MEMBRANE POTENTIALS:

RESTING MEMBRANE POTENTIAL
ACTION POTENTIAL

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ION CHANNELS

- Ions move: concentration (from higher to lower) and electrical gradient (+ve and –ve attract)

- Leaky/non gated channels: K+, Na+ leak channels

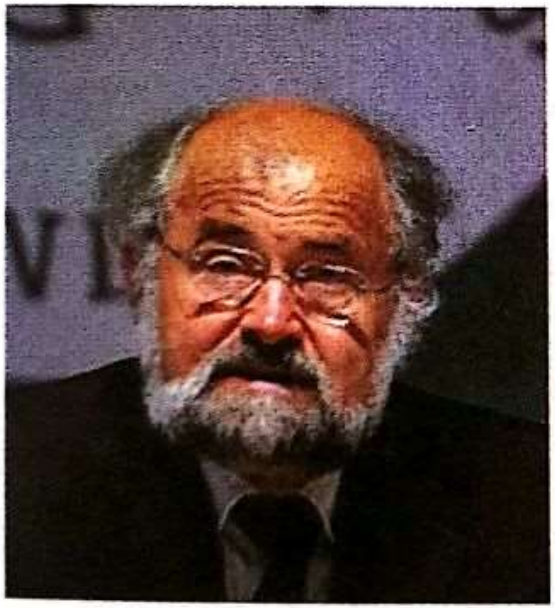
- Gated channels:

1) VOLTAGE GATED: K+, Na+, Ca++

2) ligand gated

* ATP driven pumps: Na+ K+ ATPase pump

Scientists contributed



Erwin Neher

Bert Sakmann

The 1991 Nobel Prize in Physiology or Medicine was awarded to two German scientists, Erwin Neher and Bert Sakmann for creating the experimental measuring device that conclusively proved the existence and function of ion channels.

Comprehensive textbook of Physiology, Dr. G K Pal.

