Lecture 1. Functions of the cell membrane. Mechanisms for transporting substances through the membrane. Membrane potentials. Resting potential and action potential

- Physiology - biomedical science that studies the vital functions of the whole organism and its parts - systems, organs , tissues, cells - to identify the causes , mechanisms and patterns of life of the organism and its interaction with the environment.

Methods of study

- Observation
- Experiment

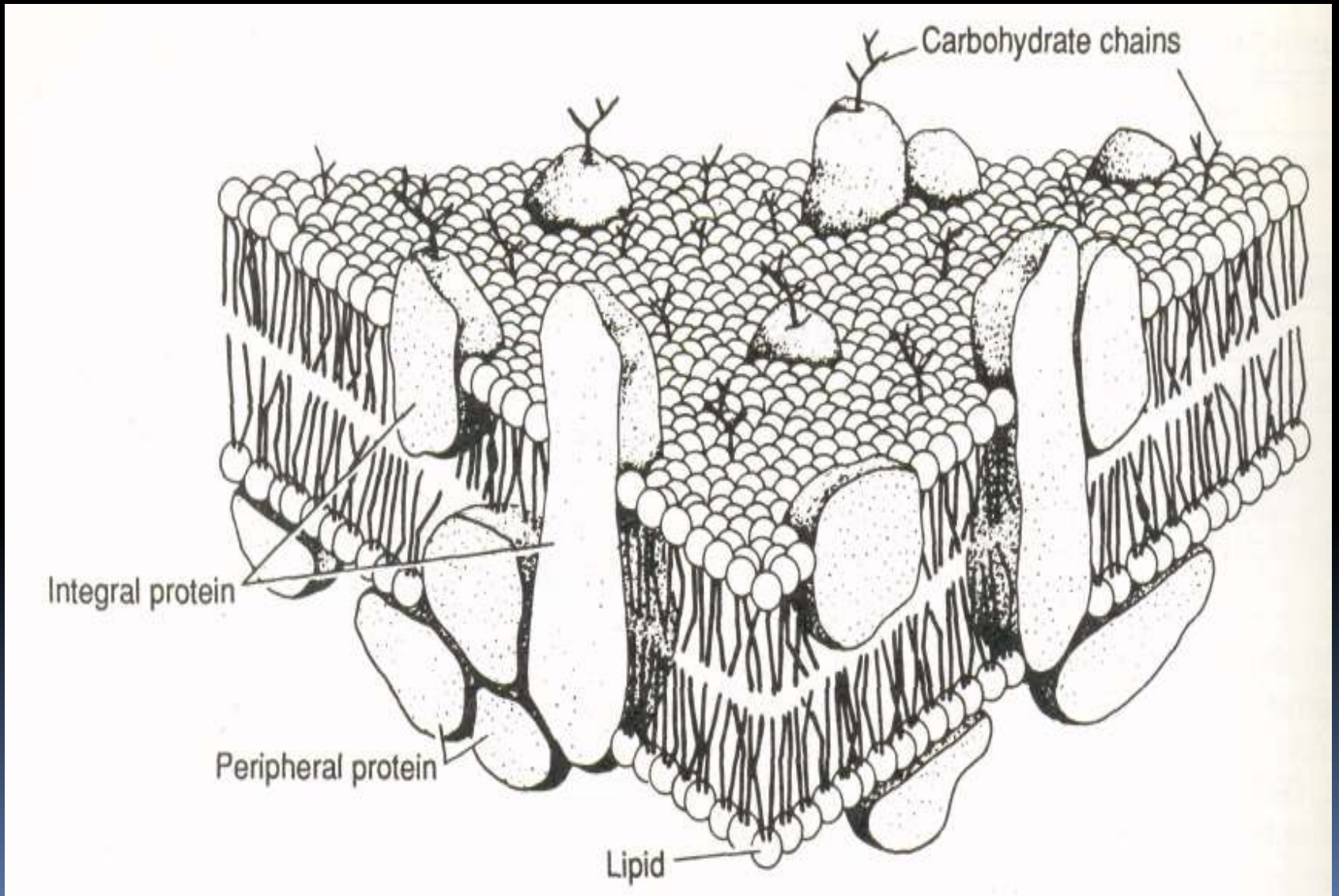
- acute

- chronic

- Modeling

PHYSIOLOGY OF EXCITABLE TISSUE

The fluid mosaic model of membrane structure



Functions of biological membranes

- 1.Structural
- Maintain shape of cells & intracellular organelles
- Form the cytoskeleton
- 2. Barrier
- Compartmentalization (separate cell space into individual compartment)
- 3. Membranes perform ADHESION of cells. This property determines the existence of multicellular organisms

- 4. Antigenic. It consists in the fact that on the cell membrane there are protein structures characteristic of the cells of the tissue of this organism. These structures are designed for mutual "recognition" of cells. Due to their presence, it is possible to implement the body's immune defenses. This function plays an important role in organ transplantation, donor blood transfusion.
- 5. Electrogenic. Is that on both sides there is a difference in the concentrations of K +, Na +, Ca2 +, Cl- and other ions. Plasma membranes are virtually impermeable to negatively charged cytoplasmic protein molecules, have limited permeability to Na +, and are freely permeable to K + and Cl-.

