Musculoskeletal Physiology

(I) Physiology of Excitable Tissues : Nerve and Muscle (namely Skeletal Muscle)

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Lecture 4&5

The Action Potential and Properties of Nerve Fibers

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Lecture 2&3 :- nerve action potential &properties of nerve fibers

Objectives

- By the end of this lecture, the student should be able to:

- Appreciate Changes that occure through the nerve after stimulation by threshold (effective) stimulus

- Define and draw giving membrane potential in mV and time course in msec and label all components such as threshold (firing level), depolarization,spike overshoot, repolarization and positive after potential

-Identify different types of voltage –gated channels

-Correlate the conductance changes with opening (activation) or closing (inactivation) of relevant gates.

- Distinguish between a local potential and an action potential.

-Define absolute and relative refractory period on basis of excitability changes

- Classify neurons by using letters or numbers on basis of diameters and velocity.

- Define myelin sheath,myelinated and unmyelinated nerve fibers

- Describe differences in the propagation of action potential in myelinated and unmyelinated nerve fibers.

- Define all and none law.

- Differentiate monophasic, biphasic and compound action potential.

Changes that occur in the nerve after stimulation by an effective stimulus are:-

1-Electrical changes

2- Excitability changes

3-Thermal changes

4-Chemical changes

1- Electrical changes
The nerve action potential

-The nerve action potential

It is potential difference along nerve membrane after stimulation

by **Threshold** (effective)stimulus

-

-Nerve signals (impulses) are transmitted as nerve action potentials conducted along the nerve fiber as a wave of depolarization to its end

-The channels necessary for nerve action potential are:-

Voltage gated Na+ & k+ channels

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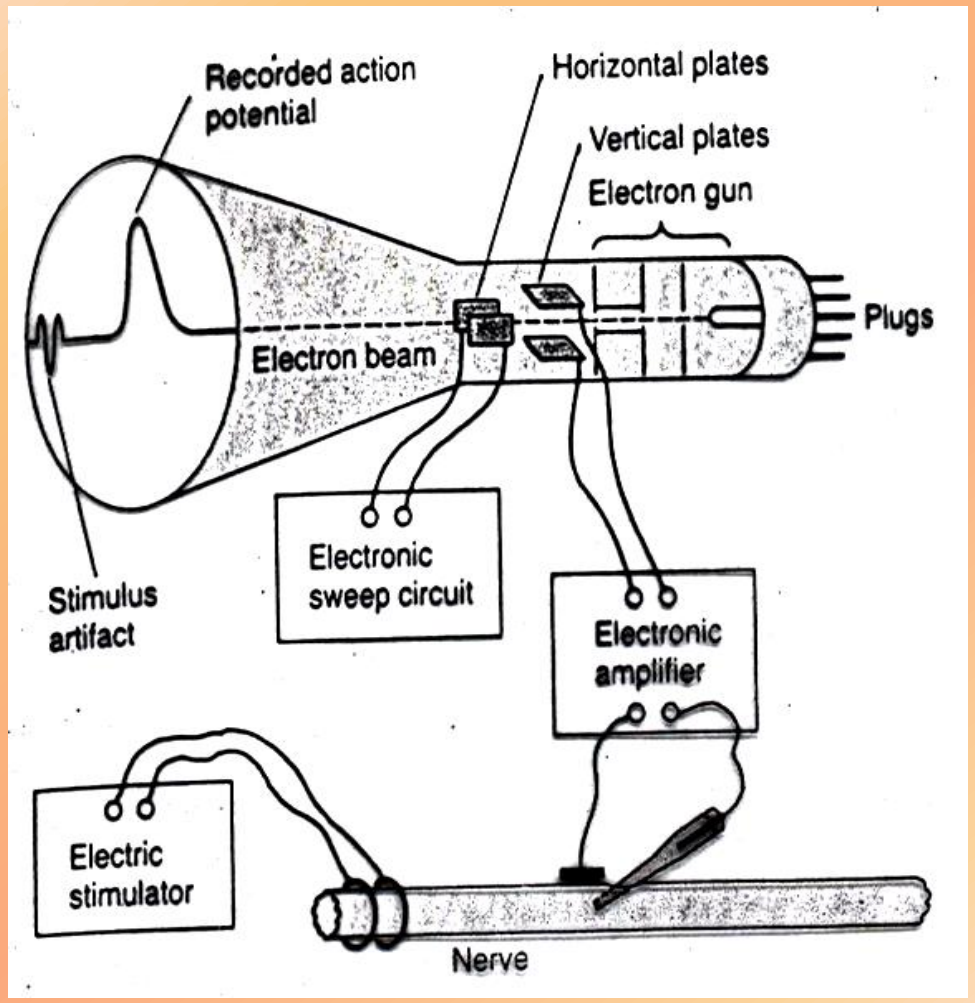
During action potential we use oscilloscope to measure rapid changes in membrane potential



