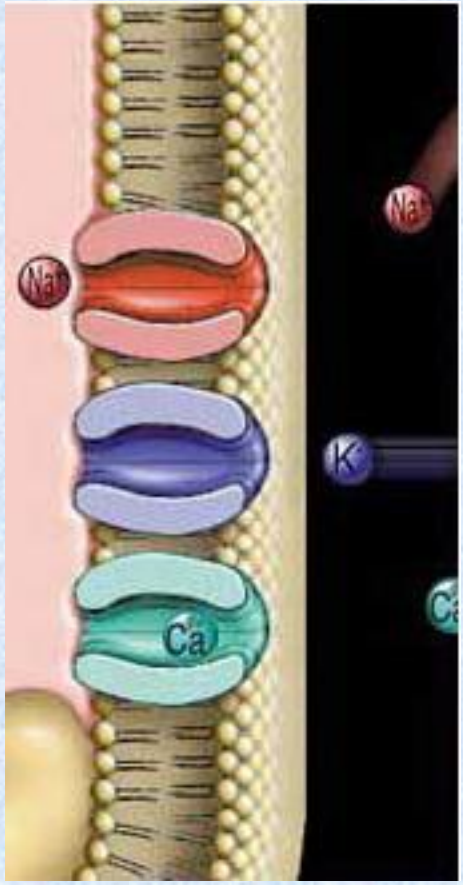

Musculoskeletal Physiology

(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 occur 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 level(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.

Types of Nerve Fibers

Classification According to Myelination

1- myelinated : have myelin sheath
(diameter more than 1um)

1-type A fibers

-(as somatic (motor) nerves to skeletal muscles)

2-type B fibers

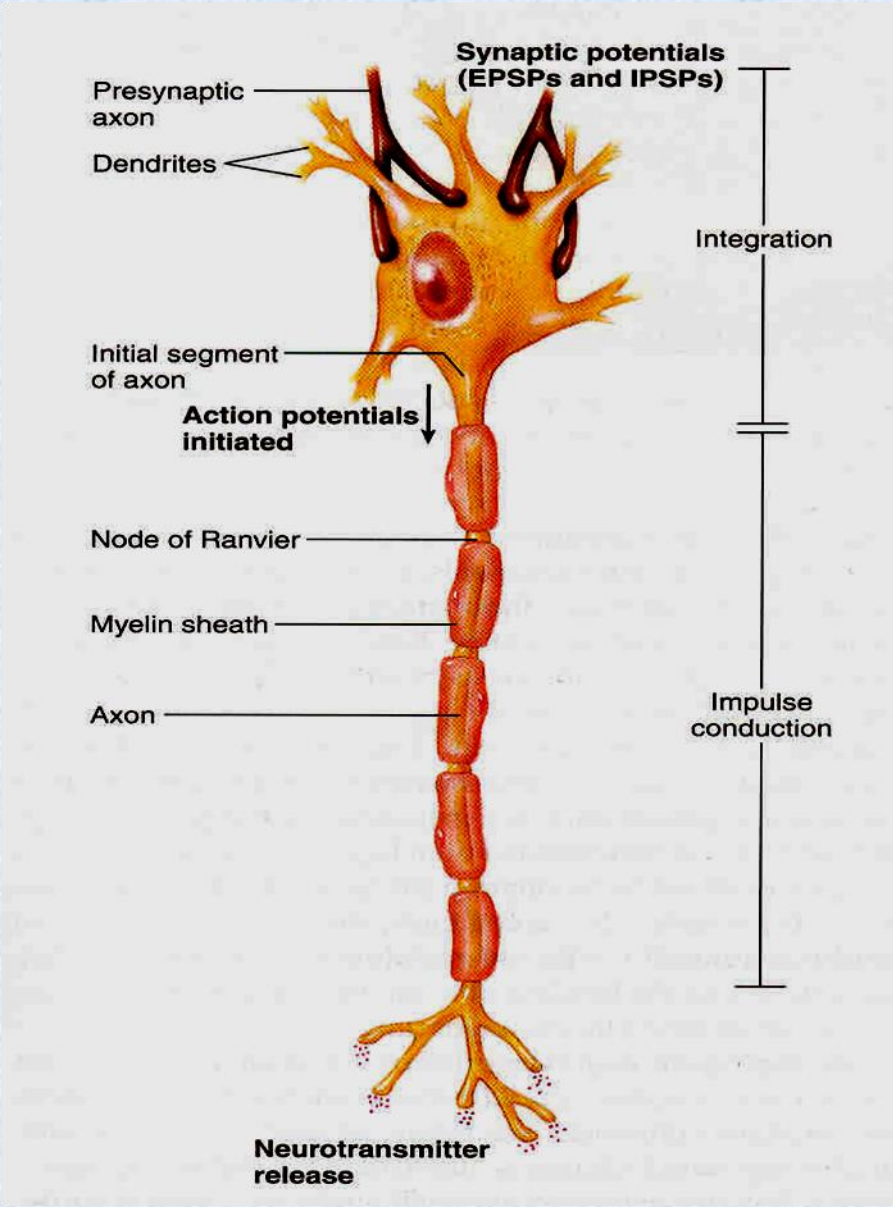
-(as preganglionic autonomic nerves).

