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THERMODYNAMICS OF BIOLOGICAL SYSTEMS

Third edition, revised and expanded

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Introduction

Biology as a science is one of the oldest in the world.

Already in the Old Testament, dating back more than 3,000 years, there is specific biological information about the plant and animal world, recommendations are given on the diet, the use of certain types of vegetation for food.

The works of many great scientists of antiquity have come down to our time: Aristotle, Avicenna and others who made a huge contribution to the understanding of biological processes. Nevertheless, for the entire centuries old history of biology, due to the exceptional complexity of the subject being studied, scientists have not it was possible to fully reveal the secrets of the mechanisms and driving forces that ensure the viability of living organisms.

Suffice it to say that even the very definition of life up to now is not unambiguous. In this regard, for all the time of its formation, up to the beginning of the 20th century, biology as a science relied on various hypotheses and theories that periodically refuted each other as it developed and received new scientific data.

A fundamentally new step in biology was the work of Erwin Simonovich Bauer "Theoretical Biology", published in 1935.

In this work, he was the first to establish that living organisms are always in a state of thermodynamic disequilibrium, which contradicted the then popular theory of thermodynamic equilibrium (the first and second principles of thermodynamics). Almost simultaneously with E. Bauer, in 1931 Lars Onsager discovered the first general relations (reciprocity relations) of nonequilibrium thermodynamics in a linear, weakly nonequilibrium domain. Onsager reciprocity relations were the first significant result in nonequilibrium thermodynamics – the thermodynamics of irreversible processes.

Later, the main works in the field of the theory of nonequilibrium thermodynamics were carried out by a Belgian physicist and physical chemist, winner of the Nobel Prize in 1977 Ilya R. Prigozhin.

Nevertheless, to date, despite the huge accumulated material, biology is mainly a descriptive science. Obtaining this or that biological information is often achieved statistically, through a huge number of experiments and observations. As a result, a number of the most important scientific data is still

unavailable. As an example, we can cite the problem of quantifying the combined effects on living organisms of several different physical and chemical loads.

Therefore, one of the most important tasks of modern biology is to determine the laws describing the physical and mathematical principles and processes of functioning of living organisms.

This publication contains new materials that allow us to understand the nature of the human factor, its patterns and its impact on the environment.

Chapter 1

Thermodynamics and Bauer's "Universal Law of Biology"

1.1. On the formation of thermodynamics as a science

Thermodynamics is the science of the most general properties of macroscopic material systems in various states relative to thermodynamic equilibrium, and of the processes of transitions between these states. To date, thermodynamics contains two main sections:

1. Equilibrium thermodynamics (thermodynamics of isolated systems)

It was mainly developed in the mid-19th – early 20th century and contains three laws - three "Beginnings":

- in the middle of the 19th century, J. R. Mayer, J. Joule and G. Helmholtz formulated the first law of thermodynamics - "The first beginning of thermodynamics".

- in 1850 by R. Clausius, and independently of him in 1851 by W. Thomson, the "Second principle of thermodynamics" was formulated.

- in 1906 V. Nernst formulated the "Third Principle of thermodynamics".

2. Nonequilibrium thermodynamics (thermodynamics of open systems) was developed in the 20th century. Contains two main subsections:

- weakly nonequilibrium thermodynamics, the foundations of which were developed in 1931 by L. Onsager;

- strongly nonequilibrium thermodynamics, mainly developed by G. Haken, I. Prigozhin and R. Tom in the middle of the 20th century.

The first work in the field of nonequilibrium thermodynamics in biology is the book by E. Bauer "Theoretical Biology" published in 1935, in which the "Universal Law of Biology" was formulated.

1.2 Basic terms and provisions of thermodynamics

A system is a collection of material objects (bodies), limited in some way from the environment.

Depending on the nature of interaction with the environment, thermodynamic systems are divided into three types:

- 1) Isolated – a system that does not exchange either matter or energy with the environment;
- 2) Closed – a system that can only exchange energy with the environment and cannot exchange matter;
- 3) Open – a system that exchanges both energy and matter with the environment.

Only open thermodynamic systems really exist, since it is impossible to create an ideal thermos. Closed and isolated systems exist only conditionally.

Living organisms are open systems. The state of any thermodynamic system is characterized by two groups of parameters:

- Intense thermodynamic parameters (pressure, temperature, etc.), independent of the mass or number of particles in the system;
- Extensive thermodynamic parameters (total energy, entropy, internal energy), depending on the mass or number of particles in the system.

Changing the parameters of a thermodynamic system is called a thermodynamic process.

The energy of the system (W) can be represented as a combination of two parts: dependent on the motion and position of the system as a whole (W_c) and independent of these factors (U):

$$W = W_c + U. \quad (1.1)$$

The second component of this set U is called the internal energy of the system.

It includes the energy of thermal motion of particles, as well as chemical and nuclear energy, which determines the translational, vibrational and rotational motion of molecules, intramolecular interaction and vibration of atoms, the energy of rotation of electrons.

The internal energy in turn is divided into free energy and bound energy.

Free energy (G) is that part of the internal energy that can be used to perform work.

Bound energy (W_b) is the part of energy that cannot be turned into work:

$$U = G + W_b. \quad (1.2)$$

In thermodynamic systems in which there are gradients of temperature, concentrations of components, chemical potentials, irreversible processes of thermal conductivity, diffusion, and chemical reactions occur.

These processes are characterized by thermal and diffusion flows, chemical reaction rates, etc.

They are called by the general term "flows" and are denoted by J_i , and their causes (deviations of thermodynamic parameters from equilibrium values) are thermodynamic forces (X_k).

The relationship between J_i and X_k , if the thermodynamic forces are small, is written in the form of linear equations:

$$J_i = \sum_{k=1}^m L_{ik} X_k. \quad (1.3)$$

Here $i = 1, 2, \dots, m$.

1.3. General information about equilibrium thermodynamics

1.3.1. The first law of thermodynamics

The first law of thermodynamics is one of the three basic laws of thermodynamics, which is the law of conservation of energy for systems in which thermal processes are essential.

According to the first law of thermodynamics, a thermodynamic system (for example, steam in a heat engine) can perform work only at the expense of its internal energy or any external energy sources.

The first law of thermodynamics explains the impossibility of the existence of the eternal an engine of the 1st kind, which would perform work without drawing energy from any source.

The essence of the first law of thermodynamics is as follows:

When a thermodynamic system is informed of a certain amount of heat Q , in general, the internal energy of the system ΔU changes and the system performs the work A :

$$Q = \Delta U + A. \quad (1.4)$$

Equation (1.4), expressing the first law of thermodynamics, is the definition of the change in the internal energy of the system (ΔU), since Q and A are independently measurable quantities.

The internal energy of the system U can be found, in particular, by measuring the operation of the system in an adiabatic process (that is, at $Q = 0$): $A_{\text{ad}} = -\Delta U$, which determines U up to some additive constant U_0 :

$$U = U + U_0. \quad (1.5)$$

The first law of thermodynamics states that U is a function of the state of the system, that is, each state of a thermodynamic system is characterized by a certain value of U , regardless of which way the system is brought into this state (while the values of Q and A depend on the process that led to a change in the state of the system). When studying the thermodynamic properties of a physical system, the first law of thermodynamics is usually used in conjunction with the second principle of thermodynamics.

1.3.2. The second law of thermodynamics

The second law of thermodynamics is the law according to which macroscopic processes occurring at a finite speed are irreversible. Unlike ideal (lossless) mechanical or electrodynamic reversible processes, real processes associated with heat exchange at a finite temperature difference (i.e. flowing at a finite speed) are accompanied by various losses: friction, diffusion of gases, expansion of gases into the void, the release of Joule heat, etc. Therefore, these processes are irreversible, that is, they can spontaneously flow in only one direction.

The second law of thermodynamics arose historically when analyzing the operation of thermal machines.

The very name "The second law of thermodynamics" and its first formulation (1850) belong to R. Clausius: "... there is no process in which heat would pass spontaneously from colder bodies to more heated bodies".

Moreover, such a process is impossible in principle: neither by direct transfer of heat from colder bodies to warmer ones, nor by using any devices without using any other processes.

In 1851, the English physicist W. Thomson gave a different formulation of the second law thermodynamics: "Processes are impossible in nature, the only consequence of which would be lifting the load produced by cooling the thermal reservoir".

As can be seen, both of the above formulations of the second law of thermodynamics are practically the same.

This means that it is impossible to implement an engine of the 2nd kind, i.e. an engine without loss of energy for friction and other related losses.

In addition, it also follows that all real processes occurring in the material world in open systems are irreversible.

In modern thermodynamics, the second principle of thermodynamics of isolated systems is formulated in a single and most general way as the law of increase of a special function of the state of the system, which Clausius called entropy (S).

The physical meaning of entropy is that in the case when the material system is in complete thermodynamic equilibrium, the elementary particles that make up this system are in an uncontrolled state and commit various random chaotic movements. In principle, it is possible to determine the total number of these possible states.

The parameter that characterizes the total number of these states is entropy.

Let's look at this in a simple example.

Let an isolated system consist of two bodies "1" and "2" having unequal temperature $T_1 > T_2$. Body "1" gives off a certain amount of heat Q , and body "2" receives it. At the same time, there is a heat flow from the body "1" to the body "2". As temperatures equalize, the total number of elementary particles of bodies "1" and "2" in thermal equilibrium increases.

As this number of particles increases, so does entropy. And as soon as there will be a complete thermal equilibrium of bodies "1" and "2", entropy will reach its the maximum value. Thus, in a closed system, the entropy S for any real process either increases or remains unchanged, i.e. the change in entropy $\delta S \geq 0$. The equal sign in this formula takes place only for reversible processes. In the state of equilibrium, when the entropy of a closed system reaches a maximum,

no macroscopic processes in such a system, according to the second law of thermodynamics, are impossible.

It follows that entropy is a physical quantity that quantitatively characterizes features of the molecular structure of the system, on which the energy transformations in it depend.

The connection of entropy with the molecular structure of the system was first explained by L. Boltzmann in 1887. He established the statistical meaning of entropy (formula 1.6). According to

Boltzmann (high orderliness has a relatively low probability)

$$S = k \ln P, \quad (1.6)$$

where k is the Boltzmann constant, P is the statistical weight,

$$k = 1.37 \cdot 10^{-23} \text{ J/K}.$$

The statistical weight P is proportional to the number of possible microscopic states of the elements of a macroscopic system (for example, different distributions of the values of coordinates and pulses of gas molecules corresponding to a certain value of energy, pressure and other thermodynamic parameters of the gas), i.e. it characterizes a possible discrepancy in the microscopic description of the macrostate.

For an isolated system, the thermodynamic probability W of a given macrostate is proportional to its statistical weight and is determined by the entropy of the system:

$$W \sim \exp \left(\frac{S}{k} \right). \quad (1.7)$$

Thus, the law of entropy increase has a statistical-probabilistic character and expresses the constant tendency of the system to transition to a more probable state. It follows that the most likely state achievable for the system is, is one in which events occurring in the system at the same time are statistically mutually compensated.

The most probable state of a macrosystem is a state of equilibrium, which it can, in principle, achieve in a sufficiently long period of time. As stated above,

entropy it is an additive quantity, that is, it is proportional to the number of particles in the system. Therefore, for systems with a large number of particles, even the smallest relative change in the entropy per particle significantly changes its absolute value; a change in the entropy standing in the exponent in equation (1.7) leads to a change in the probability of this macrostate W by a huge number of times.

This fact is the reason that for a system with a large number of particles, the consequences of the second principle of thermodynamics are practically not probabilistic, but rather reliable. Extremely unlikely processes accompanied by any noticeable decrease in entropy require such huge waiting times that their implementation is practically impossible.

At the same time, small parts of the system containing a small number of particles experience continuous fluctuations accompanied by only a small absolute change in entropy.

The average values of the frequency and size of these fluctuations are as reliable a consequence of statistical thermodynamics as the second beginning of thermodynamics itself.

The literal application of the second principle of thermodynamics to the Universe as a whole, which led Clausius to the wrong conclusion about the inevitability of "heat death the universe", is illegal, since in nature, in principle, absolutely isolated systems cannot exist.

As will be shown later, the processes occurring in open systems obey other laws and have other properties.

