CONTENTS

Chapter 1
BASICS OF VITAL ACTIVITY

1.1. GENERAL PROPERTIES OF LIVING ORGANISMS

In contrast to the inorganic world, living organisms in the process of evolutionary development have embodied a number of qualitatively new properties.

The fit of living beings in the space-time continuum of the surrounding world. The Earth, as a planet, was formed about 4.5 billion years ago. Living organisms in their most primitive form appeared about 0.5–1 billion years ago. Consequently, living organisms fit into the surrounding phenomena of the inorganic world on Earth: the gravitational attraction of the Earth, the gas environment of the atmosphere, the temperature of the air, seas, and oceans, and Earth's electromagnetic field. The properties of the environment surrounding living organisms are reflected in the biological properties of living beings (P.K. Anokhin).

The environment, in which living organisms fit in, is a space-time continuum of events (A. Einstein). This means that all events on Earth are closely connected in time and space. This is not a chaotic series of events, but their material and informational organization. The organization of events in the physical world is primarily determined by the ratio of the planets in the solar system, and first of all by the ratio of the Earth and the Sun. In the space-time continuum of the surrounding world, episodic events, such as atmospheric precipitation, earthquakes, etc., are present. Along with this, there are events that periodically repeat with a regular rhythm. They are the change of the seasons, the tide and flow of the oceans, as well as the change of day and night. Living beings, in their organization, reflect both episodic and repeated events of the world surrounding them. Particularly important for vital activity are the effects that periodically repeat throughout the life of one generation.

Isolation of living beings. Living beings not only fit into the space-time continuum of the external world but also isolate themselves from inanimate nature.

Isolation is performed in a universal way with the help of phospholipid membranes. It is characteristic that the membranes of different cells, the shells of sea urchin eggs and the membranes of nerve cells, are almost identical in structure. The membranes make it possible for living organisms to contrapose themselves

to the aquatic environment, in which they primarily evolved, to actively influence their environment, and to make their organization more advanced. Isolation is predisposed for the formation of functional properties of living subjects.

Irritability. The membranes are irritated by various environmental factors called excitants. Excitants are divided into:

- physical (mechanical, temperature, electrical, etc.);
- chemical (acids, alkalis, salts, hormones, mediators, etc.);
- physical-chemical (changes in osmotic pressure, reactions of the internal environment, ionic composition, etc.);
- biological (bacteria, viruses, etc.);
- informational, carrying, along with physical and chemical properties, certain information, resulting from the interaction of living beings and the physiological processes occurring in them. They include various emotional states, signals of calls and dangers in animals, human speech, etc.

Irritability is the ability of living beings to react to the action of excitants by changing their protoplasmic properties, primarily by changing the structure of the components of their cell membranes. The two types of irritability are distinguished: non-specific and selective.

Non-specific (trigger) irritability does not depend on the quality of the excitant. It is the result of internal processes that occur under the influence of external excitants in the living object itself, primarily in its cell membranes. This process resembles the process of pulling the trigger of a gun. The excitant gradually takes the molecular changes in the cell membranes to a critical level and generates a specific reaction in the living object.

Specific (selective) irritability appears predominantly in relation to the action of biologically active substances, in particular, medicinal substances. Certain parts of the cell membrane were shown to have receptor zones — special protein molecules that are most sensitive to the action of certain chemicals, with which they interact in a "key–lock" form. These structures are called molecular receptors. Chemical substances, **ligands**, specifically interacting with the receptor, cause biochemical reactions in the cell membrane and protoplasm. Selective irritability is also associated with the diameter of the protein ion channels of the membranes, through which molecules of only a certain size can penetrate.

Irritability is the primary manifestation of the reaction of living beings to external environmental factors. During the evolution of living beings, irritability transformed into the excitability of nervous and muscular tissue.

Memory. The universal property of living objects is memory, i.e., the ability to record molecular changes caused by one or another excitant, store signs of these changes, and subsequently reproduce this information.

The property of memory is most clearly manifested in relation to re-acting excitants. However, single strong effects are also remembered, especially those that cause emotional reactions in living beings. It is characteristic that the mechanisms of memory are principally the same in living objects of different levels of organization. They are associated with the functioning of the universal genetic apparatus.

An anticipatory reflection of reality. a general property of living objects described by P.K. Anokhin, is the ability of anticipatory reflection of surrounding events. This property of living beings is closely associated with the signal value of conditional excitations discovered by I.P. Pavlov.

