Hierarchy of biological rhythms, chronodiagnostic and bio-feedback

Sergey L. Zaguskin

1 Kabardino-Balkarian State University
   Russia, 360004, Nalchik, Chernyshevskogo str. 173
   *Corresponding author
   phone: +7 (918) 514-49-67, e-mail: zaguskin@gmail.com

Abstract
An overview of the author’s original works dedicated to the hierarchy of biological rhythms, chronodiagnostic and bio-controlled chronophysiotherapy is presented herein. Stability of biosystems is based on harmony of discrete spectra of their biological rhythms with a spectrum of normal cosmoheliogeophysical rhythms. According to the extent, the nature and the sort of the phase-related, systematic and hierarchical desynchronoses it is possible to diagnose and forecast the condition and the resistance of biosystems at their respective level. An efficient management of life is possible by bio-synchronization of an external physical action with the phases of increasing of energy supply for the respective responses of a biosystem. A prerequisite for bio-resonance is a multi-frequency parallel resonant capture. An invariant ratio of biological rhythms periods in their hierarchy explains an exclusive sensitivity of the biosystems to biologically significant information influences under their high noise immunity to influences having a single constant frequency or showing an abnormal range of frequencies. Chronodiagnostic identifies disorders (desynchronoses) at the early preclinical stage of a disease. Bio-controlled chronophysiotherapy allows eliminating not only the symptoms, but also the causes of diseases (desynchronoses) in an organism.

Keywords
Chronobiology, Desynchronosis, Pulse rhythms, Rhythms of breathing, Bio-control, Chronodiagnostic, Chronophysiotherapy

Hierarchy of biological rhythms
The origin of the simplest living cell was a result of an integration at least of two interdependent consumers of external energy from their common source. The energy consumers differ in rates and density of energy used by them. This is the main prerequisite for their timing as endogenous biological rhythms. The most labile and the least energy intensive functional processes are as follows: intracellular motions, secretion, electrical activity and depositing of substances. Processes demonstrating most pronounced time-lag and energy intensive nature are those referred to biosynthesis of macromolecules and microstructures. The emergence of convariant reduplication exclusively in combination with the functional processes of a protocell through the common energy source has resulted in the origin of a living cell. A similar division between fast functional, low-energy consuming and slow, energy-intensive structural processes may be also possible at the level of the organism, biocenoses and the biosphere (Figure 1 and 2 herein).

An intermediate value of the regulation lag has energy generation at the level of the cell and other biosystems (see Figure 1 herein). The functional processes receive the priority of the energy-related authorization and regulation referred to biosynthesis in the cell (to restore the structures of other biosystems) at the initial stage of growth of their energy input. However, an increasing energy input due to enhancing of the function is maintained even upon the normalization of the functional processes. Now, in its turn, it leads to an increase in the flux density sufficient for the authorization and regulation of the biosynthetic and the other structural processes. Normalization of biosynthesis and a reduction of the energy flux density again changes over the priority to the energy supply for the functional processes. The alternation of predominance between the functional and biosynthetic processes is maintained as endogenous biological rhythms and as retention of “a sustainable inequilibrium” in the cell [2]. The similar mechanism responsible for changing of the priority of energy supply between the functional and the structural (biosynthetic, recovery) processes exist at other hierarchical levels of biosystems (see Figure 1 and 2 herein).

The biological clock in a cell, as in any other biosystem, is hierarchically built in the same manner. It includes a mechanism to change the direction of motion...
of the pendulum, or, in other words, of the change-over of the phases of the corresponding biological rhythm for biosystems at any hierarchical level (circahoradian, circadian, seasonal rhythm etc.). A change of the phases of a biological rhythm is determined by periodic switching-over of the priorities of energy supply from the fast less-energy-consuming functional processes to higher energy intensive structural processes having the greater lag. Then the priority of the energy authorization and regulation goes to the functional processes again. Due to non-linearity of the negative feedback in the energy input and due to an interaction among the processes, having differences in their rates and energy demands, through the common energy supply, all biological rhythms show their varying periods. Even the most stable circadian biological rhythms demonstrate on the average a departure of 1-2 hours. A correction to reach 24 hours always takes place by exogenous rhythms (light, temperature). As to the circadian biological rhythms, the respective indicators (“the clock’s hands”) of the current phase are the relation between synthesis and consumption of carbohydrates and fatty acids [12], and the level of melatonin synthesis acts as the phase switch.