1.3.3. The third law of thermodynamics

The third law of thermodynamics is the law of thermodynamics formulated by V. Nernst in 1906 (Nernst's thermal law), according to which the entropy S of any system tends to a finite limit for it, independent of pressure, density or phase, when the temperature (T) tends to absolute zero. The third law of thermodynamic allows us to find the absolute value of entropy, which cannot be done on the basis of the first and second law of thermodynamics. In classical thermodynamics (first and second laws) entropy can be determined only up to an arbitrary additive

constant S_0 , which practically does not interfere with most thermodynamic studies, since the entropy difference (S_0) in different states is actually measured.

According to the third law of thermodynamics, at $T \rightarrow 0$, the value of $\Delta S \rightarrow 0$.

Max Planck in 1911 gave a different formulation of the third law of thermodynamics - as a condition for the vanishing of the entropy of all bodies when the temperature tends to absolute zero:

$$\lim_{T \rightarrow 0} S = 0. \quad (1.8)$$

Hence $S_0 = 0$. This makes it possible to determine the absolute values of entropy and other thermodynamic potentials. Planck's formulation corresponds to the definition of entropy in statistical physics through the thermodynamic probability (W) of the state of the system $S = k \ln W$.

At absolute zero temperature, the system is in the basic quantum mechanical state if it is non-degenerate, for which $W = 1$ (the state is realized by a single microdistribution). Therefore, the entropy S at $T = 0$ is zero.

In fact, with all measurements, the tendency of entropy to zero begins the discreteness of the quantum levels of the macroscopic system, which leads to the phenomena of quantum degeneracy, can appear much earlier than it can become significant at $T \rightarrow 0$.

It follows from the third law of thermodynamics that absolute zero temperature cannot be reached in any final process associated with a change in entropy, it can only be asymptotically approached.

1.4. General information about nonequilibrium thermodynamics

As mentioned above, classical thermodynamics (its three "beginnings") studies thermodynamic equilibrium, reversible processes.

For nonequilibrium processes, it establishes only inequalities that indicate the possible direction of these processes.

The fundamental works of I.R. Prigogin established, that all thermodynamics is divided into three large areas: equilibrium, in which entropy production, flows and forces are zero, weakly nonequilibrium, in which thermodynamic forces are "weak", and energy flows are linearly dependent on

forces, and strongly nonequilibrium, or nonlinear, where energy flows are nonlinear, and all thermodynamic processes are irreversible.

The main task of nonequilibrium thermodynamics is the quantitative study of nonequilibrium processes, in particular, the determination of their velocities depending on external conditions.

In nonequilibrium thermodynamics, systems in which nonequilibrium processes occur are considered as continuous media, and their state parameters are considered as field variables, that is, continuous functions of coordinates and time.

Weakly nonequilibrium (linear) thermodynamics considers thermodynamic processes occurring in systems in states close to equilibrium.

Thus, linear thermodynamics describes stable, predictable behavior of systems striving for a minimum level of activity.

The first works in this field belong to Lars Onsager, who in 1931 for the first time discovered the general relations of nonequilibrium thermodynamics in a linear, weakly nonequilibrium domain - "reciprocity relations".

Their essence is purely qualitatively reduced to the following: if the force is "one" (for example, temperature gradient) for weakly nonequilibrium situations affects the flow "two" (for example, diffusion), then the force "two" (concentration gradient) affects the flow "one" (heat flow).

It follows that in a weakly nonequilibrium region, the laws of equilibrium thermodynamics practically apply, the system does not strive for anything and its behavior in most cases is quite predictable.

Strongly nonequilibrium thermodynamics considers processes occurring in systems whose state is far from equilibrium. When the thermodynamic forces acting on the system become sufficiently large and take it out of the linear domain into a nonlinear one, the stability of the state the system and its independence from fluctuations is significantly reduced.

In such states, certain fluctuations increase their effect on the system, forcing it to evolve to a new state when it reaches the point of bifurcation – loss of stability, which may be qualitatively different from the original one. Thus, the self-organization of the system takes place. Moreover, it is believed that the development of such systems proceeds through the formation of increasing orderliness.

On this basis, the idea of self-organization of material systems arose.

All material systems, from the smallest to the largest, are considered open, exchanging energy and matter with the environment and being, as a rule, in a state far from thermodynamic equilibrium. This property of material systems allowed, in turn, to determine a number of new properties of matter.

Here are some of them.

- all processes are irreversible, as they are always accompanied by energy losses;

- entropy S in open systems has two components: deS – characterizes entropy exchange with the outside world; diS – characterizes irreversible processes inside;

- matter has the property of self-organization.

I. Prigozhin's studies of living matter as open material systems were mainly focused on the comparative analysis of the organization of structures of living and inanimate matter, thermodynamic analysis of glycolysis reactions and a number of other works.

1.5. Bauer's "Universal Law of Biology"

Along with the theoretical work of physicists on the problems of the laws of thermodynamics, the same problem, but applied to biology, was dealt with by the theoretical biologist E. Bauer at the beginning of the 20th century. At that time, biology as a science was not yet sufficiently developed. The composition of cells and their basic functions were not yet known, and it was generally accepted that life was some substance with special properties. In the microscope, the living matter of various living organisms looked almost the same in the form of cells with a jelly-like mass (which was called protoplasm).

The main task that E. Bauer set himself was to determine the basic thermodynamic properties of living substances, for which he took protein molecules in a special, non-equilibrium state.

Despite a number of erroneous assumptions, the fundamental scientific achievement of E. Bauer in this work is an irrefutable proof that living organisms can only be in a stable nonequilibrium thermodynamic state. E. Bauer formulated the "Universal Law of Biology" in the following wording:

"All and only living systems are never in equilibrium and perform constant work at the expense of their free energy against the equilibrium required by the laws of physics and chemistry under existing external conditions".

In essence, this law is the First law of thermodynamics of biological systems.

E. Bauer also formulated the "Principle of stable disequilibrium of living systems":

"It is characteristic of living systems that they, due to their free energy, produce the work of counteracting the expected equilibrium".

Later, the theory of E. Bauer was fully confirmed by the works of I. Prigozhin, G.Haken and R. Tom. According to I. Prigozhin: "... both the biosphere as a whole and its various components, living or inanimate, exist in highly non-equilibrium conditions. In this sense, life, which obviously fits into the framework of the natural order, appears to us as the highest manifestation of the processes of self-organization occurring in nature".

1.6. Passive and active thermodynamic systems

As mentioned above, in modern thermodynamics, thermodynamic systems are classified as follows:

- isolated, exchanging neither energy nor matter with the environment;
- closed, not exchanging with the environment substance;
- open, exchanging energy and matter with the environment.

In addition, thermodynamic systems are also classified as adiabatic, if there is no energy exchange of the system with the environment, homogeneous (for example, gas in a vessel) and inhomogeneous (water and steam or a mixture of gases in a vessel), stationary and mobile, and others.

All of these systems, except for open ones, can be considered only as some local, special cases of open thermodynamic systems, since the state of the external environment around thermodynamic systems is continuously changing as a result of the continuous movement of macroscopic objects of these systems in space.

Depending on the degree of interaction of thermodynamic systems, the thermodynamic processes within these systems also continuously change – in the range from weakly nonequilibrium to highly nonequilibrium, up to phase transitions, as a result of which new flows of energy and matter are created.

However, the processes occurring inside thermodynamic systems may have qualitatively different character:

- redistribution of existing energy in them, for example, heat along the rod.

Let's call such thermodynamic systems passive.

- conversion of one type of energy into another, for example, during operation, chemical or nuclear reactions and in other cases. Such systems include various types of engines: thermal, internal combustion, electric and others, as well as living organisms.

Let's call such thermodynamic systems active.

Let's consider the thermodynamic processes occurring in these systems in more detail.

1.6.1. Analysis of the basic properties of passive thermodynamic systems

If between two passive thermodynamic systems, for example I and II, if there is a temperature gradient, then, in accordance with the 2nd principle of thermodynamics, an energy flow will arise between them, directed from a more heated system to a less heated one.

In a steady-state thermodynamic process, for example between infinitely large thermodynamic systems whose temperature practically does not depend on time, it can be described by the Fourier heat equation:

$$J_q = -k \text{grad} T(x), \quad (1.9)$$

where J_q is the heat flux vector – the amount of energy passing through a unit area (energy flux density) per unit time perpendicular to the x axis, k is the thermal conductivity coefficient, T is the temperature.

In the case of an unsteady thermodynamic process, in which thermodynamic systems I and II with initial temperatures T_1 and T_2 , respective, exchange

thermal energy among themselves, and at the same time the temperatures of these systems change accordingly, the latter can be described by the equation

$$J = f(t) = \frac{-k(T_1 - T_2)}{t} \rightarrow 0. \quad (1.10)$$

From here:

$$t = \frac{-k(T_1 - T_2)}{J} \rightarrow \infty. \quad (1.11)$$

From (1.11) follows:

- 1) *Macro-objects of passive thermodynamic systems continuously strive for thermodynamic equilibrium, but never reach it;*
- 2) *Passive thermodynamic systems, between which energy is exchanged, are always in an unstable nonequilibrium thermodynamic state.*

Thus, the thermal energy of each of these two passive thermodynamic systems can be represented as:

$$Q(t) = Q_{\lim} \pm \Delta Q(t), \quad (1.12)$$

where:

Q_{\lim} is the value of the thermal energy of the equilibrium state of the thermodynamic system to which it tends,

$\Delta Q(t)$ is the residual thermal energy of the nonequilibrium state of the thermodynamic system involved in energy exchange.

1.6.2. Analysis of the basic properties of active thermodynamic systems

When the process of functioning of active thermodynamic systems has been established for a certain time, the latter, in accordance with the 1st beginning of thermodynamics, is accompanied by a constant release or absorption of thermal energy.

At the same time, the internal thermal energy of these systems does not change

$$Q_i = \text{const}, \quad (1.14)$$

and their thermodynamic state can be defined as nonequilibrium stable:

$$Q_{\text{ns}} = Q_i + W_{\text{ce}} + Q_T, \quad (1.14)$$

where W_{ce} is the converted energy, Q_T is the thermal energy released into the environment.

Thus, active thermodynamic systems in the process of their functioning are always in a stable nonequilibrium thermodynamic state.

This definition is not difficult to confirm with the following examples.

In an internal combustion engine, oxidation reactions of the fuel supplied to it occur, as a result of which a significant amount of thermal energy is released, used by means of appropriate drives, for example, for the movement of a motor vehicle.

Since, according to the first principle of thermodynamics, the coefficient the efficiency of such an engine is $\eta < 100\%$, the corresponding heating of its body and other parts occurs to a certain level at which the density of incoming energy becomes equal to the density of energy released into the atmosphere.

This condition must certainly be fulfilled, because otherwise, if the engine overheats, it will fail.

Similar processes occur with living organisms.

Their vital activity is based on the chemical processing of food, as a result of which the energy they need is released, spent on kinetic and thermal energy, as well as on the synthesis of organic substances in the case of their growth and weight gain.

Let's consider these processes on the example of the human body.

In the course of his life, he takes food daily containing a certain amount of energy, consumes a certain amount of oxygen and other substances.

However, as a result of this, neither its mass nor its chemical composition practically changes for quite a long time, for example, several months.

At the same time, a person performs physical work every day, expending kinetic energy, and also constantly, within certain limits, maintains his body temperature about 36.60 °C.

Thus, it is obvious that the energy consumed by a person from the external environment is converted, as mentioned above, into other types of energy: kinetic and thermal, when that his internal energy remains constant on average.

Returning to the law formulated by E. Bauer, we note that his mistake is that he compared the active thermodynamic system of living organisms with passive thermodynamic systems.

In fact, there are no special properties of living organisms that do not comply with the laws of physics and chemistry.

Chapter 2

Biological rhythms as a way of existence of living matter

2.1. Historical background

People have known about the existence of biological rhythms since ancient times.

Already in the "Old Testament" precise instructions are given about the correct lifestyle, nutrition, alternating phases of activity and rest. Many outstanding scientists of antiquity wrote about it: Hippocrates, Avicenna and others.

The founder of chronobiology, the science of biorhythms, is considered to be a German doctor Christopher William Gufeland, who in 1797 drew the attention of colleagues to universality rhythmic processes in biology: every day life repeats itself in certain rhythms, and the daily cycle associated with the rotation of the Earth around its axis regulates the vital activity of all living things, including the human body.