The stages of acion potential are:-

1-RMP:-At the resting state(no stimulation) the membrane is polarized (-ve inside= -90 mv)

2-Depolarization:- sudden Na inflow (influx) → polarizesd state is lost & potential rises to positive values (reach zero & overshoot to +ve values).

3-Repolarization:- Na channels close & K channels open & K outflow (outflux)to outside → restoration of the normal –ve RMP.

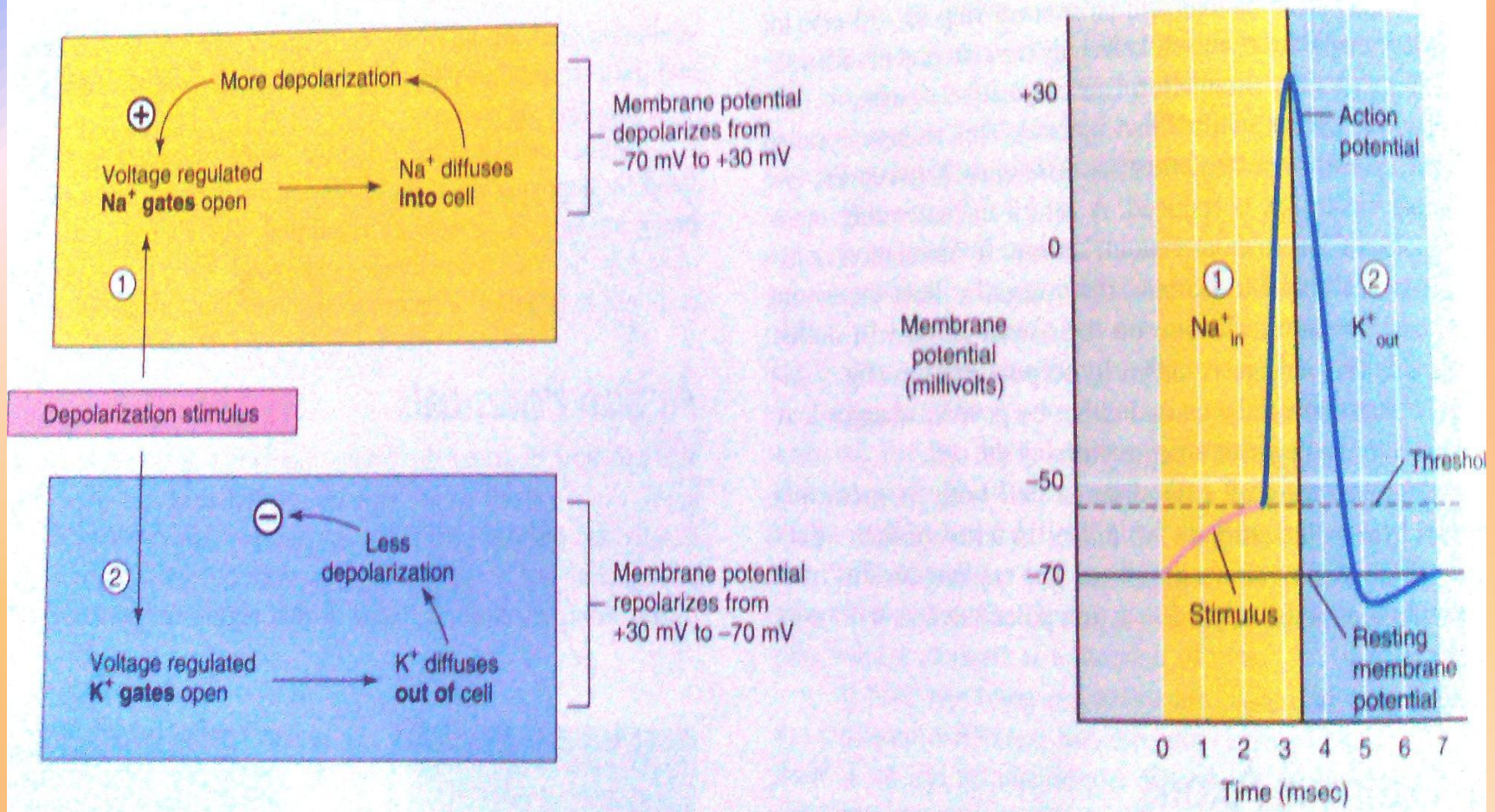


Figure 7.13 Depolarization of an axon affects Na^+ and K^+ diffusion in sequence. (1) Na^+ gates open and Na^+ diffuses into the cell. (2) After a brief

Summary of events that causes AP:-

1-Initiation of Action Potential (AP) & +ve feedback vicious circle opens Na channels CAUSING DEPOLARIZATION STAGE

- **-90 mv is the resting potential**

a- **Gradual depolarization stage:-**

- **Threshold stimulus (**A stimulus strong enough)**--------- cause voltage gated Na channels to open & Na influx rises resting potential from -90 towards zero**
- **as membrane potential raises ---------- open more Na channels & more Na influx (+ve feedback vicious circle) until all voltage gated Na channels open.**
- **A sudden increase in membrane potential from -90 to -65 mv cause explosive opening of all Na channels & Na conductance is 5000 times great → massive Na+ influx,**

so -65mv is called firing level..