Anticipatory reflection of reality is primarily related to periodically repeated impacts on living organisms (Fig. 1.1)B

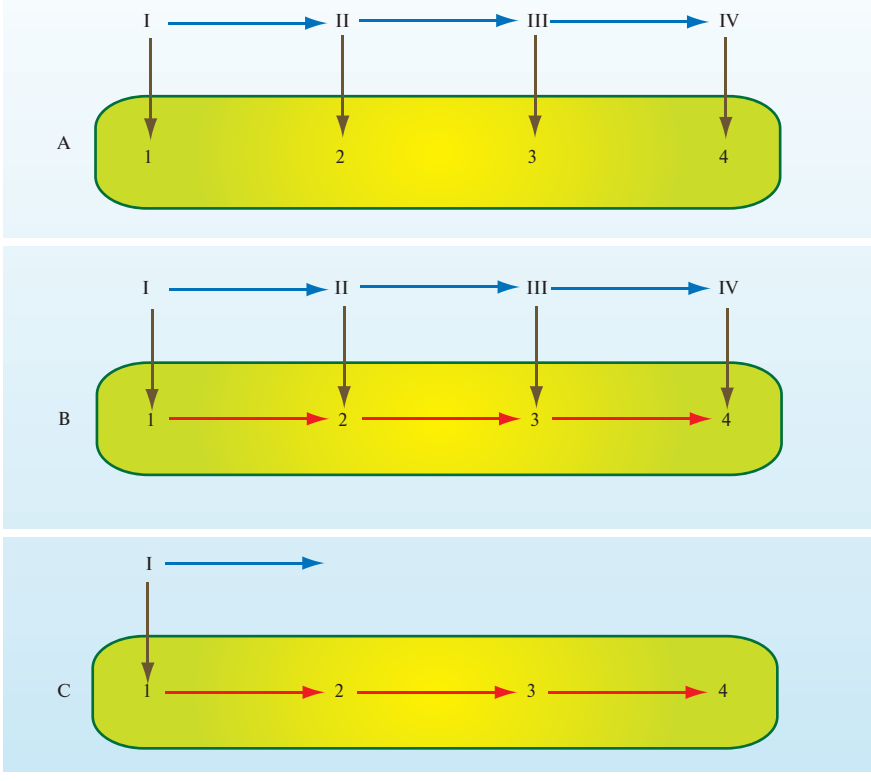


Fig. 1.1. Anticipatory reflection of reality is one of the properties of living matter: A, B, C — the stages of occurrence of the anticipatory reflection of reality in an organism (I, II, III, IV — the sequence of events in the external environment; 1, 2, 3, 4 — the sequence of internal processes in an organism)

Each subsequent impact of the external environment keeps the corresponding molecular changes in the living organism. With the multiple repeated impacts, molecular changes in the organism are connected with each other into a chemical continuum. Due to this, during the next action of the first external excitant, the entire sequential chain of molecular changes occurs rapidly. Molecular changes in the organism anticipate subsequent external excitation.

1.2. MEMBRANE POTENTIAL OF EXCITABLE CELL TISSUES

Polarization of cell membranes

According to the relation of external irritation, the tissues of the body are divided into non-excitable (epithelial, connective, bone) tissues and excitable (nerve and muscle) tissues. With irritation, excitation occurs in nerve or muscle tissue, which spreads through this tissue from the place of irritation.

Under the conditions of functional rest in the absence of stimuli, the superficial membranes of the cells of the excitable tissue are polarized. The inner surface of the membranes has a negative charge, and the outer surface has a positive charge. This is associated with the activity of sodium, potassium adenosine triphosphatase (Na^+, K^+-ATP-ase), an enzyme that is embedded in the superficial membrane of the excitable cell and, due to the energy released during the cleavage of adenosine triphosphatase (ATP), pumps K^+ ions into the cell and transfers Na^+ ions out (Fig. 1.2). In the intracellular fluid, the content of K^+ ions is 20–30 times greater than in the extracellular fluid. Within the cell, they are bound to negatively charged cytoplasmic proteins. The content of extracellular Na^+ is 10–15 times greater than intracellular ones. Extracellular fluid also contains 20–30 times more Ca^{2+} and Mg^{2+}, which is the result of the activity of membrane enzymes. Cl^- ions balance the positive charge of cations in the extracellular fluid, and therefore their extracellular content is 15–25 times greater than in the intracellular fluid.