The first serious scientific research in this area began to be conducted at the beginning 20th century, including Russian scientists I.P. Pavlov, V.V. Vernadsky, A.L. Chizhevsky and others.

By the end of the 20th century, the fact of the rhythmicity of biological processes of living organisms began to be considered one of the fundamental properties of living matter and the essence of the organization of life.

However, the nature of biorhythms was unclear until recently.

As happens in such cases, biorhythm studies were a process of accumulating information, identifying properties and patterns by statistical methods, and practical use issues were considered.

As a result, two scientific directions have emerged in the science of biorhythms: chronobiology and chronomedicine.

One of the main works in this field can be considered the classification of biological rhythms developed by F. Halberg in 1964 (circadian rhythms).

However, the nature of biorhythms and their role in the functioning of living organisms remained unclear to him and his followers.

2.2. The nature of biorhythms. Analysis of thermodynamic properties of biological systems

Returning to the works of E. Bauer, discussed in Chapter 1, we note that, theoretically assuming the presence of structures providing thermodynamic disequilibrium, E. Bauer did not establish how living organisms constantly maintain this nonequilibrium thermodynamic state.

Disequilibrium means, says E. Bauer, that all structures of living cells at the molecular level are pre-charged with "superfluous", excessive energy in comparison with the same inanimate molecule, which is expressed in the inequality of potentials, in the created a chemical or electrical gradient, whereas in an inanimate closed system, any gradients are distributed uniformly according to the entropy rule.

Bauer calls this "extra" energy existing in living cells at any level "structural energy" and understands it as deformation, disequilibrium in the structure of a living molecule.

To determine how living systems provide a state of stable disequilibrium, we will analyze the thermodynamic processes occurring in living organisms.

As it is known from biology, the production of free energy from food and its consumption to ensure their vital activity is carried out by living organisms using biochemical reactions of metabolism, which are metabolic cycles.

The metabolic reactions that continuously occur in cells are complexes of various biochemical reactions of cleavage and synthesis of substances by various metabolic pathways.

Since metabolism occurs in cycles, then in cells in accordance with these continuous periodic changes in the concentrations of substances occur in cycles, involved in numerous biochemical reactions. Figure 2.1 shows a graph of intracellular fluctuations in calcium concentration as an example.

As can be seen from figure 2.1, intracellular calcium fluctuations are a continuous periodic process.

Among all biochemical reactions, a special role is played by reactions of synthesis from molecules of carbohydrates and fats contained in nutrients, adenosine triphosphate (ATP), accompanied by energy consumption, and reactions of its subsequent cleavage, accompanied by the release of energy.

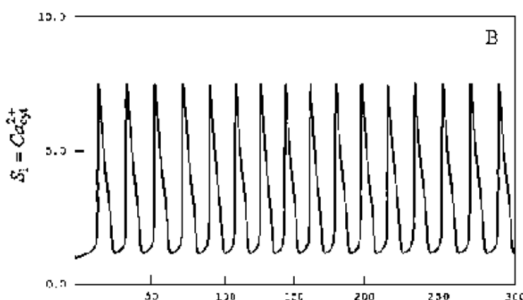


Figure 2.1. Graph of intracellular calcium fluctuations

The structure of ATP is shown in figure 2.2.

As can be seen from Figure 2.2, ATP consists of three phosphate groups (α , β and γ), nitrogen base residues (adenine) and sugar residue (ribose).

When the phosphoanhydride and phosphoester bonds are broken, energy is released.

Phosphate groups can be split off step by step by dissolving in water (hydrolysis) and formation of orthophosphate or inorganic phosphate and adenosine diphosphate ADP, and then, after the cleavage of ADP, and adenosine monophosphate with the release of energy at each stage:

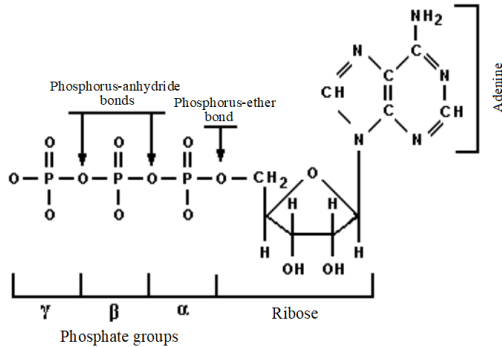
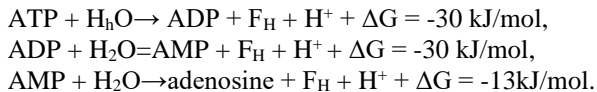


Figure 2.2. Structure of ATP



Here F_H - inorganic phosphate, H^+ - positive hydrogen ion, ΔG is the change in the free energy released during the separation of the terminal phosphate group.

Usually, cells extract energy from ATP during cellular respiration, splitting off only one phosphate group from its molecule.

Figure 2.3 shows an example of a simplified graph of ATP synthesis-cleavage cycles.

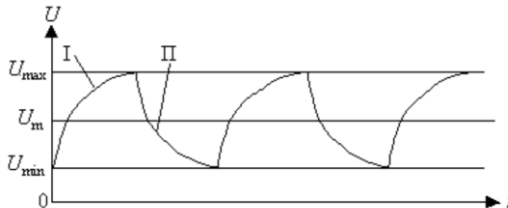


Figure 2.3. Simplified graph of ATP synthesis-cleavage

U is the amount of ATP in the cell;

I is the synthesis process; II is the cleavage process

As can be seen from the graph in figure 2.3, the processes of ATP synthesis depicted on it (curve I), and ATP cleavage (curve II) represent a continuous sequence of cycles, with both processes proceeding according to laws close to exponents.

The upper and lower limits of the concentration of the biochemical substances U_{\max} and U_{\min} are determined by the positive and negative feedbacks present in the cells, which will be discussed below.

The rate of biochemical reactions is regulated by appropriate biochemical catalysts that accelerate these reactions and inhibitors, slowing them down, as can be seen from figure 2.4, where an example of the scheme of the mechanism of regulation of enzymatic reactions is presented.

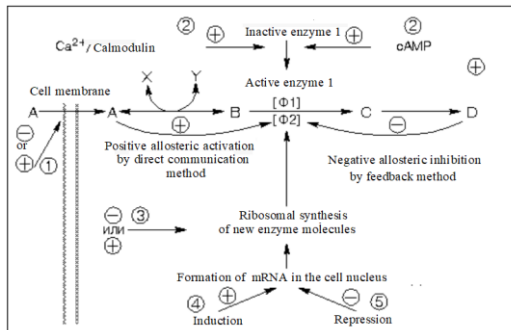


Figure 2.4. Example of the regulation scheme of enzymatic reactions

In figure 2.4, the numbers enclosed in circles indicate the likely areas of hormone action. 1 - change in membrane permeability; 2 - transition of the enzyme from inactive to active form; 3 - change in the rate of mRNA translation at the ribosomal level; 4 - induction of new mRNA formation; 5 - repression of mRNA formation.

Graphs of alternations of ATP synthesis and cleavage and corresponding alternations of energy expenditure and release are shown in Fig. 2. 5.

As can be seen from figure 2.5, as a result of successive alternations of cycle of biochemical reactions of synthesis and cleavage of ATP, in which thermodynamic processes of costs and energy release occur respectively, the

amount of energy released is greater than consumed. The average value of the difference between the energy released and consumed is equal to $W_a > 0$.

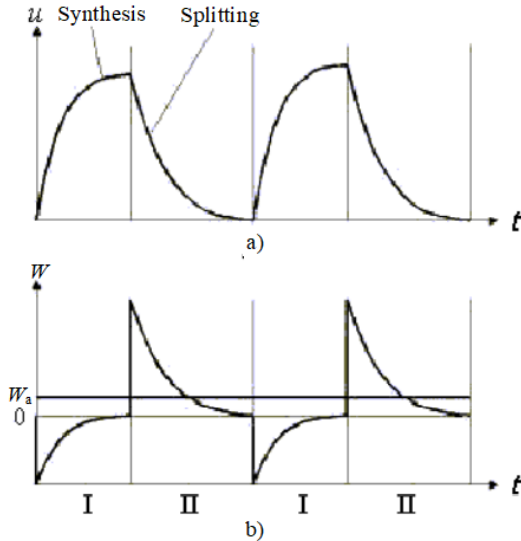


Figure 2.5: a) Graph of alternating phases of synthesis and cleavage of substances;

b) The schedule of alternating phases of energy consumption and release;

I – phase of energy consumption;

II - phase of energy release;

W_a is the average effective resultant value of the released energy.

The value of the W_a energy directly depends on the reaction of the cell to the effects of the internal and external environment in the form of enzymatic regulation of the processes of synthesis and cleavage of ATP.

Sensors that determine the speed and nature of metabolic processes in cells, they are allosteric modulators and hormones that continuously control their thermodynamic state.

The stability of the nonequilibrium thermodynamic state of cells is provided as follows:

- at the minimum value of the nonequilibrium thermodynamic state of the cell the sensors turn on the mode of splitting ATP, as a result of which their energy begins to increase, reaching a certain maximum value;

- at the maximum value of the nonequilibrium thermodynamic state of the cell, the sensors turn on the ATP synthesis mode, at which the energy of the body begins to decrease.

Thus, the principle of ensuring the stability of the nonequilibrium thermodynamic state of cells is that the magnitude of their nonequilibrium thermodynamic state always continuously fluctuates within the limits determined by allosteric modulators and hormones.

Let's consider thermodynamic processes at the level of organs, systems and the body as a whole using the example of the human body.

Since each cell is a full-fledged microorganism in a stable nonequilibrium thermodynamic state, the resulting with these cells, organs, systems and whole organisms are also in a stable nonequilibrium thermodynamic state. Moreover, since all biochemical processes in these cells are interconnected, the functioning of organs, systems and integral organisms is ensured by corresponding cumulative synchronous integral oscillations of the nonequilibrium thermodynamic state of cells.

This is expressed in periodic fluctuations of physiological parameters (functional shifts) of organs, systems and the whole organism. A good example here is the sequence of contractions and relaxes of the heart muscle: when the heart muscle contracts, the cells that enter it have synchronous processes of splitting ATP, and when relaxing, the processes of ATP synthesis.

Moreover, with successive cycles of contraction and relaxation of the heart muscle in these processes, it is statistically significant simultaneously, integrated and synchronously a huge number of cells produce the corresponding biochemical reactions, each of which performs its role as part of the heart muscle.

At the same time, the heart rate is determined by the thermodynamic state of the whole organism and can fluctuate depending on the load experienced by the body within sufficiently large limits.

Similarly, the corresponding oscillatory processes occur in the respiratory system, the central nervous system and others.

Here it is necessary to pay attention to the fact that in any physiological processes not absolutely all cells involved in this process behave like soldiers, clearly fulfilling their prescribed role.

As already mentioned above, living organisms are open thermodynamic systems in which various irreversible processes continuously occur. Therefore, the conditions of existence and vital activity of each cell are constantly changing and, accordingly, their roles in the integral processes occurring in organs and systems are changing (redistributed). However, statistically, in

as a result of the action of a huge number of cells, they eventually produce the actions for which they are intended, in this case, successive contractions and relaxation of the heart muscle in the required rhythm.

In the human body, all organs and systems react to the effects of loads. Of these, the cardiovascular system reacts most clearly and promptly, since stopping her work, even for a few minutes, can lead to the death of the body.

The respiratory system works somewhat more freely, but within fairly strict limits, the periodic processes of which a person can consciously regulate to a small extent.

In an even freer mode of oscillation, some centers of the brain, the digestive system and others work. A person can afford in certain it can disrupt the rhythm of sleep and wakefulness, the rhythms of food consumption, etc.

However, the magnitude of all these parameters largely depends on the general state of the organism and on environmental conditions.

Since the organs and systems of a living organism, in particular the human body, perform a variety of functions, the periods of fluctuations in the parameters of these organs and systems, as well as the patterns of changes in these fluctuations can be very different.

When perceiving pulses of light or sound, the periods of oscillation are fractions of seconds. In some types of work, the periods of fluctuations caused by them (in combination with other fluctuations) can be days, weeks, and even months.

At the same time, regardless of anything, all types of physiological fluctuations are continuous sequences of cycles corresponding to energy fluctuations in energy consumption and release.

Thus, the principle of ensuring the stability of the nonequilibrium thermodynamic state of living organisms (biological systems) as at the level

The process of energy consumption and release at the level of cells, organs, systems and whole organisms consists in continuous alternations of energy consumption and release through cycles of ATP synthesis and cleavage controlled at appropriate levels.

