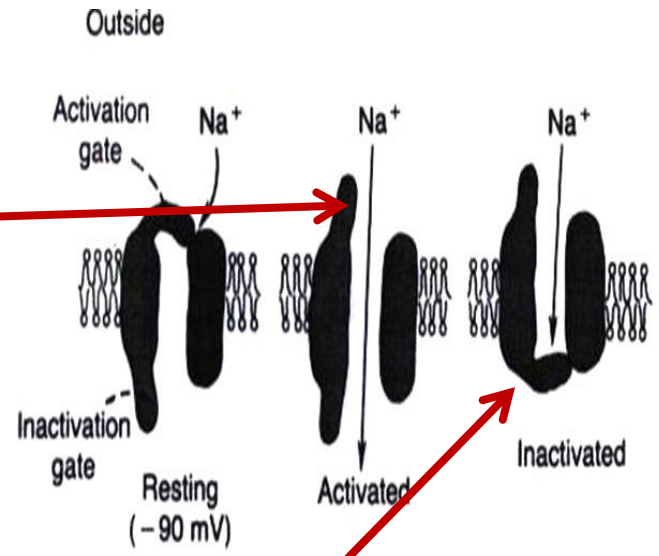
Activated State of Sodium Channel

(2) Activated state : when a Threshold Depolarizing Stimulus 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 open) →
- permeability to Na+ becomes increased 500 to 5000 times → Na+ influx
- N+ flows into the cell in large amounts , depolarizing it more & more , until there is reversal of MP .

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

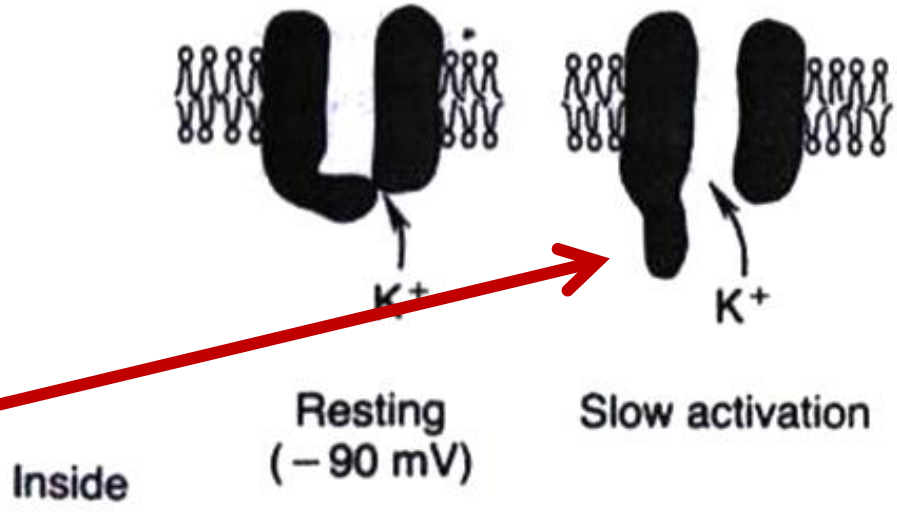
- → in this case , while the activation gate is still open , the inactivation gate is closed



After the AP , 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).

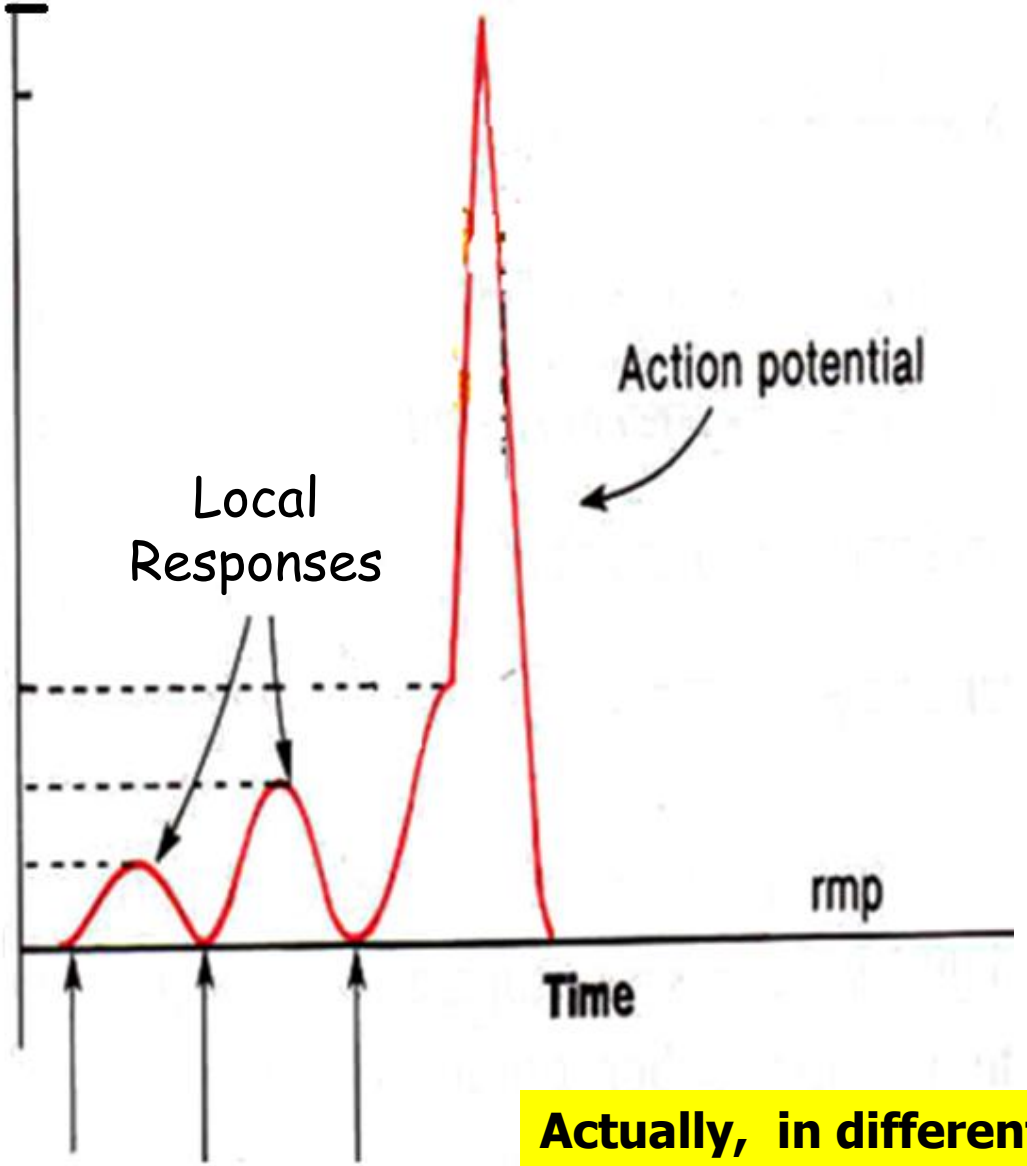
The Voltage-Gated Potassium Channel

- Has one gate only .
- During the resting state , the gate of the potassium channel is closed , and K+ can not pass through it .
- Shortly after depolarization , when the sodium channel begins to be inactivated , the potassium channel opens .
- → K+ exits (called K+ Efflux) → Repolarization