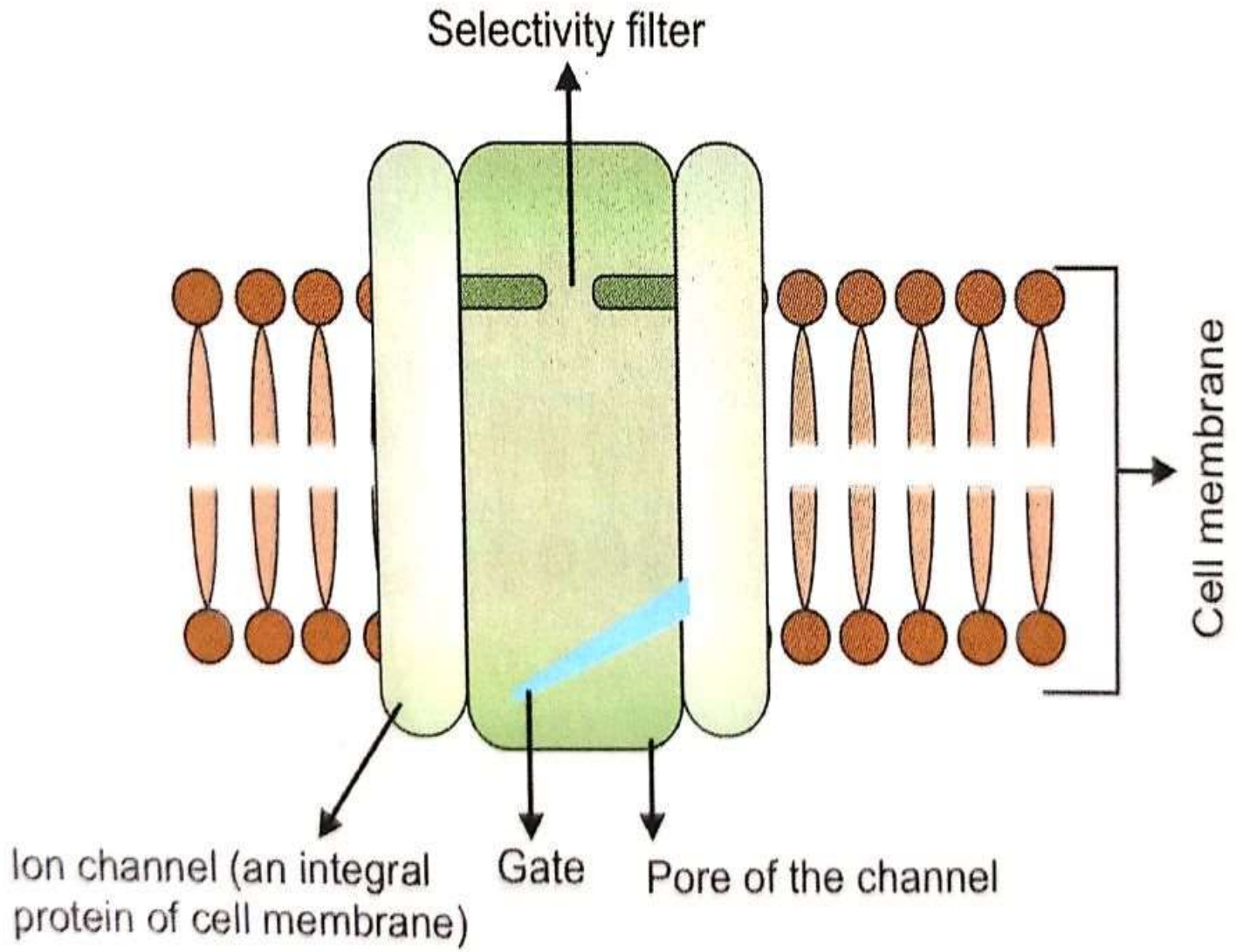


Fig. 6.1: A typical ion channel. Note the presence of selectivity filter and the gate.

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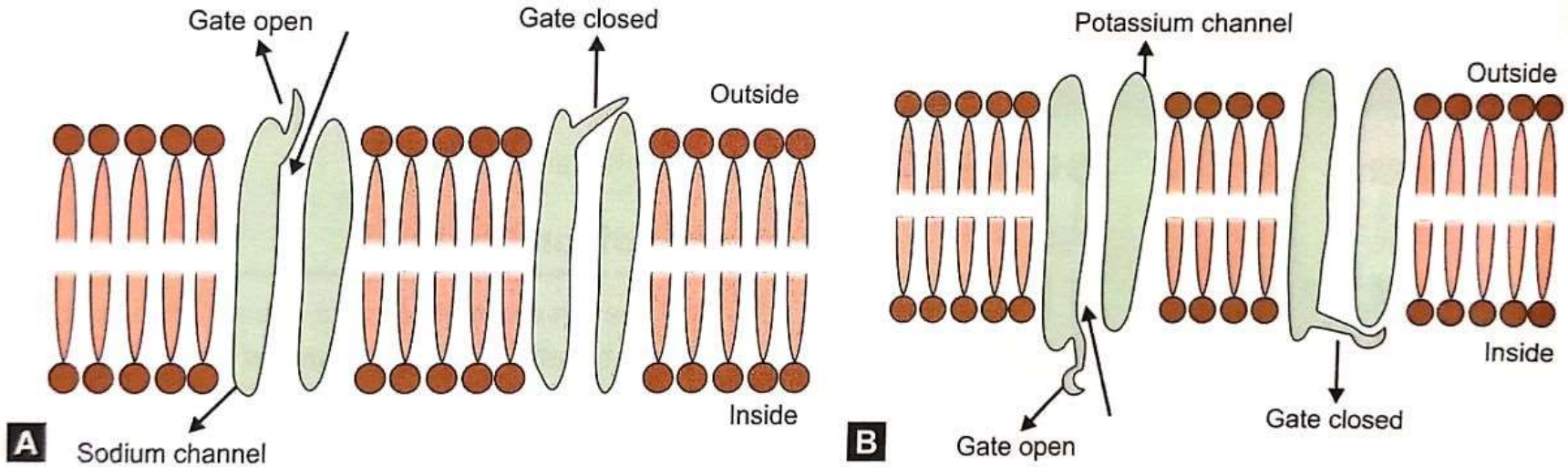

Figs. 6.2A and B: Gating mechanism of ion channel. Arrow indicates passage of ions through the gate when gate opens. (A) Gate is present on the outer side in sodium channel; (B) Gate is present on the inner side in potassium channel.

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Na+ channels

- LEAKY/NON GATED: RESTING STATE
- VOLTAGE GATED: WHEN STIMULATED
- 2 GATES: OUTER ONE: ACTIVATION GATE
  INNER ONE: INACTIVATION GATE
- DURING REST: INACTIVATION GATE: OPEN
  ACTIVATION GATE: CLOSED
- STIMULUS: ACTIVATION GATE: OPENS (BOTH GATES: OPEN)
- AT +35 (END OF DEPOLARISATION):
  INACTIVATION GATE: CLOSE
  ACTIVATION GATE: OPEN

* END OF REPOLARISATION: INACTIVATION GATE: OPEN
  ACTIVATION GATE: CLOSED

RESTING MEMBRANE POTENTIAL (RMP)

Definition- potential difference exists across the biological cell membrane under resting state. It is called rmp.

Normal value- it is -90 mv in skeletal muscle fiber. In nerve cell body it is -70 mv.

Recording- by microelectrodes (diameter of tip less than 1 micron) connected to cathode ray oscilloscope (CRO)

NORMAL VALUE OF RMP

-90 MV

NERVE FIBER/AXON, SKELETAL MUSCLE & CARDIAC MUSCLE FIBER

-65 TO-70 MV

FOR NERVE CELL BODY OR NEURON

-50 TO -30 MV

FOR SA NODE, AV NODE & SMOOTH MUSCLE

-10 MV

FOR RBCS

- # CAUSES OF NEGATIVE RMP:
- 1) Permeability of K+ ions is 100 times more than that of Na+ ions because size of hydrated K+ ion is less than hydrated Na+ ion so K+ ions can easily pass through K+ leak channels.
- number of k+ leak channels is more than Na+ leak channels, due to concentration gradient, K+ ions continuously diffuse outside the cell leading to net deficit of positive charge inside (causing negativity inside).

