University of Zagreb
Faculty of Electrical Engineering and Computing

Biomedical Instrumentation

Origin of bioelectric potentials

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Outline

- Introduction
  - Definition of BME
- Origin of bioelectric signals
  - Most commonly measured bioelectric potentials
  - Resting potentials
  - Action potential
  - Receptor potentials

Human physiology

- Science on vital processes and functions in living organisms
- BME students have special interest in:
  - Electrophysiology
  - Control mechanisms

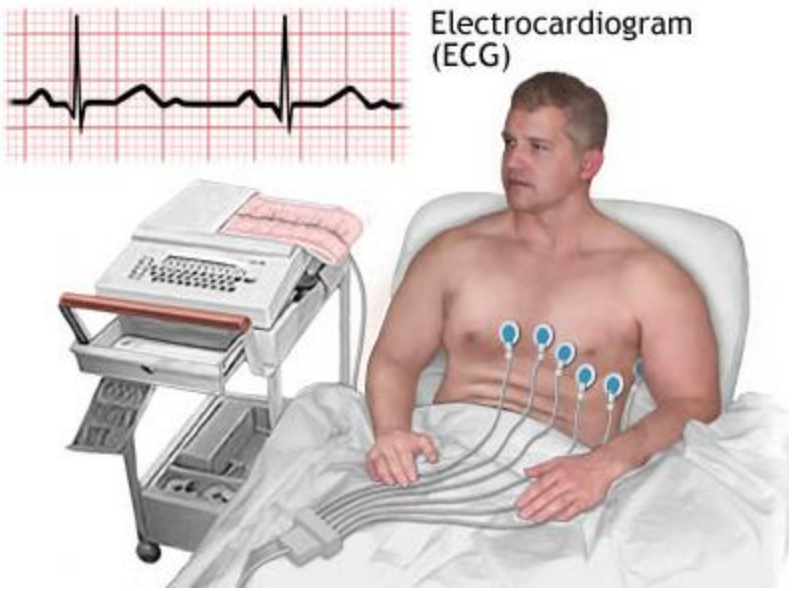
"A man is a machine, extremely complex, but still a machine" (Arthur Vander)

Electrophysiology

- Study of electric properties of biological cells and organs
- Includs measurement of voltage changes and currents from cell level to organ level
- In neuroscience, potentials of nerve cells and action potentials are measured

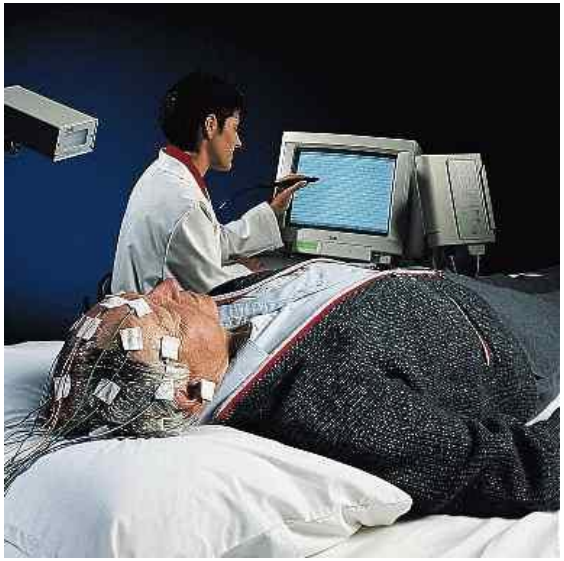
Types of electrophysiological measurements

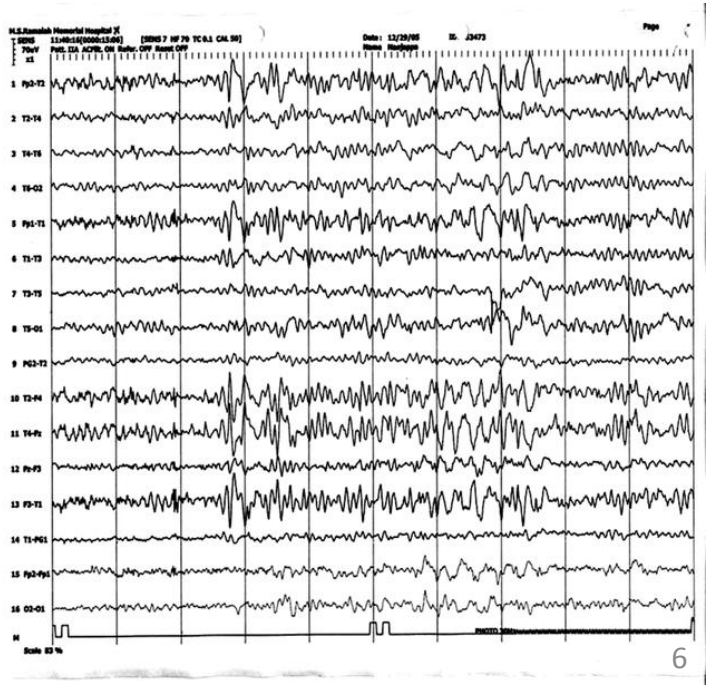
- **Electrocardiography** (abb. ECG or EKG)- a standard noninvasive procedure for recording electrical potentials of the heart. The record (electrocardiogram), consists of waves that relate to the electrical activity of the heart during each beat. Results - printed on paper or displayed on monitor.



Types of electrophysiological measurements

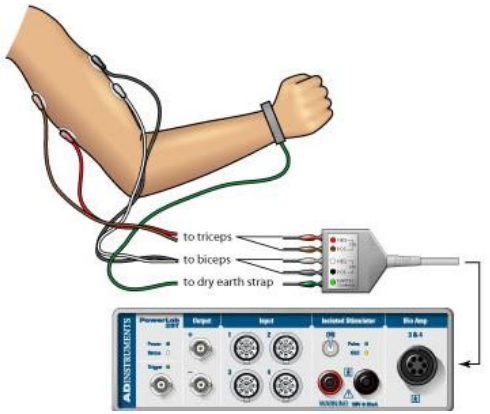
- **Electroencephalography** (EEG)- a standard noninvasive procedure for recording electrical activity of the brain. The record (electroencephalogram), consists of curves that relate to the spontaneous electrical activity of millions of neural cells of the brain. The recording lasts for 20-40 min and is printed on paper or displayed on monitor.





Types of electrophysiological measurements

- Electromyography (EMG)- recording of the electrical activity produced by skeletal muscles.



- Electrooculography (EOG) - measuring the resting potential of the retina. The resulting signal is called the electrooculogram.

- Other methods: Electroretinography, Audiology, Electrogastrography ...