Reversal Potential
= + 35 -40 mV

Reversal Potential
= + 35 to +40 mV



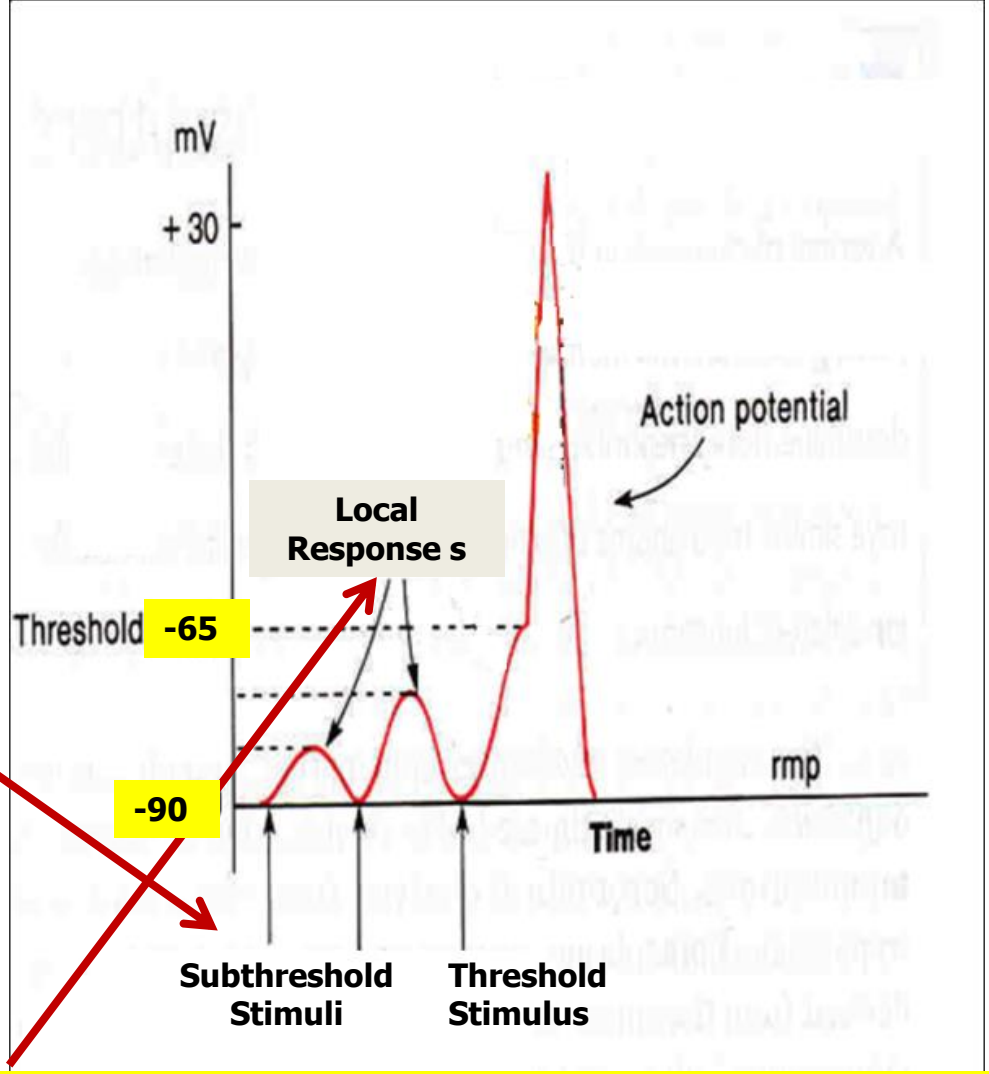
Threhold
Potential (Firing Level)
= -65 mV

RMP= -90 mV

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

Actually, in different nerve cells , threshold ranges between -50mV and -65 mV

- Q : What is a Subthreshold Stimulus ?
- A : it is a weak stimulus, not strong enough to carry the MP to the Threshold Level
- i.e., it may depolarize the membrane to less than threashold level → fails to produce AP , and can produce only Local Response



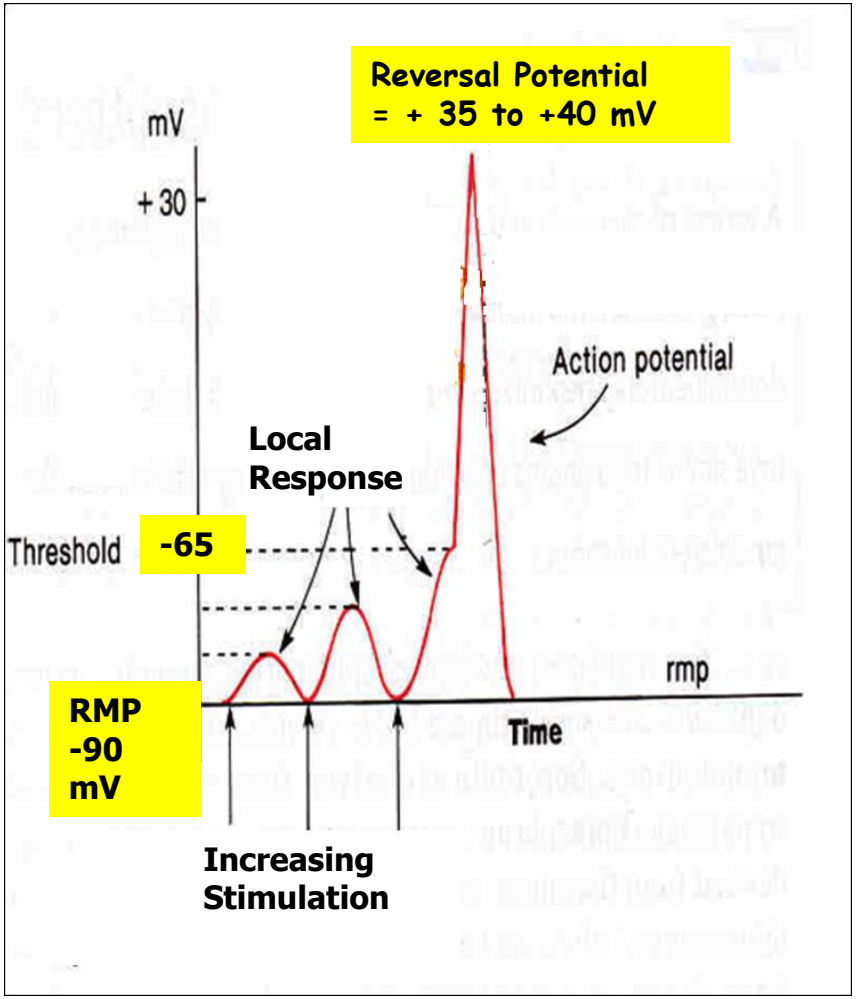
Q : What is a Threshold Stimulus ?
A : it is a stimulus strong enough to depolarize the membrane & move the MP to Membrane Threshold Level = -50 to -65 mV Which is the firing level at which the Action Potential is triggered

Graded Potential (Local Response) :

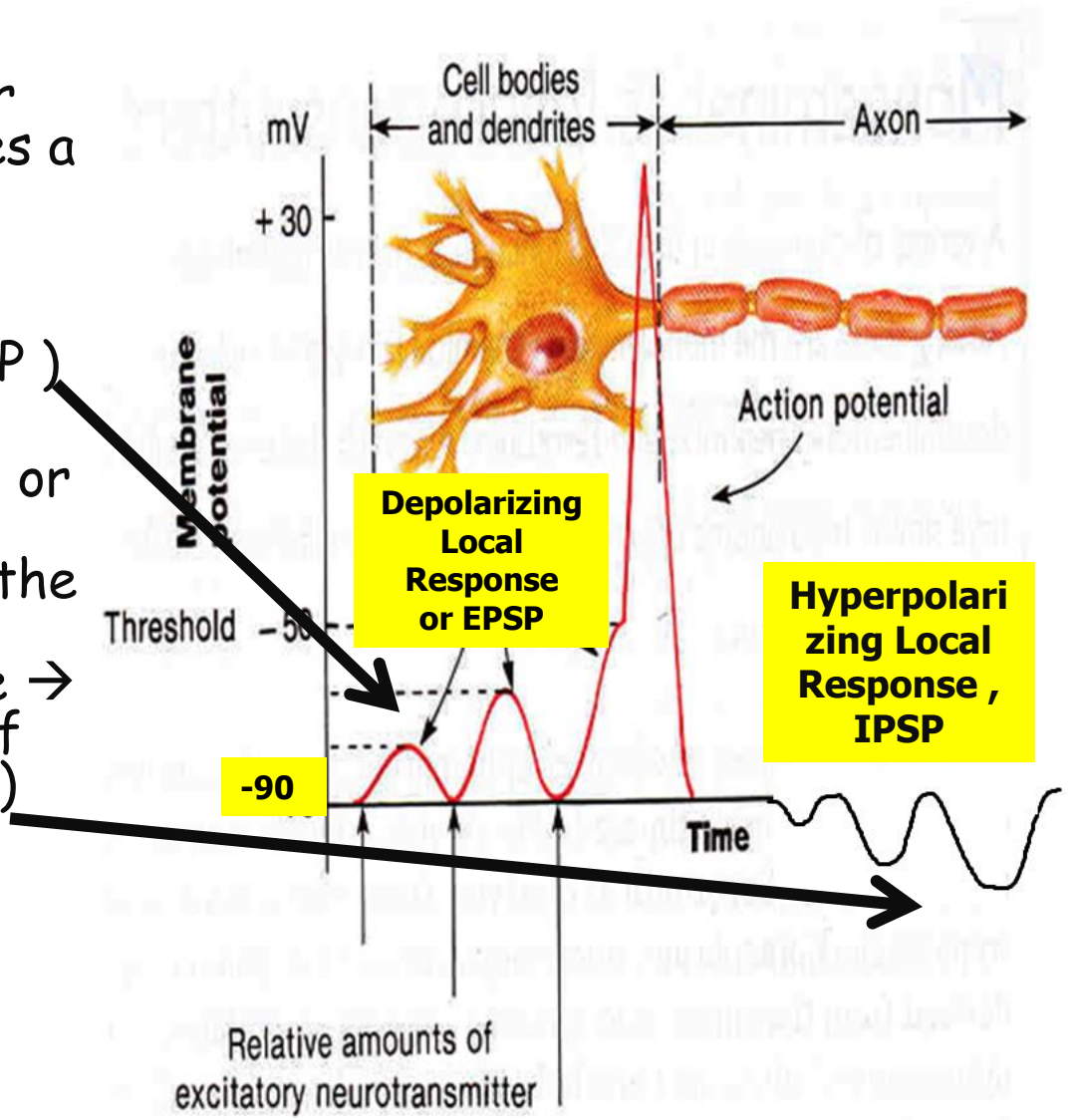
- ✓ Stimulation of the neuron by a weak subthreshold stimulus produces a local, non-propagated potential which is measurable only in the immediate vicinity of stimulated point , but not farther than that .
- ✓ It does not obey All-or-None Law