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 around the nerve fiber**
- **-Interrupted at nodes of Ranvier (2-3 micron) at the junction between 2 cells.**

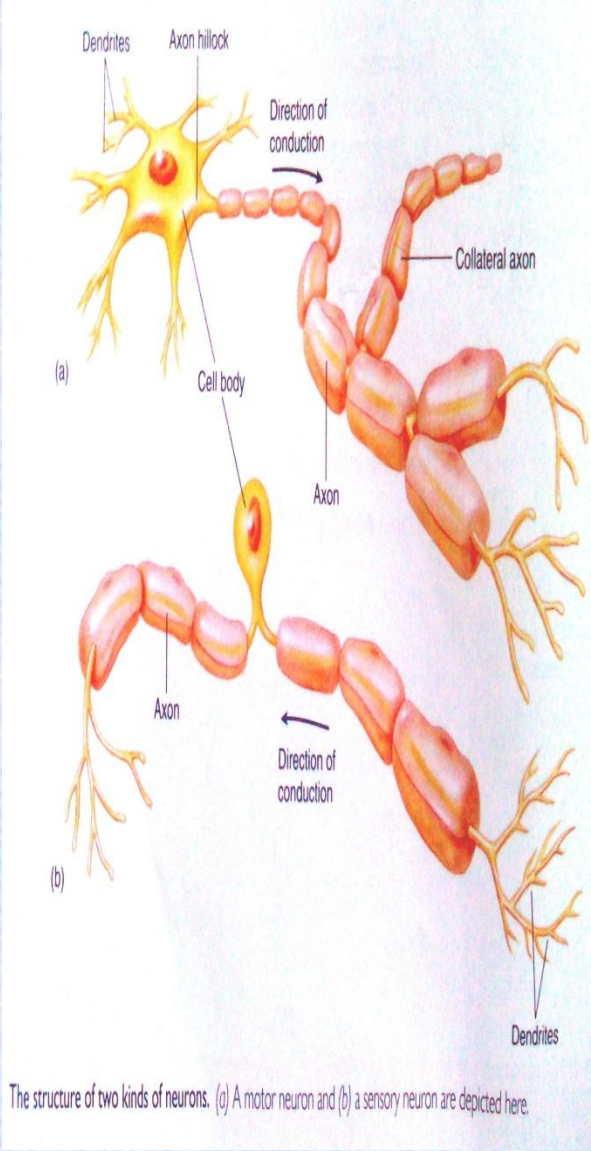
Functions of myelin sheath

1-insulator/ makes ion flow across the membrane much more harder & decrease ion flow through the membrane (decreases ion leakage)

3- increase conduction velocity (because ionic currents need to " jump " (from one node of Ranvier to the next)

4-protection

5- conserve energy during transmission of AP



The structure of two kinds of neurons. (a) A motor neuron and (b) a sensory neuron are depicted here.

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**

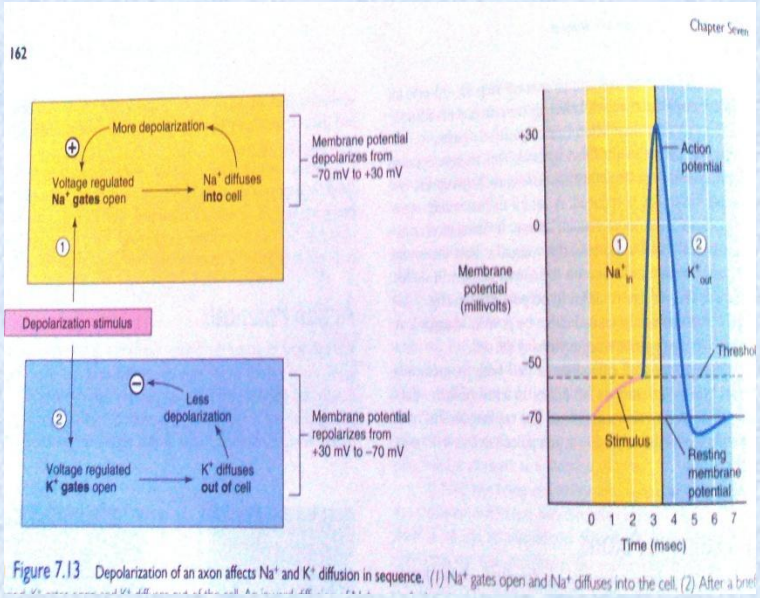


Figure 7.13 Depolarization of an axon affects Na^+ and K^+ diffusion in sequence. (1) Na^+ gates open and Na^+ diffuses into the cell. (2) After a brief

The nerve action potential

-The nerve action potential

It is potential difference along nerve membrane after stimulation by (Threshold = effective) stimulus