Human body structure

- Chemical elements
- Cells
- Tissue – group of similar cells
- Organ – group of similar tissues
- System – functional complex made of different organs
- Organism – functional complex of 11 systems

Human body composition - the structural level

- Chemical level
- Cellular level
- Tissue level
- Organ level
- System level
- The level of the organism

Human body chemical composition

- Most represented elements (approx. 99,3%):
  - Hydrogen (H) 63%
  - Oxygen (O) 26%
  - Carbon (C) 9%
  - Nitrogen (N) 1%

Human body chemical composition

- Minerals (approx 0,7%):
  - Calcium (Ca)
  - Phosphorus (P)
  - Potassium (K)
  - Sulphur (S)
  - Sodium (Na)
  - Chlorine (Cl)
  - Magnesium (Mg)

Human body chemical composition

- Other elements (<0,01%):
  - Iron (Fe)
  - Iodine (I)
  - Copper (Cu)
  - Zinc (Zn)
  - Manganese (Mn)
  - Cobalt (Co)
  - Chromium (Cr)
  - Selenium (Se)
  - Molybdenum (Mo)
  - Fluorine (F)
  - Tin (Sn)
  - Silicon (Si)
  - Vanadium (V)

Human organism consists of

Fluids

(approx. 2/3 of the weight)

+

Tissues

(groups of similar cells)

Liquids

- Intracellular fluid (approx. 40%)
- Extracellular fluid (approx. 20%)
  - Interstitial fluid (approx. 16%)
  - Plasma (approx. 4%)
- The remainder (6-10%) consists of:
  - Blood
  - Lymphatic fluid
  - Urine
  - Cerebral spinal fluid

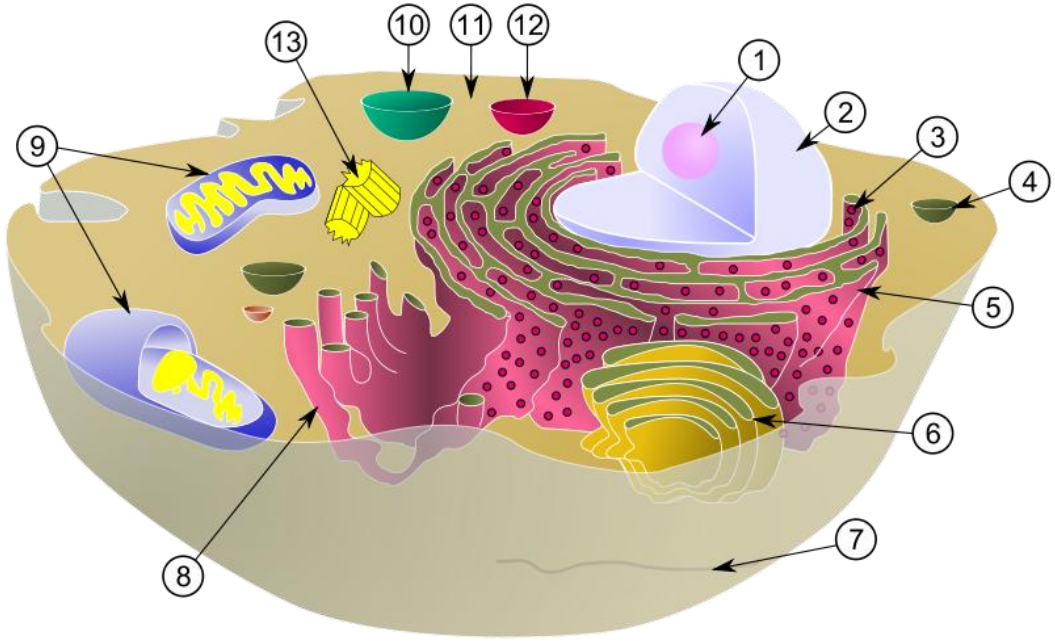
Tissues

NERVOUS (Neural)	MUSCLE (Muscular)	CONNECTIVE	EPITHELIAL
1. NERVOUS (Neural)	1. SKELETAL (Voluntary)	1. FILAMENTARY (Fibrous)	1. VESSELS (Vascular)
2. GLIA CELLS (Cells for excitacion of brain metabolism)	2. SMOOTH (Involuntary)	2. FAT (Adipose)	2. GLAND (Gladular)
	3. CARDIAC (Involuntary)	3. CARTILAGINOUS	3. SKIN
		4. BONES (Osseous)	4. HAIR (Cilia)

Cell

- Human organism consists of approx. $75 \cdot 10^{18}$ cells (75.000.000.000.000.000.000)
- Cell diameter ranges from 0,2 - 120 µm
- Most cells range from 10 - 20 µm in diameter
- Organisms of different sizes (man or elephant) consist of cells similar in dimension, only the number of cells is different

Cell structure



Subcellular components

(1) nucleolus
(2) cell nucleus
(3) ribosome
(4) vesicles
(5) rough endoplasmic reticulum (ER)
(6) Golgi
(7) Cytoskeleton
(8) smooth endoplasmic reticulum
(9) mitochondria
(10) vacuole
(11) cytoplasm
(12) lizosom
(13) centrioles

Cell membrane

- Cell membrane is semipermeable lipid bilayer made of lipids and proteins that separates the intracellular part from the extracellular environment
- Thickness of 10 nm
- Semipermeable - the pore width 8 nm
- Dielectric constant $\varepsilon = 5$, spec. capacity C = 0.5 to 1 $\mu F/cm^2$

- Transit of substances (in and out of cells) is regulated by
  - Diffusion (from regions of higher concentration to regions of lower concentration)
  - Osmosis (diffusion of water through a semipermeable membrane)
  - Active transmission (from region of lower concentration to regions of higher concentration, requires energy)