- 2) Negatively charged protein ions, sulfate ions and phosphate ions are non diffusible. hence they cannot leave the cell causing negativity inside.

- 3) Na+ K+ pump: this pump pushes 3 Na+ ions outside the cell in exchange of 2 K+ ions inside the cells causing net loss of positive charge inside.

UNEQUAL DISTRIBUTION OF IONS INSIDE & OUTSIDE THE CELL

1) presence of -ve charged nondiffusible anions (PO4-, proteins) inside the cell.

Gibbs-donnans equilibrium

2) Na-K pump

(which create more na in ecf & more k in icf.)

GIBBS-DONNAN'S EQUILIBRIUM

1. **Solutions on either side of the membrane (intra and extracellular fluids) are electrically neutral, i.e. The total charges on cations are equal to those of anions.**

2. **The product of diffusible ions on one side of membrane is equal to the product of diffusible ions on the other side.**

3. **Presence of non diffusible ions on one side changes the concentration of cations and anions.**

Nernst or diffusion potential

Equilibrium potential at which there is no net diffusion of ion in any direction, when membrane is permeable only to that ion.

At this stage, the electrical force developed because of diffusion of ions will be exactly equal but opposite to force due to concentration gradient and net diffusion of the ions stops.

- Nernst potential for different ions can be calculated by Nernst equation.

- Emf (mv) =

- 61 log concentration of ion inside the cell

  concentration of ion outside the cell.

NERNST POTENTIAL

- Cl– = –70 MV,
- K+ = –94 MV,
- Na + = +61 MV.

GOLDMANN HAS PREPARED AN EQUATION FOR FINDING OUT RESTING MEMBRANE POTENTIAL, BY CONSIDERING:

(i) **POLARITY** OF ION

(ii) **CONCENTRATION GRADIENT** FOR ION ACROSS THE CELL MEMBRANE

(iii) **PERMEABILITY** OF THE CELL MEMBRANE FOR THE ION.

GOLDMANN'S EQUATION IS AS FOLLOWS:

$$\text{EMF (millivolts)} = -61 \cdot \log \frac{C_{Na^+_i} P_{Na^+} + C_{K^+_i} P_{K^+} + C_{Cl^-_o} P_{Cl^-}}{C_{Na^+_o} P_{Na^+} + C_{K^-_o} P_{K^+} + C_{Cl^-_i} P_{Cl^-}}$$

Under the resting state cell membrane is most permeable to K+ ions.

RMP is mainly caused due to diffusion potential for K+ ions

Thus diffusion potential caused by diffusion of diffusible ions (mainly K+ ions) is the main cause of development of resting membrane potential.

ACTION POTENTIAL:
HODGKIN AND HUXLEY IN 1950

1) **DEFINITION**
2) **PHASES (DEPOLARIZATION, REPOLARIZATION)**
3) **COMPONENTS AND IONIC BASIS OF AP**
4) **CHARACTERISTICS OR PROPERTIES OF AP**
5) **RECORDING OF AP (BY CRO)**
6) **AP IN OTHER EXCITABLE TISSUES**

ACTION POTENTIAL

SELF PROPAGATIVE WAVE OF DEPOLARIZATION WHICH IS PRODUCED WHEN A THRESHOLD STIMULUS IS GIVEN TO AN EXCITABLE TISSUE (NERVE, MUSCLE ETC).

ACTION POTENTIAL

- **ADEQUATE/THRESHOLD STIMULUS**
- **REVERSAL OF MEMBRANE POTENTIAL**
- **DEPOLARIZATION PHASE**
- **REPOLARIZATION PHASE**