The main ions that form the resting potential and the action potential are Na^+ and K^+ ions. Na^+ ions along the concentration gradient attempt to enter the cell, but at rest the membrane is impervious to them. Therefore, a high concentration of Na^+ ions remains outside the membrane. The membrane is partially permeable for K^+ ions and they passively travel along the concentration gradient and exit the cell through potassium pores. These pores are formed by membrane proteins and are called K^+ ion leakage channels. The released ions accumulate near the outer surface of the membrane, since large negatively charged anions of cytoplasmic protein molecules persist on the inner surface of the membrane, which electrostatically attract K^+ ions.

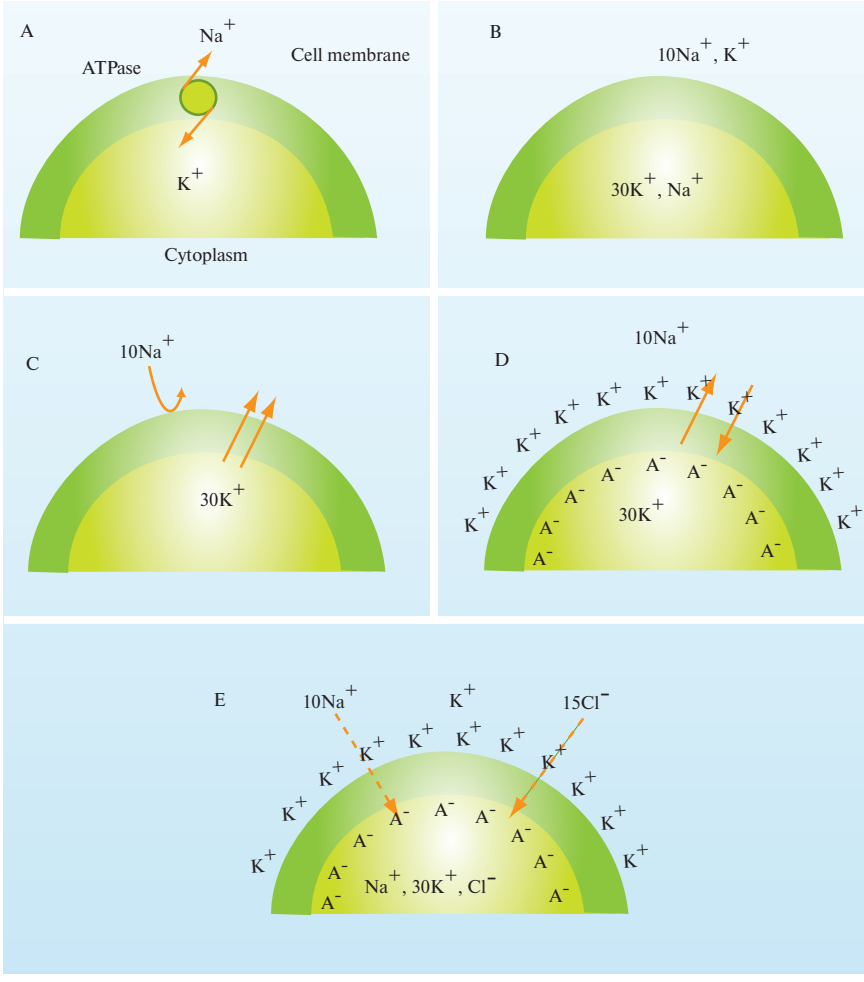


Fig. 1.2. The sequence of ionic processes of spontaneous polarization of the cell of excitable tissue: A — active transport of Na^+ and K^+ ions; B — heterogeneous distribution of extracellular and intracellular Na^+ and K^+ ions; C — passive release of K^+ ions along the concentration gradient; D — occurrence of the potassium equilibrium potential. K^+ ions move outward along the concentration gradient and inward along the electrostatic gradient; E — Cl^- ions are distributed asymmetrically to the distribution of K^+ ions. a slight passive entry of Na^+ and Cl^- ions changes the value of the potassium equilibrium potential

