Lecture 4. Physical processes in biological membrane.
Resting and action potentials of human excitable tissues cells

Goals
- to consider physics of some transport mechanisms across human cell membrane
- to quantify electrogenic ions transport across human nerve cell membrane

Objectives
- characteristics of human cell membrane basic structures
- classification of human cell membrane transport mechanisms
- physics methods vital activity electric processes dynamics registration

1. Human cell membrane basic structures
2. Electrogenic ions transport mechanisms across human cell membrane
3. Human nerve cell resting and actions potentials
4. Physics methods to record and quantify human vital activity electric processes
5. Conclusions
6. Information resources

1. Human cell membrane basic structures

The principal components of the plasma membrane are lipids - phospholipids and cholesterol, proteins, and carbohydrate groups that are attached to some of the lipids and proteins

Carbohydrate groups are present only on the outer surface of the plasma membrane and are attached to proteins, forming **glycoproteins**, or lipids, forming **glycolipids.**

The proportions of proteins, lipids, and carbohydrates in the plasma membrane vary between different types of cells.

For a typical human cell proteins account for about 50 percent of the composition by mass, lipids of all types account for about 40 percent, and the remaining 10 percent comes from carbohydrates.

The structural basis of the membranes is the **lipid bilayer.** The majority of the embrane **lipids** are **phospholipids.**

The membrane lipids are of **amphiphilic nature** - they consist of **polar head-group** and in most cases of **two parallel apolar hydrocarbon chains** containing 14 – 18 carbon atoms per chain. The hydrocarbon chains may be saturated, or may contain one or more double bonds.

Phosphatidylcholine (lecithin) molecule is a component of every biological membrane.

Cholesterol, another lipid composed of four fused carbon rings, is found alongside phospholipids in the core of the membrane.

In aqueous medium lipid molecules are ordered so that the polar groups turn towards the aqueous phase and get into electrostatic interaction with one another and with dipolar water molecules.

The hydrophobic parts are linked by van der Waals forces inside the membrane.

The structural basis of the membranes is the lipid bilayer resulting in easily changing liquid cristalline structure of the membrane

The lipid is of easily changing liquid cristalline structure because of lipid molecules behavior.

The membrane **proteins** are intercalated into “fluid” lipid layer to an extent depending upon their geometric and charge configurations, determined by their amino acid content and sequence.

Membrane proteins may extend partway into the plasma membrane, cross the membrane entirely, or be loosely attached to its inside or outside face.

The currently accepted **fluid mosaic model** for the structure of the plasma membrane was first proposed in 1972. This model has evolved over time, but it still provides a good basic description of the structure and behavior of membranes in many cells.

According to the fluid mosaic model, the plasma membrane is a mosaic of components, primarily, phospholipids, cholesterol, and proteins. These move freely and fluidly in the plane of the membrane. In other words, a diagram of the membrane is just a snapshot of a dynamic process in which phospholipids and proteins are continually sliding past one another.

2. Electrogenic ions transport mechanisms across human nerve cell membrane

The cell membrane is selectively permeable to ions and organic molecules and controls the movement of substances in and out of cells.

K^+-, Na^+- and Cl^-- ions are considered as electrogenic determining human nerve cell function as electric processes.

The movement of substances across the membrane can be either "**passive**", occurring without the input of cellular energy, or "**active**", requiring the cell to expend energy in transporting it.

The **sodium-potassium pump**, which is also called Na^+/K^+- ATPase, transports Na^+ ion out of a cell while moving K^+ ion into the cell. Na^+/K^+- pumps brings two K^+ ions into the cell while removing three Na^+ ions per one ATP molecule energy consumed

The Na^+/K^+- pump is an important ion pump found in the membranes of all cells.

The activity of Na^+/K^+- pumps in nerve cells is so great that it accounts for the majority of their ATP usage.

The cell possesses K^+- and Na^+-leakage channels that allow these cations to diffuse down their concentration gradient.

The neurons have far more K^+-leakage channels than Na^+- leakage channels. Therefore, potassium diffuses out of the cell at a much faster rate than sodium leaks in.

Because more cations are leaving the cell than are entering, this causes the interior of the cell to be negatively charged relative to the outside of the cell.

Clorine ions (Cl^-) tend to accumulate outside of the cell because they are repelled by negatively-charged proteins within the cytoplasm.

The cell possesses K^+- and Na^+-leakage channels that allow these cations to diffuse down their concentration gradient.

3. Human nerve cell resting and actions potentials

The difference in total charge between the inside and outside of the cell is called the **resting membrane potential**.

The Goldman-Hodgkin-Katz equation predicts actual membrane potential for a cell that results from the contribution of electrogenic ions

$$V_m = \frac{RT}{F} \ln\left(\frac{p_K[K^+]_o + p_{Na}[Na^+]_o + p_{Cl}[Cl^-]_i}{p_K[K^+]_i + p_{Na}[Na^+]_i + p_{Cl}[Cl^-]_o} \right)$$

V_m = the membrane potential, volts
p_{ion} = the permeability for an ion, meters per second
$[ion]_0$ = the extracellular concentration of an ion, moles per cubic meter
$[ion]_i$= the intracellular concentration of an ion, moles per cubic meter
R = the ideal gas constant
T = the temperature, Kelvins
F = Faraday's constant, coulombs per mole

At the resting potential all voltage-gated Na^+ channels and most voltage-gated K^+ channels are closed. The Na^+/K^+-transporter pumps K^+ ions into the cell and Na^+ ions out.