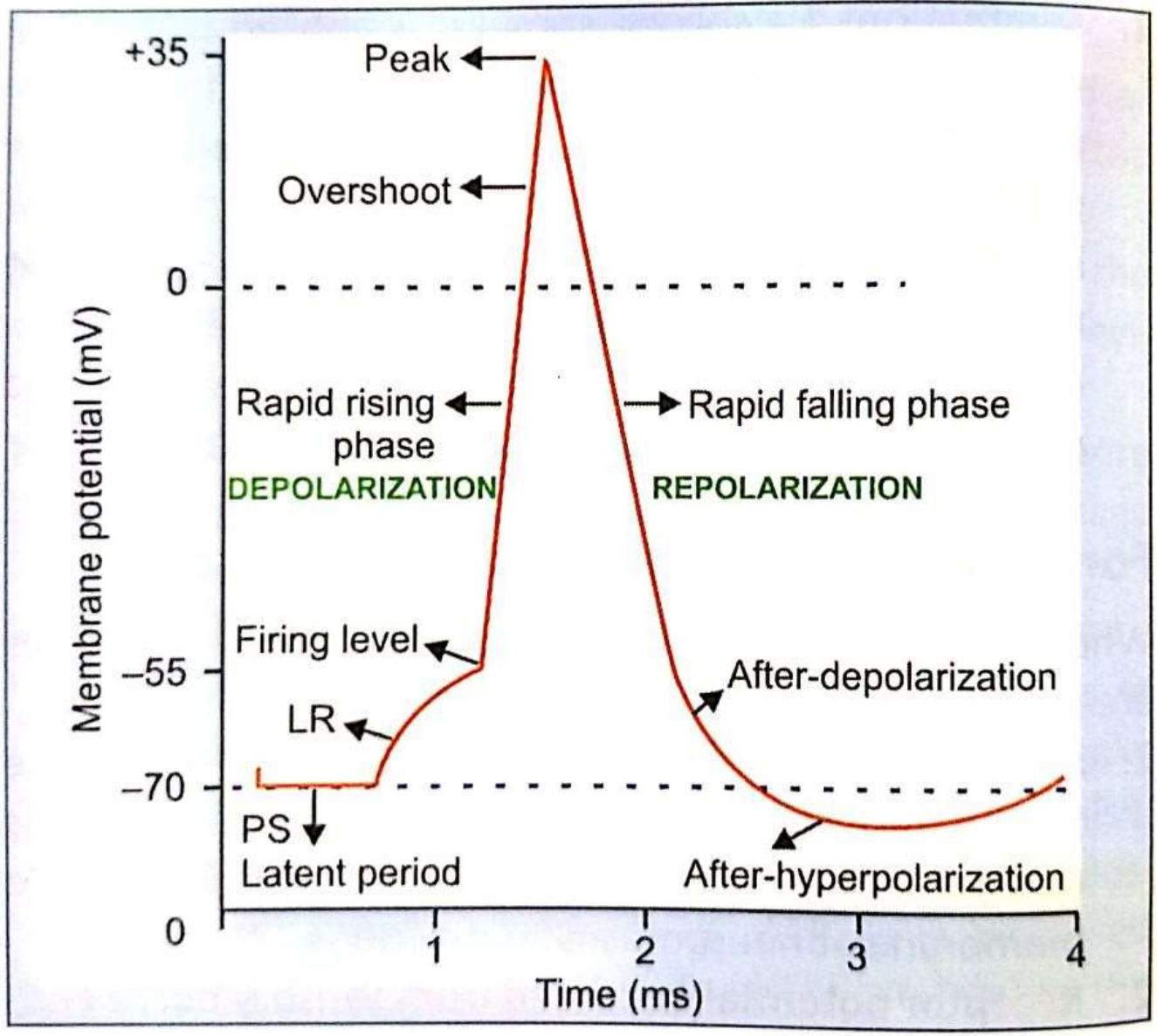

Fig. 23.3: Phases of action potential recorded from a neuron. Note, depolarization phase, overshoot and peak; and repolarization phase consists of rapid falling phase and after-depolarization. (LR: Local response; PS: Point of stimulation).

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Components and ionic basis of AP

Depolarization Firing level	**-90 mv to +35 / VG fast Na+ chann.** **- 60 Mv: Hodgkin's effect:+feedback**
Spike potential & overshoot	**steep part of AP, part of AP above 0 mv**
Repolarization : initial: fast, Slow: **- after potential**	**+35 to -90 / VG K+ channels: exit of K+** **slow repolarization- decreased K+ gradient- slow exit of K+**
+after potential	**hyperpolarization – delayed closure of VG K+ channels: exit of more K+**

Latent period	**Time taken by AP to reach recording E along axon.**
Threshold / **Firing level**	**VG fast Na+ channels open rapidly** **+ feedback: Hodgkin's effect**
Stimulus artifact	**current leak from stimulating E to recording E.**

FUNCTIONS OF Na+ K+ PUMP

1. **The pump helps in creating & maintaining unequal concentrations of Na+ & K+ ions inside & outside the cell.**

2. **It helps in maintaining & regulating the cell volume.**

3. **It acts as electrogenic pump and therefore contributes little bit in the RMP.**

4. **After the passage of no. of impulses along the nerve fiber, it brings the ionic concentration of the fiber back to normal. It is called recharging.**