Unlike chemical oscillatory systems with a constant oscillation period, all biological rhythms demonstrate their period variability. The reason to provide the variability is that there are always many spontaneously arising, irregular endogenous factors available, which produce their influence on the lag of the energy regu-

---

**Figure. 1. Hierarchy of biosystems.** Left: green links are functional processes; right: blue links are structural processes; in the middle: red links represent energy regulation.
Due to the time differences in the functional and structural (biosynthetic) processes, the living cell along with the other biosystems has acquired new properties. This is memorizing of the history of input influences and effects; it is not only some trace changes, but also a long-term memory with maintaining selective sensitivity to some usual, regularly occurring, time parameters of the biologically significant influences and effects. These are the properties of adaptation, training and learning, specialization and some new possibilities and capabilities of the evolutionary adaptation and complexity. The problem of ageing of cells as a result of minimizing energy consumptions, when adapting and learning & training, has been solved in evolution by three ways: 1) by maintaining growth through functional induction of biosynthesis of new macromolecules and eliminating defective macromolecules and microstructures; 2) through a change of generations (reproduction), though at the expense of the loss of the biological information acquired in ontogenesis at the epigenetic level; 3) through the differentiation of stem cells into cells of a given type. Similarly, at the expense of the loss of memory and ontogenetic phenotypic adaptations, genetic mutations and selection, life is saved at the level of the organism, the biocenosis and the biosphere. And it is a human being alone, who has exclusively invented a completely new way of storage and saving of the information obtained by him in the ontogenesis that remains ready-made available for the next generations.

The relative lag of structural changes, as compared with the same level of the functional ones, allows biosystems ignoring random signals, possessing memory and providing presets to regularly occurring, biologically significant, signals. At the same time, the signature functional effects provide for "an advanced reflection going ahead"[1] of the most likely expected responses of a biosystem. Due to the advanced reflection (expectation), a biosystem gains in a principle manner in its stability. The appearance of the differences in the energy intensity and the lags in the regulation between the functional and structural (biosynthetic) processes should be attributed to the hysteresis dependence of the sol-gel transitions of the energy supply parameters. In particular, changing in the rate of the ATP synthesis and its consumption under the influence of varied rates...
and lags of the regulation of the intracellular processes depends on the local sol-gel ratio in a particular compartment of the cell [4].

When a living cell first originated, the duration of the transition processes, time constants of feedbacks and time periods of rhythms of the functional and structural processes differed by a factor of \( \pi^7 \) (see Figure 1.2 herein). “The current structure is a product of the yesterday's kinetics” [10]. The biological significance of such differences between the structure and the function of biosystems at the same level is to provide a reduced sensitivity to random, erroneous, unaccustomed information and a pre-specified selectivity of biologically significant, adequate, regularly appearing, signals. A large lag (by a factor of \( \pi^7 \)) of the structure against the function at the same level allows biosystems avoiding memorizing of some random effects in the structure and fixing the selective sensitivity to the regularly occurring, biologically meaningful, information signals.

As shown in [11], evolution of elementary open catalytic systems (EOCS) demonstrates a tendency in increasing of the common and useful energy capacity of the base reaction. By applying this statement to evolution of biosystems, it may be assumed that their progressive complexity from the primary cells to the multi-level differential biosphere in its existing form has also been followed the direction of increasing flux densities of energy used. Evolution of the biosphere, upon the origin of new levels of the integration of biosystems and their further progressive complexity was possible only in the case, when an increase in the energy flux density, at least temporary and local, would give energy gains and elevate the stability thereof (even at the expense of change of generations).

The emergence of new major levels of the biological integration (MLBI), it is thought to be similar to the EOCS evolution [11], is based on overcoming some constitutional constrains of increasing of the averaged density fluxes of energy used. MLBI covers the following: the biosynthetic self-replicating cycles - BSRC, cells, organisms and biocenoses as subsystems of the biosphere (see Figure 1 herein). The MLBI are qualitatively new autonomous structures. By increasing the average consumption of the external energy, they are capable of a centralized parametric energy regulation of the function \((u, v, w, \text{left side in Figure 1 herein})\) and the structure \((k, l, m, \text{right side in Figure 1 herein})\) of their subsystems and elements, using feedbacks of all elements. This gives a gain in energy supply for slower processes, which however globally cover the entire biosystem. Increased sustainability through an energy benefit for each element in the formation of intermediate levels of the biological integration (ILBI) takes place by increasing dispersion and consequently the maximum density of fluxes of the used energy to overcome the kinetic limits.