Transmission of a signal within a neuron (from dendrite to axon terminal) is carried by a brief reversal of the resting membrane potential called an **action potential**.

The formation of an action potential can be divided into five steps.

1. A stimulus from a sensory cell or another neuron causes the target cell to depolarize toward the threshold potential.

2. If the threshold of excitation is reached, all Na^+ channels open and the membrane depolarizes.

3. At the peak action potential, K^+ channels open and K^+ begins to leave the cell. At the same time, Na^+ channels close.

4. The membrane becomes hyperpolarized as K^+ ions continue to leave the cell. The hyperpolarized membrane is in a refractory period and cannot fire.

5. The K^+ channels close and the Na^+/K^+ transporter restores the resting potential.

4. Physics methods to record and quantify human vital activity electric processes

Electrocardiography

Attaching electrodes to the body surface allows the voltage changes within the body to be recorded after adequate amplification of the signal.

A galvanometer within the ECG machine is used as a recording device. Galvanometers record potential differences (voltages) between two electrodes.

ECGs are merely the recordings of differences in voltage between two electrodes on the body surface as a function of time.

ECG Lead. Pair of two electrodes connected to electrocardiograph with wires constitute a LEAD. A lead measures voltage difference between two electrodes.

Stylus (needle) of ECG machine moves up and down with changing voltage. Waves are recorded on ECG paper which moves beneath the stylus –ECG recording

Types of Leads

Limb leads: I, II, III - Bipolar leads; aVR, aVL, aVF –Unipolar leads.

Chest leads: V1, V2, V3, V4, V5, V6 –Unipolar leads.

During each heartbeat, the spread of the action potential through the heart causes potential differences between depolarized and polarized cells. The conducting nature of body fluids transmits these potential differences so that they can be detected at the surface by electrodes. The signals are very much reduced in size by their passage through the body having typical values of 1 to 2 mV. They need amplifying before they can be recorded, electrodes must be placed in particular positions, and the patient must be relaxed so that no other signals interfere with the heartbeat. Their display over time is called an electrocardiogram **(**ECG), and their study, electrocardiography, is a method of diagnosing various diseases and conditions of the heart.

A typical ECG includes the following important features, which are usually referred to by letter labels:

- the **P-wave** due to the depolarization and contraction of the atria;
- the **QRS-wave** due to the depolarization and contraction of the ventricles;
- the **T-wave** due to repolarisation and relaxation of the ventricles.

Controlling the heart's action. All muscular activity is associated with the changes in electrical potentials, which result from the migration of ions. The regular pumping action of the heart is controlled by special muscle cells, the **sinoatrial (SA) node** or **pacemaker**, located in the right atrium. This produces an electrical stimulus about 70 times a minute and initiates the depolarization of the nerves and muscles of both atria. These contract and pump blood through one-way valves (tricuspid and mitral) into the ventricles. Repolarisation follows as ions move to reduce the potential, and the muscles relax. The electrical signal then passes to the **atrio-ventricular (AV) node**, which initiates the depolarization of the two ventricles.

Equivalent dipole. The voltage differences among resting, depolarized, and repolarizing cells function as a battery. The various charges that are present are summated and are termed an **equivalent dipole**.

The total charge that is present depends on the mass of tissue involved as well as the magnitude of the membrane potentials.

The cardiac dipole is a vector quantity because it has both magnitude and direction. Vectors are represented as arrows with arrowhead indicating the direction and the length of the arrow indicating the magnitude.

The surface potential, or the magnitude of the voltage recorded at the body surface, is a function of electrode position and the orientation and magnitude of the dipole (fig. 5).

By convention, a wave of depolarization approaching the positive electrode results in an upward deflection of the ECG tracing. A wave of depolarization proceeding parallel to an electrode axis (the line connecting two electrodes) produces the maximal deflection for that dipole. A depolarization wave perpendicular to the electrode axis produces no net deflection of the tracing.

Vector loops. The instantaneous cardiac vector represents the electrical vector generated by the cardiac dipole during the depolarization process. This vector begins at the zero isopotential point and inscribes a loop as the tissues are depolarized. Three loops can be recorded during one cardiac cycle (fig. 8). The **P loop** is caused by atrial depolarization; the **QRS loop** is caused by ventricular depolarization; and the **T loop** results from ventricular repolarization. Atrial repolarization cannot be recorded with standard techniques because of the prolonged time course and the small voltages involved.

The **P loop** is small and is directed leftward and inferiorly, resulting in a positive P wave in the three bipolar limb leads.

The normal **QRS loop** is inscribed counterclockwise and is directed leftward, interior and posterior.

5. Conclusions

1. Excitable tissues functions are of physics electric nature.
2. K^+-, Na^+- and Cl^-- ions are considered as electrogenic determining human nerve cell function as electric processes.
3. Attaching electrodes to the body surface allows the voltage changes within the body to be recorded after adequate amplification of the signal.

The voltage changes recorded provides quantitative data for evidenced diagnosis of excitable tissues functional state.

6. Information resources

1. https://courses.lumenlearning.com/boundless-ap/chapter/transport-across-membranes/
2. https://www.biotopics.co.uk/A15/Transport_across_cell_membranes.html
3. http://hyperphysics.phy-astr.gsu.edu/hbase/electric/dipole.html
4. https://www.examfear.com/notes/Class-12/Physics/Electrostatic-Potential/815/Electrostatic-Potential-due-to-an-Electric-Dipole.htm
5. https://www.slideserve.com/milo/the-electric-dipole