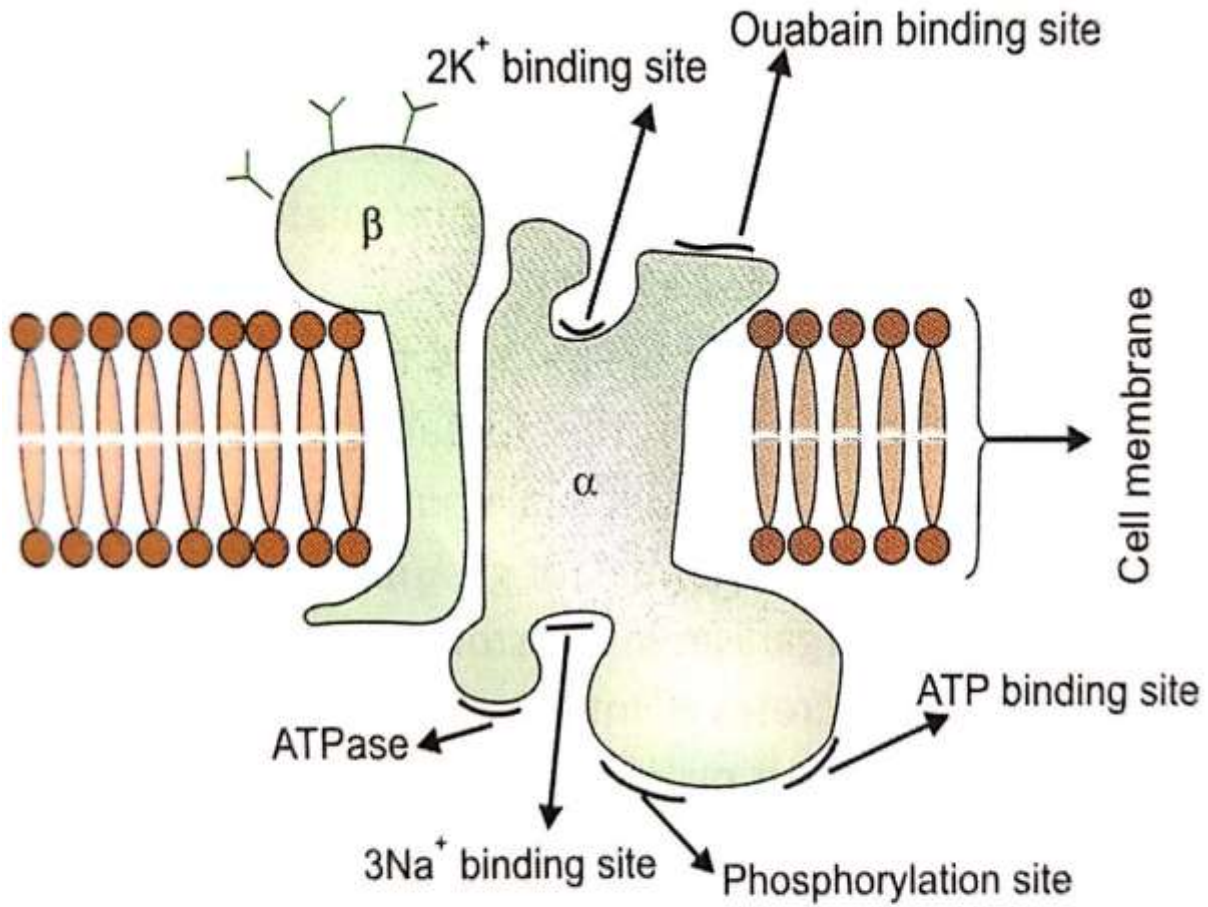

Fig. 6.8: Structure of Na^+-K^+ ATPase. It has a small β subunit and large α subunit. The extracellular surface of α subunit contains binding sites for two K^+ and ouabain, and intracellular surface has binding sites for three Na^+ and one ATP, a phosphorylation site and an ATPase site.