-

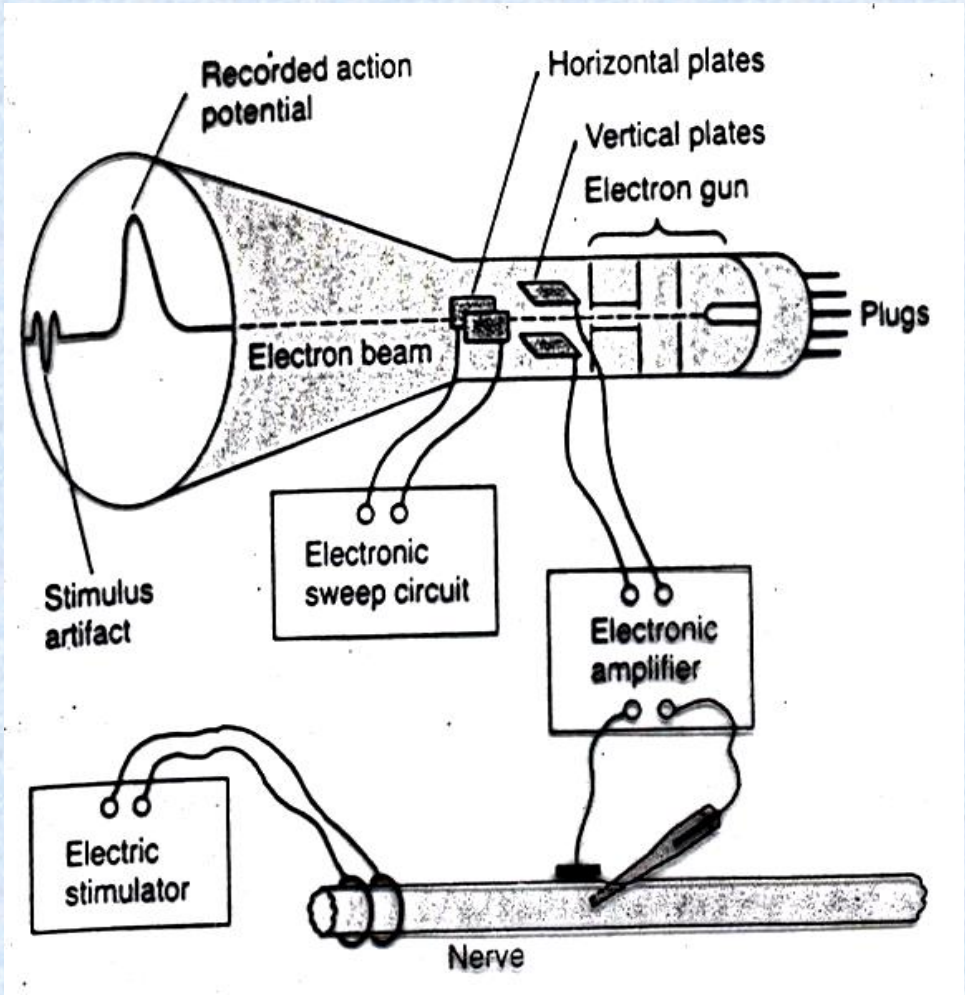
-Nerve signals (impulses) are transmitted as nerve action potentials conducted along the nerve fiber as a wave of depolarization to its end.

-The channels necessary for nerve action potential are:-

Voltage gated Na+ & k+ channels

-

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



Summary of 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.