- 6. Catalytic
- Many membrane proteins are enzymes
- Can only fulfill their function only if they were in the membrane
- 7.Receptor
- Some membrane proteins are receptors, can recognize & bind certain hormones, mediators & modulators which can initiate physiological change in cells
- 8.Transport
- Most of the charged, polar and hydrophilic substances cannot penetrate membrane freely, they need special transport system
- Most penetrating proteins can function as transport proteins

Functions of membrane proteins

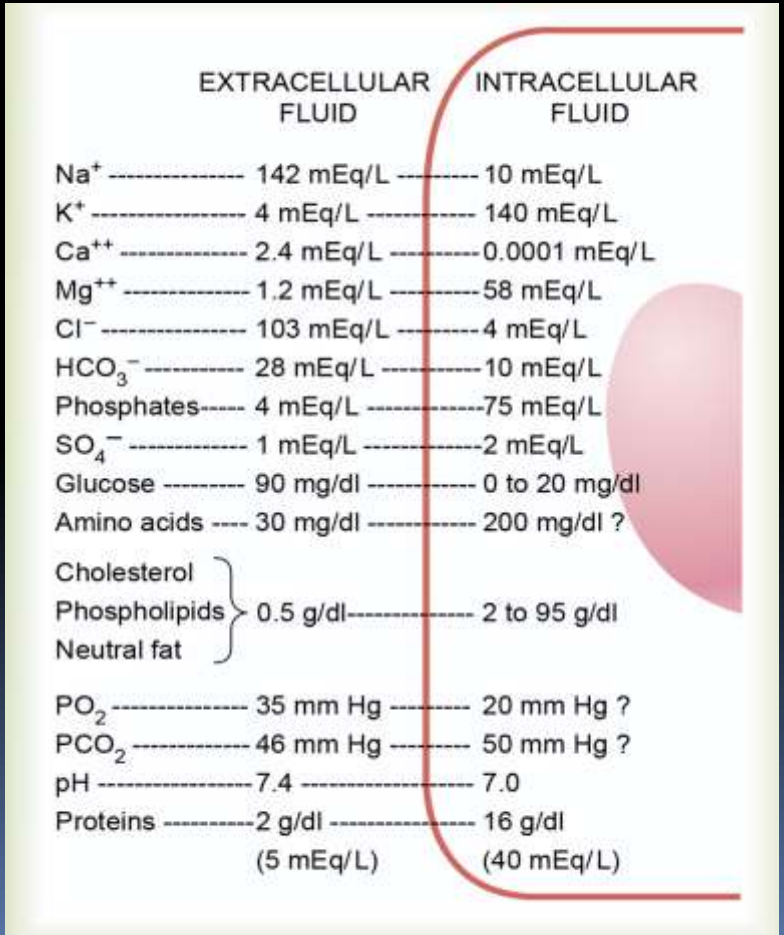
- Transport
- Structure
- Receptors
- Enzymes
- Antigens

BIOMEDICAL IMPORTANCE

- Gross alterations of membrane structure can affect water balance and ion flux and therefore every process within the cell. Specific deficiencies or alterations of certain membrane components lead to a variety of diseases.

- Examples include the lysosomal absence of acid maltase, causing type II glycogen storage disease; the lack of an iodide transporter, causing congenital goiter; and defective endocytosis of low-density lipoproteins, resulting in accelerated hypercholesterolemia and coronary artery disease

Chemical compositions of extracellular and intracellular fluids.



	EXTRACELLULAR FLUID	INTRACELLULAR FLUID
Na^+	142 mEq/L	10 mEq/L
K^+	4 mEq/L	140 mEq/L
Ca^{++}	2.4 mEq/L	0.0001 mEq/L
Mg^{++}	1.2 mEq/L	58 mEq/L
Cl^-	103 mEq/L	4 mEq/L
HCO_3^-	28 mEq/L	10 mEq/L
Phosphates	4 mEq/L	75 mEq/L
$SO_4^=$	1 mEq/L	2 mEq/L
Glucose	90 mg/dl	0 to 20 mg/dl
Amino acids	30 mg/dl	200 mg/dl ?
Cholesterol, Phospholipids, Neutral fat	0.5 g/dl	2 to 95 g/dl
PO_2	35 mm Hg	20 mm Hg ?
PCO_2	46 mm Hg	50 mm Hg ?
pH	7.4	7.0
Proteins	2 g/dl (5 mEq/L)	16 g/dl (40 mEq/L)

Transport Across Membranes

- 1. **Macrotransport**
- **2. Microtransport**

Macrotransport

- 1. **Endocytosis**

- A. Phagocytosis
- B. Pinocytosis

- 2. **Exocytosis**

Microtransport

- 1. Passive
- 2. Active

Passive transport

- 1. Simple diffusion
- 2. Facilitated diffusion
- 3.Osmosis

Simple diffusion

- **Movement of molecules in response to a concentrational gradient.**
- **It doesn't need energy**

Facilitated diffusion

- **It doesn't need energy too, but needs special carries**

Osmosis

- The process of movement of water caused by a concentrations difference of solutions is called osmosis.