The first kinetic limits of an increase in the maximum density of used energy for each MLBI are achieved due to formation of the first intermediate levels of the biological integration (ILBI), representing an energy integration of homogeneous elements. For the structural entities, they are homogeneous microstructure of the cells (HMC), tissues, populations and biomes. As to the functional entities, they are as follows: homogeneous compartments of a cell (HCC), ensembles or functional units (FE); families, herds, flocks; functional systems of homogeneous biocenoses (FSOB). The energy advantage of an integration of this sort is provided by a coordination (shifting) of the activity phases of the homogeneous elements, similar to the case, when individual energy consumers from different time zones are united into their common grid network.

The second kinetic limits are reached, when heterogeneous elements are united into the second type of ILBI: they are heterogeneous microstructures of the cell (HMC), organs, consortia, regions; heterogeneous compartments of the cell (HCC), the functional systems of an organism (FSO), the functional systems of dissimilar organisms (FSDO) and those of biocenoses (FSB). An energy gain from the integration of the elements with different kinetics and energy is also obvious, since this contributes to a more complete and faster consumption of external energy. All ILBI in contrast to MLBI are not capable to energetically synchronize their elements. The regulation of the elements therein is carried out only on the basis of energy competition with their closest neighbors. This gives an advantage as compared to the central regulation in solving tactics (fast), but local-type tasks.

Some relict biological rhythms, inherited from the procaryotic biosphere, have periods approximately 3 times smaller than the fundamental ones, and the fundamental biological rhythms demonstrate 3 times shorter periods than the coordinating biological rhythms at the same integration levels (see Figure 2 herein). This eliminates a parametric resonance and provides the relative autonomy of the adjacent levels. The periods of the biological rhythms of the adjacent levels of the integration of biosystems differ by dozens
of times (10-30): this eliminates the capture of the period both from the lower and the upper level.

Discreteness of the temporary organization of complex biosystems with step PI (π) can be explained by their protection from a parametric resonance (more than 2), including from the lower and upper level rhythms (π2). Such values of a step of the temporal hierarchy of biological rhythms correspond to the discreteness of sizes of animals between taxa of different ranking established in [14]. It can be assumed that such step is associated with the hierarchy of the energy linkage between the local and integrating processes. In the simplest case with a ball-shaped biosystem, a cooperative energy linkage of elements (each with each) is slowing down by a factor of π, as aggregates of aggregates - by a factor of π2, and as aggregates of the third orders - by a factor of π3. However, an actual deviation of the biosystem shape from its spherical shape, the origin of the blood circulatory system, sending signals as nerve pulses lead to an enhancement of the kinetic perfection only. And an increase in the energy density is only possible at the expense of the other parts of the biosystem as a result of the spatio-temporal organization (alternating). Consequently, an integral rhythm of the structure will slow down as is the case with the rhythm in the ball-shaped biosystem.

The emergence of associations of the sol-gel structures corresponding to the existing genes (viruses), for the first time has split the times of the functional (x, y, z) and the structural (p, r, s) processes. This is a fundamental difference of the living systems from the non-living ones. The energy parametric regulation by BSRC w0 acted as feedback with a period equal to r0, the rhythm of the elongation (joining of amino acids in protein synthesis at the ribosome) (see Figure 1 herein). Thus these unique structures have lost their direct functional changes (the regulation by the lower elements). Hence appeared is the parametric energy regulation of derepression and replication of genes in the absence of a direct inheritance of acquired properties. We can say that life came into being, when the spatial organization of BSRC (see Figure 1 herein) in the protocell provided the circuit through the energy parameterization not only of the function of their elements (w0), but also in the form of r0 of the same energy flux - the structural organization of genes. Thanks to this for the first time a stable hierarchy of interrelated (through the distribution of the overall flux of the input energy) oscillatory circuits developed, which were adequate to the hierarchy of the external environment oscillation periods.