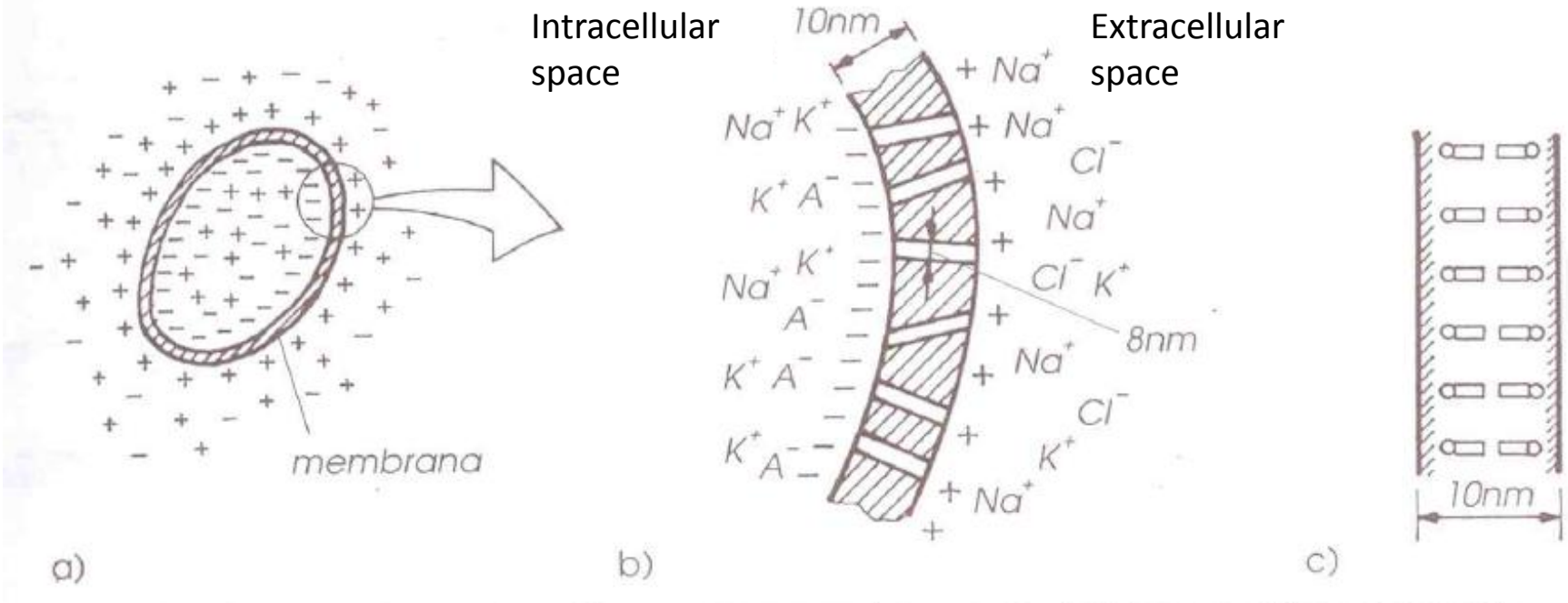
- State of the membrane is determined by two main factors:
  - Concentration gradient (diffusion coefficient, D)
  - Electric field (E)

Concentration in the cell and out of the cell

	Out (mM/l*)	In(mM/l)
Na^+	**142**	**10**
K^+	**5**	**141**
Ca^{2+}	5	<1
Mg^{2+}	3	58
Cl^-	103	4
HCO^{3-}	28	10
Phospates	4	75
Amnino acids	30	200
Glucose	90	0 do 20

* mM/l, millimol per liter

Cell membrane



a) Cell polarization b) part of the membane c) structure of the membrane

- Potassium ions (K+) exit the cell easily, while A- is hard to come out of the cell
- Na+ is hard to enter, whereas Cl- enters the cell easily
- Na-K pump ejects Na+ more efficiently than injecting K+
- Therefore, outside the cell there is an excess of positive charge and the inside of the cell is negatively charged

Diffusion through semipermeable membrane - the passive process

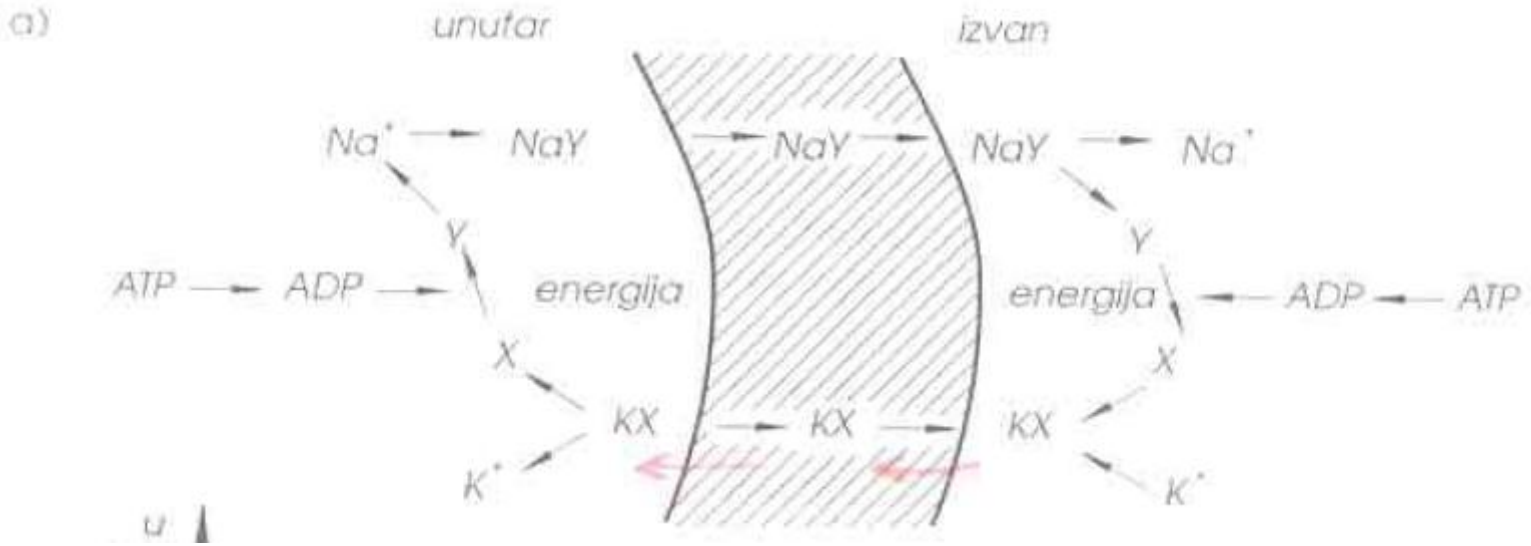
- Fick's law $$\frac{\mathrm{d}m_i}{\mathrm{d}t} = S \cdot D \cdot \frac{\mathrm{d}c_{ix}}{\mathrm{d}x}$$

m_i = amount of (a particular) substance i [mol]
t = time [s]
S = membrane surface [m^2]
D = diffusion coefficient [m^2/s]
dc_{ix} / dx = concentration gradient [mol/m^3] of a particular substance i at the possition x

- diffusive flux goes from regions of higher concentration to regions of lower concentration, and it is proportional to the concentration gradient (in space).