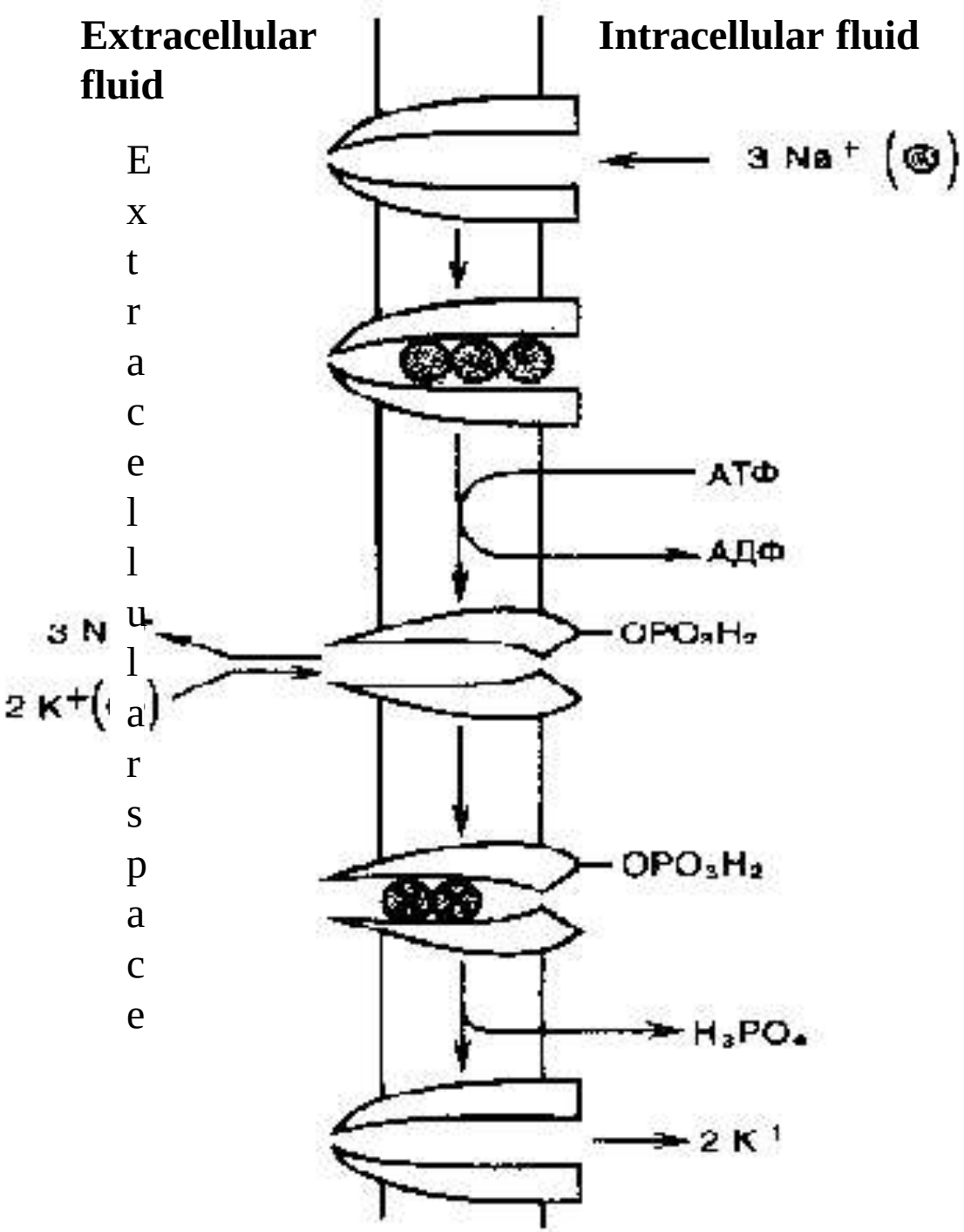
Active transport

- Goes against concentration gradient and requires energy.
- 1. Primary
- 2. Secondary