Action potential (AP) :

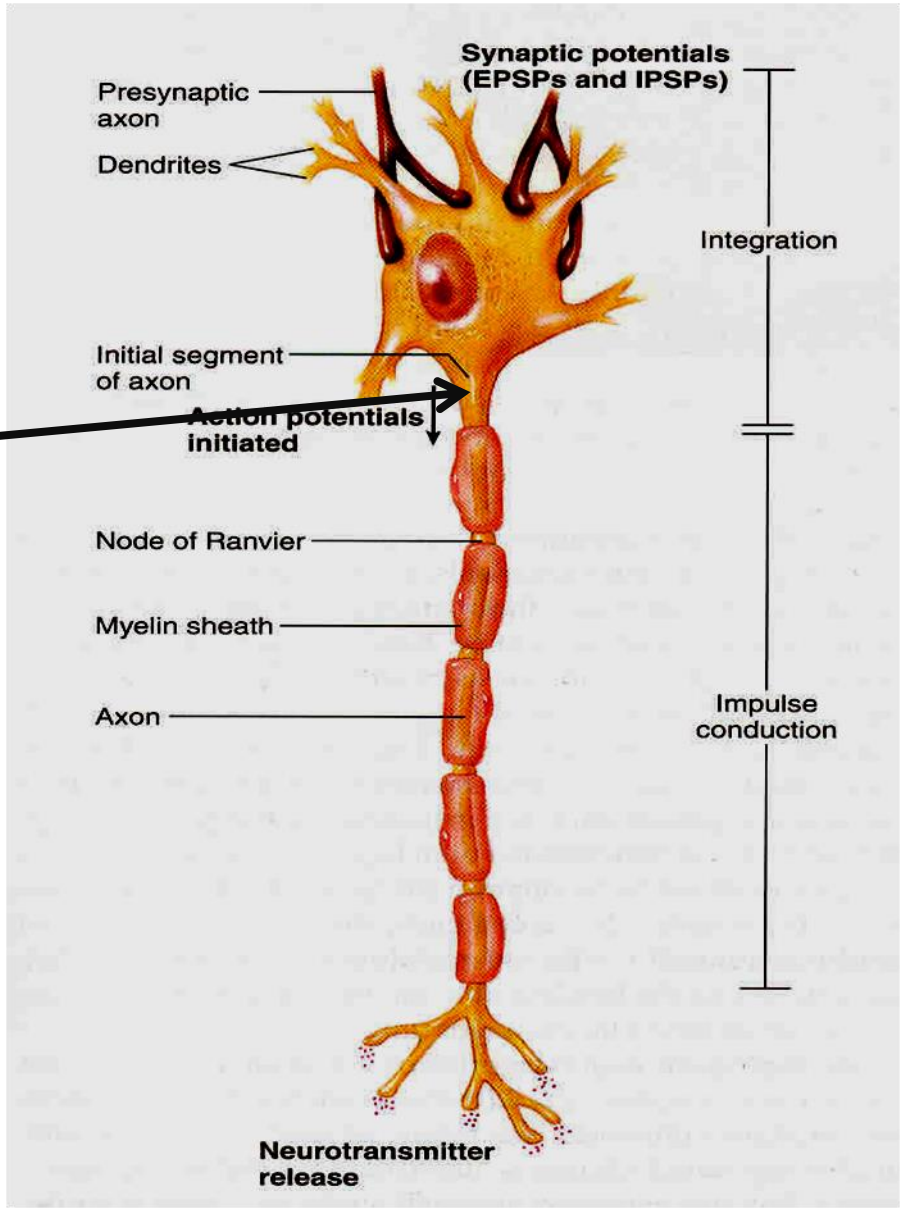
- ✓ AP is the MP value in case of a cell that is generating a propagated electrical potential
- ✓ It can be measured anywhere along the nerve
- ✓ It obeys All-or-None Law
- • At the peak of the AP , the value of the MP reaches +35 to +40 mV



- In case of local responses :
- (a) If the stimulation is excitatory (opening sodium or calcium channels) , it produces a depolarizing local response → which makes the inner side of the membrane less negative (reduces , depolarizes the MP)
- (b) If the stimulation is inhibitory (opening potassium or chloride channels) , it →increases , hyperpolarizes the membrane → producing a hyperpolarizing local response → (which makes the inner side of the membrane more negative)
- And makes the cell more difficult ton excite .
- **At synapses , where neurotransmitters mediate opening of channels , (a) mentioned above is called Excitatory Postsynaptic Potential (EPSP) , and (b) is called Inhibitory Postsynaptic Potential (IPSP) .**