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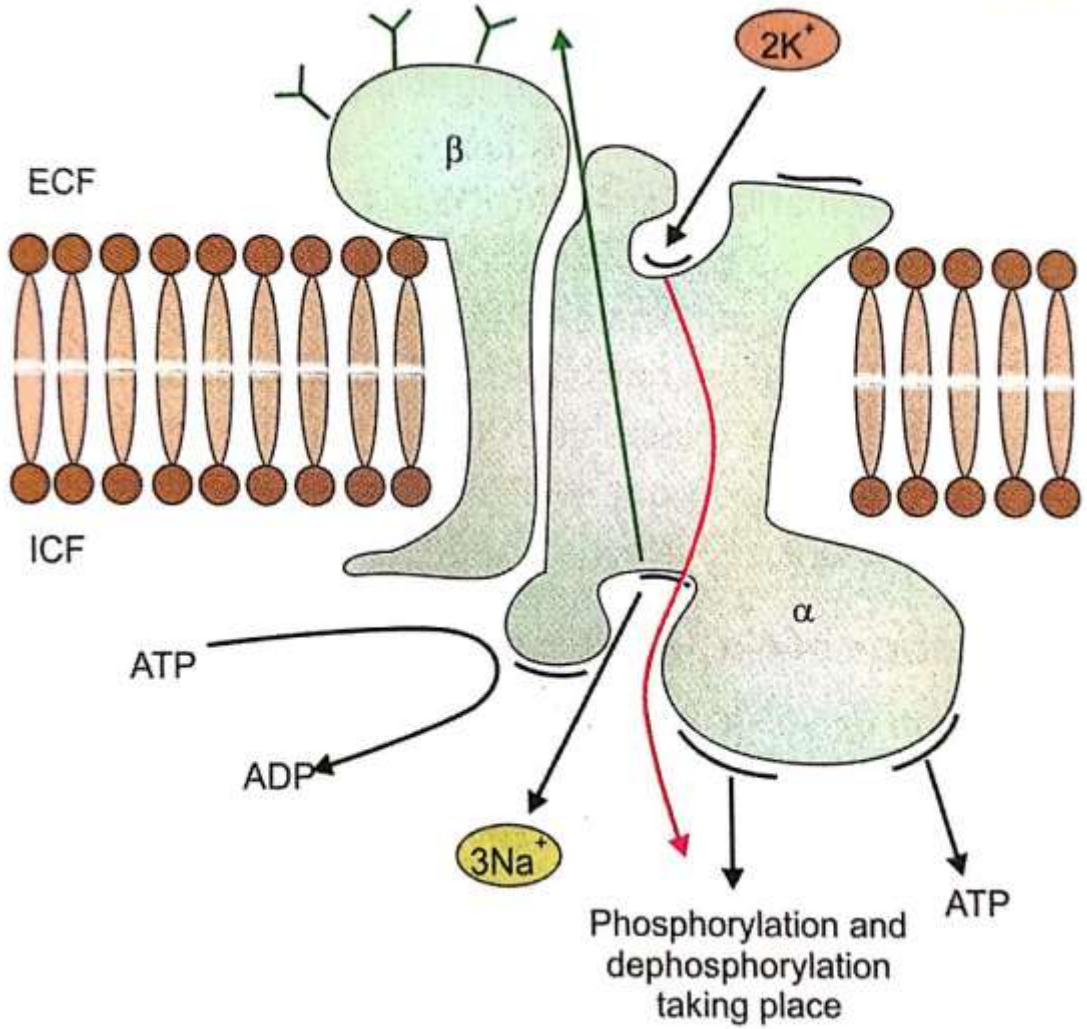

Fig. 6.9: Mechanism of action of Na^+-K^+ ATPase. Binding of three Na^+ and one ATP to their respective sites on α subunit activates ATPases that converts ATP to ADP. This causes phosphorylation of α subunit that changes its configuration and transfers 3 Na^+ to ECF. K^+ binds to K^+ binding site on the extracellular surface that causes dephosphorylation of α subunit and transfers two K^+ from ECF into the cell. Thus, three Na^+ are pumped out for entry of two K^+ into the cell, and one ATP is hydrolyzed.

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RECORDING OF AP

- **Monophasic AP**: one electrode outside and other in the nerve: positive deflection only: cro
- **Biphasic AP**: both electrodes outside nerve: one negative and other positive deflection
- **Compound AP**: from nerve trunk having myelinated and unmyelinated nerve fibers: sum of all AP's

LOCAL POTENTIAL, ELECTROTONIC POTENTIAL

- Subthreshold stimulus
- Small amount of voltage gated na+ channels open
- Firing level of -60mv is not reached.
- Positive side=depolarizing :catelectrotonic potential) or
- Negative side= hyperpolarizing anelectrotonic potential.
- E.G. EPSP, IPSP, receptor potential, pacemaker potential.

LOCAL POTENTIAL:

- Cannot propagate, do not have refractory period and they do not follow all or none law.
- Do not have any threshold or latent period

ACTION POTENTIAL:

- Propagative, has refractory period and follows all or none law.
- It has threshold or latent period

INITIATION OF ACTION POTENTIAL

- IN A MOTOR NEURON ACTION POTENTIAL :BEGINS FROM THE AXON HILLOCK REGION BECAUSE VOLTAGE GATED na+ AND K+ CHANNELS ARE MAXIMUM AT THIS PART.

- In sensory neurons action potential begins in first node of ranvier.

- These areas (axon hillock and first node of ranvier) are called as trigger zones.

Na+ CHANNELS

- IN MYELINATED NEURONS, THE NUMBER OF na+ CHANNELS PER SQUARE MICROMETER OF THE MEMBRANE IS AS FOLLOWS-

- Cell body 50-75
- *Axon hillock* ***350-500***
- *Nodes of ranvier* ***2000-12000***
- Axon terminals 20-75
- Channels are maximum in nodes of ranvier and axon hillock region.

- **Channelopathies:** the diseases resulting in structural or functional defects of ion channels are called channelopathies.

PROPERTIES OF NERVE FIBERS/ACTION POTENTIAL

- Excitability: action potential
- Conductivity: saltatory conduction
- Refractory period:
  Absolute/relative
r
* Summation
* Accomodation
- Infatigability
- All or none law

CONDUCTION / PROPAGATION OF ACTION POTENTIAL

- Conducted along whole membrane in both direction without decrement.

- Circuit of current (current sink) or circular current flow : start between stimulated area and adjacent areas.