- K+ ions can easily leave the cell, creating an excess positive charge and the potential difference occurs - diffusion takes place until the electric field is established and it stops the process of diffusion

Sodium - Potassium Pump – an active process



- Na^+ + Y-complex= NaY molecule + Na-pump = Out Na^+ + X
- K^+ + X-complex = KX molecule + K-pump = In K^+

- For each inserted K + ion, 2-5 Na + ions are ejected
- Na-K pump requires energy:

ATP = ADP + energy

ATP - adenosine triphosphate, ADP - adenosine diphosphate

Resting potential

The resting potential of a cell - Nernst equation

Δu = potential difference [V]

R = universal gas constant = 8,314 J/molK

T = absolute temperature (0K = -273 °C)

n = valence of chemical elements whose concentration is considered, potassium in this case

c_{Ki} , c_{Ko} = concentration of ions inside and outside the cells (for potassium, see table on slide 19)

F = Faraday constant = 96,5 C/mol

E = electric field [V/m]

$$\Delta u = \frac{R \cdot T}{n \cdot F} \ln \frac{c_{k1}}{c_{k2}}$$

$$\Delta u = 61.5 \log \frac{c_{Ko}}{c_{Ki}} [\text{mV}]$$

$$\Delta u = -85\,\text{mV}$$

$$T = 37\,[°\text{C}],\ c_{Ko} = 5\,[\text{mol/l}],\ c_{Ki} = 141[\text{mol/l}]$$

Electric field on the membrane

$$E = \frac{\Delta u}{d} = \frac{85\,[\text{mV}]}{10\,[\text{nm}]} = 85\,[\frac{\text{kV}}{\text{cm}}]$$

Resting potential

Bioelectric potentials are a result of electrochemical activity of excitable cells (in neuros, muscular or glandular system)

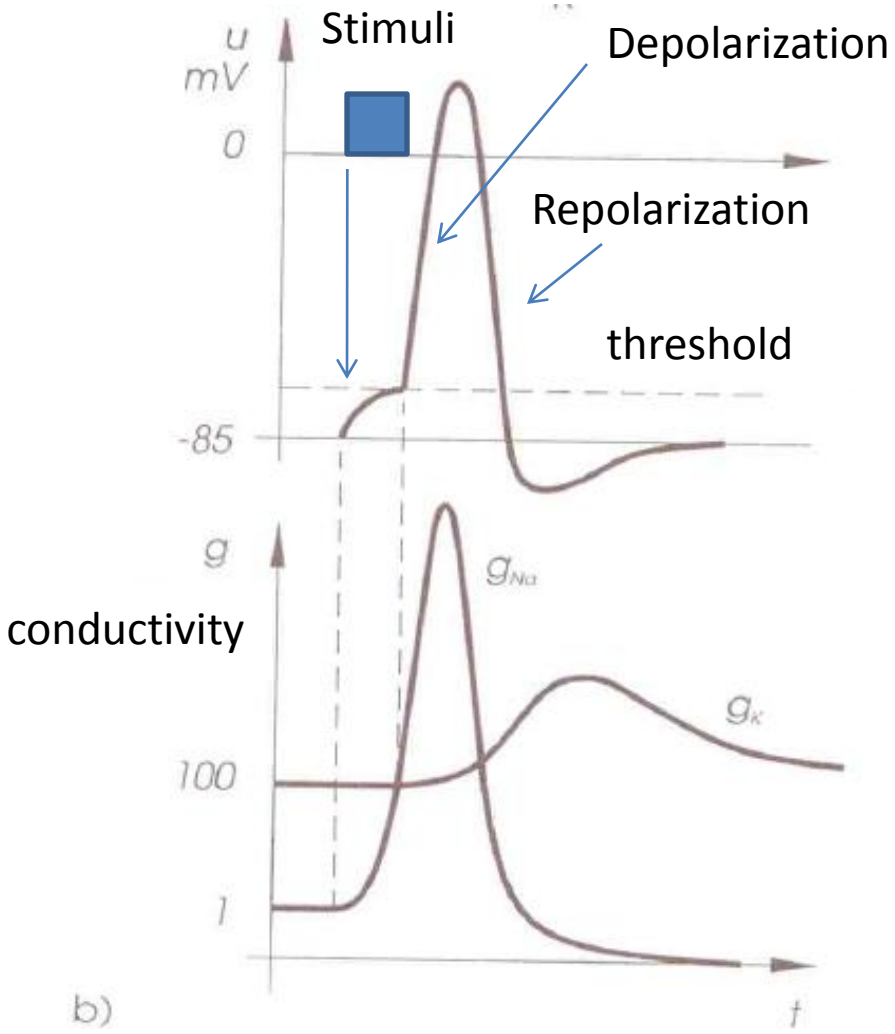
The resting potential of a cell – steady difference in electric potentials between internal and external environment of the cell.

Typical values of resting potentials are in range of -50 mV to -100 mV (reference point out of the cell).

Action potential

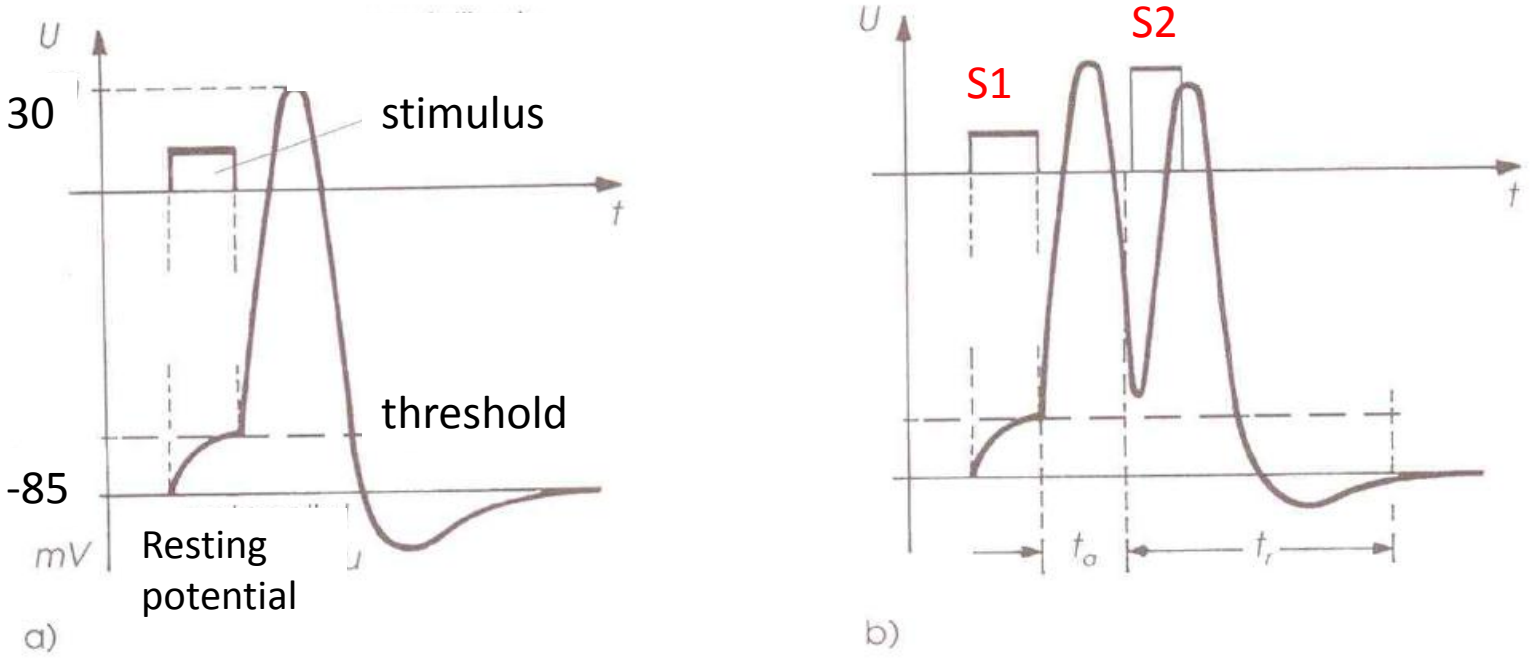
- Stimulus:
  - Mechanical
  - Chemical
  - Electrical