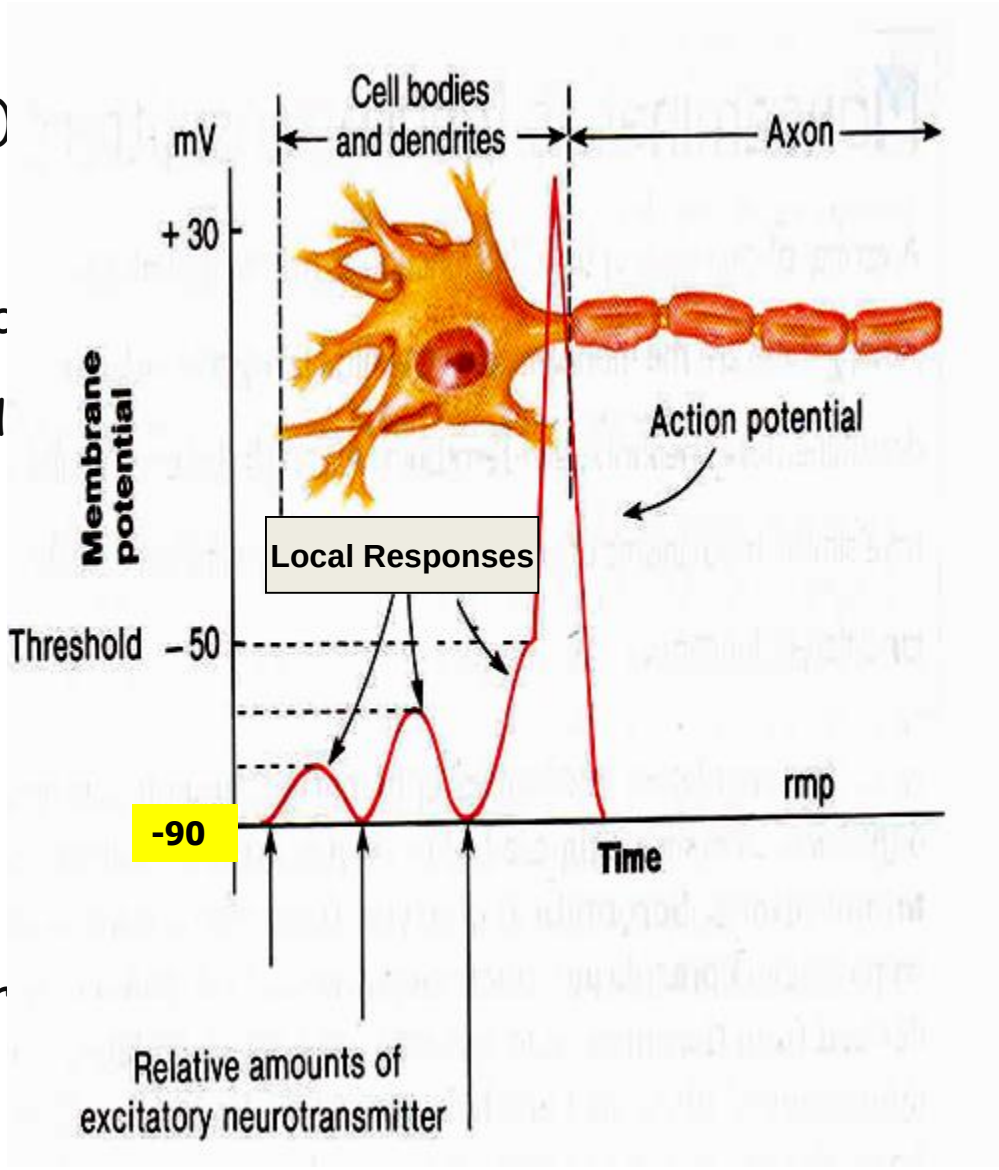


- In all above cases the -ve or +ve sign refers to the inside of the membrane .
- In nerves , the AP is generated at the initial segment of the axon , which is called <u>Axon hillock</u>
- but , by contrast , a local responses can be generated at any membrane area if the stimulation is sufficient



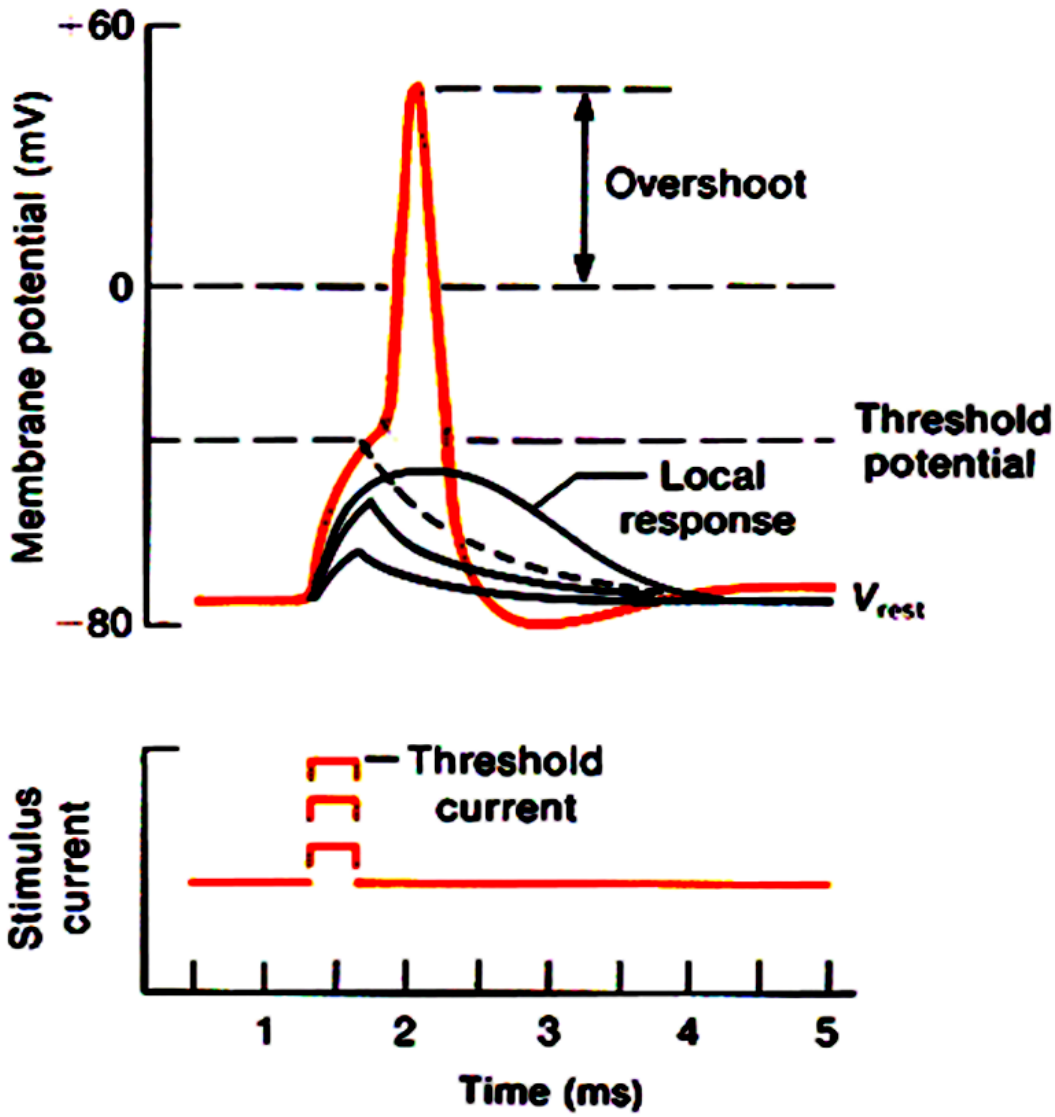
- **Summary :**

- A/ When the cell is inactive (resting) → we call the MP : Resting Membrane Potential (RMP) .
- B/ When the cell is stimulated weakly by subthreshold stimulus → a small number of voltage-gated channels open → we get only stim a Local Response (which is graded and does not propagated).
- C/ However , if the stimulus is Threshold Stimulus i.e., strong enough to carry the MP to its Threshold Level → it opens many voltage-gated sodium channels open → and action potential (AP) is generated .
- The AP differs from local response in that it is (1) not graded obeys All-or None Law) , and (2) propagated (conducted for long distances .