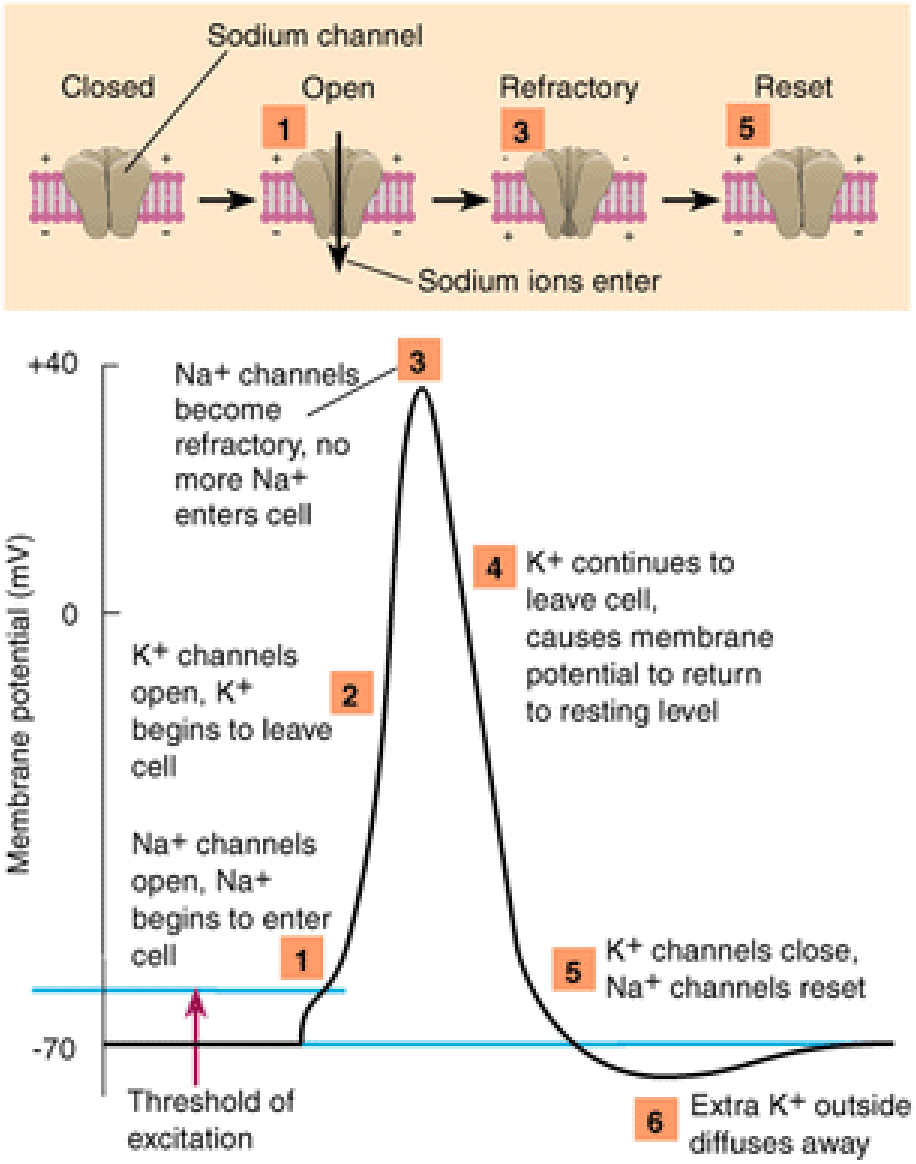
b-Depolarization occurs & membrane potential reach zero value & overshoot to reach + 35 mv (reversal of polarity) occurs & the inside of the cell becomes +ve

The peak of AP is reached at (+35 - +40 mV).

- All Na + channels become refractory & no more Na+ entry

- At + 35 mv all Na channels begin to close suddenly (Depolarization ends)

▶ The Movements of Ions During the Action Potential



c-Repolarization :- due to high K conductance (flow) to outside (K outflux) by openning of all K channels

(& zero flow of Na to inside as all Na channels close)--> - causes negativity inside

-Membrane returns to resting potential (drop from +35mv towards zero then to negative resting potential -90 mv)

D- positive after potential (In some nerves) **membrane potential becomes more negative than resting level,**

(because many K channels remain open & K outflux continue- ⟹ causing more –ve inside = hyperpolarized)

-(positive after potential is wrong terminology it is historical one)

.

E- Re-establishment of Na & K ionic gradients & return to resting potential:-

a- Na that had influxed in & K that had oufluxed out returned to original state by Na-K pump (active process - need ATP & ATPase)