Primary active transport

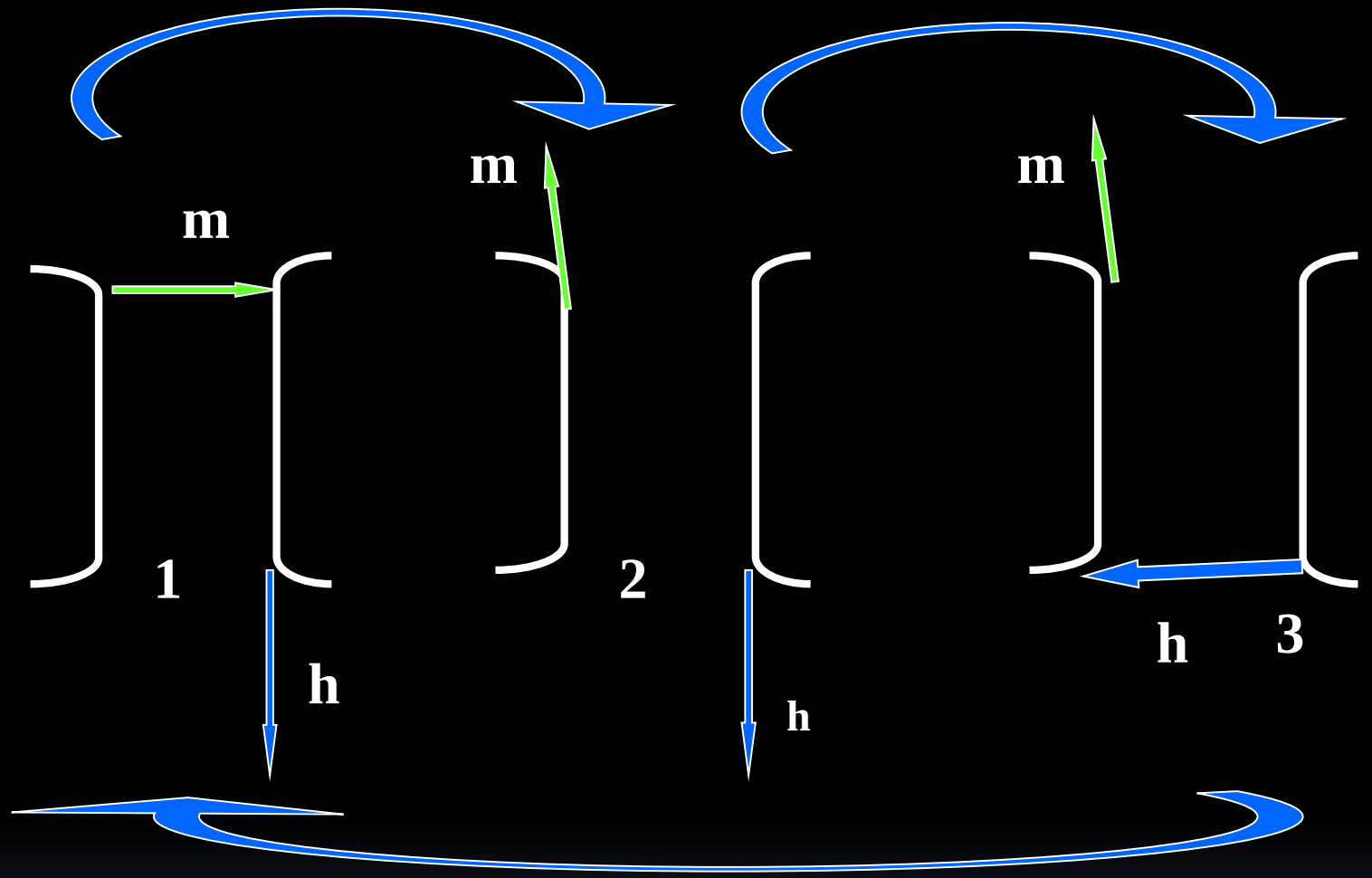
- This is transportation of the ions with the help of special enzymatic transport systems (ATP-ases)

- E.g. Na / K – pump


Extracellular fluid
Intracellular fluid
Extracellular space
3 Na+
АТФ
АДФ
3 N
2 K+
OPO3H2
OPO3H2
H3PO4
2 K+

Gating of Protein Channels

- . 1. *Voltage gating.*
- . 2. *Chemical (ligand) gating.*



The number of opened channels regulates membrane permeability

Equilibrium potential

- **Equilibrium state** – is such an electrical charge on the membrane which completely balances the concentration gradient for a certain ion & the current for this ion is equal **o.**
- **Potassium equilibrium potential =**

  -97,5 mV (E_{K^+} = -97,5 mV)

Mechanisms for maintaining ionic asymmetry

- The electric charge on the membrane promotes the entry of potassium into the cell and inhibits its exit
- The sodium-potassium pump is an active transport that transports ions across the membrane against a concentration gradient

depolarization

- Occurs at the opening of sodium channels
- **Sodium enters the cell:**

❖ decreases negative charge on the inner surface of the membrane

❖ Decreases electrical gradient

❑ ***Level of depolarization depends on the number of opened sodium channels***

CRITICAL LEVEL OF DEPOLARIZATION E_{CR}

- Charge on the membrane which opens max amount of sodium channels
- This number of opened channels is critical for further development of action potential
- «evelange» sodium influx
- sodium influx is 20 times more than potassium efflux
- ***Regenerative depolarization starts***