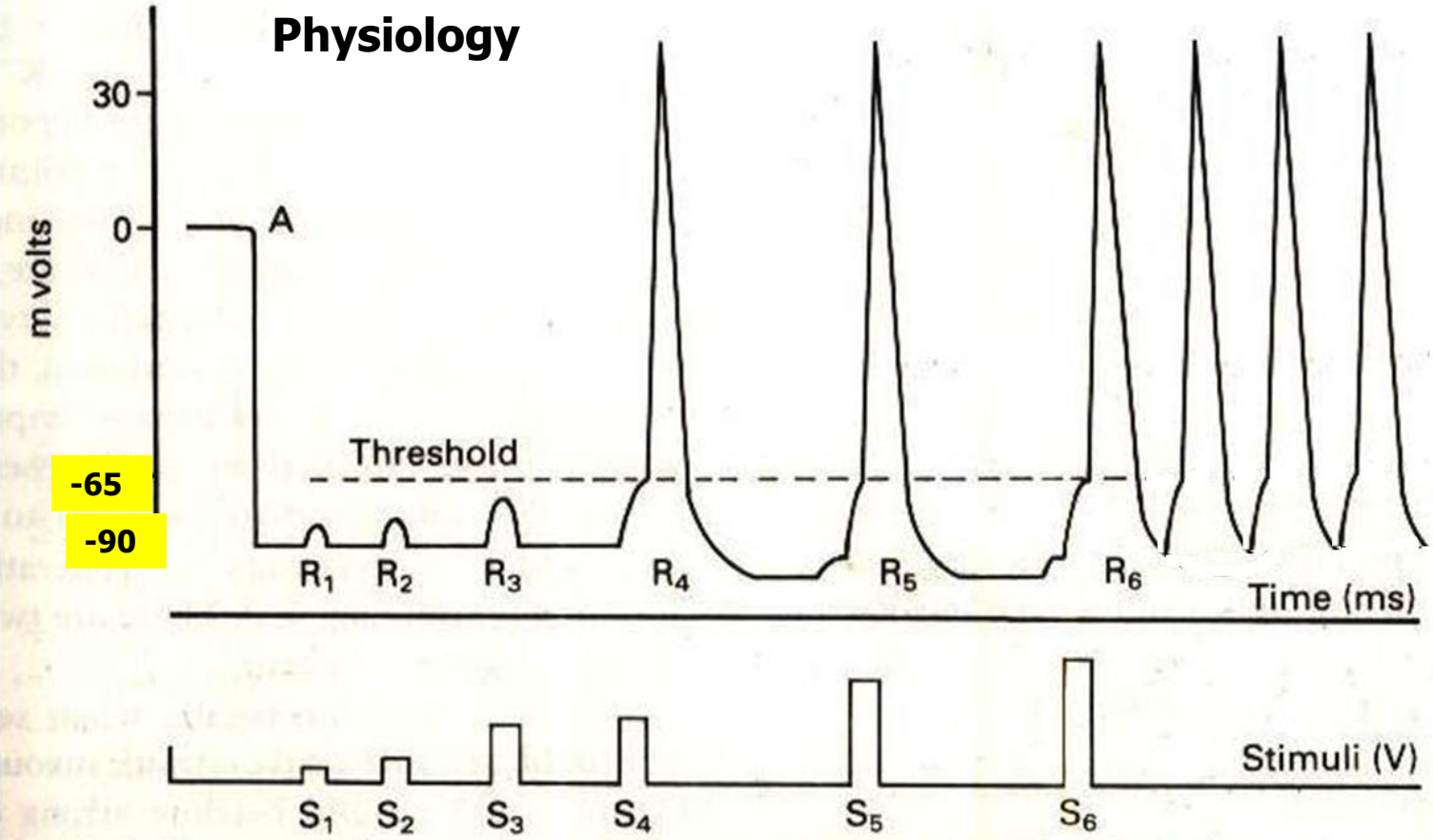
AP obeys All-or-None Law

Local Respnse does <u>NOT</u> obey All-or-None Law



Action potential produced by a nerve cell membrane in response to a depolarizing stimulus that brought the membrane to the threshold potential. Smaller polarizations failed to evoke the all-or-none response.

Reference : Taha S Ahmed in Concise Human Physiology



Effect of strength of electrical stimulation. A, point of entry of microelectrode into the cell. Local graded responses (R_1, R_2 and R_3) are produced when subthreshold stimuli (S_1, S_2 and S_3) are applied. Response R_4 is due to a threshold stimulus. Responses R_5 and R_6 are due to supra threshold stimuli (S_5 and S_6). Note that the AP does not increase in amplitude with increased strength of stimulation.

Increasing stimulation will NOT increase the amplitude (height) or duration (width) of AP , but will increase frequency of AP

Threshold stimulus : the minimal stimulus which produces an AP
أقل كمية من التحفيز يمكن أن تسبب نبضة كهربائية

Subthreshold Stimulus

تحفيزأقل من الثرشهولد لا يستطيع توليد آكشن بوتنشيال ولكنه قادر علي إستجابةمحلية Local Response

Suprathrehold Stimulus

تحفيزأكثر من الثرشهولد لا يستطيع زيادة الآكشن بوتنشيال طولا أو عرضا و لكنه يسبب زيادة سرعة ترديد (تكرار) الآكشن بوتنشيال

Threshold level of the MP: the value of the MP at which a stimulus can produce an AP
قيمة فولطاج غشاء الخلية التي يمكن منها إستهلال النبضة الكهربائية

The Action Potential (AP)
(nerve impulse & muscle AP)

- We need to describe 3 types of event

✓(1) Electrical changes in the cell-membrane أو التغيرات الكهربائية التي نرصدها علي الخليّة في مختلف مراحل الآكشن بوتنشيال

(depolarization , repolarization & hyperpolarization)

✓(2) Ionic changes underlying the electrical events (N+ influx and and K+ efflux) التغيرات الأيونية

✓(3) Excitability changes التغيرات الأستثارية & refractory periods وفترات الممانعة (when will be the cell ready to respond to a second stimulus & produce AP after the first one (preceding one)

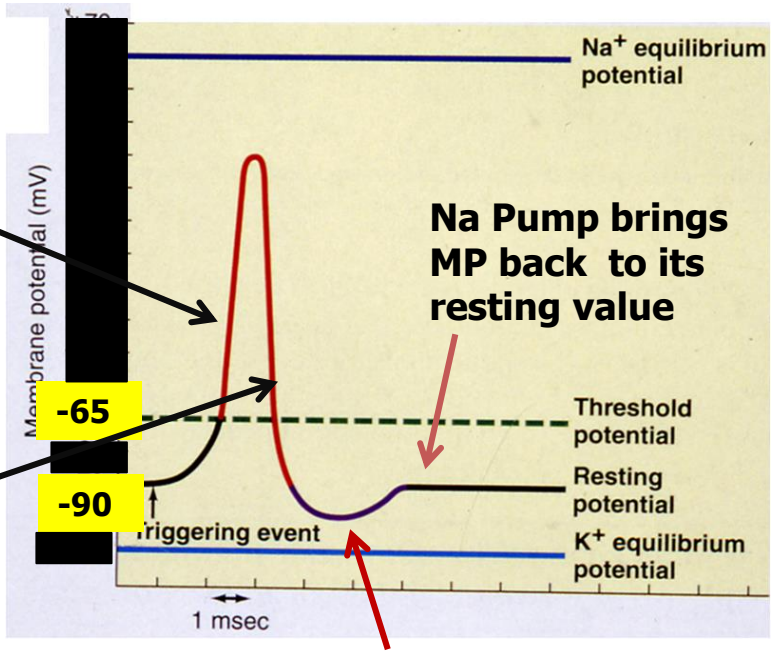
A/ Electrical Changes During the Nerve Action Potential

- ✓ **We need to start from the baseline i.e., Resting State of the cell i.e, at the RMP**
- ✓ **A threshold Stimulus will lead to →**
- ✓ **(1) Depolarization phase مرحلة إزالة الأستقطاب Of the AP ,**

which soon (within about one millisecond) will be followed by

(3) Repolarization phase . مرحلة إعادة الأستقطاب

(3) In some neurons there is a 3rd phase called Hyperpolarization



Hyperpolarization (positive after-potential)

B/ Permeability (Conductance) Changes During the AP

As mentioned before, in a resting cell the membrane permeability to K+> Na+ (due to K+ leak channels) & the RMP= -90 mV (-70 to -90n mV) .

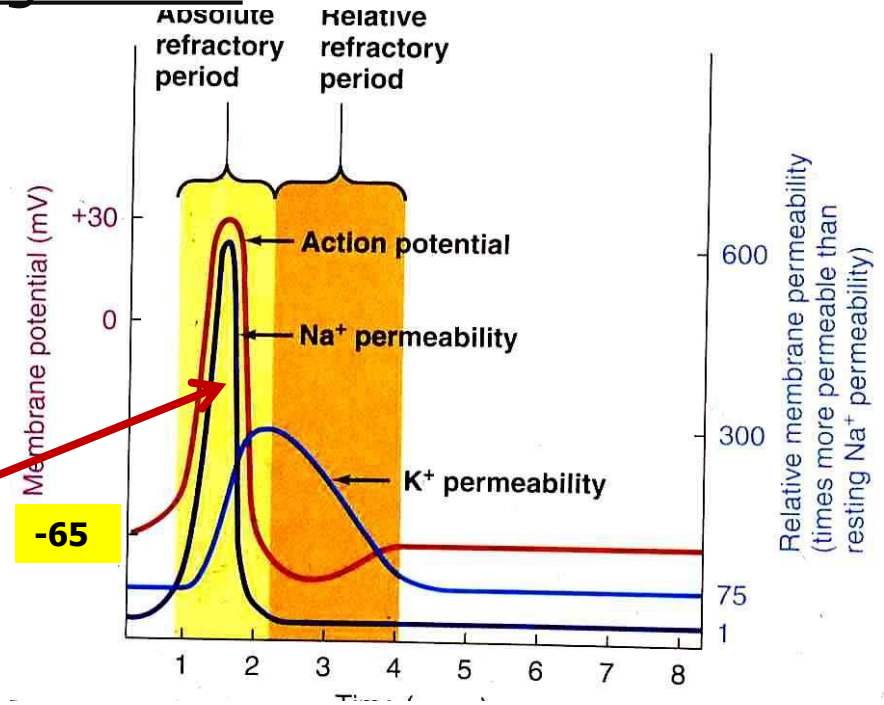
(1) A stimulus strong enough to carry the MP to the threshold level -65 mV) causes →