The hierarchy of biological rhythms shows a good agreement practically with all major cosmogeliogeo-physic rhythms, recorded on the surface of the Earth: this is the natural frequency of the ionospheric waveguide, infrasound and micro-pulsations of the geomagnetic field of classes Rs1, Rs2 and Rs5, pulsation of the Sun, cycles by Niedermueller, Cortie, Wolf, Patterson, Grebby and Milankovitch, climatic rhythms and seasonal rhythm of a galactic year. Not all biosystems show the same sensitivity to these external rhythms. It is possible that a number of the rhythms with a short period have even lost their importance they have had at the early stages of life evolution. They differ dramatically in their power and amplitude fluctuations. However, for the development of multi-level life the ratio of their periods is critical. This is the basis for bio-resonance allowing biosystems to combine their high noise immunity with an extremely high sensitivity to biologically meaningful, appropriate influences made by the other biosystems.

**Chronodiagnoses**

The evolutionary classification of biological rhythms in the hierarchical biosystems allows suggesting that there may be some new methods of diagnostics and forecasting of state of the biosystems from the cell to the biosphere based on detections of various disagreements among the biological rhythms and disorders of their fractal structure. Chronodiagnoses can be made by evaluation of availability and assessment of values of phase-related, systematic and hierarchical desynchronoses. In contrast to the methods of disease diagnostics by the presence of structural disorders in a human body (with the use of x-raying examination technique, ultrasound examination, tomography), chronodiagnoses is possible at an early, preclinical stage of disease progression according to functional desynchronoses, when structural disorders do not manifest themselves. According to a shift of acrophase, changes in the amplitude and the mesor of the circadian biological rhythm and according to the appearance of the ultradian and infradian biological rhythms, it has become possible to reliably and very simple detect even the first signs of progressing of various diseases and changes in the functional state of the human organism, taking into account ageing and occupational specifics [8, 13, 18].

We proposed some original methods of early diagnostics by the presence of some systemic and hierarchical disagreements among biological rhythms [3,5]. Dis-
orders of harmony of biological rhythms are recorded not by changes in their absolute values, but according to their deviation from the normal invariant ratios. For example, a system desynchronosis, as a deviation from the normal ratio of the heart rate to the respiratory rate value (from 3 to 5), has the same value for a human and a mouse, as well as for an elephant, despite the differences in the absolute values of the periods of their given biological rhythms in these organisms. System desynchronoses are recorded as a disagreement in the ratio between the periods of the rhythms at the same level. For example, a system desynchronosis according to a deviation from the ratio of the rhythms of the heart rates to the respiratory rates at the organ level indicates a disorder of the vegetative status of an organism. Abnormalities of the ratio of biological rhythms in numbers of the populations in a biocenosis bear witness to ecological ill-being. A hierarchical desynchronosis between biological rhythms found at different levels, but referred to the same type (function, energy or structure) allows predicting a direction of processes at a specific level from the cells to the biosphere.

Fresh opportunities for chronodiagnostics have been opened by the theory of non-linear oscillations and dynamic chaos [20]. It is proved in [19] that the multi-fractal heart rhythm structure and dominant influence thereon by breathing rhythm under the normal conditions may substantially differ at the early stages of ontogenesis and pathology. Today there are many various approaches to studies on the heart rate and respiratory rhythm variability based on non-linear dynamics methods [15, 16, 17, 19]. Since the time of completion of the first research works on the above subject, the non-linear dynamics techniques have confirmed that they are really a powerful tool for an analysis of biological rhythms. The non-linear symbolic dynamics method [20] was used as a pioneering technique with the encoding “words” of varying non-fixed lengths, including construction of the respective scattering diagrams to take into account the RR-interval minima and maxima on ECG [5]. Also very informative, according to our research, is the diagnostic methods to detect disorders of the systemic coordination in the performance of the individual subsystems. The first class of the disorders of the systemic coordination may be revealed, when comparing the rhythms of different periods taken at the same level of the organization. For example, for the level of the organs and organism systems, a disorder can be detected according to the ration of the heart rate value to the respiratory rate. Such a disorder is capable not only characterizing the early signs of a disease of the heart and respiratory organs, but also of predicting unfavorable vegetative responses under stressful loading or under developing a sustainable sympathicotonia or vagotonia. The second class of the systemic disorders is found to be an abnormality of an optimal balancing and harmonizing of the rhythms of different periods, in our case it refers to the heart rhythm relationship in different periods.

In our research, we pioneered in applying the method of non-linear symbolic dynamics [20], which deals with the encoding "words" of different non-fixed length. The fact that up to 90% of power of the frequency spectrum in an intervalogram account for very low and ultra-low frequencies, and their physiological and diagnostic value remains unknown [9], suggests that the methods of non-linear dynamics of the R-R periods ECG allow obtaining more accurate data and more direct information used for diagnosing and predicting the condition of patients.