Threshold of depolarization

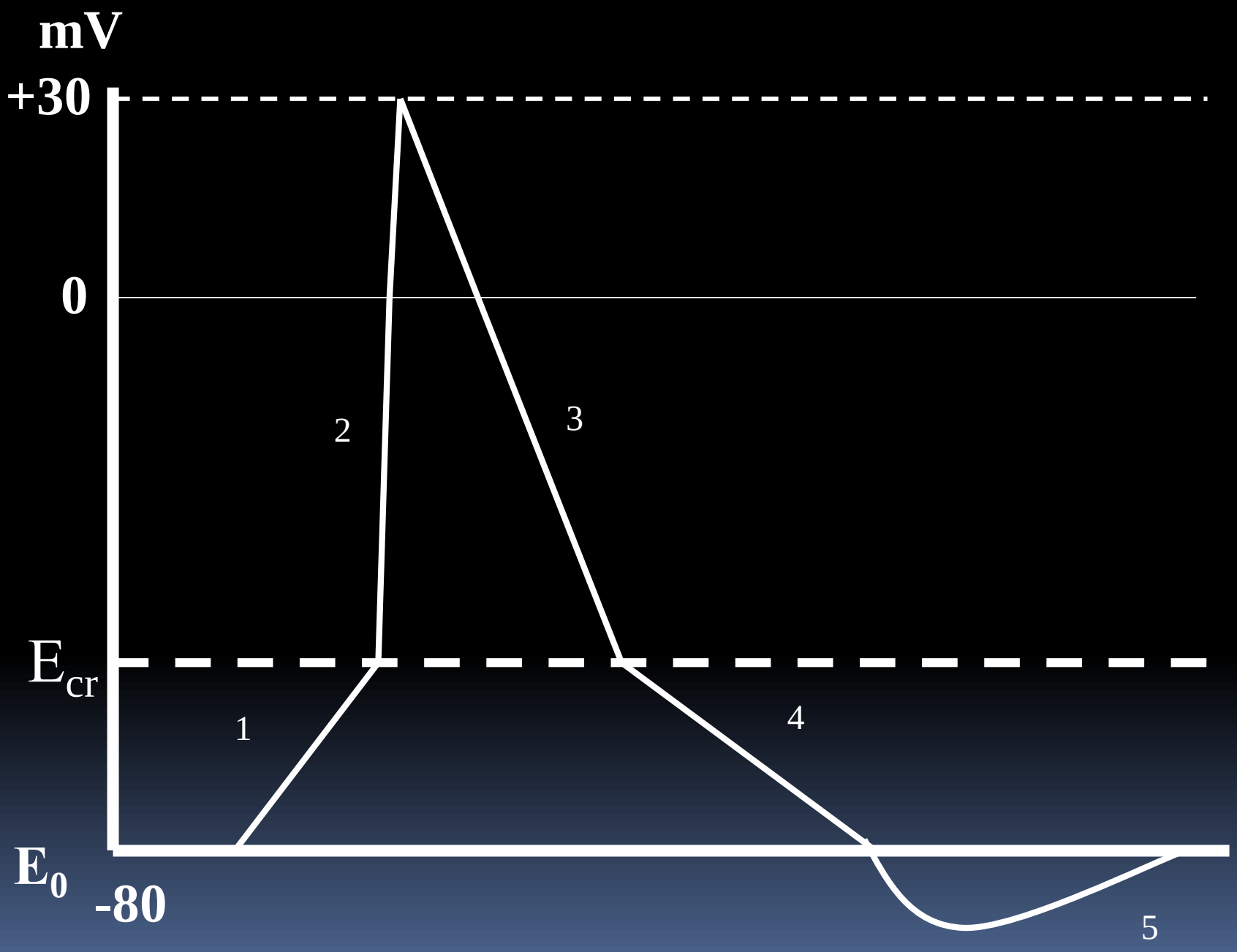
- Difference between resting potential (E_o) &critical level of depolarisation (E_{cr})

$$\Delta V = E_o - E_{cr}$$

- Is in inverse proportion to excitability – the lower is the threshold, the higher is excitability of the membrane

ACTION POTENTIAL (AP)

- Action potential (AP) is a difference of potentials between depolarized and non-depolarized parts of the membrane, which occurs as the result of quick membrane depolarization with the following restoration of membrane potential.
- AP magnitude is 120-130μV, its average duration is 3-5 msec (in different tissues it may be from 0,01 msec to 0,3 sec)