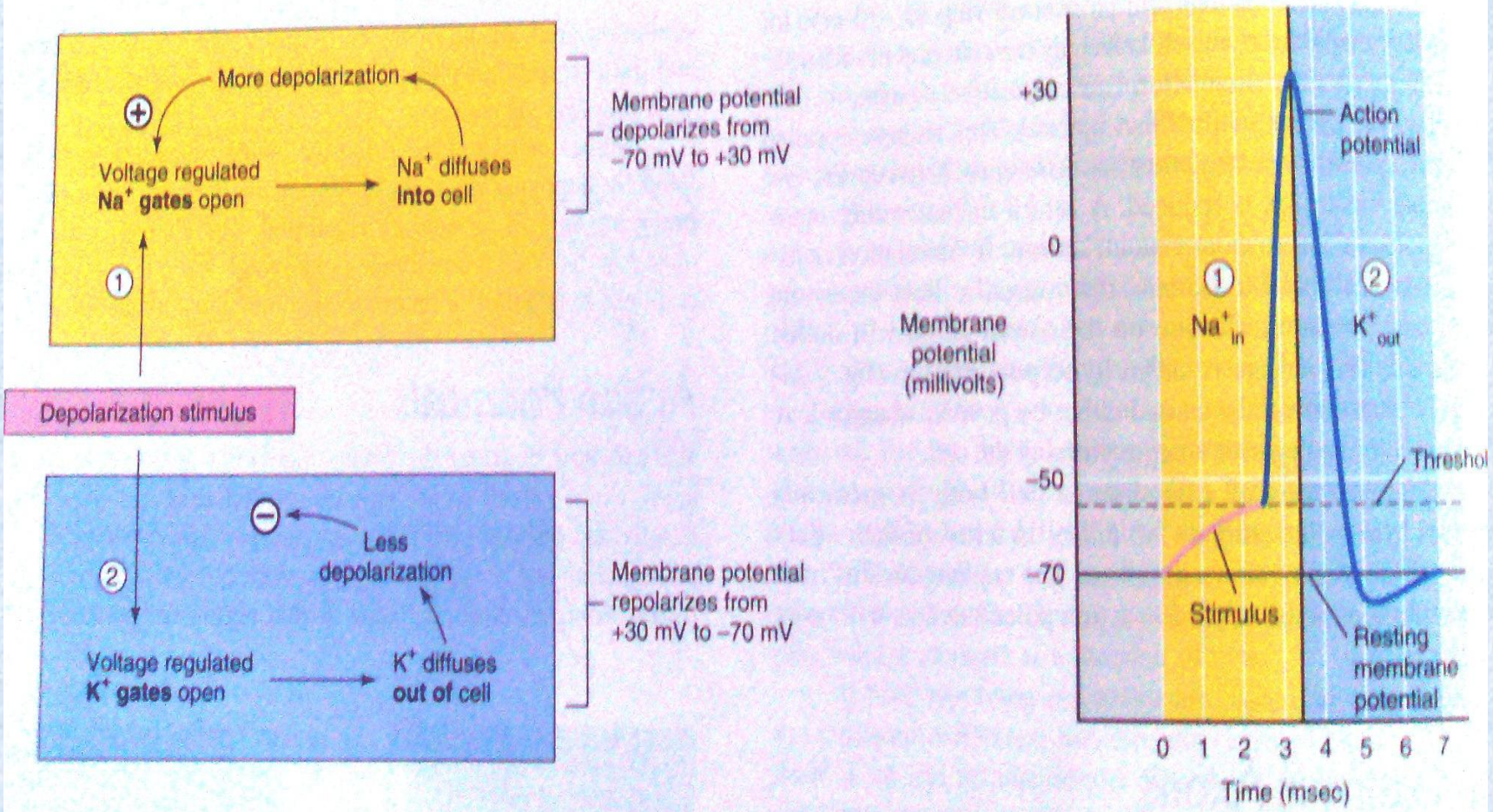


Figure 7.13 Depolarization of an axon affects Na^+ and K^+ diffusion in sequence. (1) Na^+ gates open and Na^+ diffuses into the cell. (2) After a brief

Summary of events that causes AP (spike potential):-

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

a- Gradual depolarization stage:-

- **Threshold stimulus (**An effective stimulus strong enough)**->>>>> >to cause voltage gated Na channels to open & Na influx to inside nerve membrane >>>>>>>rises resting potential from-90 towards zero**

- **Rise of membrane potential >>>>>> open more Na channels & more Na influx (+ve feedback vicious circle) until all voltage gated Na channels open.**

- **The 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 stage:-

- **Sharp & rapid depolarization occurs & membrane potential reach zero value & then overshoot to reach + 35 mv (reversal of polarity)** occurs & the inside of the cell becomes **+ve**

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

- **At this value all Na + channels become refractory (begin to close suddenly & no more Na+ entry)**

& Depolarization ends

c-Repolarization (return to polarized state):-

Cause:- due to high K conductance(flow) to outside of nerve membrane by openning of all K channels >>>>>> (K outflux carrying positivity to outside & raising negativity inside)

(Also 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)