Hence, in addition to the "Universal Law of Biology" by E. Bauer, the second law of biology can be formulated, which is stated in the following wording:

2.3. The second law of thermodynamics of biological systems

The principle of ensuring the stability of the nonequilibrium thermodynamic state of living organisms (biological systems) both at the level of cells and at the levels of organs, systems and whole organisms, it consists in continuous alternations of energy consumption and release through controlled cycles of synthesis and splitting of ingredients involved in biochemical reactions.

The following consequences follow from this law:

1. In living organisms, no process can occur continuously, but must alternate with the opposite direction: inhale with exhale, work with rest, wakefulness with sleep, synthesis of substances with splitting, etc.

2. The state of a living organism is never static, and all its physiological and energy parameters are always in a state of continuous fluctuations relative to average values, both in frequency and amplitude.

The physiological fluctuations of living organisms described above, which have been observed by mankind for many thousands of years, are biorhythms.

Thus, the nature of biorhythms is continuous alternation of phases consumption and release of energy through controlled reactions of synthesis and cleavage of ATP, aimed at ensuring a stable nonequilibrium thermodynamic state of biological systems.

2.4. Natural and forced frequency of biorhythms

In living organisms, the vital activity of each cell, each organ, each system and the whole organism are characterized by corresponding complexes of biological rhythms, the parameters of which are closely interrelated and determined by both the internal properties of the corresponding elements of the organism, and their role in the composition of an organ or system, as well as the habitat. For example, the heart rate of a person in a calm state is 58-75 beats / min., and when a heavy load can reach 160 or more, cycles of biochemical

reactions associated with the digestion of food occur, for example, from 3 to 5 times a day, depending on the diet, etc. Because every living organism has its own way it is unique, it will be characterized by an optimal lifestyle corresponding only to it: sleep and wakefulness time, diet regime and composition, appropriate environment, necessary physical activity and much more. In this regard, for such a living of the organism will be characterized by biological rhythms corresponding only to its physiological parameters.

However, in real life, such a regime is impossible, since it cannot exist in isolation from the conditions of its environment.

What are the conditions of this situation?

One of the main conditions is the sleep-wake cycle period equal to 24 hours.

This condition is determined by the period of rotation of the Earth around its axis.

Another basic condition is that a person lives in a society, and therefore must obey its rules, in particular the regime of the day, work and rest time meal time, etc.

Therefore, in most cases, certain parameters of the biorhythms of each the organism is forced.

Figure 2.6 shows an example of idealized typical fluctuations of functional shifts of the human body, which are a generalization of biorhythms of such physiological parameters as body temperature, arterial systolic and diastolic pressure, reactions to light and sound, heart rate.

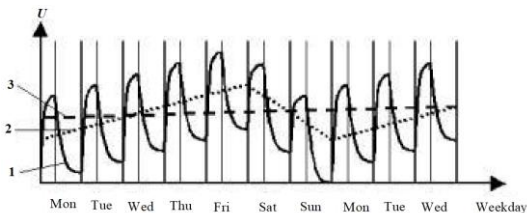


Figure 2.6. Idealized typical fluctuations of functional shifts of the human body

1 – daily fluctuations of the functional shift; 2 – week average effective fluctuation of the functional shift; 3 – the average effective value of the functional shift.

As can be seen from figure 2.6, generalized periodic fluctuations of functional shifts of the human body are both daily and weekly in nature.

How does the human body coordinate its own and forced parameters of biorhythms?

Here it is necessary to pay attention to the fact that all the processes occurring in the human body under the conditions of its own biorhythms are absolutely necessary for its vital activity, since otherwise there will be an accumulation of values of non-regenerating functional shifts, which can lead to loss of working capacity, diseases and death.

As examples, a graph of changes in functional shifts can be given, 2.6, which reflects the accumulation of residual functional shifts and their recovery during rest days, or well-known cases of loss of performance as a result of prolonged lack of sleep, severe physical or mental fatigue, and others.

Therefore, forced periods of biorhythms of the organization of biochemical processes the cycles of sleep and wakefulness, work and rest, nutrition and other cycles are adjusted by the body so that all the functions necessary for its vital activity fit into these compulsory frameworks. In particular, a person determines for himself the type of work activity, the time and duration of sleep, the type of rest, the range of food, sports and much more. Besides, this correction is also largely due to the ability of the organism to phenotypic adaptation. As numerous studies in the field of chronobiology and chronomedicine show, the properties of living organisms, and in particular humans, to correct their own biorhythms are very individual.

2.5. About the problem of biological clocks

In 1729, de Maran, the scientific secretary of the Paris Royal Academy of Sciences, noticed that bean leaves move regardless of the time of day and light. In 1758 year Dumel repeated de Maran's experiments, placing plants in a deep cave - in the darkness, where the temperature was unchanged both day and night. The movements of the leaves continued, but after many days these movements faded, but from the flash of light the movements resumed as before. This is a property of wildlife to change its circadian activity scientists called the biological clock vital activity. Since then, many well-known scientists have been engaged in the study of the nature of the biological clock: Frisch, Bunning, Pitendrich,

Hastings, Halberg and others. They believe that in every cell of animals and plants there are certain genes that determine the circadian (circadian) frequency of vital activity. The intracellular "clock" sets its course for the periods of light and dark time of day and does not depend much on temperature changes. Moreover, in the central nervous system of animals there are "main" clocks that control the clocks of other cells.

However, so far this clock has not been found. Analyzing this problem from the point of view of nonequilibrium thermodynamics, we obtain the following.

To ensure their vital activity, living organisms must always be in a stable nonequilibrium thermodynamic state, any changes in the parameters of the external environment immediately cause certain changes in the course of biological processes in them. However, the work of the biological clock, according to the ideas of adherents of this hypothesis, should not depend on the influence of external parameters environment, which can lead to a loss of stability of the nonequilibrium thermodynamic state of biological systems. Thus, the hypothesis of the existence of a biological clock is apparently erroneous.

Chapter 3

Theoretical foundations of adaptation

3.1. General information about adaptation

Living organisms have the property of adapting to environmental conditions.

A large number of works are devoted to the problems of adaptation, mainly containing facts or various theories offering various scientific explanations of the observed processes, including P.K. Anokhin, F.Z. Meerson and others.

There are two types of adaptation: genotypic and phenotypic.

According to the definition of the Great Medical Encyclopedia (BME): "...genotypic adaptation occurs due to the selection of cells with a certain genotype, conditioning endurance". This definition is not perfect, since it does not reflect what kind of loads endurance refers to, since in most cases, by acquiring some advantages, living organisms lose others. If, for example, a plant tolerates a hot, arid climate well, then, most likely, it will not tolerate cold and humid.

As for phenotypic adaptation, there is currently no strict definitions of this term.

According to the definition of BME, "... phenotypic adaptation occurs as a protective reaction to the action of a damaging factor".

According to F.Z. Meerson's definition, "Phenotypic adaptation is a process developing in the course of individual life, as a result of which an organism acquires a previously absent resistance to a certain environmental factor and thus gets the opportunity to live in conditions previously incompatible with life, ..."

Similar definitions of adaptation are also known by other authors.

However, neither the definition given in the BME nor the definition of F.Z. Meerson reflects in the full extent of the properties of living organisms to phenotypic adaptation. If we analyze the definition of phenotypic adaptation given in the BME, it becomes obvious that limiting the adaptation process only by the presence of a damaging factor is apparently unjustified.

Indeed, if a non-damaging factor acts, for example, drinking water with a different salt content, to which you need to get used, or moving to a zone of a different time zone, then in these cases the body is also rebuilt due to the properties phenotypic adaptation. As for the definition given by F.Z. Meerson, it also does not sufficiently cover the area in which phenotypic adaptation manifests itself.

The main reason for the ambiguity of the definitions of genotypic and phenotypic adaptation is that when defining these concepts, there is no basic criterion for the viability of organisms – the stability of their nonequilibrium thermodynamic state.

Therefore, the following version of the definition of genotypic and phenotypic adaptation is proposed:

Genotypic adaptation is a change in the gene pool of a species by natural selection according to the indicator of maximum stability of a nonequilibrium thermodynamic state.

Phenotypic adaptation is the property of an organism to change its biological parameters under constantly changing environmental conditions to ensure the stability of a nonequilibrium thermodynamic state.

Genotypic adaptation will not be considered in this textbook.

As for phenotypic adaptation, its processes can be conditionally divided into two types:

1. Operational phenotypic adaptation, as a result of which the organism, through appropriate operational physiological reactions, continuously reacts to all short-term factors affecting its vital activity, without changing the average values of its functional systems.

2. Stable phenotypic adaptation, as a result of which, with prolonged exposure to environmental factors the average values of its functional systems have changed, as a result of which the body has become more adapted to these factors.

The issues of determining the nature of adaptation and its basic laws by analyzing biological processes based on the principles of the vital activity of living organisms as open thermodynamic systems in a stable nonequilibrium thermodynamic state will be considered below.

3.2. The essence of phenotypic adaptation processes

As was established by the second law of biology, the stability of the nonequilibrium thermodynamic state of biological systems is ensured by the continuous alternation of phases of energy consumption and release through controlled reactions of synthesis and cleavage of ATP.

However, along with the reactions of ATP synthesis and cleavage in living organisms, a large number of other vital biochemical reactions occur in the form of metabolic cycles.

The execution time of the complete cycle of biochemical reactions is determined by the smallest the average value of the reaction rate in each phase of the cycle. Moreover, the parameters of the processes of biochemical reactions in cells are not constant. On the contrary, they are constantly changing both for some internal reasons and due to external environmental influences.

With any impact on the cell: changes in environmental parameters, the composition of food and others, in response, numerous changes in biochemical reactions and physical condition occur in it, aimed at maintaining its viability – ensuring the stability of its nonequilibrium thermodynamic states. In particular, this is expressed in changes in the rates of alternation of cycles of metabolic processes, the volumes of substances entering into reactions, the rate of receipt of food and other ingredients, the period of cell division, energy potential,

average life time, content and speeds of other vital processes, as well as mass and geometric parameters.

Such reactions in some cases can ensure the viability of living organisms with changes in environmental parameters within very large limits: at an altitude of more than 80 kilometers and at a depth of eleven kilometers in the ocean at a pressure of a thousand atmospheres, in mines at a depth of 4 kilometers, in lifeless deserts and in the saltiest of lakes - the Dead Sea, in the contours of nuclear reactors, at very low concentrations of nutrients and other conditions.

It should be noted that the plasma membrane, organelles and other elements of cells according to their physical characteristics, they are quite plastic. Therefore, in the process of vital activity, when exposed to loads, their sizes and shapes continuously change within certain limits.

The properties of phenotypic adaptation of multicellular living organisms are determined by the combined properties of cells, organs and systems of which they consist, to respond to certain loads.

For example, as a result of training the human body, the latter can significantly increase muscle mass, physical strength and endurance, when changing the place of residence is getting used to a different climate, changing time zones and other loads.

Based on the above, it is possible to formulate the essence of the properties of living organisms to phenotypic adaptation in the following wording:

The properties of phenotypic adaptation of living organisms are based on the frequency of alternating phases of energy release and consumption and consists in physical and biochemical changes in cells, organs and the body as a whole, aimed at maintaining a stable non-equilibrium thermodynamic state with changes in environmental parameters.

3.3. The work of the mechanism of phenotypic adaptation

To analyze the work of the mechanism of phenotypic adaptation, consider as an example the behavior of a cell when exposed to a certain load. At the same time for to maintain the stability of its nonequilibrium thermodynamic state, the cell will need to increase the volume and rate of ATP synthesis and cleavage.

(Simultaneously with these changes in reactions in cells, many others, included in the corresponding metabolic pathways, also change).

When such a load is applied to the cell, enzymes will be activated in it, increasing the rate of biochemical reactions in the first phase – the intake phase nutrients and synthesis of ATP from them. This phase under the action of enzymes will occur in an accelerated mode until an increased amount of synthesized ATP is reached. When a critical amount of ATP is reached in the cell, the phase of ATP synthesis will switch to the phase of ATP cleavage due to the action of feedbacks.

During the ATP cleavage phase, completely different biochemical reactions occur, mainly hydrolysis reactions, as a result of which ATP is converted into ADP with the release of energy.

These reactions will also proceed in an accelerated mode until the minimum amount of ATP is reached.