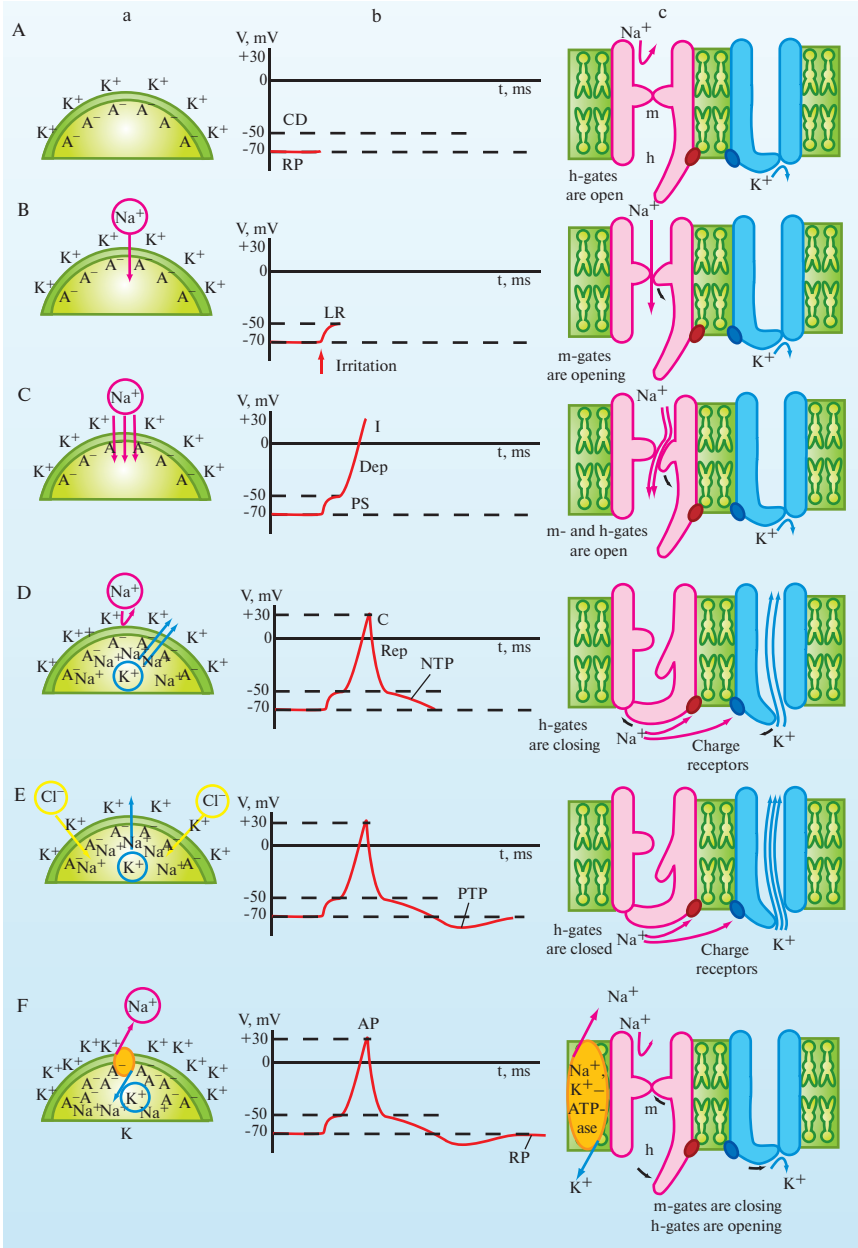
Therefore, less than 1% of K^+ ions exit the cell. a dynamic equilibrium between the concentration gradient of K^+ ions occurs, which determines their release from the cell, and the electrostatic gradient, which causes the termination of the release of K^+ ions and their accumulation on the outer surface of the membrane. On the membrane, **potassium equilibrium potential** occurs, which is one of the most important causes of cell membrane polarization at rest.

The recording of the level of membrane polarization is performed using glass microelectrodes, which are inserted into the cell without causing the destruction of the surface of the membrane. The potential difference between the microelectrode on the outer surface of the membrane with a positive charge, and the tip of the microelectrode on the inner surface of the membrane that is negatively charged, generates a current between the electrodes, which is recorded by electronic devices. The intracellular method of recording the cell membrane charge level determines that the analysis of changes in the value of membrane polarization is performed on the inner surface of the membrane. The value of the resting potential ranges from −50 to −100 mV, which is due to the different activity of ATP-ase and the different number of pores for K^+ ions in different excitable cells.