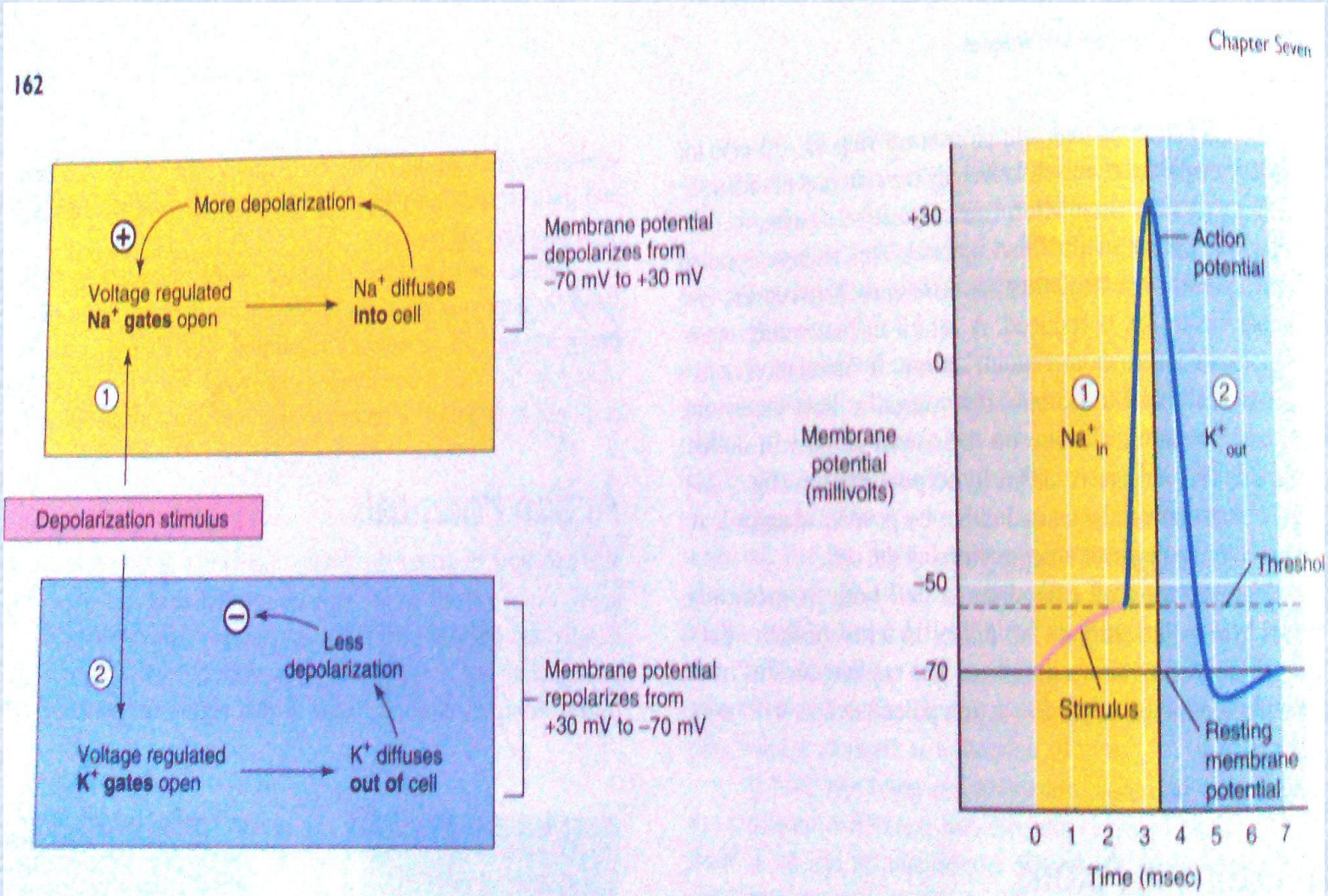


Figure 7.13 Depolarization of an axon affects Na^+ and K^+ diffusion in sequence. (1) Na^+ gates open and Na^+ diffuses into the cell. (2) After a brief

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 state)

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

.

E- Re-establishment of Na & K ionic gradients & return to resting membrane 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 so keep some K+ inside(raise positivity inside)

-Gain of these two processses is:-

K remain inside causing some positivity to raise potential towards -90 mv

- 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

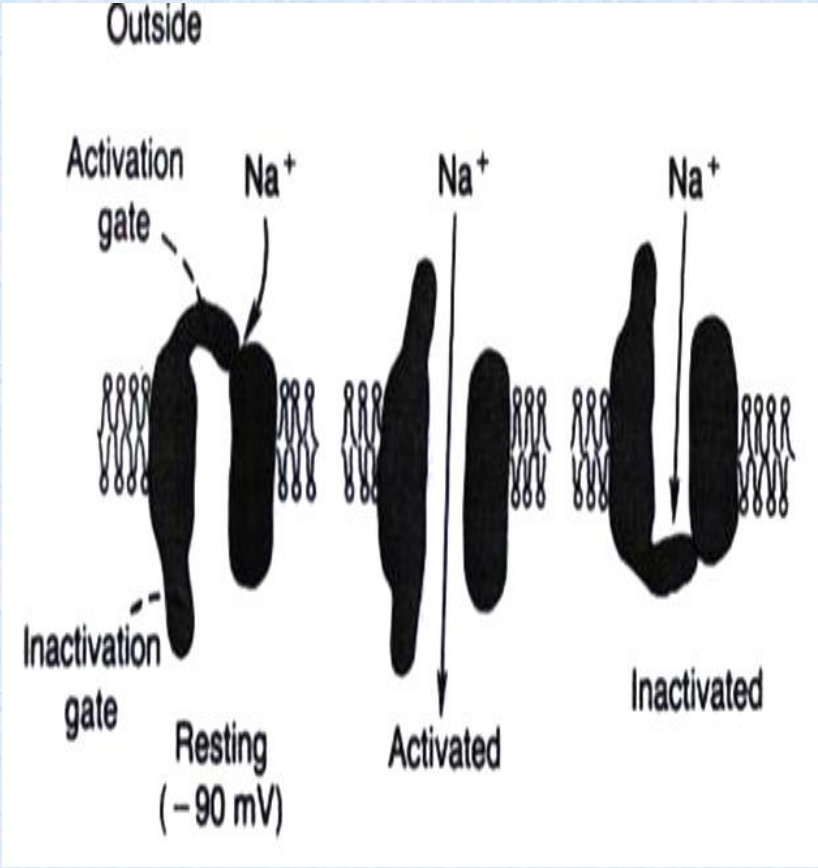
2- K voltage –gated channels important for repolarization

A- Voltage –gated Na channels:-

- -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 -90 to -65mv, conformational change occur & activation gates open (now both gates are open) & Na influx causing depolarization