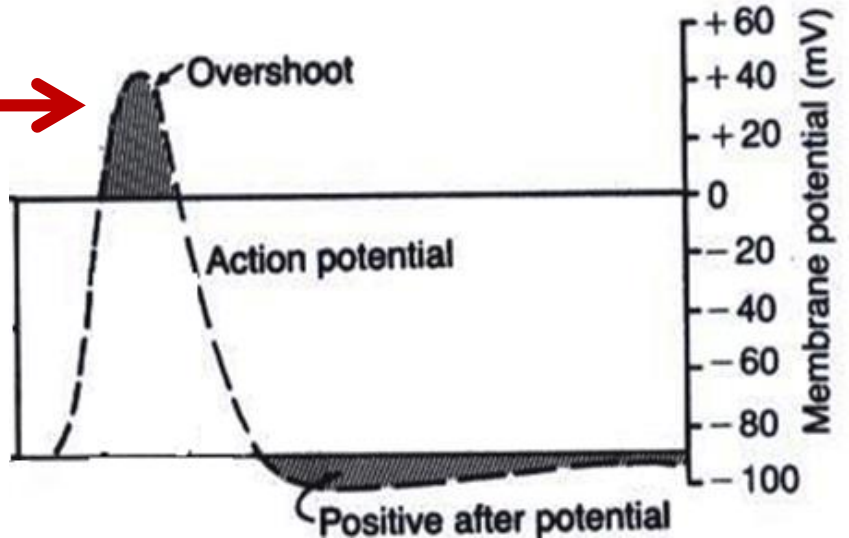
explosive activation of voltage-gated Na+channel → 5000 fold increase inNa+ conductance

(permeability) →massive Na+ influx

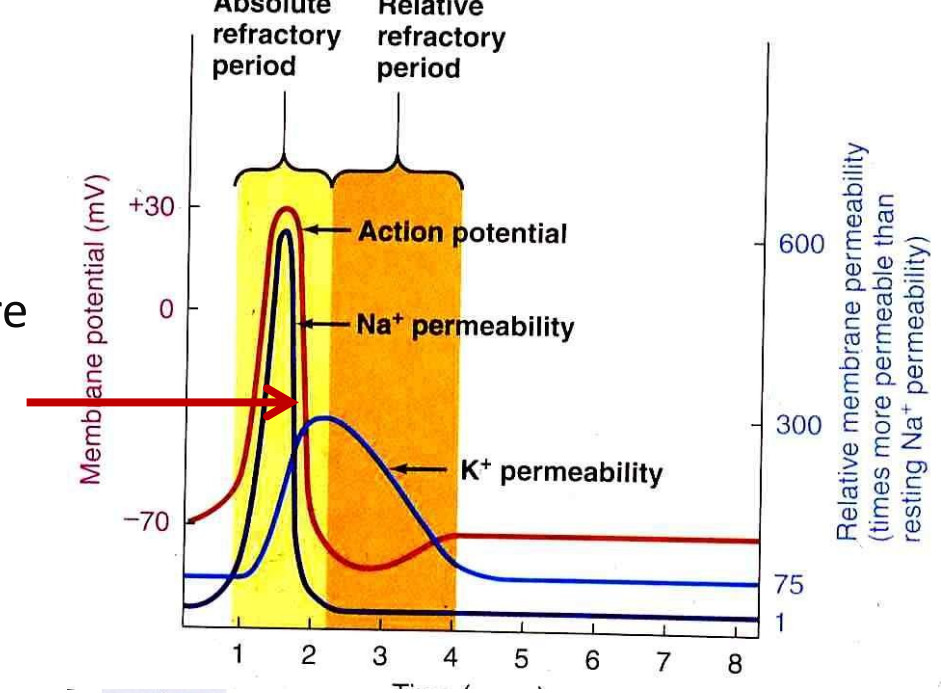
(inflow)→depolarization.

- **Then overshoot (reversal of MP) occurs as the inside of the cell becomes +ve ; & the peak of AP is reached at +35 - +40 mV.**



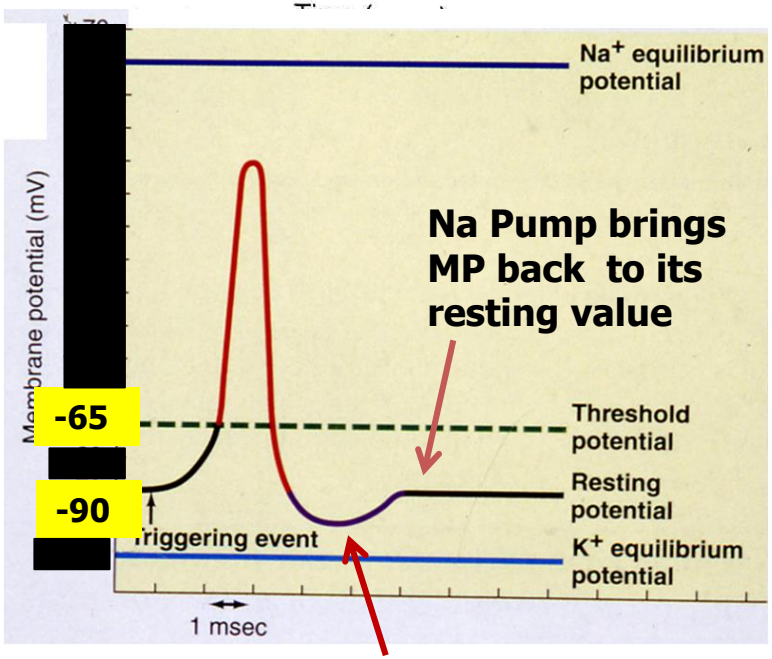


(2) Repolarization phase is due to delayed opening of K+ channels (Na+ channels are already inactivated) → rapid K+ efflux (outflow , exit) → the MP quickly returns toward the resting level .



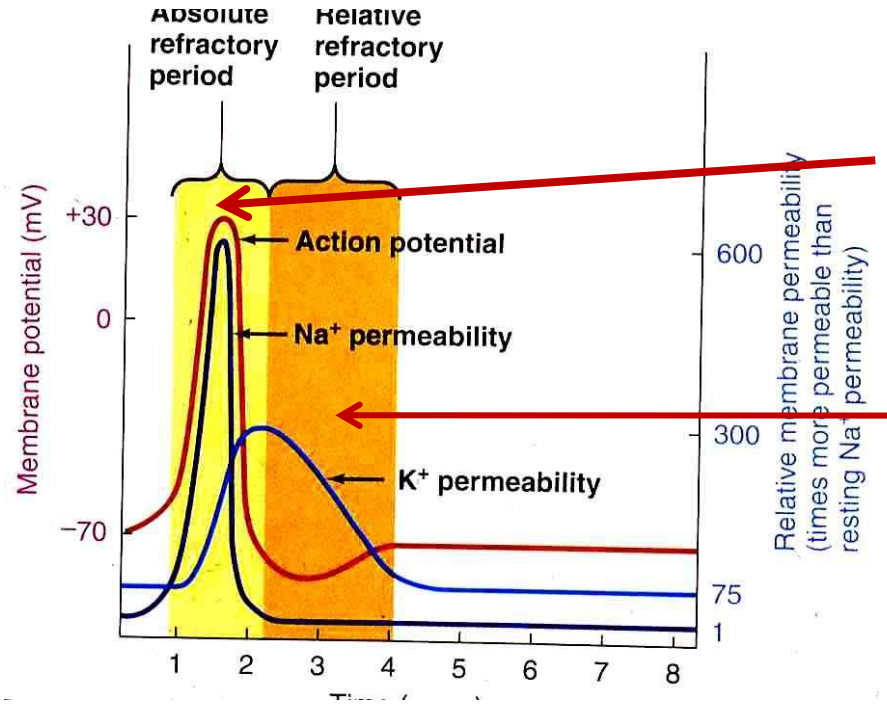
(3) In some nerves there is a Positive After Potential, due to continued outflow of K+, which causes the membrane to becomes hyperpolarized

- However , the Na+-K+ pump soon restores the MP to the resting (RMP) level .