Figure 3. Three scatter plots displaying the mm-intervals in a healthy human (left), in a patient with stagnant heart failure (center) and in an atrial fibrillation patient (right). On the axes the mm-intervals in milliseconds are plotted.
When constructing a scatter diagram to indicate the lows and highs of the mm-R-R intervals, there we can reveal some new features in its structure: instead of a single cloud, which is found on the scatter diagram of the R-R intervals, we can find several clouds of the localization of the dots. The appearance of these clouds can be explained by the fact that each time interval of a prevailing activity of the parasympathetic or sympathetic nervous system is characterized by a different number of the heart beats. Therefore, the mm-scatter diagram reflects the complete hierarchy of the R-R interval rhythms (see Figure 3 herein).

Figure 3 exhibits some mm-scatter diagrams, which are typical for patients, suffering from diseases, versus that in a healthy individual. Differences in them are clearly seen even without any additional analysis tools. An mm-scatter plot of an ill patient displays some differences in its shape and demonstrates blurred lines of cloud configurations. An assessment of the actual shapes of the clouds and the dot distributions therein allows drawing a diagnostic conclusion. In particular, under pathology, a lesser number of clouds can be identified, and their shapes show a stronger differentiation. A comparative analysis of a large number of such scatter plots completed by us has shown that there are distinct differences detected in the ill patients versus healthy individuals, and in addition there are some significant differences identified in patients with different types of pathology. A visual qualitative assessment of such mapping is easy and simple for express chronodiagnostics, for a quick identification of the presence and extent of pathology, of a tendency in disease progression and an assessment of the effectiveness of the treatment. However, to objectively quantify various mm-scatter diagrams, Y.V. Gurov developed a tutorial program of an identification of the scanned images for differentiated diagnostics of heart diseases. It is not excluded that this analysis of the heart and breathing rhythms solely would allow diagnosing diseases of the other organs in the organism, too, similar to the pulse diagnosis plasticized by Avicenna applied to diagnose abnormalities and diseases of different organs. So far, an application of this method has demonstrated the capability of differentiated chronodiagnostics of a variety of cardiac diseases. For these purposes, used is the quantitative method of character non-linear dynamics.

Treating vocabularies of long words (having a length of more than two characters), we can notice that, starting with words containing 8 characters in length, the average volume of the vocabulary for a group of healthy people is less than that for groups of patients suffering from stagnant heart failure and with atrial fibrillation. Recordings made in patients with a diagnosis of the syndrome of sudden death, the vocabulary volume is found to be consistently lesser, as compared to the other three groups. Such differences in the volume of the vocabularies can be explained by the fact that for healthy individuals, there are significantly less forbidden words of a short length that eliminates the need of a "regulation" of the rhythm by longer words. For the sudden cardiac death syndrome typical is the presence of multiple abnormalities in the heart rhythmicity. Apparently, their appearance is a consequence of the fact that the regulation by the long words leads to a dysregulation. In particular, the sudden cardiac death is characterized by very long words (up to 1000 characters in a word), that is not the case with the other three groups, where the maximum length of the periodic words reaches in average 30-60 characters.

The frequency rate of forbidden words in healthy people is associated with their age. The greater the age, the more forbidden words. In groups of unhealthy individuals, the volume of the vocabulary made of two-character words seldom reached a limit of 125 words. In the group of patients suffering from stagnant heart failure only 5 patients of 44 were identified, whose vocabulary volume amounted to 125. In the group of patients with atrial fibrillation 18 individuals of 84 and in 3 of 19 individuals in the sudden cardiac death groups the forbidden two-character words appeared even in the first two submatrices in the graph (see Figure 4 herein).

Figure 5 herein gives an illustrative example of pie charts, which are descriptive of the occurrence of some specific words in the symbolic dynamics. According to the charts, we can make conclusions on the status and the presence of a disease in a particular patient, if any, in a very easy way. So, Figure 5, on the left, shows a diagram of a healthy individual, and another diagram, given on the right in the same Figure, characterizes an ill patient. The difference between these two charts is that in case of a healthy subject, in the symbolic line, we can find a great variety of the words that manifests itself in the fact that there are almost no white stripes available, which meet the forbidden transitions. At the same time, an ill individual is characterized by a large number of the forbidden transi-
tions and offsets of the distribution of the words. In the symbolic line, the repetition of the same words is often found.