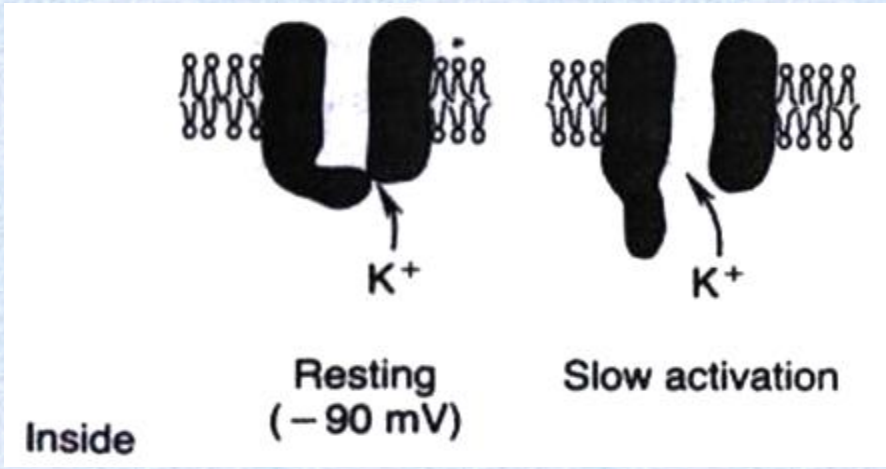
3- Inactivation state:- inactivation gates close slowly while the activation gate is still open & they close completely at + 35 mv & stops Na influx & repolarization begins.



B -Voltage –gated K channels:-

1- Only one gate,

a-at RMP (resting state) the gate of K is closed & no K pass to out.



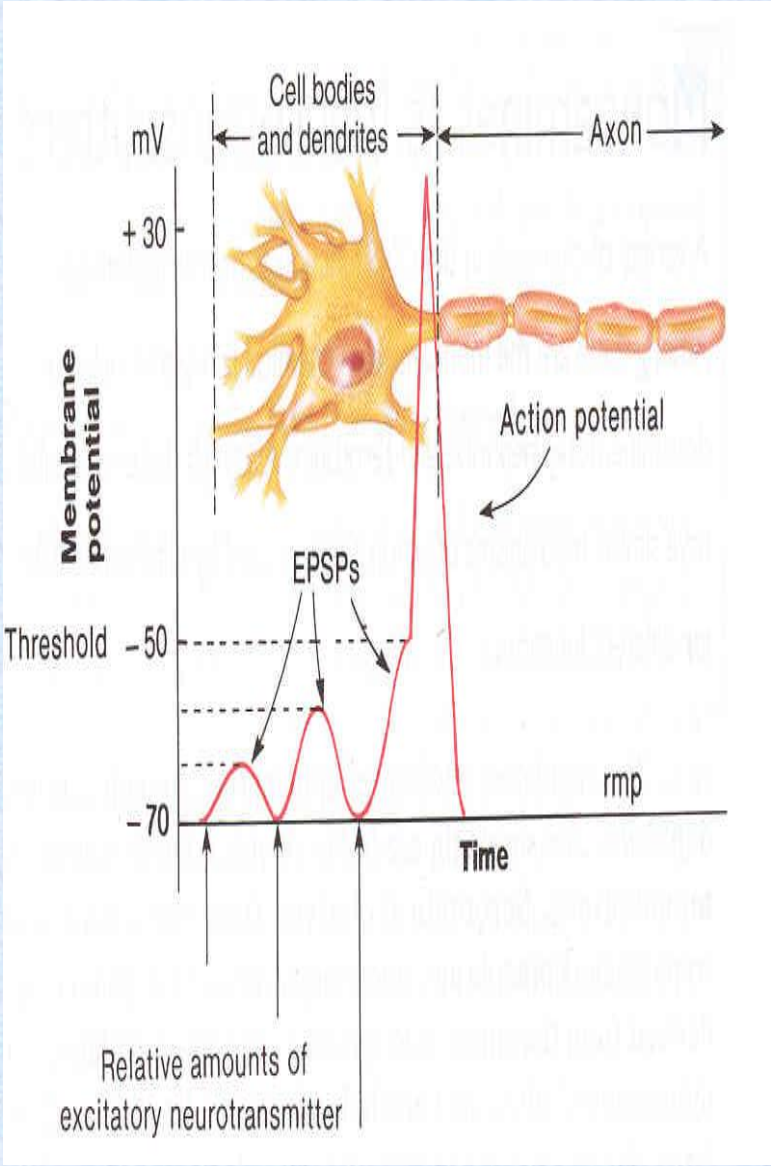
- b- after stimulation & between -90 to zero mv, the potassium channel opens slowly & K outflux begins slowly
- - They open completely only when Na gates close & when Na influx stop) causing rapid repolarization

-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 generation of AP, this is acute subthreshold potential
(which is graded متدرج and does not propagate). It should increase to threshold level to produce AP.