- Sudden increases of membrane conductance for Na + ions (1000 times more) - change in polarity of the voltage - depolarization



Action potential, showing depolarisation and repolarisation b) Changes in conductivity for sodium and potassium during the action potential

Action potential



a) Action potential b) Two consecutive action potentials, caused by stimuli S1 and S2. Note that the magnitude of S2 is larger than magnitude of S1

- After commencement of the action potential , the process can not be stopped by any subsequent stimulus - as long as this state lasts we are talking about the **absolute refractory period t_o**
- When the process starts to calm down and return power to the value at rest, it is possible to re-trigger action potentials using more intense stimulus, even though the voltage has not reached the value at rest - the time when it is possible to re-create the action potentials with a greater intensity of stimulus is called **the relative refractory time, t_r**

Action potential

- The course:
  - The stimulus reaches the threshold
  - Increasing membrane permeability for Na + ions
  - After that, permeability for K + increases and Na + ions permeability decrease
  - Reducing permeability for K + ions
  - Active ejection of Na + and injection of K + ions

Action potential

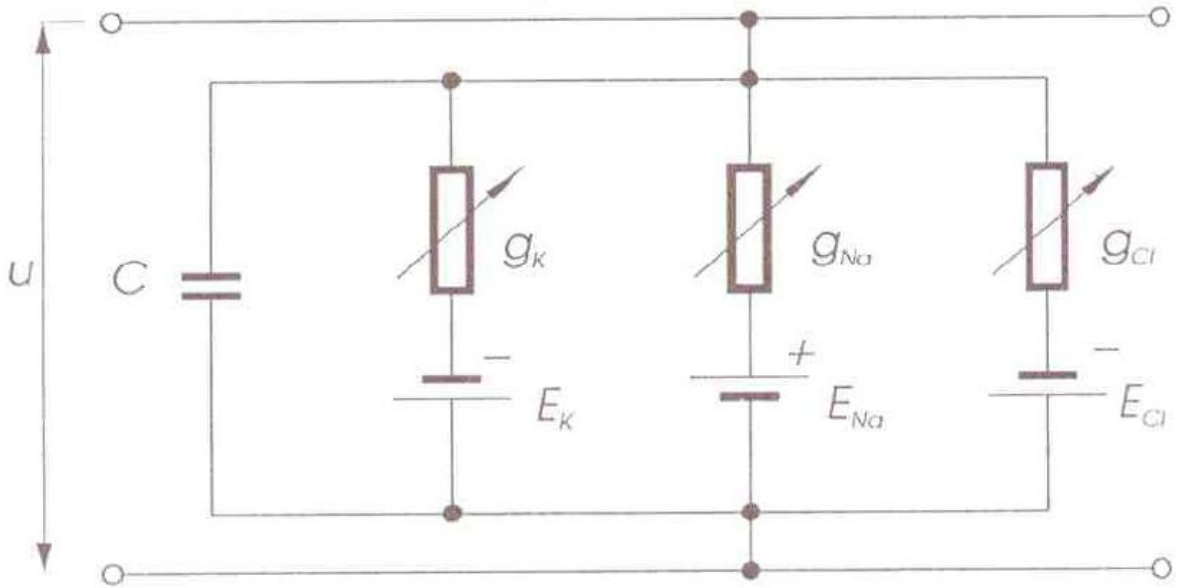
- Excitable cells have the ability to conduct action potentials when adequatly stimulated.
- An adequate stimulus causes depolarisation of the membrane large enough to reach and exceed the stimulation threshold of the membrane.
- Adequate excitation causes an **action potential**, which follows the all –or-none rule. The action potential travals along the membrane at constant velocity and without attenuation.
- At rest, the cell is said to be **polarized**.
- After the cell is excited, the potenetial is decreasing – **depolarisation** of the cell membrane.
- Returning of the cell potential to the resting value is called **repolarisation**.
- After repolarisation, for a short period of time, the cell potential is increased which is called **hyperpolarisation**. During that period, a stimulus has to be of larger magnitude in order to excite a cell.