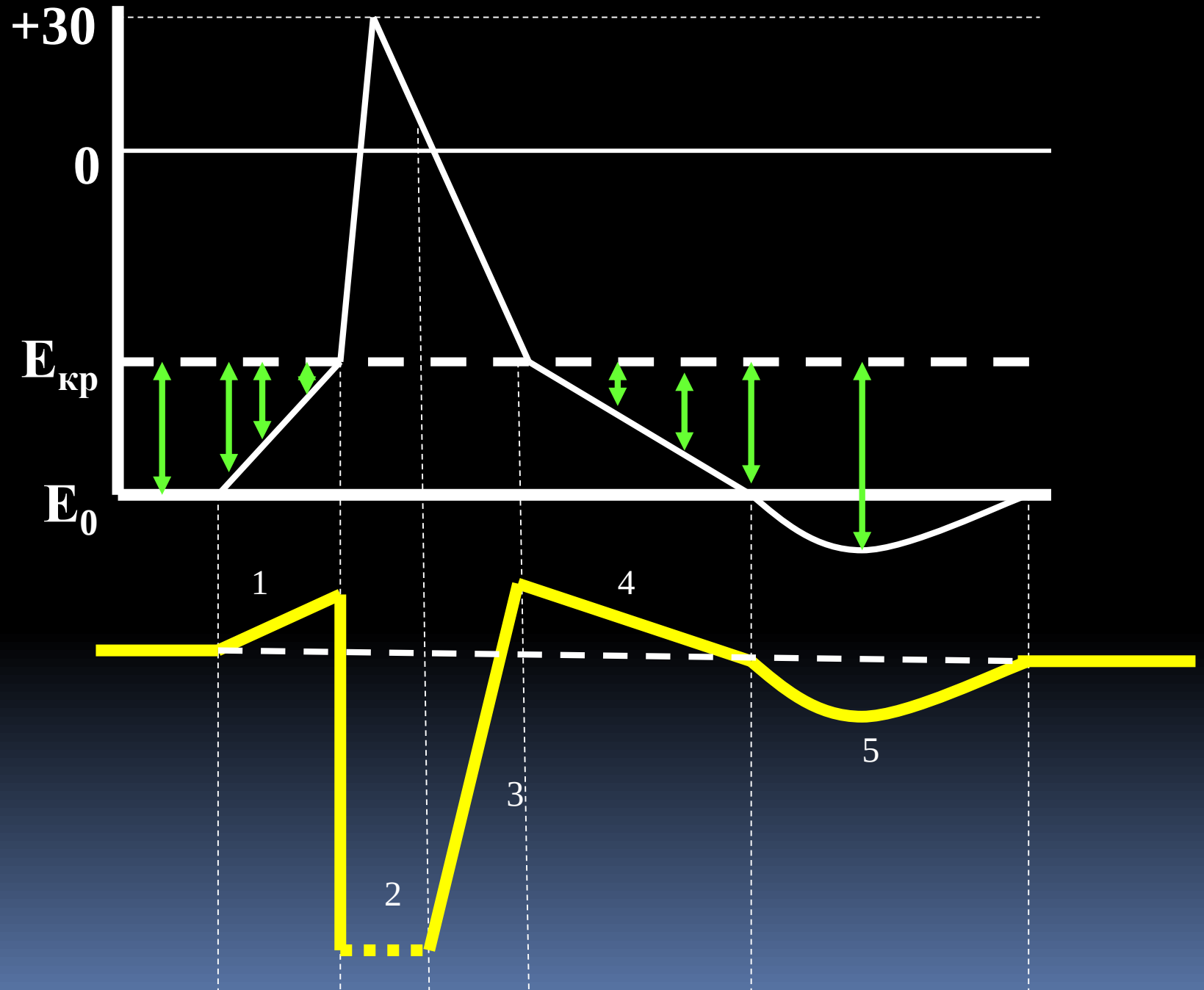

mV
+30
0
E_{cr}
E_0
-80
1
2
3
4
5

Excitability changes during AP development

- Excitability is in inverse proportion to depolarization threshold

$$\Delta V = E_0 - E_{cr}$$

- $\uparrow \Delta V \longrightarrow$ excitability $\downarrow$
- $\downarrow \Delta V \longrightarrow$ excitability $\uparrow$


+30
0
$E_{кр}$
E_0
1
2
3
4
5

LABILITY

- **Lability (functional mobility)** is the largest number of action potentials an excitable substrate is capable of generating per second in response to frequently recurring stimuli.
- Lability = 1000ms/abs.ref.phase.

- L. of the nerve is equal to = 1000/2=500 imp/s
- L. of the muscle = 1000/3=330 imp/s
- L. of synapse = 1000/8= 125 imp/s.

Advantages of electrical stimuli

1. **Constructs biological processes (biopotentials)**
2. **Easy to change in:**

- *Force*
- *Time*
- *Steepness of force growth*

LAWS OF IRRITATION

- **LAWS OF IRRITATION** is a complex of laws which point out the requirements for a stimulus able to cause AP.
- **Polar law –** on the extracellular application of constant rectangular current excitation occurs under cathode on closed circuit and under anode on the opened circuit.