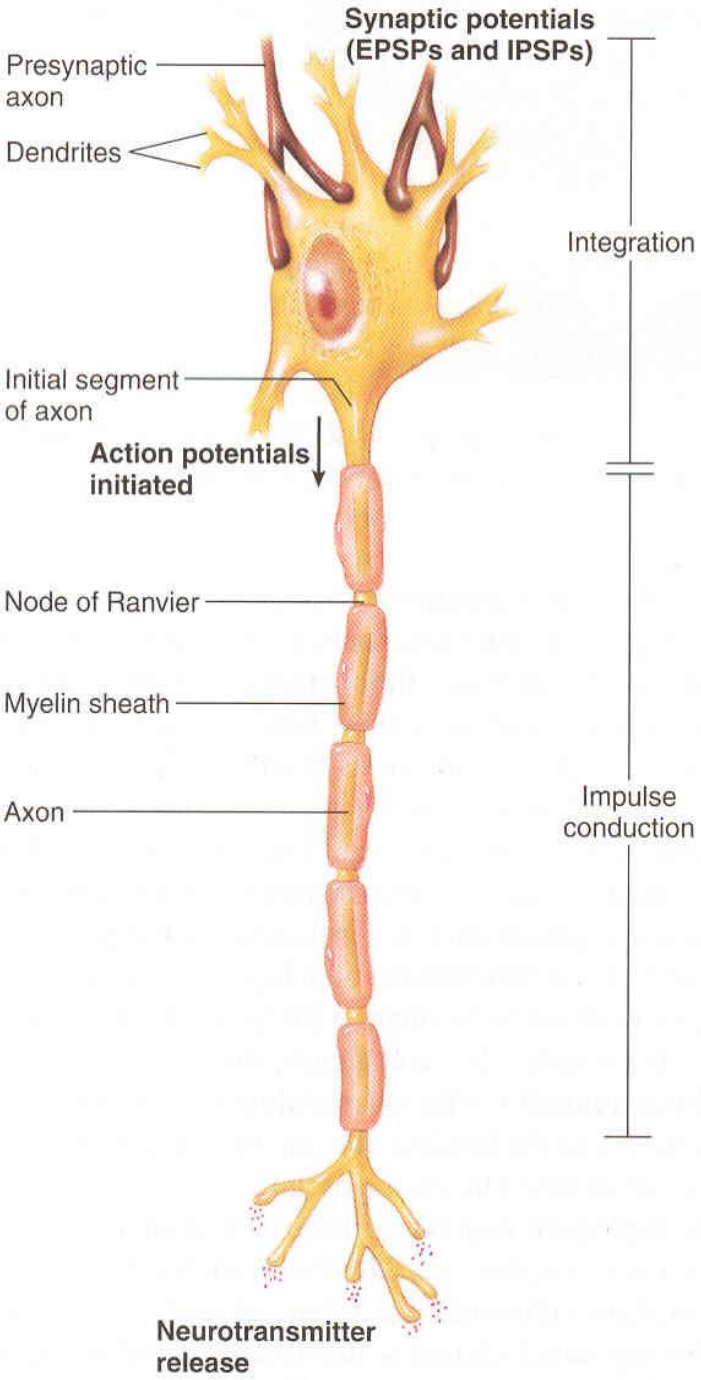
-The AP differs from local response in that AP is:-

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



All or nothing principle:-

- The nerve respond to a threshold stimulus maximally or does not respond at all (there are no half solutions)
- Once threshold stimulus applied, it gives AP spread all over the nerve fiber
- -its intensity (peak amplitude) can not increase by increasing stimulus intensity (or by suprathreshold)
- subthreshold stimulus can not elicit action potential (but produce a local response which 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

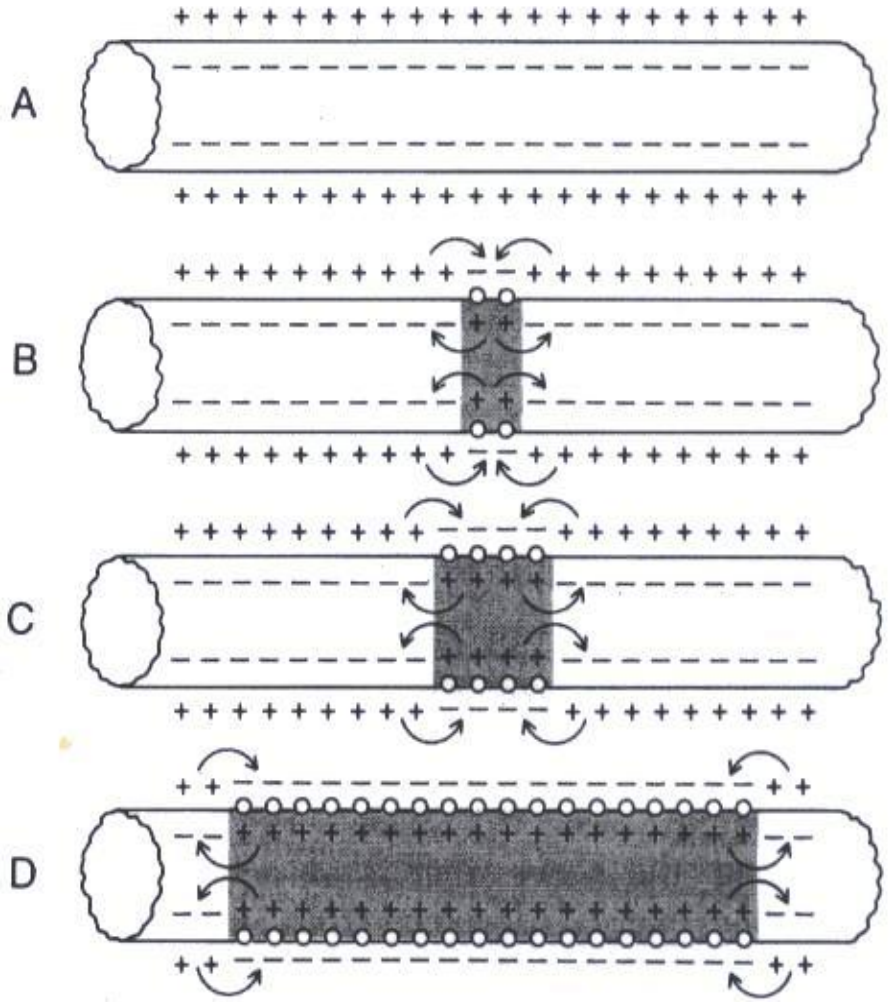


Figure 5–8 Propagation of action potentials in both directions along a conductive fiber.