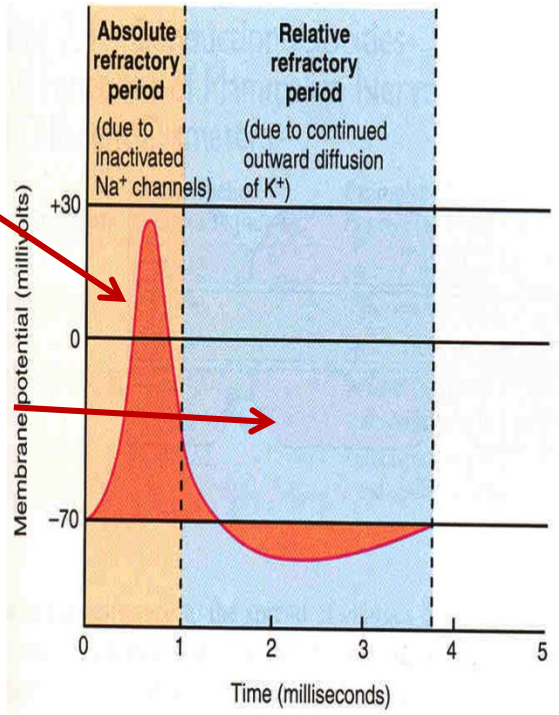
Hyperpolarization (positive after-potential)

C/ Excitability Changes During the AP



فترة الرفض المطلق

فترة الرفض النسبي



Meaning : when can the cell respond to a second stimulus (after the first stimulus which produced the first AP)

متي تكون الخلية مستعدة للأستجابة لمحفز تاني بعد المحفز الأول الذي سبب الآكشن بوتنشيال الأول ، الأصلي)

(1) Absolute Refractory Period : where no stimulus , however strong , can produce a second AP . It is due to inactivation of Na+ channels .

(2) Relative Refractory Period : a stimulus higher than threshold is needed to produce an AP . Due to continued outflow of K+ .

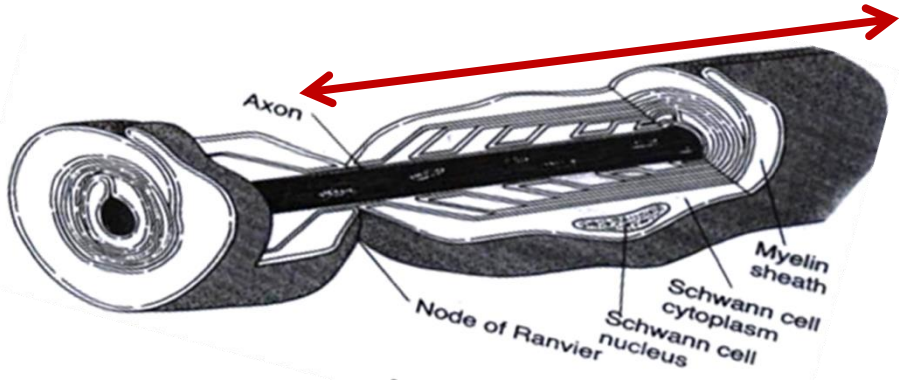
Types of nerve Fibers

- Nerve fibers can be classified in 2 ways :

A/Classification According to Myelination

(2) Myelinated Fibers →

✓ Myelin sheath الغمد أو الغطاءالمايايني covers the axis cylinder , separated by Nodes of Ranvier (naked , uncovered parts) at 2-3 Micron intervals



(2) Unmyelinated : without myelin sheaqth

B/Classification According to Diameter

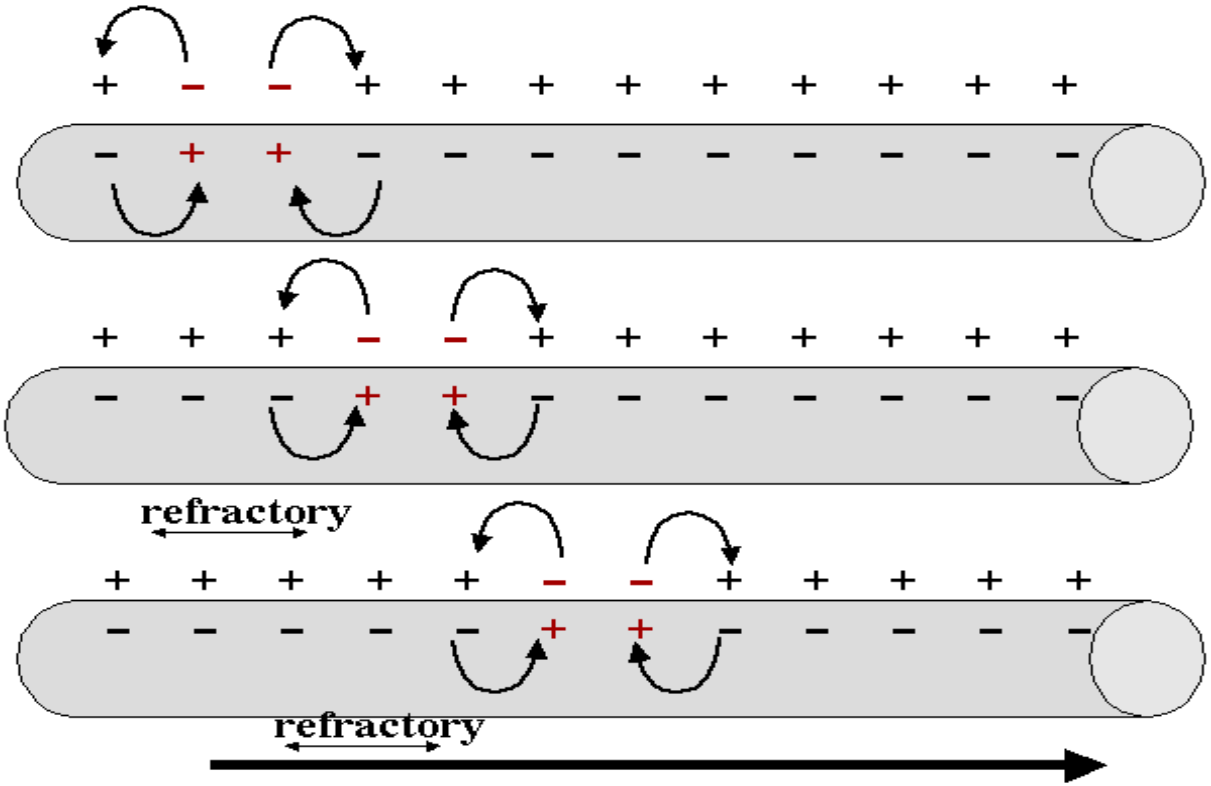
- A, B & C fibers
- Diameter : A> B> C
- Because conduction velocity depends upon diameter , A are fastest and C are slowest
- A and B are myellinated
- C are unmyelinated

Propagation (Conduction) of Action Potential

- In both myelinated and

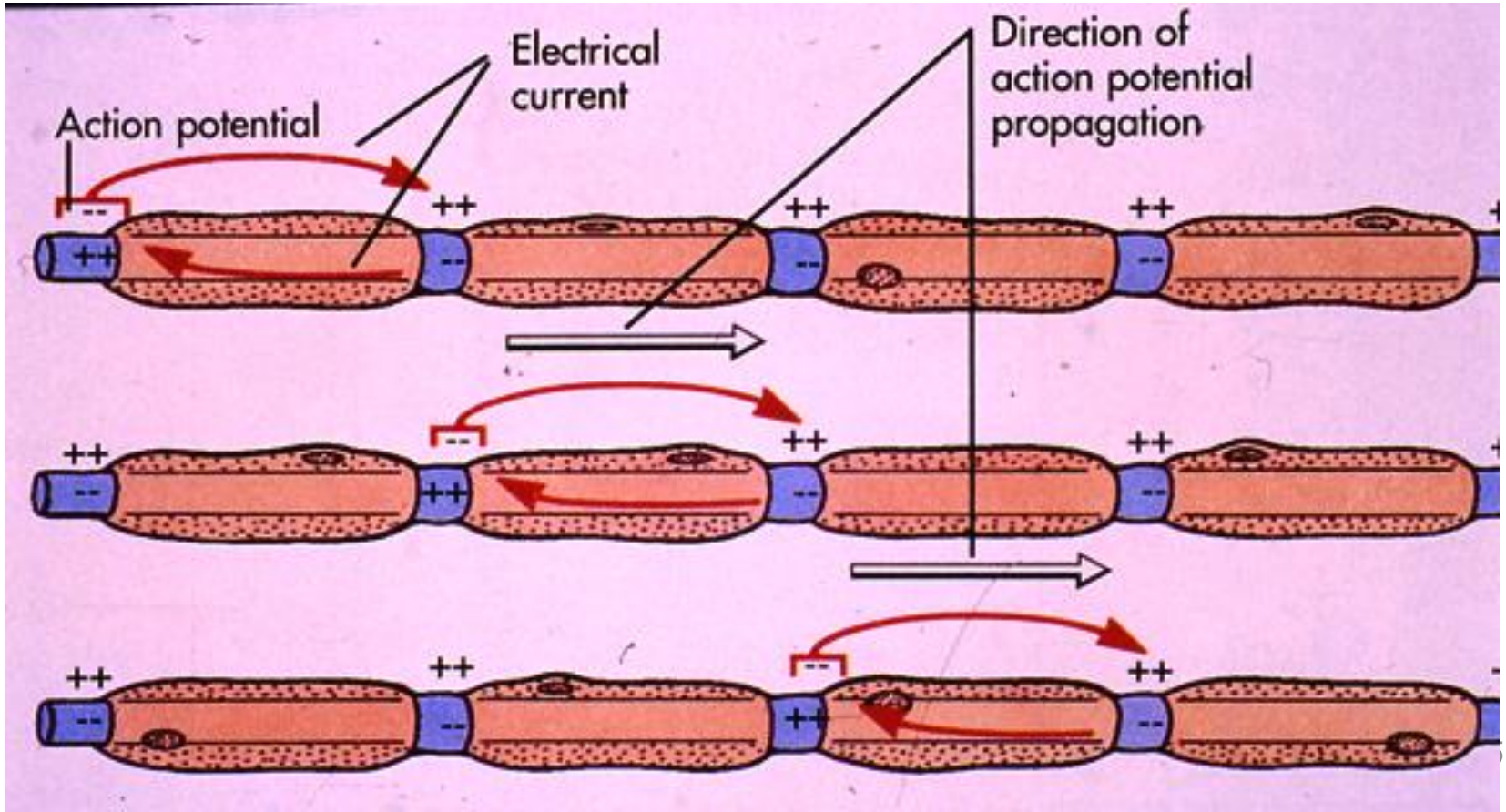
Unmyelinated nerve fibers impulses arepropagated (conducted) by <u>Sodium Ionic Current Flows تيارات أيونية /كهربائية</u>