b- Closure of some K channels

- Duration of nerve action potential is 1-1.5 ms

The factors necessary for depolarization & repolarization are :-

1-Na voltage –gated channels important for both depolarization & repolarization

2- K voltage –gated channels important for repolarization

A- Voltage –gated Na channels:-

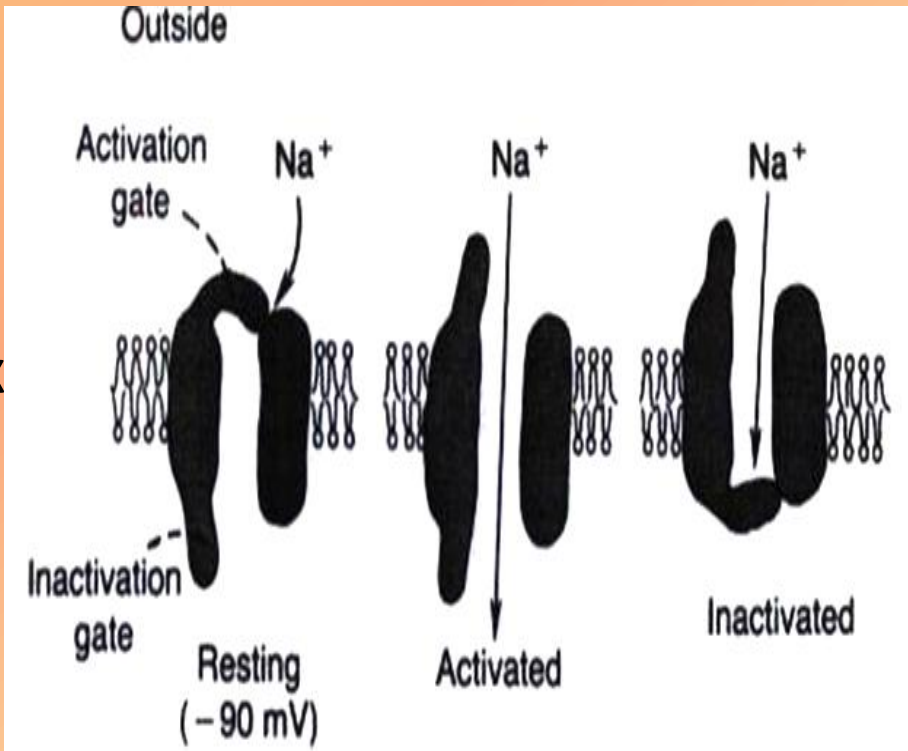
O

- -outer activation gates& inner inactivation gates.
- 1-Resting state:-at RMP -90 mv activation gates close & inactivation gates open
- No Na entry.

2- Activated state:-after stimulation, the membrane potential rises at a voltage between -70 to -50mv, conformational change occur & activation gates open (now both gates are open)& Na influx

3- Inactivation state:- inactivation gates close slowly while the activation gate is still open

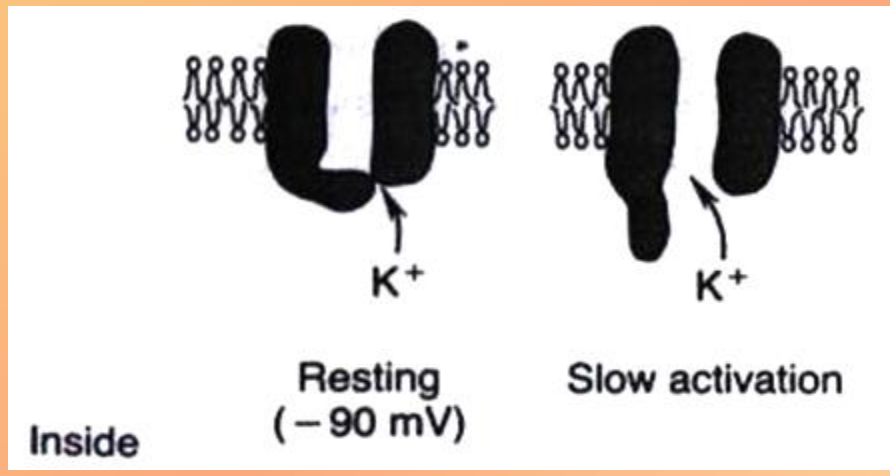
stops Na influx & they close completely at + 35 mv & repolarization begins.



B -Voltage –gated K channels:-

1- Only one gate,

- at RMP (resting state) the gate of K is closed & no K pass to out.
- 2- after stimulation & between -90 to zero mv, Shortly after depolarization , when the sodium channel begins to be inactivated , the potassium channel opens slowly & K outflux begins causing repolarization
- (they open completely only when Na gates close & when Na influx stop)



-Acute local potential (acute local response):

A very weak stimulus (not threshold) can cause local change in membrane potential
e.g from -90 to -85 mv which is not sufficient for regeneration of AP, this is
acute subthreshold potential
(which is graded and does not propagated). which should increase to threshold level to produce AP.

-The AP differs from local response in that AP is:-

(1) not graded
(2) obeys All-or None Law
(2) propagated (conducted for long distances .