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 conductance is 5000 folds , at the same time voltage gated K channels begin to open slowly

3- During depolarization :- Na conductance / K conductance > 1000 fold

4- 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 voltage gated K channels & no K+ conductance

2-Excitability changes

the ability to respond to a second stimulus

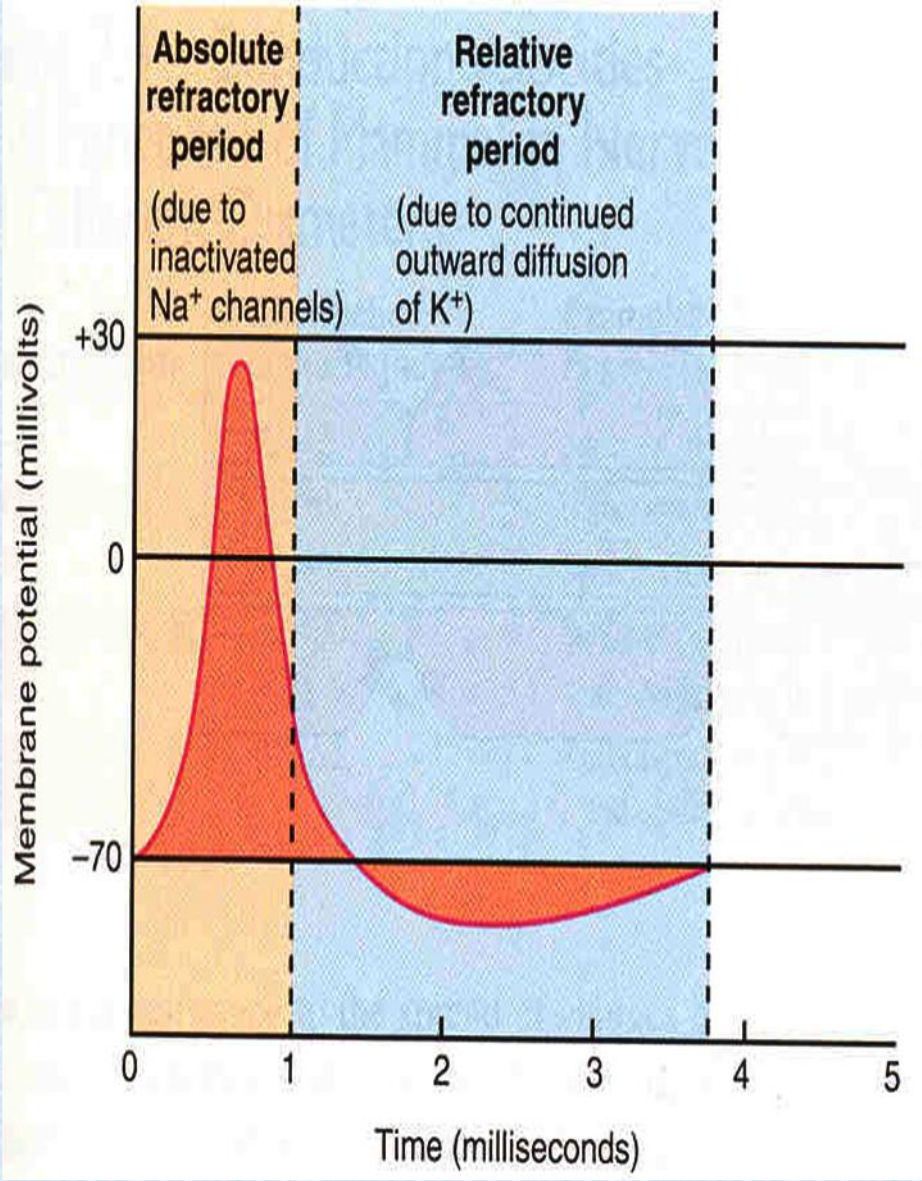
1-Latent period

2-absolute refractory (متمرد)period

- During depolarization & early repolarization

- during it the nerve can not excited by a a second stimulus & a second spike 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 stimulus can not open further Na channels



3- Relative refractory period:-

-It is during the late third of repolarization (½ to 1/4 absolute refractory period in its duration)

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

Why suprathreshol stimulus?

because :_

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

2- rapid flow of K to outside during repolarization oppose any stimulation to occur (so need stronger stim to cause a new AP.)

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

1- in myelinated nerve fibers by:-

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 (100 m/sec in large myelinated nerve fibers in comparison to 0.25 m/sec in small unmyelinated nerve fibers)

2-Conserve energy for axon because only nodes depolarize (need little energy for re-establishment of Na&K ions).

3-Insulation by myelin sheath allow repolarization to occur rapidly (with many K channls have not open)

2- Non- myelinated nerves by :-

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

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 means one in one direction then second in second direction