These reactions, taking place with the participation and under the control of enzymes, will also be accompanied by enhanced synthesis of the latter. Changes in the course of biochemical reactions lead to biological and physical changes in the cell: the rate and volume of reactions, mass, shape, geometric dimensions.

Figures 3.1 and 3.2 show graphs of changes in neutrophil mass and spectral cell mass densities (data from the All-Russian Research Institute of Optical and Physical Measurements).

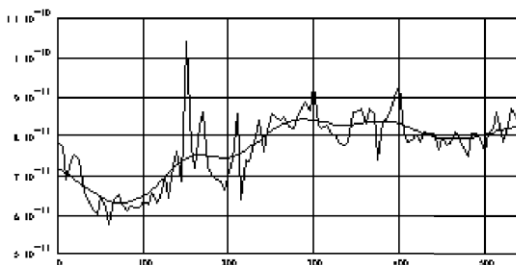


Figure 3.1. Graph of neutrophil mass change. Abscissa axis: minutes; ordinate axis: grams

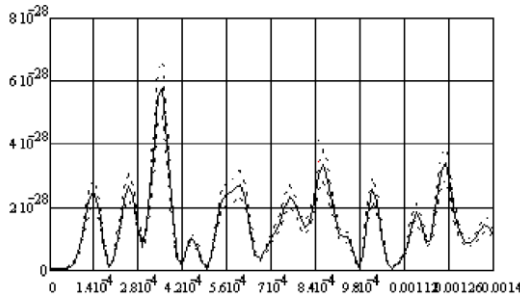


Figure 3.2. Graph of the spectral density of the cell mass. Abscissa axis: Hz; ordinate axis: g^2/Hz

In the event that the load is small and acts on the cell for a short time, then after its removal, all the parameters of the cell (both parameters of biochemical reactions and physical) will quickly return to their original state.

As mentioned above, this type of phenotypic adaptation is operative. Figure 3.3 shows an example of operational phenotypic adaptation.

As can be seen from figure 3.3, during the time t_F of the action of the load E_m , a functional shift of the oscillation process of the physiological parameter u occurs.

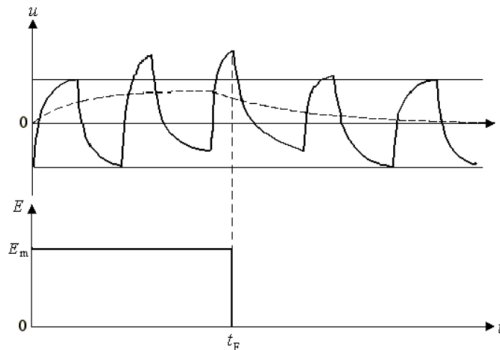


Figure 3.3. An example of operational phenotypic adaptation

After the termination of the load, the functional shift is restored to its original state. But if the load acts for a long time, then, due to the cyclic nature of

metabolic processes, stable changes in its physical and biochemical parameters will gradually occur in the cell: geometric dimensions and mass will change, the limits of regulation of biochemical reactions, the rate of division and more.

When the load is removed after that for a long time, due to the same cyclic nature of metabolic processes, a steady return to the initial parameters will occur in the cell for a sufficiently long time.

It is not difficult to see this by the example of athletes' training.

As a result of long-term training, there is almost always a significant increase in muscle mass.

However, if the training stops, the muscle mass eventually returns to its previous parameters.

With biochemical and physical changes in cells that do not exceed the maximum permissible, phenotypic adaptation processes in them can be considered conditionally reversible.

This is due to the fact that, as stated in Chapter 1, all matter is open systems and all processes taking place in the material world are irreversible.

Indeed, the return of the organism to the initial parameters can and does occur in principle, but already in its other state.

During the phenotypic adaptation and its return to the initial parameter, the body will change to a certain extent, in particular, it will become older.

Certain changes took place in his organs and systems, biochemical reactions began to occur differently due to the intake of other food, the weather and a lot of others environmental parameters that change continuously.

Considering the processes of restructuring multicellular organisms, it should be noted that they, to one degree or another, but always affect all organs and systems.

It should also be noted that organs and systems have very different properties of reactions to loads.

Some organs and systems react to the effects of loads very quickly, for example, the cardiovascular system, and some very slowly, for example, the already mentioned process of changing muscle mass.

Therefore, the volume of restructuring processes in the body under the influence of loads largely depends on both the duration of exposure to these loads and their nature.

3.4. Basic patterns of reactions to loads

3.4.1. Reactions to a single load

As mentioned above, the effects on cells of various loads lead to corresponding changes in the course of biochemical reactions occurring in them, as well as to biological and physical changes: the speed and magnitude of reactions, mass, volume, shape, geometric dimensions.

To determine the regularity of the dependence of such reactions on the load, consider the effect on the body of a single load in the form of a rectangular pulse.

Figure 3.4 shows a simplified graph of the regularity of changes in a certain functional shift u when the body is exposed to a rectangular pulse load E_1 acting during a time interval $T = t_2 - t_1$.

It should be noted here that in fact, a living organism always reacts not only to the magnitude of the load, but also to the rate of its increase.

In addition, in nature, in principle, there are no pulses of absolutely rectangular shape - there are always leading and trailing fronts that change according to certain laws, with certain finite parameters.

In this case, to simplify the task, these issues are not considered.

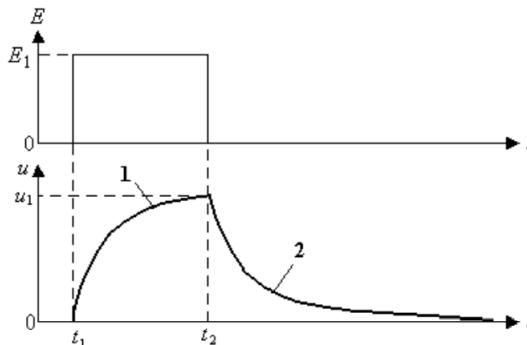


Figure 3.4. Simplified graph of the regularity of changes in the functional shift

As can be seen from figure 3.4, when the body is exposed to a load E_1 of duration $T = t_2 - t_1$, a certain functional shift u occurs and begins to increase in the

body, which reaches its maximum value u_1 at the moment of termination of the load t_2 (curve 1). After removing the load E_1 , the functional shift u is restored to its original value according to a law close to the exponent (curve 2). The observed pattern of changes in the functional shift shown in Figure 3.4 is the result of a large complex of biochemical enzymatic reactions, caused by the impact of load E_1 .

An attempt to mathematically describe such reactions was made back in 1913 by German scientists L. Michaelis and M. Menten.

As a result of their research, they derived a law describing the kinetics of substrate changes in an enzymatic reaction:

$$\frac{ds}{dt} = \frac{\mu_0 s}{K_m + s}, \quad (3.1)$$

where s is the concentration of the substrate, μ_0 - maximum speed, K_m - the Michaelis constant - is numerically equal to the concentration of the substrate at which the reaction rate is half of the maximum possible.

The graph of the dependence of the reaction rate as a function of the initial concentration of the substrate s is shown in Figure 3.5.

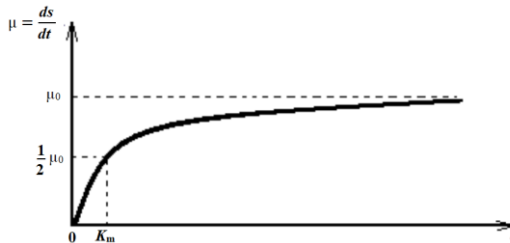


Figure 3.5. Michaelis - Menten Law

However, the Michaelis-Menten law describes only one catalytic reaction, and then with several not entirely realistic assumptions, in particular, such as the absence of other forms of the enzyme in solution.

In our case, it is necessary to analyze the regularity of changes in the functional shift as the final cumulative result of the entire complex of biochemical reactions involved in its formation.

In this regard, to describe the cumulative process of the body's reactions to some single load (Fig.3.4), expressed in the growth of the corresponding functional the shift and the reaction of the recovery of this shift after the load is removed, mathematical formulas can be used based on the results of practical studies of these processes and the construction of appropriate graphs.

In particular, the regularity of the increase in the functional shift u (Fig.3.4, curve 1) can be described by the formula (3.2.)

$$u = u_1(1 - e^{-kt}), \quad (3.2)$$

and the process of restoring the functional shift of u_1 towards the initial state (Figure 3.4, curve 2) can be described by the formula (3.3):

$$u = u_1 e^{-kt}. \quad (3.3)$$

As can be seen from formula (3.3), $u \rightarrow 0$ for $t \rightarrow \infty$.

Hence, it follows that it is impossible to determine the exact recovery time of the functional shift t , at which $u = 0$.

With certain changes in the magnitude of the load E_1 and the duration of its exposure T , the pattern of growth and restoration of the functional shift u will change accordingly, since at the same time different amounts of ingredients with corresponding concentration dynamics will take part in biochemical reactions.

Let's consider the dependence of changes in functional shifts u on changes in the magnitude of the load E .

Figure 3.6 shows the patterns of changes in functional shifts u at different absolute values of the load E .

As can be seen from figure 3.6, with an increase in the absolute magnitude of the load E , acting for equal periods of time T , the magnitude of the functional shifts u increases.

At the same time, their recovery time also increases: $T_3 > T_2 > T_1$.

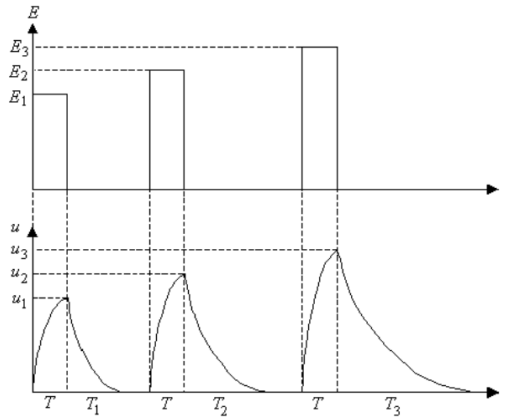


Figure 3.6. Dependence of changes in functional shifts u on changes in the magnitude of the load E .

Next, consider the dependence of changes in the magnitude of functional shifts u on the duration of the load E .

In figure 3.7 the regularities of changes in functional shifts u at different load times E : $t_1 < t_2 < t_3$ are shown.

As can be seen from Fig. 3.7, with an increase in the duration of exposure t to the same load E_m , the magnitude of functional shifts u increases. At the same time, their recovery time increases $T_3 > T_2 > T_1$.

Thus, the recovery time T of functional shifts u depends both on the magnitude of the load E and on the duration of its impact t .

The magnitude and duration of the effects of loads on the body can be different, but they are always limited in maximum values. Depending on the magnitude of the load, the processes of biochemical reactions change accordingly, and as a consequence - physiological processes.

With minor loads, both in magnitude and duration of action, to which the body is sufficiently adapted (let's call them normal), the functional shifts caused by them are quickly restored to their original values after the loads are removed.

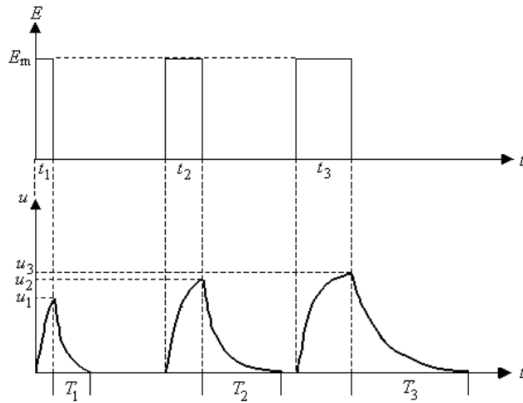


Figure 3.7. Dependence of changes in the magnitude of functional shifts u on the duration of the load E_m .

At the highest or longest possible load due to enzymes, changes in the rate of biochemical reactions and the volume of reagents involved in them reach the limit values. After removing such loads, the body needs quite a long time to restore the functional shifts caused by them.

When loads exceeding the maximum permissible loads are applied to the body, it is enough there is a high probability of damage, disease or death of the body. As a result of such loads, as a rule, there is no complete restoration of the functional shift.

Figure 3.8 shows an example of a graph of the response of a functional shift to an unbearable load (noise from an explosion) that caused an acoustic injury, and the process of restoring hearing after an acoustic injury.