All or nothing principle:-

-i.e The nerve respond to a threshold stimulus maximally or does not respond at all (there are no half solutions)

-- Once threshold stim applied it gives AP produced & spread all over the nerve ,its intensity can not increased by increasing stimulus intensity (or by suprathreshold)

- subthreshold stimulus can not elicit action potential (but a local response (EPSP) can be produed it does not obey this law)

Direction of propagation of AP:-

- In one direction from axon hillok to nerve terminal

- (experimentally) if nerve stimulated at its midportion , AP pass in both directions

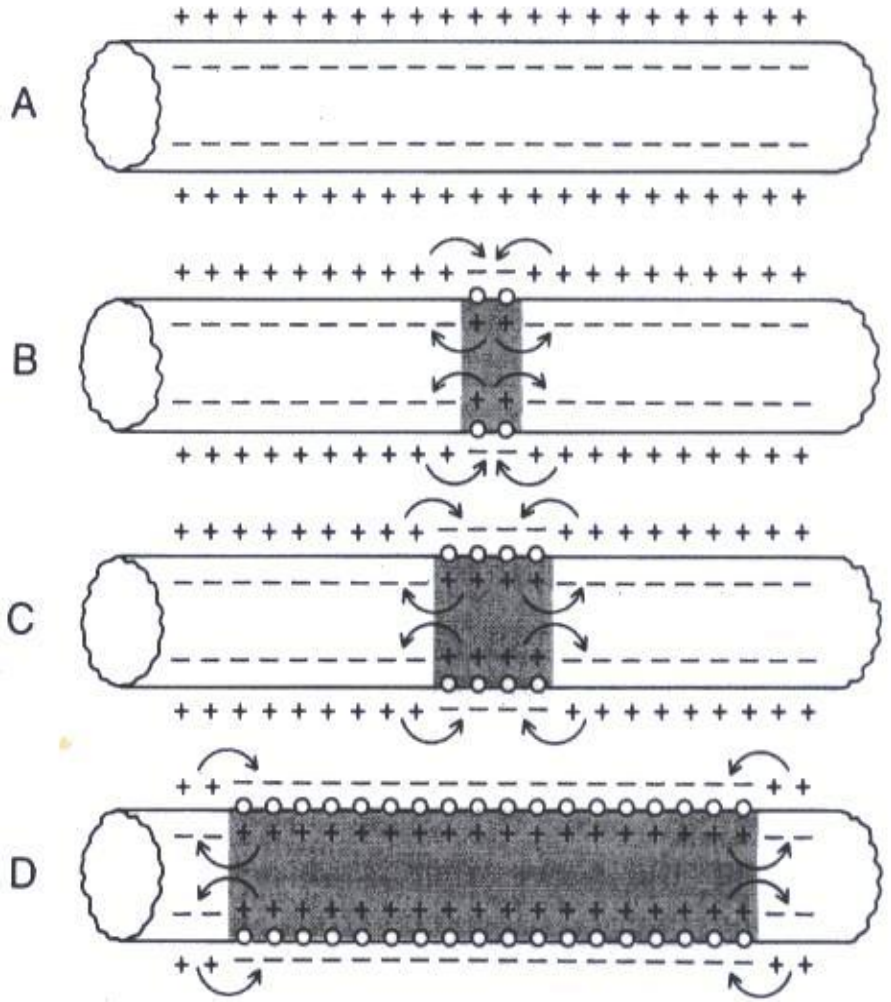


Figure 5–8 Propagation of action potentials in both directions along a conductive fiber.

Under Artificial condition of electrical stimulation in the laboratory

Na & K conductance (flow) during action potential:-

1-At resting state , before AP:-

K conductance through K leak channels is 50-100 times as Na.

2- At onset of action potential:-

voltage gated Na channels activated & Na conductanceis 5000 folds, at the same time voltage gated K channels begin to open slowly

- At depolarization Na conductance/ K conductance >1000 fold

3- At peak of AP Na channels close & voltage gated K channels open&,
K conductance increase

-- At repolarization the ratio Na conductance/ K conductance decreases.