Cell membrane model

- Hodgkin and Huxley – Nobel prize, 1963

Resting potential *u*

Intracellular medium



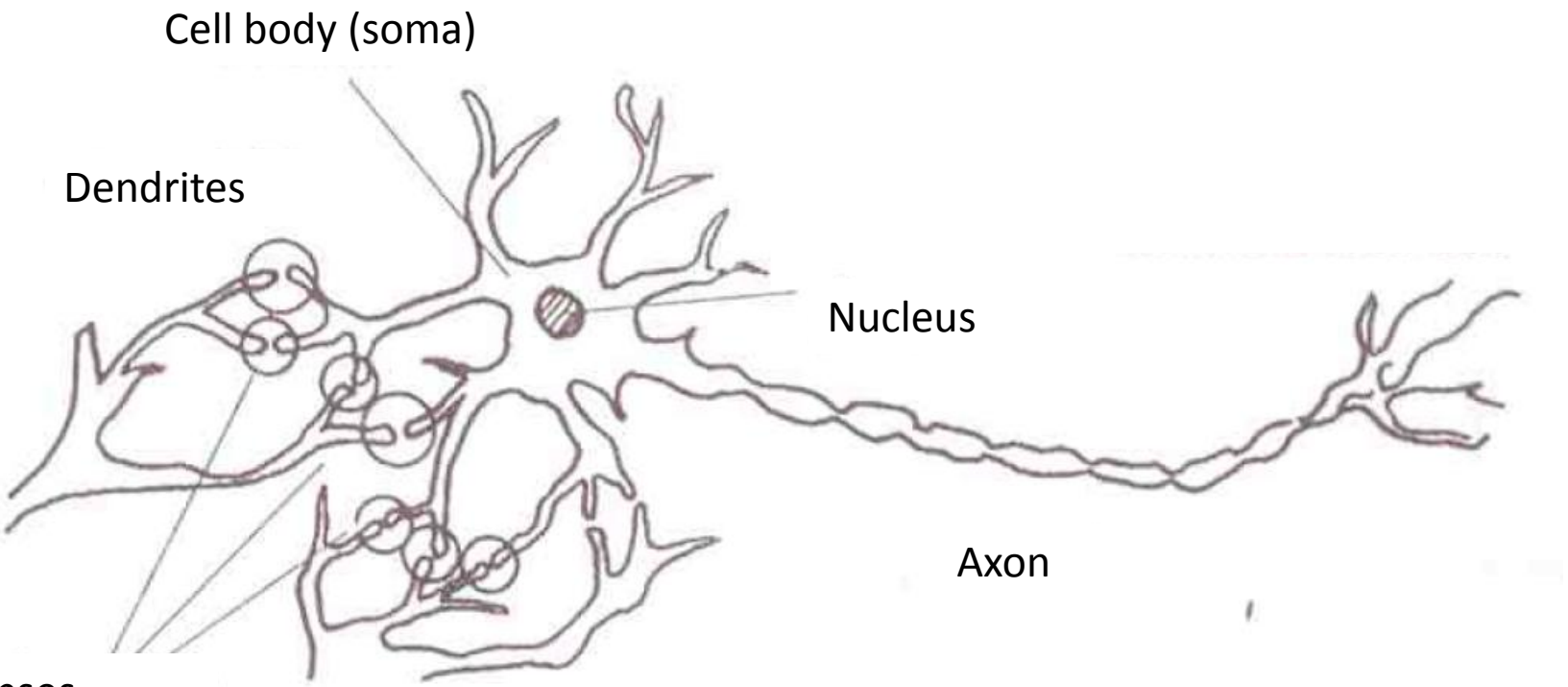
Extracellular medium (liquid)

Diagram of network equivalent circuit of a cell membrane showing voltage sources of main ions E_i, membrane conductances g_i and membrane capacitance C.

Nerve cell

Signals are transmitted from neuron to neuron via an action potential, when the axon membrane rapidly depolarizes and repolarizes.

https://www.youtube.com/watch?v=ifD1YG07fB8



Intercommunicating links between neurons (neuro-neuro junctions) are called synapses.

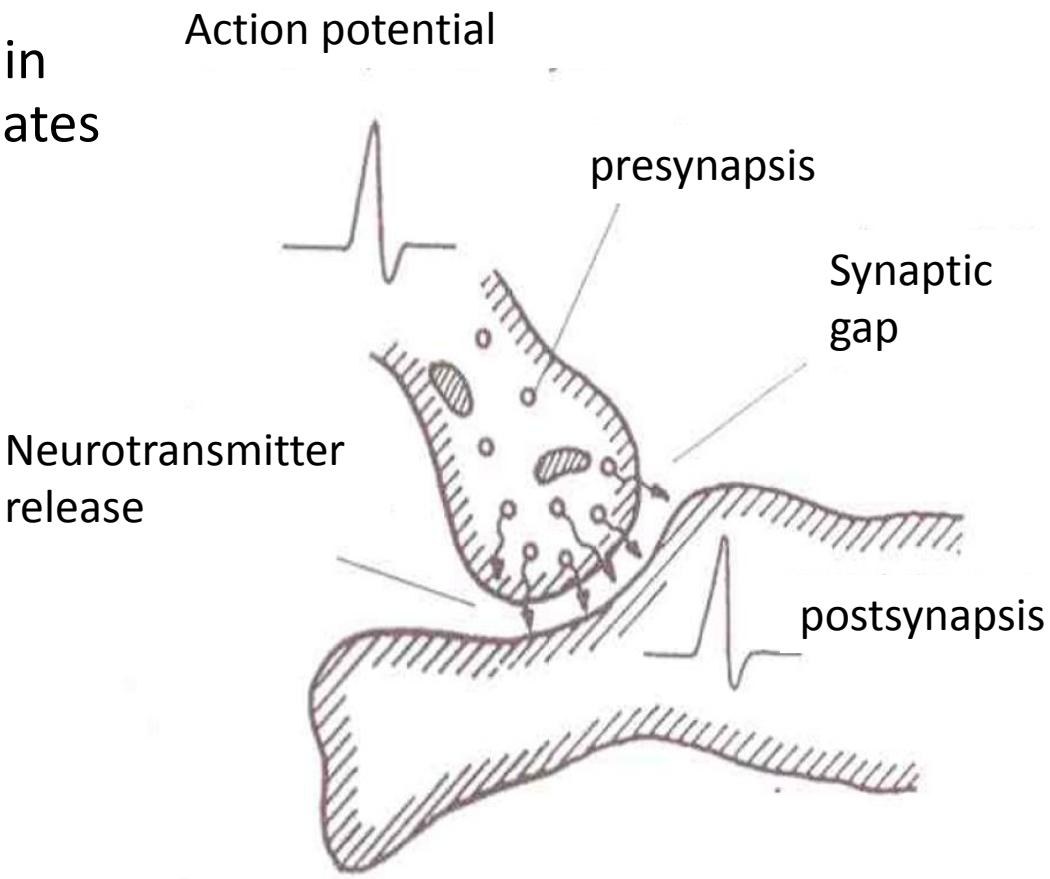
Source: Boundless. “Nerve Impulse Transmission within a Neuron: Action Potential.” *Boundless Biology*. Boundless, 21 Jul. 2015. Retrieved 22 Oct. 2015 from https://www.boundless.com/biology/textbooks/boundless-biology-textbook/the-nervous-system-35/how-neurons-communicate-200/nerve-impulse-transmission-within-a-neuron-action-potential-762-11995/