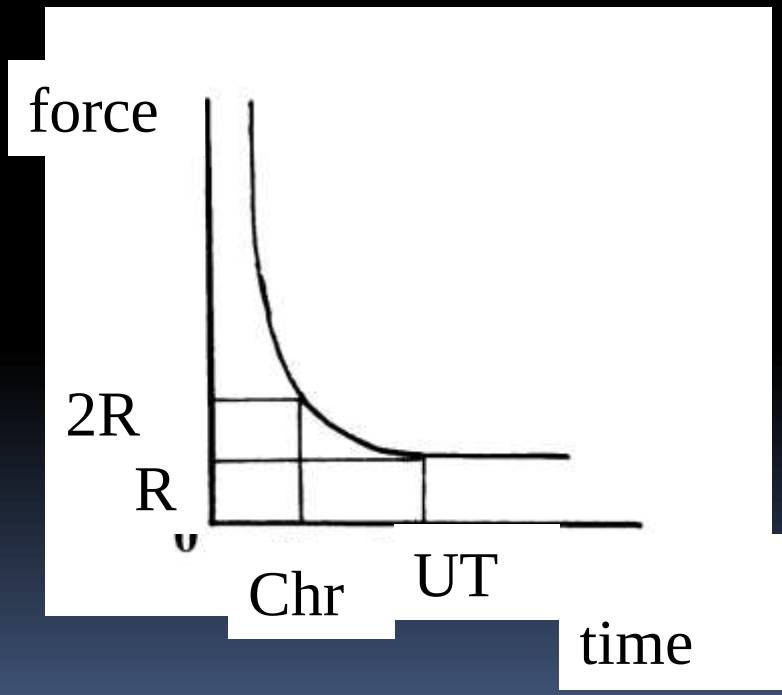
- **Law of force** – to cause AP stimulus should have certain force not lower than the threshold one.
- **Law of time** – to cause AP stimulus should be applied during the time not shorter than the threshold one.
- **Law of steepness** – to cause AP stimulus should have certain steepness not lower than the threshold one.

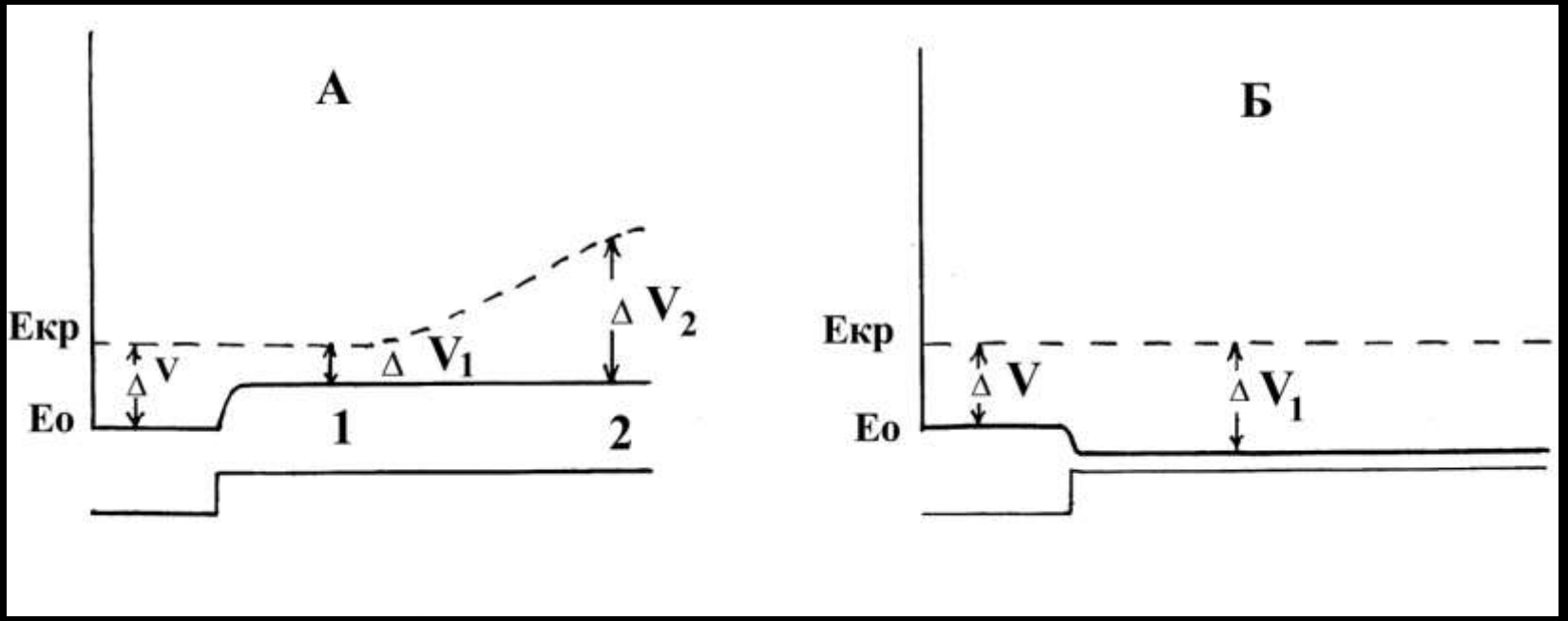
FORCE-TIME CURVE

R – reobase – minimum force that causes AP

UT – utilization time – minimum time of 1 reobase application to cause AP.