As can be seen from Fig. 3.8, the graph of the growth of the functional shift u under the influence of an unbearable load (curve 1) represents a steep characteristic, passing in the upper part into a horizontal line, indicating the transition of the reaction to the mode of the limit value of the functional shift – the consequence of which was acoustic trauma. The process of restoration of functional shift (curve 2) – restoration of hearing after acoustic trauma – occurs only partially.

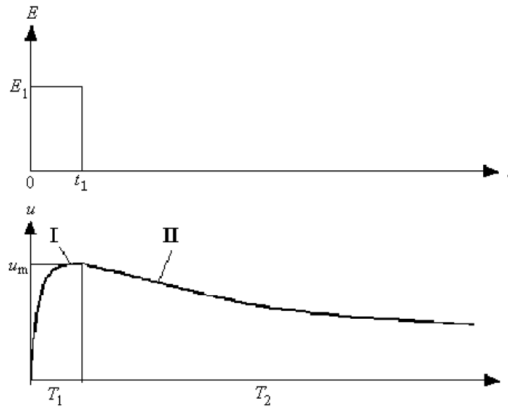


Figure 3.8. Graph of the functional shift response to an unbearable load.

Thus, the loads affecting the body can be divided into three categories: normal, elevated and intolerable with the following definitions:

- normal loads – loads that do not cause any consequences from their action;
- increased loads – loads that can affect the body without consequences for only a limited time;
- unbearable loads – loads that can lead the body to diseases, injuries, or death.

3.4.2. The body's reactions to periodic stress

Loads affecting living organisms are quite often not only single, random, but also periodic in nature.

As already mentioned above, the most frequent periodic nature of loads is associated with the rotation of the Earth around its axis and around the Sun.

In addition, in humans, it may be associated with production processes, work and rest regimes, and other reasons.

The body's response to a periodic load depends on what this load is, its magnitude, frequency parameters, and more.

Let's consider as an example the impact on the human body of normal periodic physical activity of a rectangular shape.

Figure 3.9 shows: a graph of periodic alternation of loads E (a) and a graph of the corresponding functional shifts u (b).

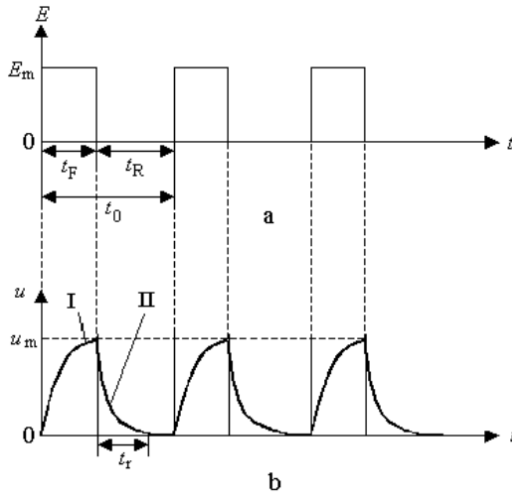


Figure 3.9. The graph of fluctuations of the functional shift u from the influence of normal periodic load E

As can be seen from Graph a in figure 3.9, the human body is periodically affected by a load of E_m with a period t_0 , duration t_F and pause t_R .

As can be seen from graph b in figure 3.9, during the time of exposure to t_F load E_m , a reaction occurs in the human body, expressed in the form of an increase in the functional shift u , which reaches the u_m value by the end of the exposure time. During the pauses between loads of duration t_R , the functional shift E is restored, which actually reaches its original value of 0 during t_r . (it was stated above that it is impossible to determine the exact recovery time of the functional shift). As can be seen from graphs a and b, $t_r < t_R$, and the patterns of growth of functional shifts u under subsequent loads E_m are identical.

This means that by the beginning of the next load, the body has fully recovered from the previous one. Consider the case of the impact on the body of periodic increased load E_m , at which $t_r > t_R$.

Figure 3.10 shows a graph of the impact on the body of periodic increased load.

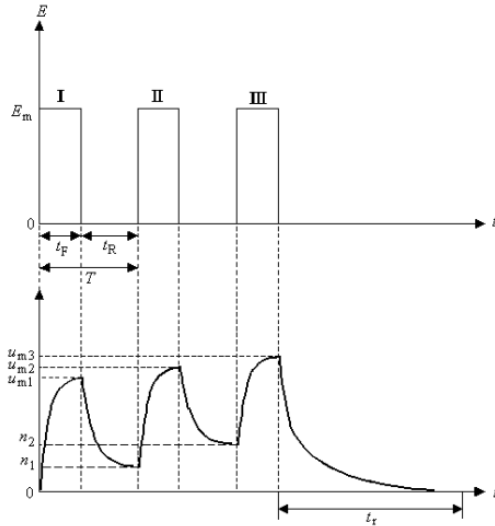


Figure 3.10. The graph of fluctuations of the functional shift u under the influence of increased periodic load E

As can be seen from the graph in figure 3.10, the effect on the body of an increased load I by the value of E_m and duration t_F causes an increased functional shift u_{m1} , which does not have time to fully recover during the pause t_R and by the time the load II arrives, the residual value of the functional shift is n_1 .

As a result of the action of load II, the functional shift u increases and reaches the value $u_{m2} > u_{m1}$, which also does not have time to fully recover before the arrival of load III and its residual value is already $n_2 > n_1$.

The impact of load III causes an increase in the functional shift u to the value u_{m3} . And only during a long pause t_r , the functional shift u is fully restored.

Such a pattern of growth of functional shifts with incomplete recovery is observed quite often.

As examples, cases of growth of functional shifts during the working week and their full recovery over the weekend, with shift work schedules in extreme conditions (week after week), etc. can be given.

3.5. The main patterns of phenotypic adaptation

3.5.1. Operational phenotypic adaptation

As mentioned in section 3.1, operational phenotypic adaptation is an organism's response to all short-term factors affecting its vital activity, without changing the average values of its functional systems.

The properties of operational phenotypic adaptation of multicellular living organisms are determined by the result of the combined properties of cells, organs and systems of which they consist, to respond to certain loads by changing the processes occurring in them. They use various types of biochemical processes to preserve the stability of the nonequilibrium thermodynamic state.

The regularities of reactions of living organisms to loads during operational phenotypic adaptation have actually already been considered in sections 3.4.1 "The body's response to a single load" and 3.4.2 "The body's response to a periodic load".

3.5.2. Stable phenotypic adaptation

3.5.2.1. Stable phenotypic adaptation under the influence of a constant single load

When considering the processes of operational phenotypic adaptation, it was established that when the body is exposed to any loads changes corresponding to these loads occur in it during cycles of biochemical reactions.

If such a load in its magnitude corresponds to normal or increased, occurs relatively rarely and for a short time, then each time after its termination, the cell's operating mode is restored to its original level, since this requires little time.

If such a load acts for a long time, and breaks between loads relatively short, as a result of numerous cycles of metabolism, certain physical changes gradually increase in the cell.

As a result, after some time, an increased or decreased amount of nutrients begins to constantly enter the cell, and an increased or decreased amount of reagents participate in biochemical reactions.

Thus, the mode of functioning of the cell under conditions of constant action of the load becomes normal for it, and it will be maintained all the time of its action.

The graph of such a process is shown in figure 3.11.

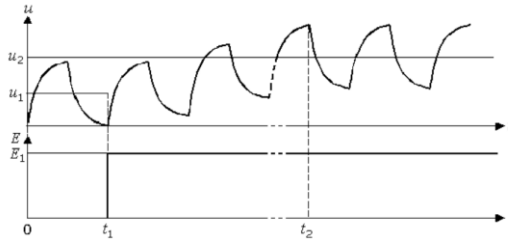


Figure 3.11. The process of stable phenotypic adaptation

As can be seen from figure 3.11, before the start of the E_1 load, in the time period $0 - t_1$, the average value of the functional shift oscillations was u_1 . As a result of phenotypic adaptation over a long period of time $t_2 - t_1$ of the action of the load E_1 there are changes in the course of biochemical reactions, as a result of which the average value of the fluctuations of the functional shifts u_1 increases to the value u_2 , which becomes constant under the conditions of constant exposure to the load E_1 .

With prolonged removal of the load, phenotypic adaptation will occur in the opposite direction to the initial level, since its value is below the maximum permissible.

It should be noted that in real conditions, the load is not applied instantly, but increases over a certain time.

In addition, living organisms react not only to the magnitude of the load, but also to the rate of its increase (therefore, athletes, in order to reduce the magnitude of the impact of the load, pre-"warm up" before performing the appropriate exercises).

Figure 3.12 shows an example of a graph of real changes in the fluctuations of functional shifts u under the action of a constant load E_1 .

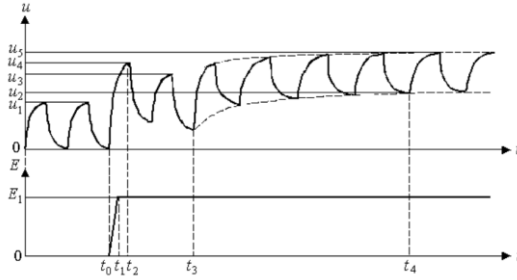


Figure 3.12. Example of a graph of changes in the fluctuations of functional shifts u under the rapid action of a constant load E_1

As can be seen from the graph in Figure 3.12, before the start of the load E_1 , the fluctuations of the functional shift are in the range $(0 - u_1)$.

The load E_1 on the body begins to act from the moment t_0 , increasing over a period of time $t_0 - t_1$ from the value 0 to the value E_1 .

During the time interval $t_0 - t_2$ of the action of the load E_1 , the upper limit of the fluctuations of the functional shift u increases sharply from the value u_1 to u_4 .

This is explained by the body's reaction to two simultaneously affecting load parameters: the value of E_1 and the rate of its increase: $v = dE_1/dt$.

During the time interval $t_2 - t_3$, the functional shift u is slightly restored, reaching the upper limit of the u_3 level, since restoration of the functional shift caused by the action of the load growth rate parameter.

Then there are changes in the oscillations of the functional shift u , determined only by the action of the load value E_1 : the range of oscillations of the functional shift decreases with a simultaneous increase in the average level of its value.

This is due to the exponential dependence of the magnitude of the functional shift u on the load E_1 . Moreover, changes in the minimum and maximum values of functional shifts will occur according to identical laws, as indicated above, respectively:

$$u = u_{\min}(1 - e^{-kt}), \quad (3.4)$$

$$u = u_{\max}(1 - e^{-kt}). \quad (3.5)$$

From the moment of time t_4 , the process of restructuring the body can be considered established.

At the same time, the fluctuations of the functional shift will be constantly, during the entire duration of the load E_1 , within the limits of $u_2 - u_5$.

After the load is removed for a certain time, the functional shift u may return to values close to, but not equal to, the initial values, since irreversible processes continuously occur in the process of vital activity of living organisms

3.5.2.2. Stable phenotypic adaptation under the influence of prolonged periodic load

Let's consider the processes of stable phenotypic adaptation of living organisms under the actions of periodic loads on the example of the human body.

The main parameters of periodic loads include: absolute value, duration of action and duration of pause.

In the above analysis of the body's reactions to periodic stress, the main patterns of the impact on living organisms of this type of load were considered.

Let's determine the regularity of the adaptation process under periodic loads.

If the absolute value of the load belongs to the category of normal and the ratio of the duration of exposure to the load and pauses is such that the functional shift caused by the load is fully restored, then there is no phenotypic adaptation, since the body is already adapted to such loads.

If the absolute value of the load belongs to the category of increased, and at the same time the recovery time of functional shifts caused by the load will actually be longer than the time of pauses between loads, then the process of long-term phenotypic adaptation will begin.

At the same time, biochemical reactions will occur in the body, both the synthesis from food and the splitting of ATP in such volumes that it will be ensured stability of its nonequilibrium thermodynamic state. The process of stable phenotypic adaptation, in which the body load is periodic in nature, while causing the corresponding periodic sequences of reactions of synthesis from food and cleavage ATP, provides the possibility of significantly larger ranges of rearrangements of functional parameters than under constant load.

This is due to the fact that the periodic nature of loads allows the body to provide more quickly the processes of changes in the rates of biochemical

reactions and the volumes of reagents involved in them. The regularity of these processes has an individual character, since it is directly related to its own biological rhythms and the physiological state of living organisms.

This property of the body is quite convincingly confirmed by the processes of athletes' training, when, with the right choice of combinations of loads and rest significant indicators in sports achievements are achieved.