Transfer of stimulus - Synapse

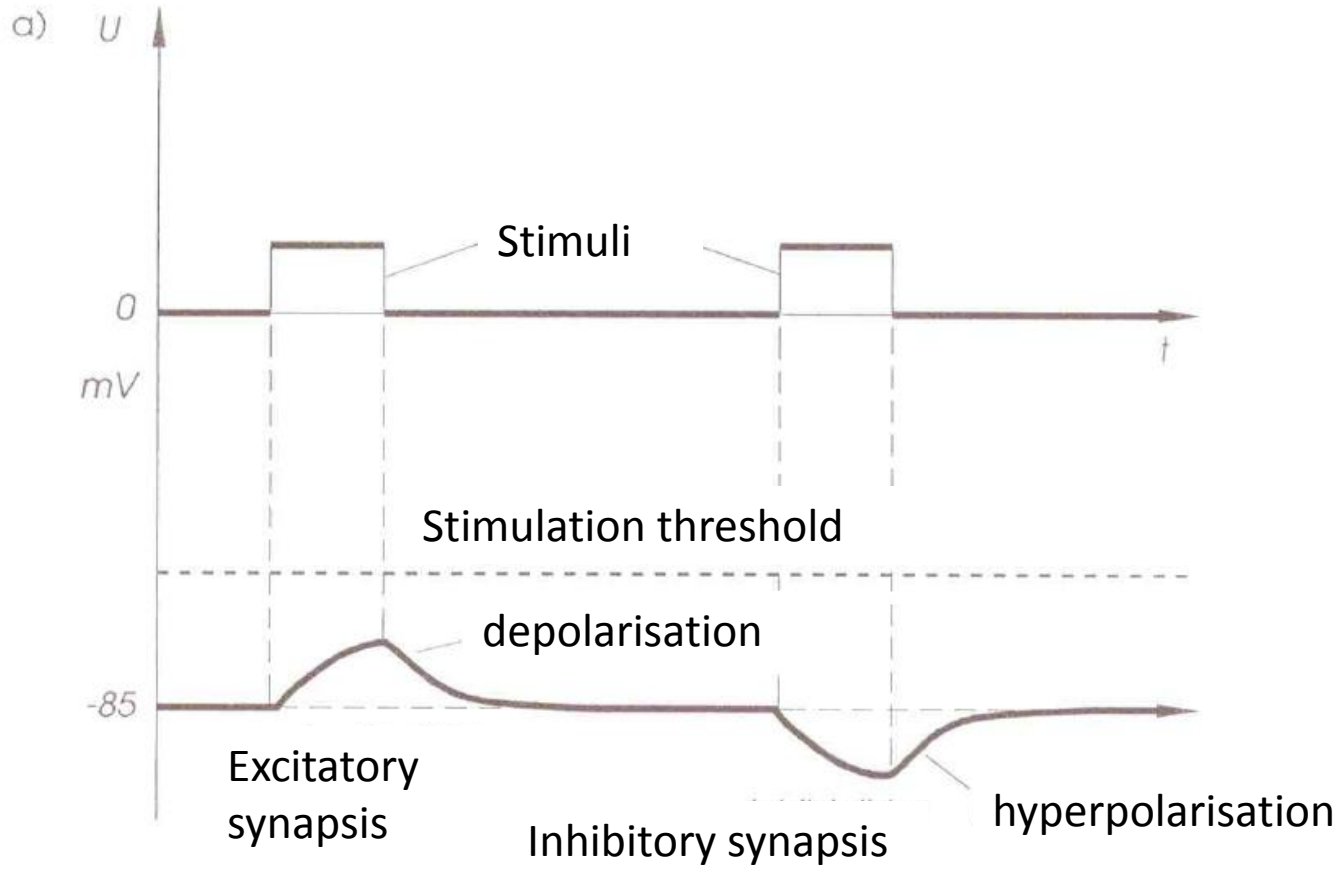
- Stimulus stimulates neurotransmitter secretion in the synaptic cleft and stimulates (or not) the next nerve cell

- Neurotransmitters:
  - Acetylcholine
  - Monoamines
  - Amino acids
  - Peptides

- Synapses can be:
  - excitation
  - inhibitory

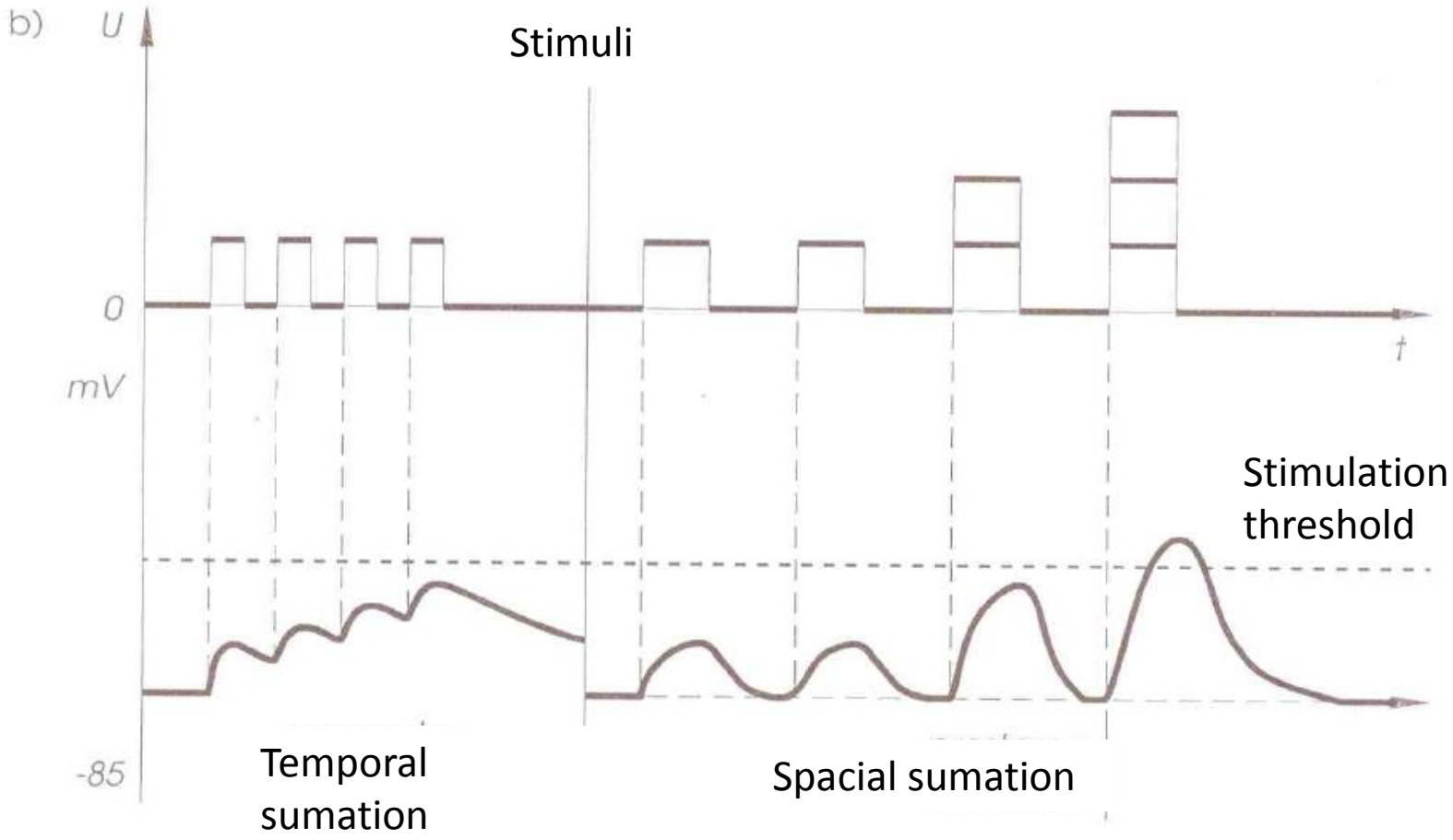


Synapse activity



Changes in resting potential caused by activity at an excitatory and an inhibitory synapse