4-At end of AP ,return to –ve potential , close K channels& no K+ conductance

2-Excitability changes: the ability to respond to a second stimulus

1-Latent period

2-absolute refractory (متمرد)period :-

- During depolarization & early repolarization

- during it the nerve can not excited by a a second stimulus & a second action potential can not be elicited whatever strength of the stimulus (even suprathreshold)

-(because all Na channels are already opened & Na influx occurred & a new stim can not open further

2- Relative refractory period:-

-It is ½ to 1/4 absolute refractory period, late third of repolarization

-it is the period during which a second action potential of low amplitude can be elicited by stimulus stronger than normal suprathreshold)

because :_

1- some Na channels still inactive so need stronger stim to open

2- rapid flow of K to outside during repolarization

Types of Nerve Fibers

Classification According to Myelination

1- myelinated : have myelin sheath

(diameter more than 1um)

1-type A

- (e.g somatic (motor) nerves to skeletal muscles)

2-type B fibers

-(as preganglionic autonomic nerves).

2- unmyelinated have no myelin sheath

(diameter less than 1um)

-type C (postganglionic autonomic &pain fibers)

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

- -**Myelin sheath** is formed by schwann cell which deposit lipid substance called sphingomyelin
- -Interrupted at nodes of Ranvier (2-3 micron) at the junction between 2 cells.

Functions of myelin sheath

1-insulator

2-decrease ion flow through the membrane

3- increase conduction velocity

4-protection

5- conserve energy during transmission of AP

Propagation of action potential(Transmission of depolarization process along a nerve =spread of nerve impulse

1- in myelinated nerve fibers:-

Saltatory conduction (jumping)

✓**- AP occurs at nods of Ranvier & directed from node to node, through axoplasm inside & ECF outside**

by jumping

APs can develop only at the Nodes of Ranvier

→ Where

(1) ions can relatively easily flow in & out

(2) there are voltage-gated channels

.

Value:-

1-↑ velocity of conduction

2-Conserve energy for axon because only nodes depolarize

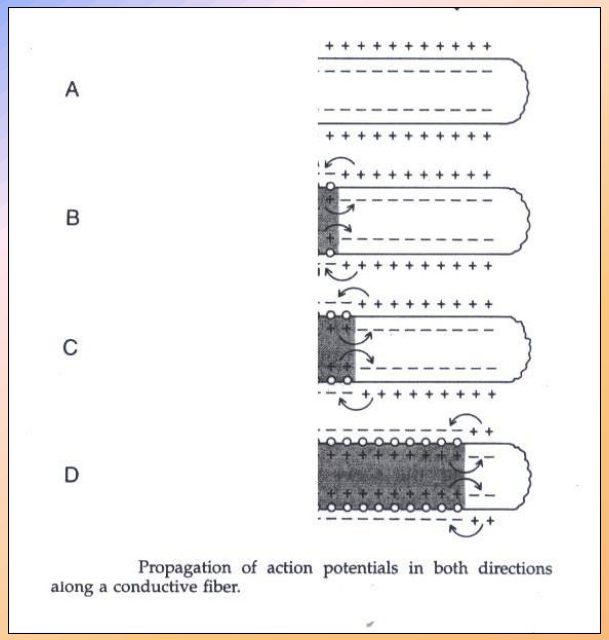
3-Insulation by myelin sheath allow repolarization to occur rapidly