Figure 3.13 shows an approximate graph of the process of stable phenotypic adaptation when exposed to periodic stress on the body.

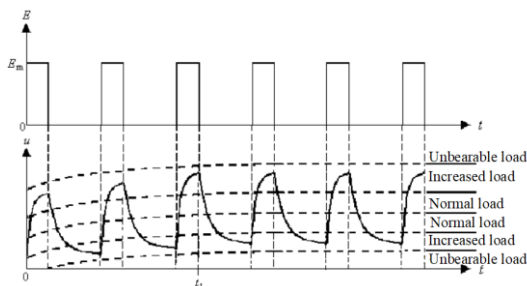


Figure 3.13. Approximate graph of stable phenotypic adaptation to periodic loads with constant parameters

As can be seen from the graph in figure 3.13, in the initial time period $0 - t_1$ of the impact of the E_m load, the functional shifts u are rearranged, in which the recovery during the pauses between loads does not occur completely.

However, from the moment of time t_1 , the process of growth and restoration of functional shifts stabilizes.

This means that the phenotypic adaptation has ended and the synthesis processes from food and ATP breakdown begin to occur at a different level.

At the same time, there is also a shift in the values of loads characterizing normal, increased and unbearable loads.

Thus, the property of phenotypic adaptation of living organisms to changing environmental conditions is due to the principle of functioning of biochemical reactions in the form of alternating sequences of cycles of synthesis and cleavage of substances.

This principle allows you to quickly and in a large range "swing" within the necessary limits the volumes of the entire complex of substances involved in an

interconnected set of biochemical reactions under certain environmental conditions, and slow them down under other conditions.

This ensures high stability of the nonequilibrium thermodynamic state of living organisms under a variety of conditions of their existence.

3.6. Phenotypic adaptation and environment

3.6.1. The main patterns of changes in environmental parameters

In the existing material world, both living and inanimate, almost all the parameters characterizing it are never constant and are subject to both periodic and random changes.

All changes in environmental parameters are due to the fact that, depending on the simultaneous impact of a variety of factors on it: weather, solar radiation, the position of the planets, the time of year and others, the degree of disequilibrium of the state of matter changes.

When the state of disequilibrium exceeds a certain critical limit matter moves to another level by self-organization, acquiring other properties.

As examples of the transition of matter to another level of self-organization, one can cite the effect of spontaneous combustion of combustible substances when their temperature exceeds a certain critical level or the transformation of water into ice at temperatures below 0° C.

Inanimate matter is always in an unstable equilibrium, weakly nonequilibrium or strongly nonequilibrium thermodynamic state, depending on its properties, environmental parameters and the level of self-organization.

Unlike inanimate nature, as already mentioned, living organisms must always be in a stable non-equilibrium thermodynamic state to ensure their vital activity.

Therefore, any changes in the parameters of the external environment immediately cause in living organisms, through feedback, corresponding changes in the course of biological processes aimed at maintaining a stable nonequilibrium thermodynamic state.

At the same time, periodic changes in environmental parameters cause corresponding periodic changes in the course of biological processes in living

organisms, and random changes in environmental parameters cause corresponding random changes in the course of these processes.

The values of environmental parameters, their composition and the pattern of changes in the habitat of living organisms are mainly determined by its geographical area and in most cases obey the relevant laws of statistics.

In general, each of the parameters of the external environment: air temperature, humidity and others, as well as their aggregates, have corresponding statistical characteristics of probability, the regularities of which usually correspond to the density law of the normal probability distribution (Fig. 3.14), expressed by the formula (3.6.):

$$\varphi(U) = \frac{1}{\sqrt{2\pi}} e^{-\frac{U^2}{2}}, \quad (3.6)$$

where $\varphi(U)$ is the probability value, U is the density of the normal probability distribution.

Populations of living organisms that live permanently in a certain environment and have undergone the process of genotypic adaptation – natural selection, in their overwhelming majority are usually well adapted to the parameters of the environment.

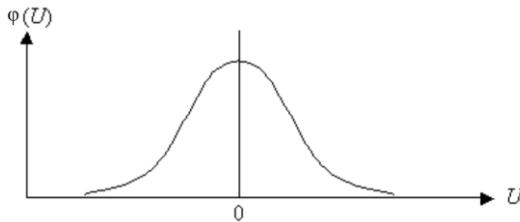


Figure 3.14. Graph of the density of the normal probability distribution

Moreover, the degree of fitness of individuals included in the population also usually corresponds to the density law of the normal probability distribution.

However, in nature there is always a certain probability that the parameters of the external environment may change so much that for most individuals of a

particular population they will become uncomfortable, in which their existence will become much more complicated, as well as unbearable – incompatible with the possibility of survival.

To characterize the external environment according to the conditions of life, we divide it into three zones: comfort, discomfort and intolerance with the following definitions:

A comfort zone is a range of cumulative environmental conditions in which the vital activity of a given type of living organisms occurs most comfortably, and the loads affecting them belong to the category of normal.

The zone of discomfort is a range of cumulative environmental conditions in which living organisms of this species are in difficult conditions of survival, and the loads affecting them belong to the category of elevated.

The zone of intolerance is a range of cumulative environmental conditions under which the vital activity of a given type of living organisms is impossible, and the loads affecting them belong to the category of intolerable.

3.6.2. External environment and vital activity of living organisms

For each species, for each population of living organisms, there is always a preferred set of conditions that are most optimally suitable for their vital activity.

For example, for some species, a wetter and warmer climate is preferable, for others, a drier and colder climate, etc.

Moreover, in each species and in each population there is a certain spread, a certain variance of requirements for environmental parameters associated with individual characteristics of individuals.

Figure 3.15 shows an example of a graph of the probability density distribution of generalized indicators of the real (curve 1) and optimal external environment for a certain type of living organisms (curve 2).

As can be seen from figure 3.15, the real characteristics of the external environment in its parameters largely, but not completely, coincide with the optimal one for the species under study.

This means that the studied species is not fully adapted to the parameters of the external environment.

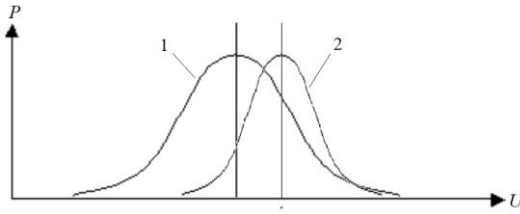


Figure 3.15. Example of probability density distribution of generalized indicators of real (curve 1) and optimal (curve 2) environmental parameters

Since the graphs are close enough, we can expect that over time, by how both genotypic and phenotypic adaptations, the species will adapt even more to this external environment.

In cases where such schedules largely do not coincide, for example, in environmental disasters, this leads to the death of the species.

However, in addition to the state of the environment, it is extremely important for living organisms how their vital activity is carried out.

To do this, we will clarify the content of the concepts widely used in modern science: "conditions of vital activity", "optimal conditions of vital activity" and "optimal vital activity":

Conditions of vital activity - a set of physical, chemical, biological and psychological factors of the external environment that affect the processes of vital activity of living organisms.

Optimal living conditions - a combination of physical, chemical, biological and other environmental factors, under which it can be provided maximum stability of the nonequilibrium thermodynamic state of living organisms.

Optimal vital activity is a set of biological, physical and other functions performed by a living organism, in which, under given environmental conditions, maximum stability of its non-equilibrium state is ensured thermodynamic state.

Figure 3.16 shows an idealized example of a graph of daily fluctuations of functional shifts of the human body in the case of its optimal vital activity.

As can be seen from the graph in figure 3.16, in order to ensure maximum stability of the nonequilibrium thermodynamic state of the human body, the range of fluctuations of functional shifts should also be maximum and be located

not only within the comfort zone, but also in the lower (for example, with inactivity) and upper (for example, with hyperdynamics) zones of discomfort.

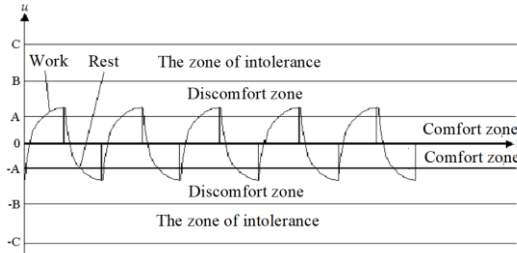


Fig. 3.16. Idealized graph of daily fluctuations of functional shifts of a person with optimal vital activity

At the same time, the values of comfort zones, discomfort and intolerance as a result of phenotypic adaptation processes will expand within certain limits, thereby ensuring maximum stability of the nonequilibrium thermodynamic state of the organism.

If all the daily fluctuations shown on the graph are identical or close to each other to a friend, this means that the body is fully recovering from the overloads experienced during the day.

The mode in which the fluctuations of functional shifts have the maximum scope, entering the zone of discomfort, and at the same time fully recover during the day, is the closest to optimal. At the same time, the body is ready for the maximum overload values for it.

When overloads occur, periodic fluctuations in the functional shifts of the body will have the form shown in figure 3.17.

As can be seen from figure 3.17, with changes in environmental parameters that cause an increased load on the E_m body, the process of fluctuations in functional shifts u changes accordingly, moving up to the intolerance zone.

When restoring the initial value of the environment, the oscillation parameters of functional shifts are also fully restored.

It should be noted that the zones of comfort, discomfort and intolerance, as well as normal, increased and unbearable loads are individual parameters for each organism.

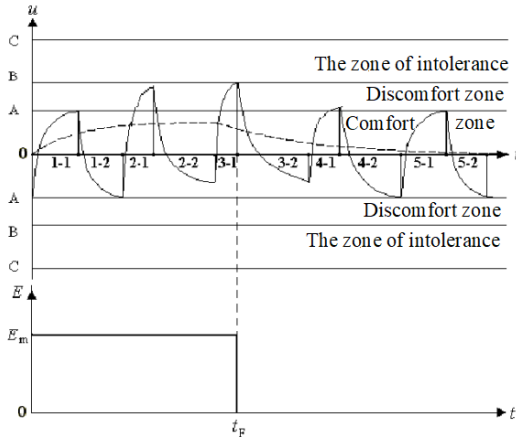


Fig.3.17. Graph of changes in periodic fluctuations of functional shifts u under the influence of load E_m

Chapter 4

Quantitative assessments of the impact of environmental parameters on living organisms

4.1. Types of quantitative assessments

Quantification of the impact of environmental parameters on living organisms is one of the most serious scientific problems.

The main difficulty lies in the fact that living organisms and the external environment are characterized by many different parameters having different natures and different units of measurement.

To date, five main methods of assessing the impact of environmental parameters on living organisms are known:

- score;
- risk assessment;
- estimation by fluctuating asymmetry;
- assessment by questionnaires;

- estimation of the recovery time of functional shifts (method Dobroborsky-Kadyskin).

The most common of them are point scores in determining the severity and intensity of work, as well as assessment using questionnaires, used in various psychological studies. Let's consider these rating systems in more detail.

4.2. Point score

The score is a list of all possible types of loads, affecting the body, each of which has a certain weight, expressed in points.

Depending on the number of points scored, a particular type of work activity or a characteristic of the external environment is evaluated in the appropriate categories.

Table 3.1 shows an example of the classification of working conditions using the points system.

The main disadvantages of the scoring method are that it is metrologically unreasonable, does not reflect all possible combinations of environmental parameters, which are often potentiating, and therefore provides very an approximate assessment of the real situation.

Table 3.1. Classes of working conditions in terms of air temperature ($^{\circ}\text{C}$, lower boundary) for open areas during the cold season and in cold (unheated) rooms

Climate zone	Classes of working conditions						
	thermal insulation of clothing	acceptable	Harmful - 3				Dangerous (extreme)
			1 degree	2 degree	3 degree	4 degree	
			3.1	3.2	3.3	3.4	
	$^{\circ}\text{C W/m}$	2	3.1	3.2	3.3	3.4	4
1A	0.71	-30	-36	-38.5	-40.8	-60	<-60.0
1B	0.82	-38	-46.2	-48.9	-54.4	-70	<-70.0
II	0.61	-23	-29.4	-31.5	-35.7	-48	<-48.0
III	0.51	-15.9	-21.3	-23	-26	-37	<-37.0

4.3. Risk assessment

Risk assessment consists of three types of procedures:

a) hazard identification, exposure assessment, dose-response assessment and risk characterization;

b) a scientific assessment of the sources (toxic properties of a chemical substance or properties of physical factors) and the conditions of their impact on a person, aimed at establishing the probability that exposed people will be affected, as well as to characterize the nature of the effects that they may have;

c) assessment of the type and severity of the danger created by the source in as a result of existing or possible exposure to a certain group of people, as well as the existing or potential health risk associated with this source.