Temporal and spatial summation

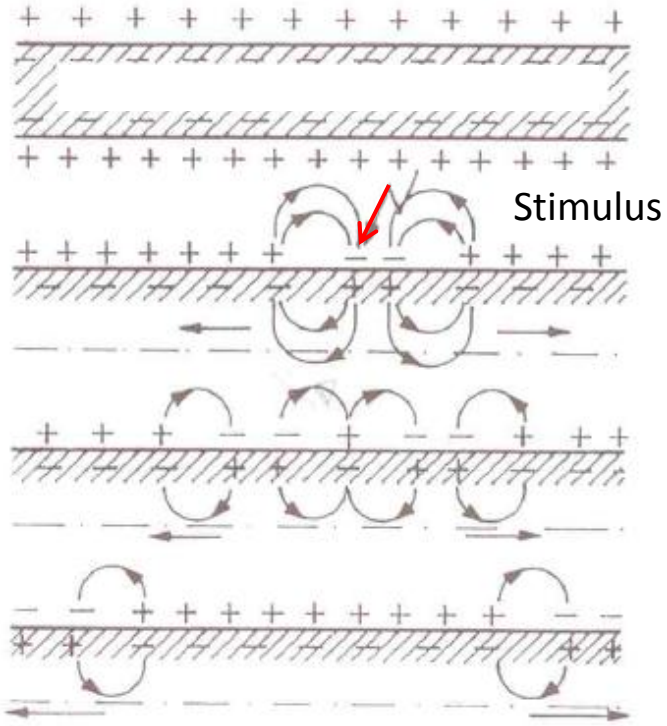


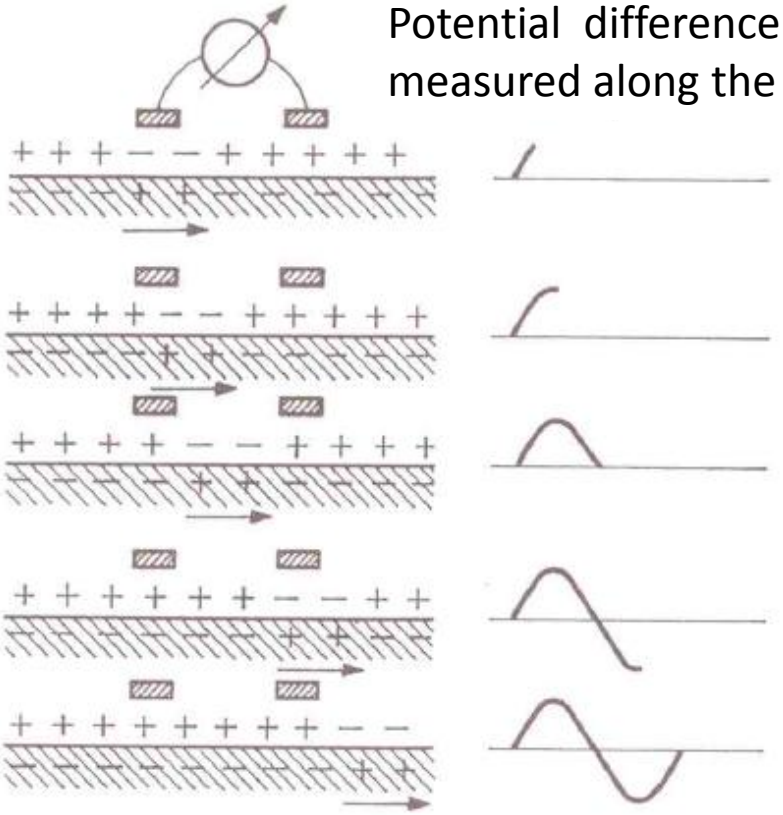
Types of synaptic connections

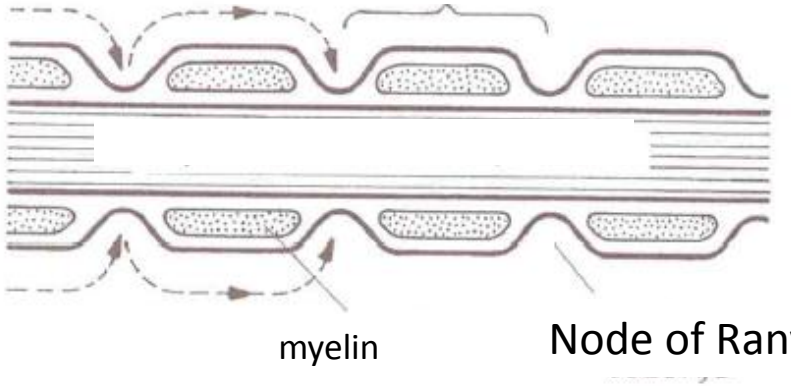
- Neuron – neuron junctions
- Neuromuscular junctions – communication links between neurons and muscle fibers. These are small regions of the muscle fiber, called neuromuscular plates.

Types of nerve fiber

- Myelinated fibers
  - Axon is insulated by a seath of myelin (lipoprotein)
  - Myelin seath interrupted every 1-2 mm nodes of Ranvier
  - Sodium ion chanells distributed unequally, more at nodes of Ranvier
  - Myelization reduces leakage currents and improves transmission properties (cable like behaviour)
  - faster propagation of action potentials
- Unmyelinated
  - Equal distribution of sodium and potassium channels
  - Leackage current sourses more expressed
  - Slower propagation along the axon (cable)







Propagation of stimuli in unmyelined and in myelined nerve fibers

Literature

- John G. Webster: Medical Instrumentation, Chapter 4, The origin of biopotentials
- R.S. Kandpur: Biomedical Instrumentation, Chapters 1.1-1.3, 2.1
- A. Šantić: Biomedicinska elektronika