2- Non- myelinated nerves:-

(local circuits)=Continuous Conduction =point to point

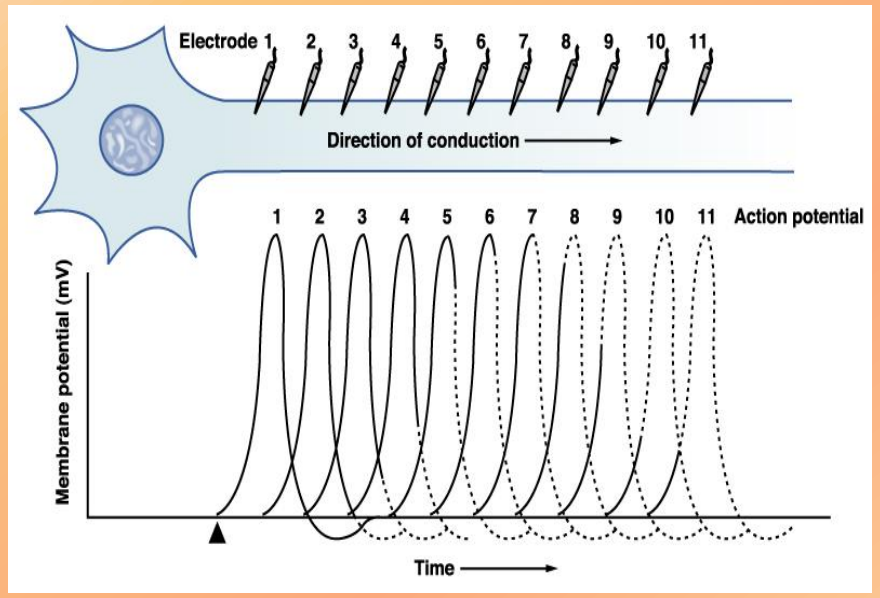
-depolarization pass by local circuits. -depolarization in an area, + ve charge carried inward by Na ions flow for several 1-3 mm in the axon core & increases the voltage inside the nerve to threshold value to cause depolarization in a new area & Na channals open & depolarization spread to new areas

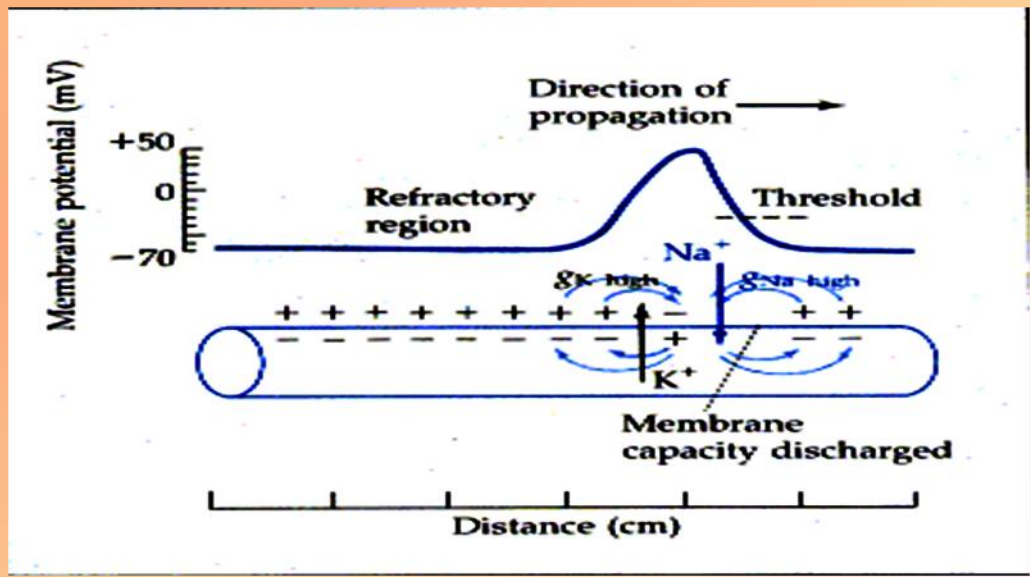
Propagation (Conduction) of AP :By Circular Current Flows



Propagation of action potentials in both directions along a conductive fiber.

Point-to –Point conducti
in unmyelinated nerve





Recording of AP:- by cathode ray oscilloscope

1-**Monophasic AP:-** one microelectrode outside & one inserted into nerve fiber

2- **Biphasic AP:-** 2 microelectodes placed on outside of nerve fibers (biphasic mean in one direction then in second direction