- ***Orthodromic:*** forward conduction (common)
- Antidromic: backward conduction: axon reflex

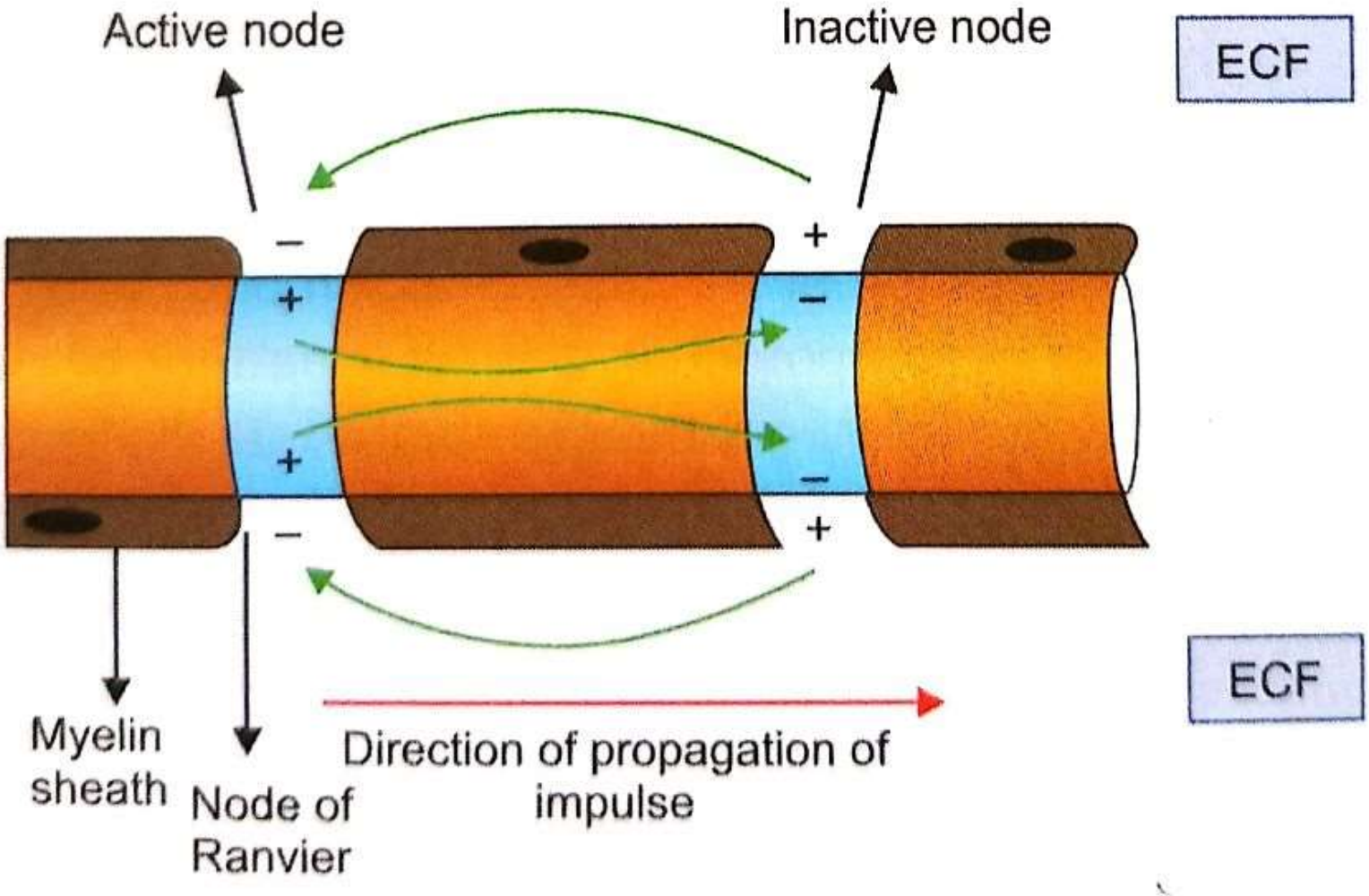

Fig. 23.9: Propagation of action potential in myelinated axon.