The method of risk assessment in most cases provides the ability to predict the impact of the external environment based on statistical data.

However, this method does not identify the main sources that determine the degree of risk in cases of combined action of many sources, and also does not give a specific quantitative biological (physiological) assessment of the magnitude of human damage.

4.4. Evaluation by bioindication

Bioindication is a method of approximate assessment of anthropogenic load by the reaction of various living organisms and their communities to it, for example, the oppression or development of phytoplankton in the aquatic environment.

Of all the variety of known methods of bioindication research, it is considered that the method of analysis of fluctuating asymmetry most fully meets the necessary criteria.

Fluctuating asymmetry is a consequence of the imperfection of ontogenetic processes, the inability of organisms to develop along precisely defined paths.

According to phenomenology, it represents small non-directional deviations of living organisms from strict bilateral symmetry.

At the same time, the differences between the parties are not strictly genetically determined and, therefore, depend mainly on external conditions.

The fluctuating asymmetry is estimated in points.

Table 3.2 provides an example of such an assessment to determine the stability of the development of living organisms by the level of asymmetry of morphological structures.

Table 3.2. The degree of deviation of the environment from the norm for the violation of the stability of development the most massive (background) species

Stability of development in points	Environment quality
1st point	Conditionally normal
2nd point	Initial (minor) deviations from the norm
3rd point	The average level of deviations from the norm
4th point	Significant (significant) deviations from the norm
5th point	Critical condition

The methodology is based on the identification, accounting and comparative analysis of asymmetry in different species of living organisms according to certain characteristics.



Figure 3.18. Scheme of morphological features used to assess the stability of the development of the hanging birch (*Betula pendula*)

- 1 - the width of the left and right halves of the sheet.
- 2 - the length of the vein of the second order, the second from the base of the leaf.
- 3 - the distance between the bases of the first and second veins of the second order.

4 - the distance between the ends of the same veins. 5 is the angle between the main vein and the second vein of the second order from the base of the leaf.

Determination of the magnitude of the fluctuating asymmetry of bilateral morphological structures when using a meristic (counting) feature in each individual is made by calculating the number of certain structures on the left and right within the specified boundaries.

The population estimate is expressed by the arithmetic mean of the difference in the number of structures on the left and on the right. When using a plastic (dimensional) feature, certain structures on the left and right are measured in each

individual. The amount of asymmetry is calculated by dividing the difference in measurements on the two sides by their sum. Let us give as an example a methodology for assessing the stability of the development of the hanging birch (*Betula pendula*). Figure 3.18 shows a diagram of the morphological features used for this assessment.

The measurement technique is as follows.

To measure, the sheet is folded in half, combining the top with the base of the leaf blade. Then the leaf is unbent and the distance from the border of the central vein to the edge of the leaf is measured by the resulting fold. To assess the degree of detected deviations from the norm, their place in the general range of possible changes in the indicator, a five-point scale is used. The main disadvantage of the method is the inability to determine the causes of fluctuating asymmetry and its very conditional quantitative assessment.

4.5. Assessment by questionnaire

Questionnaire assessment is one of the types of survey methods used to obtain empirical information concerning objective facts, knowledge, opinions, assessments and behavior.

This method is widely used in sociology, psychology, pedagogy, and other fields of science and practice (for example, in preventive medicine for large-scale identification of persons at risk of coronary heart disease).

An essential feature of the method is the mediated nature of the interaction between the researcher and the subject (respondents) who communicate with the help of a questionnaire, and the respondent himself reads the questions offered to him and records his answers himself.

4.6. Estimation of the recovery time of functional shifts (Dobroborsky-Kadyskin method)

Assessment by the recovery time of functional shifts is a method that provides a quantitative integral objective assessment of the impact on living organisms of any loads of any composition and in any combination.

The method is based on the regularity of the dependence of the recovery time of a functional shift on the magnitude of the load that caused this shift. This pattern was discussed in section 3.4.

Using the time parameter to assess the effects on living organisms the external environment solves several major problems at once:

- 1) the commensurability of environmental factors and parameters of living organisms that are different in nature and units of measurement;
- 2) objectivity of measurement results, metrological justification of measurement results;
- 3) identification of the main factors determining the nature of the impact of the external environment;
- 4) determination of the most effective ways to reduce the harmful effects of environmental parameters.

As already mentioned in section 3.4, the regularity of restoring the functional shift occurs according to an exponential law, which does not allow to accurately determine the time of its recovery.

Therefore, in this method, direct measurements of recovery time are replaced by relative measurements.

With these measurements, the relative value of the recovery time is made by analyzing the regularity of changes in the speed of the recovery process of functional shifts.

Figure 4.19 shows graphs showing four processes of functional shift recovery.



Figure 4.19. Graphs of restoration of functional shifts

As can be seen from figure 4.19, the processes of restoring functional shifts obey the same exponential law, but occur at different speeds.

Here it should be noted that various functional shifts, for example, heart rate, tremor, blood pressure or vibration sensitivity, having a different physical essence and dimension, and characterized by absolutely different physiological indicators, when analyzing their recovery processes, become commensurate, since they are compared by the same parameter – recovery time.

Therefore, for the quantitative characterization of these processes, a new physiological (hygienic) indicator was proposed - ergo capacity, with the following definition:

Ergocapacity is a physiological (hygienic) indicator characterizing the time spent by living organisms to restore functional shifts, caused by the impact of various loads on them, after their termination.

In addition to the actual measurement of the conditional recovery time of functional shifts, the time of exposure to loads that caused functional changes is of great importance shifts. In this regard, another indicator has been introduced – specific ergocapacity with the following definition:

Specific ergocapacity is a physiological (hygienic) indicator that characterizes the ratio of the recovery time of functional shifts to the time of their occurrence during the impact of loads.

A new unit of measurement, D, is proposed to quantify the specific ergocapacity.

This method, as well as the indicators of ergo capacity and specific ergocapacity have not yet been introduced into regulatory documents, but nevertheless they have found their application in hygienic studies of various types of industrial equipment: mining machines, computer workstations, air traffic controllers' workplaces and others, since as a result of the application of this method, in addition to the actual assessment of the impact of environmental parameters, due to the commensurability of these parameters and physiological indicators, it is possible to determine the most effective ways to improve it.

It should be noted that determining the regularity of the rate of recovery of functional shifts from the point of view of mathematics is quite a difficult task, in this connection, a specialized computer program was developed for this purpose "Loqus 2003.1En".

This program calculates the conditional recovery time - the ergo capacity of any functional shifts and their ratios and determines the specific ergocapacity.

Chapter 5

Symmetry and asymmetry of living organisms

5.1. The state of the problem

A large number of scientific papers have been devoted to the problem of symmetry and asymmetry of living organisms, including the human body.

To date, the most complete analysis of the state of this problem, apparently, should be considered the book by N.N. Bragina and T. A. Dobrokhotov "Functional asymmetries of man", which provides an overview of the results of numerous studies in this area.

These works included numerous detailed studies the functioning of motor asymmetry: hands, feet, body and face, sensory asymmetry: vision, hearing, smell and taste, as well as mental asymmetry.

Below, as an example, is a brief excerpt from this book regarding the motor asymmetry of the hands.

"The hand is "the most multifunctional organ of motor activity" [Roze N. D., 1970].

There are many designations of the asymmetry of the hands: right-handedness, or right-handedness; left-handedness, or left-handedness; two-right-handedness, or ambidextrous ambilevia, desnoruchie, shueruchie, equiluchie.

The most common designations are: right-handed, left-handed, ambidextrous.

Morphological signs of hand inequality are described. The right hand is longer, larger than the left hand [Ginzburg V. V., 1947]. The size of the right hand in 97% of men is larger than the left (by $\frac{1}{4}$ the size of gloves), this difference is less pronounced in women [Brandt AF, 1927]. Venous the network on the back surface is more developed on the leading hand [Gurevich M. O., 1949], where the size of the nail bed of the thumb is also greater. The muscle mass of the right arm is 6% greater than that of the left [Weber E., 1905]. The skin patterns (finger and palm dermatoglyphs) on the right and left hands are different: they are more variable in left-handed people [Voitenko V. P., Polyukhov A.M., 1986].

Functional asymmetries of the hands are diverse. In the overwhelming majority of the world's population, the right hand is superior to the left in

strength. This symmetry is expressed by the formula: $A = S / D$, where A is the asymmetry of the arms, D is the muscular strength of the right, S is the muscular power of the left hand [Kubyshkin Yu. I., 1963]. This ratio is less than one for right—handers, more than one for left—handers and equal to one for ambidextrous."

Without any doubt about the exceptional value of this book, we note that, unfortunately, it does not contain an analysis of the nature of symmetry and asymmetry of living organisms, which is really impossible in descriptive biology, which contains only statements of facts, assumptions and hypotheses.

However, the objective causes of symmetry and asymmetry of living organisms can be strictly explained from the standpoint of thermodynamics of biological systems.

5.2. Causes of symmetry and asymmetry of living organisms

The reason for the symmetry of living organisms should be considered the simple and obvious fact that it is this condition that provides the most optimal conditions for their vital activity, as a result of which the symmetrical form of organisms is transmitted from generation to generation due to genotypic and phenotypic adaptations. Moreover, not only the condition of geometric symmetry is observed here, but also the location of the center of gravity along its axis.

However, the symmetry of living organisms is not and cannot be ideal. All living organisms are somewhat asymmetric. Moreover, this asymmetry is not accidental.

We will analyze the causes of asymmetry of living organisms.

As is well known, living organisms have both unpaired organs (heart muscle, gastrointestinal tract, etc.) and paired organs (eyes, arms, legs, etc.).

Moreover, paired organs, symmetrical relative to each other, perform similar functions, collectively providing the necessary properties for the body, for example, orientation in space thanks to paired visual and auditory analyzers, ensuring a stable position due to the musculoskeletal system, and others.

To ensure the necessary mutual functioning of paired organs, they must comply with the requirements of mutual coordination.

As studies have shown, this requirement in living organisms is fulfilled by distributing the functions of the master - slave between paired organs, in which the leading organ has some advantages in its properties compared to the slave.

The advantages of the leading organ may be expressed in greater physical strength, greater reaction speed, more precise coordination and others.

Due to these advantages, the leading organ is subjected to heavy loads, since the use of its advantages in comparison with the slave is most convenient for the body.

Moreover, thanks to phenotypic adaptation, this advantage is constantly maintained.

For example, it is most convenient for a person to perform the most difficult and precise work with his right hand if he is right-handed, and auxiliary work is performed with his left.

The distribution of master–slave functions between paired organs is carried out as a result of genotypic adaptation, to a certain extent having a random personality. As practice shows, a person realizes this distribution of functions even in early childhood.

Thus, the asymmetry of living organisms is a fundamental condition for the possibility of their existence.

The degree of asymmetry of living organisms – the difference in the properties of paired organs, as follows from the numerous materials given in the above book, is quite wide. Moreover, it can change significantly due to certain environmental conditions, due to phenotypic adaptation to certain loads, age-related changes, etc. However, it is within the limits that do not violate the conditions of functioning of living organisms due to symmetry.

It follows from this that ambidextrous people with the same properties of paired organs cannot exist in principle. In fact, for these people, the difference between the properties of paired organs is not large enough.

Conclusion

The materials presented in the book showed that the applied approach to solving a number of problems of theoretical biology from the standpoint of nonequilibrium thermodynamics allowed to explain to a certain extent the essence and regularity of the functioning of living organisms and their adaptation

abilities. The new laws and regulations outlined in the work allow us to state with sufficient confidence that the driving force in the processes of vital activity of living organisms is the maximum stability of the nonequilibrium thermodynamic state, carried out by continuous alternation of cycles containing phases of ATP synthesis from nutrients and its subsequent cleavage.

The whole set of activity of cells, organs, systems and the whole organism is aimed at this main goal.

Therefore, when studying their functioning, it is necessary to proceed from the fact that all reactions and processes in living organisms are aimed precisely at this goal. Then, perhaps, the most complex processes that occur in a living organism will become more understandable, and their regularity will also be determined.

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