✓ In unmyelinated fibers , they oare contiguous متلاصقة ، متلامسة occurrring at almost each adjacent متجاورة point on the membrane .This is called <u>Continuous (Contiguous) conduction</u> of nerve impulses



✓ and in myelinated nerves there

Saltatory Conduction , where ionic currents travel by jumping from oneNode of Ranvier to the next .



Saltatory Conduction (propagation) of APs in myelinated nerves

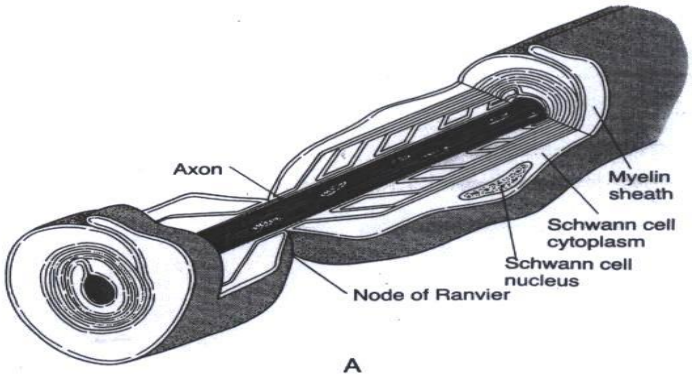
Myelin is an excellent insulator : it prevents

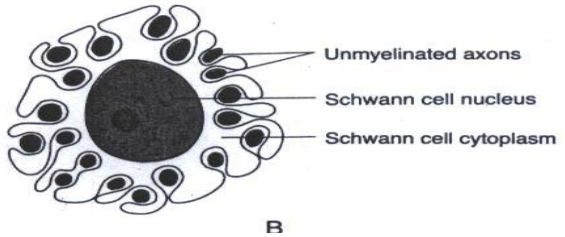
leakage تسب و فقدان (& hence loss) of ions

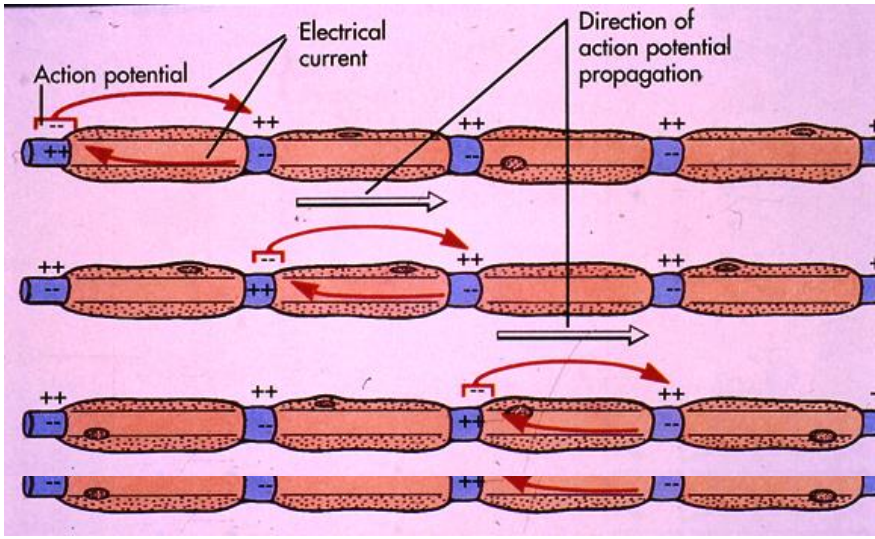
from inside the cell through membrane .

Ions are allowed to pass only at Nodes of Ranvier

- ➢ Myelin sheath makes conduction in myelinated nerves →
- ✓ (1) more economical (because it prevents leakage of ions + because N+-K+ pump only works at Nodes of Ranvier , unlike unmyelinated nerves where it works at every point in the membrane) , and
- ✓ (2) faster-conducting

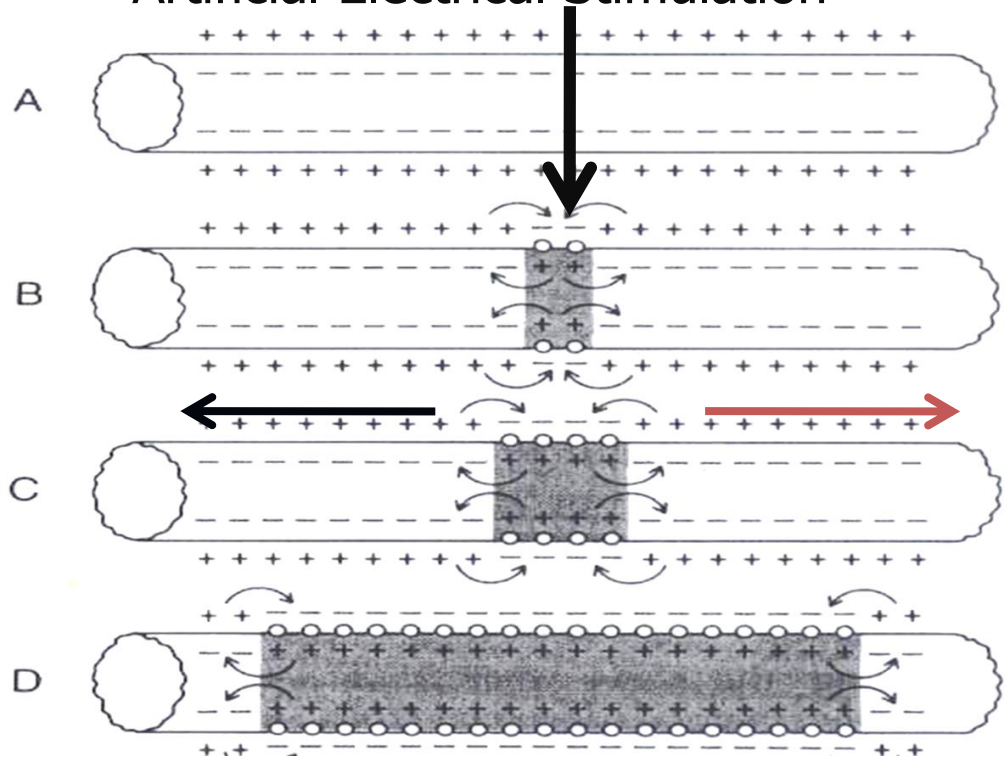






Direction of AP Propagation (Conduction)

Artificial Electrical Stimulation



✓Under Artificial condition of electrical stimulation in the laboratory , the AP propagates in both directiions .

✓But normally AP starts in axon hillock & propagates distally in one directions