Single excitation

Stimuli, acting on the excitable tissue, are divided according to the intensity on the **subthreshold**, **threshold**, and **suprathreshold**. In the case of subthreshold stimuli, the resting potential of the membrane decreases by a small magnitude at the site of the irritating electrodes. This change is called a local response. The magnitude of the local response increases with a jump in the intensity of the subthreshold irritation. In case of threshold irritation, the local response reaches the level of critical membrane depolarization and transfers to action potential, which characterizes the change in the charge on the membrane when the excitation propagates from thecirritating electrodes. In the action potential, several parts are distinguished: pre-spike, spike, negative, and positive trace potentials (Fig. 1.3).

Fig. 1.3. The dynamics of ion processes during excitation: A — state of rest in a cell of excitable tissue; B — partial depolarization underbsubthreshold irritation; C — depolarization under threshold or suprathreshold irritation; D — repolarization; E — hyperpolarization; F — return of the initial ion distribution; a — distribution of ions around the cell membrane; b — membrane potentials; c — position of the gate in the sodium and potassium voltage-dependent channels (V — voltage on the inner surface of the membrane; t — time; RP — resting potential; CD — critical depolarization; IR — irritation; LR — local response; PS — pre-spike; Dep — depolarization; I — inversion; S — spike; Rep — repolarization; NTP — negative trace potential; PTP — positive trace potential; AP —action potential)


a
b
c
A
V, mV
+30
0
-50
-70
t, ms
CD
RP
h-gates
are open
m
h
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LR
Irritation
m-gates
are opening
C
I
Dep
PS
m- and h-gates
are open
D
C
Rep
NTP
h-gates
are closing
Charge
receptors
E
PTP
h-gates
are closed
F
AP
Na+, K+–ATP-ase
m-gates are closing
h-gates are opening

In neurons and skeletal myocytes, the spike lasts for a shorter time than trace potentials, the duration and presence of which are variable. The shape and duration of action potentials vary significantly in different excitable tissues: neurons, receptors, skeletal and smooth muscle myocytes, and cardiomyocytes. Potential amplitude is also diverse in different tissues and at the same time constant in each cell. Action potential amplitude in the nerve fiber is approximately 100 mV.

The permanence of action potential amplitude is reflected in the law of excitable tissue irritation **"All-or-nothing"**, which says that in the event of subthreshold irritation, the action potential does not occur, and in the event of threshold and suprathreshold stimuli, there is an action potential of maximum amplitude. The "All-or-nothing" law applies to neurons, nerve fibers, muscle fibers, smooth muscles, and the heart muscle. This low does not apply to nerves and skeletal muscles. This is the result of the nerve fibers that make up the nerve, and the muscle fibers that form the skeletal muscle, having a different threshold of irritation.

When the action potential occurs, the processes that cause a change in membrane polarization start. During the pre-spike, a slow **partial depolarization** of the membrane occurs due to the gradual opening of membrane pores for Na^+ ions, their entry into the cell, and a partial decrease in the negative charge on the inner surface of the membrane (see Fig. 1.3, aB). When the **critical depolarization level** is achieved, the opening of all the pores for Na^+ ions occurs, and a large amount of Na^+ ions passively enters the cell along the concentration gradient, causing rapid **total depolarization**, and then **inversion** of the sign of membrane charge (see Fig. 1.3, aC). Membrane charge permutation causes the opening of the voltage-dependent pores for K^+ ions, and K^+ ions release from the cell, causing repeated polarization of the membrane, which is called **repolarization** (see Fig. 1.3, aD). Sometimes, a phenomenon of increased membrane polarization or **hyperpolarization** occurs, the ionic mechanisms of which are associated with an increased release of K^+ ions and sometimes with the entry of Cl^- ions into the cell (see Fig. 1.3, aE). Ifter the end of action potential, Na^+, K^+-ATPase pumps Na^+ ions out and K^+ ions in with a persisting resting potential of the membrane (see Fig. 1.3, aF).

The ion channels of the cell membrane are formed by membrane proteins. Each channel has the shape of a tubule in a protein molecule. The opening of the channel is blocked by projections of this protein, called the channel gate. The sodium channel has **m- and h-gates**. At rest, m-gates arPTPclosed, and Na^+ ions do not pass through the channel (see Fig. 1.3, cA). At the same time,