Chronaxy - minimum time of 2 reobase application to cause AP.





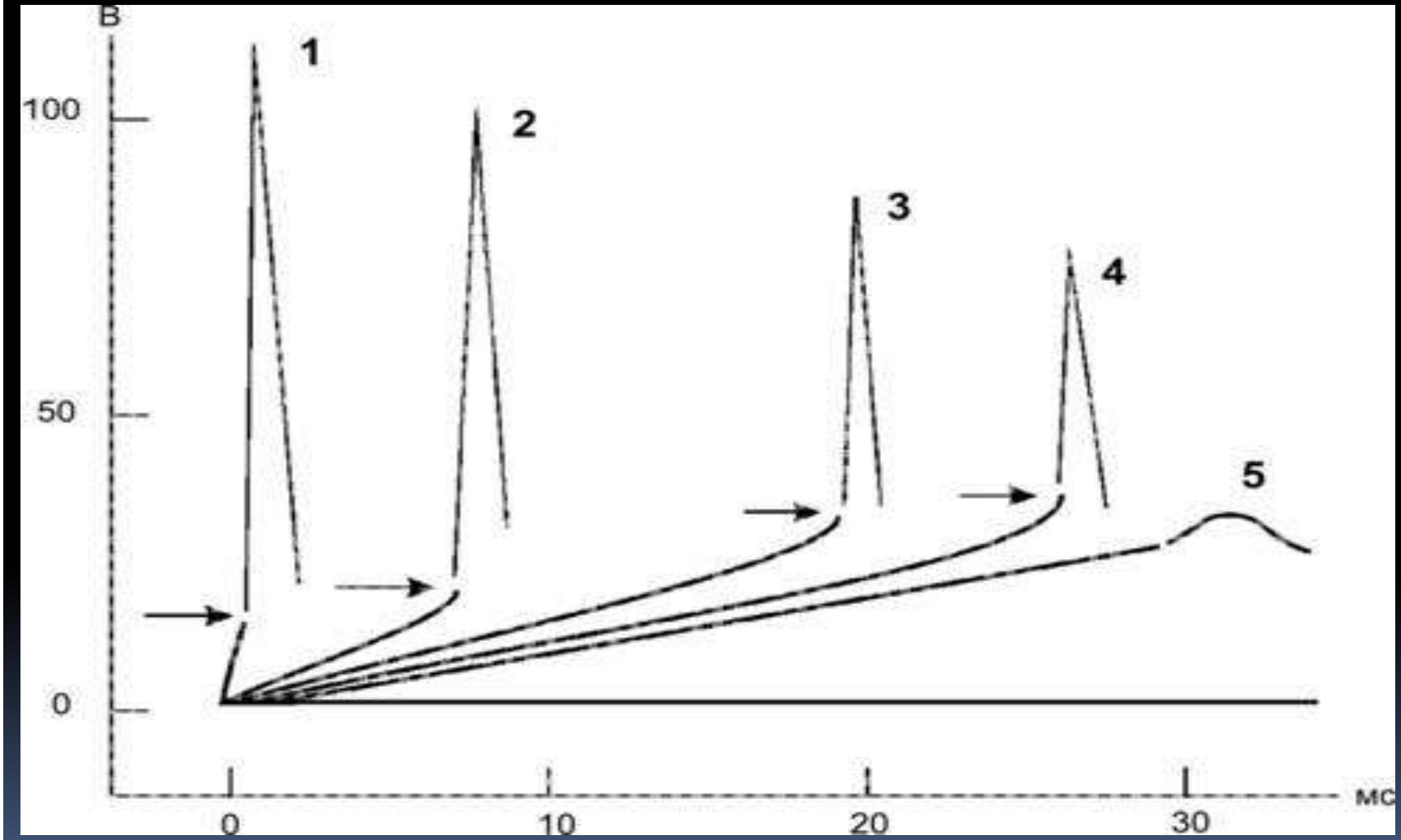
A - cathelectrotonus. 1 - initial increase of excitability: : $\Delta V_1 < \Delta V$.
2 - cathodal depression: $\Delta V_2 > \Delta V$.

B - anelectrotonus, decrease in excitability: $\Delta V_1 > \Delta V$.

Accomodation

- Is tissue ability to get adjusted to long lasting & low steepness stimulation.
- Critical level of depolarization decreases to zero
- Sodium channels don't open simulteneously & sodium influx is compensated by potassium efflux.
- There can be no regenerative depolarization & AP doesn't occur

ACCOMODATION



- 1.Guyton and Hall. Medical Physiology. Textbook. Eleventh edition
- 2.Phisiology : Textbook / Edited by V. M. Moroz, 0. A. Shandra. - Vinnytsia: Nova Knyha Publishers, 2011.