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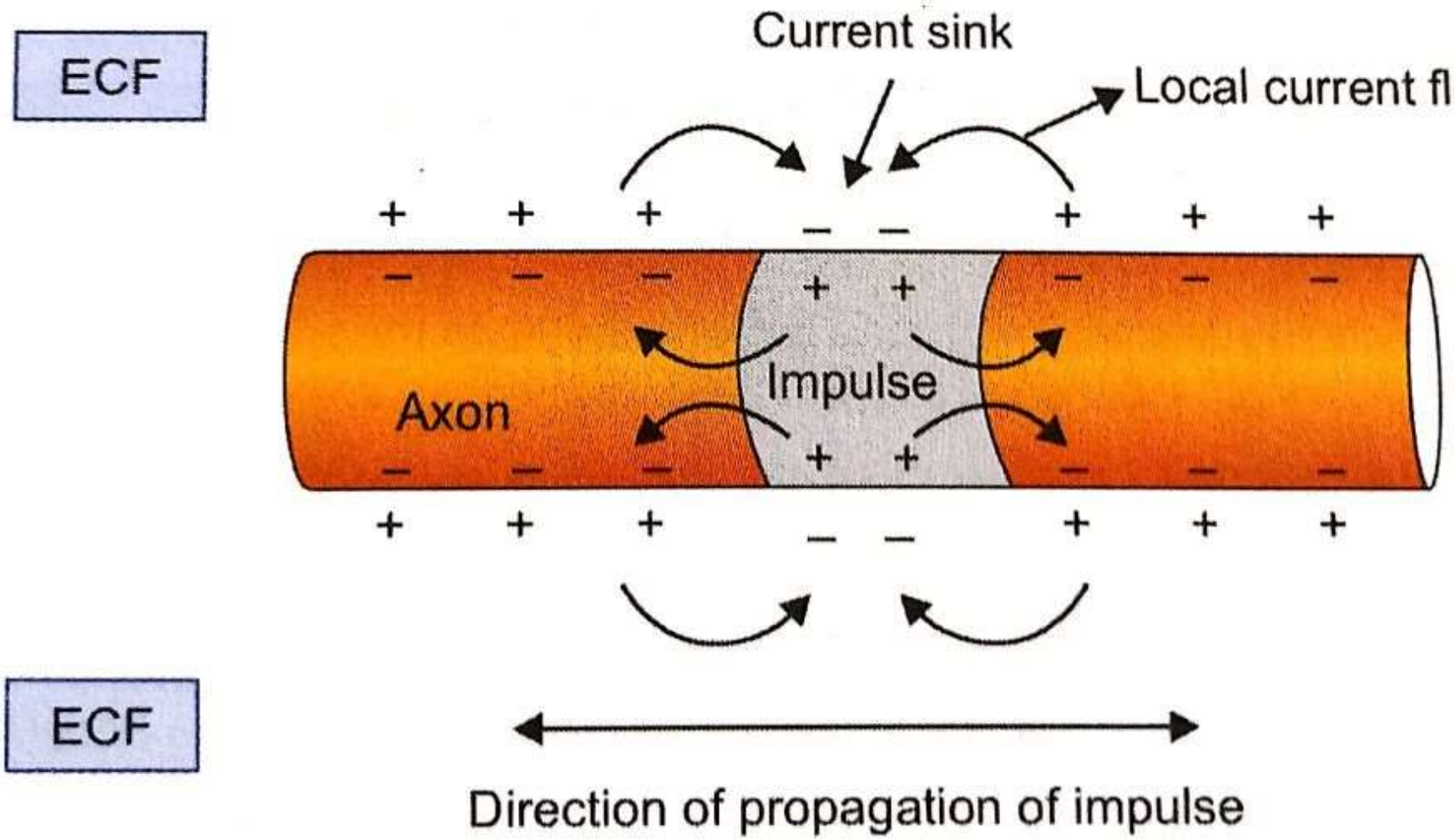

Fig. 23.8: Propagation of action potential in unmyelinated axon.

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REFRACTORY PERIOD

- Refractory means non-responsive.

- The duration for which action potential is not produced due to 2nd stimulus is called refractory period.

- **absolute refractory period**:-how ever strong the strength of stimulus, the next AP is not produced.

  from firing level until one third of repolarization.

- **relative refractory period**:-stronger stimulus.

  end of ARP to 2/3rd of repolarisation.

ONE WAY CONDUCTION

- ***ORTHODROMIC:*** FORWARD CONDUCTION (COMMON): FROM CELL BODY TO AXON TERMINAL
- ANTIDROMIC: BACKWARD CONDUCTION: RARE * AXON REFLEX
- WHY ?????
- BECAUSE AREA BEHIND STIMULATED PART IS REFRACTORY TO 2^{ND} STIMULUS, HENCE AP CANNOT

ACCOMODATION

- ADAPTATION
- IF FIRING LEVEL IS REACHED SUDDENLY, AP IS PRODUCED

- WHEN STIMULUS IS INCREASED SLOWLY TO FIRING LEVEL: NO ACTION POTENTIAL
- Na+ CHANNELS OPEN BUT GET INACTIVATED WITHIN 1 msec.

INFATIGUABILITY

- NERVE FIBER CANNOT BE FATIGUED.
- ABSOLUTE REFRACTORY PERIOD

SUMMATION

- 1 SUBMINIMAL STIMULI: NO RESPONSE
- MANY SUBMINIMAL STIMULI: GET SUMMATED, PRODUCE MINIMAL STIMULI, ACTION POTENTIAL IS PRODUCED

ALL OR NONE LAW

MINIMAL STIMULI: FULL AP

SUBMINIMAL STIMULI: NO AP

THERE'S NOTHING LIKE HALF AP

THANK YOU