So far, chronodiagnostics has not found its application in diagnostics and prediction of future states of the biocenoses and the biosphere in general. That is due to some difficulty in recording & tracing and lengths of biological rhythm periods of the biosystems, as compared with those related to chronodiagnos-

ics remain the same for biosystems of any level due to their natural fractality. Therefore, we may expect that there will be some pioneering possibilities and options for such analysis in ecology and for predicting future biosphere-associated processes.

Bio-resonance and bio-controlled physiotherapy

All regulatory communication in biological systems is of multi-frequency nature. Respectively, resonances in biological systems also can be of multi-frequency

Figure 4. Submatrices of a weight matrix of the graph for a healthy human individual (top row) versus a patient with stagnant heart failure (bottom row). White cells have a weight more than 1%, the grey cells have a weight greater than zero, but less than 1%, and the black cells show forbidden transitions.
character with an invariant ratio between the frequencies at each time under variation of the absolute values of these frequencies. They are memorized in evolution, since they do not destroy stability of biosystems under information communications among themselves and with the external environment. It has been just the multi-frequency signals, being in correspondence with the hierarchy of biological rhythms periods, to which evolutionarily the highest sensitivity has been producing. The most important difference of the biological multi-frequency resonances is that decisive for them are not the absolute values of the components, but their invariant ratio, similar to the same chord in different octaves. The phenomenon of multi-frequency parallel resonant capture is a specific property of living systems. It has been detected by us experimentally in a single nerve cell [3.7]. Only multi-frequency exposure the intrinsic rhythms of energetics of the cell has increased in a sustained manner the content and synthesis of protein in the cell (see Figure 6 herein). A single-frequency or continuous-type exposures have resulted in a temporary increase in protein content in the cell only [4].

The multi-frequency resonance was discovered by us in studies on some examples of selective intensification of biosynthesis in neurons, yeast cell budding, wheat seed germination and oppression of the vital activity of abnormal cells, which varied in the range of their intrinsic biological rhythms [7]. A proportional change in the absolute values of the periods of biological rhythms does not affect their invariant ratio: we understand the same word, no matter whether it is spoken by a male with a low frequency bass voice or by a woman with a voice showing high absolute values thereof. Due to multi-frequency codes, a signature control of signals of much shorter durations, as compared with the period of the inherent responses by a biosystem, is realized. For example, the response time of the organism to a light stimulus is comparable to the duration of the transition process of the cell membrane. In response to short and weak signals of a tree, affected by tree pests, the other trees are initiating their long-term biosynthetic reactions of protective nature. Synchronization of these transitions between certain sol-gel structures in the cell may be sufficient to relay information signals and provide the relay transmission of external influences between the cells in the organism.

This is an ancient way of information interactions that has been developed at the stage of the origin of the simplest living cell. It certainly has survived both in modern single-cell and multicellular organisms. If compared with the evolutionarily more recent neuro-humoral ways of conveying information in an or-
ganism, its main features are efficiency, low energy
demand at a high-rate signal transmission. The main
advantage of this method of signaling is a large infor-
mation capacity, because the multi-frequency encod-
ing of signals by the hierarchy of the rhythms of the
sol-gel transitions enables using biological codes fixed
by evolution, at high noise immunity. The neural and
humoral communication linkages are expensive from
the standpoint of chemical and energetic parameters,
and their appearance has been dictated by the need to
provide an address target transmission of signals that
is required by a multi-cellular organism.

The biological codes (the biological software) re-
sponsible for information communications between
biological systems, beginning with their intracellular
level, are invariant ratios of the periods of the rhythm
hierarchy. This encoding allows eliciting responses to
those signals, the intensity of which may be lower than
natural background noise. At the same time, the bio-
systems possess high noise immunity, escaping from
the single-frequency resonances occurring upon an
exposure to a fixed frequency. The levels of an intact
integral biosystem, referred to as those located above
and below, actively absorb impacts made at a fixed fre-
quency, even if the latter will be close to the average
period of the biological rhythm at a targeted level. Bio-
systems avoid single-frequency resonances due to vari-
ance in the periods of biological rhythms, among other
things. A concurrent exposure to a set of frequencies
with an invariant ratio, characteristic of a biosystem,
allows the biological system to identify these adequate
physiological information impacts of extremely low
intensity and respond to them. Thanks to these codes
the biosystems combine their high noise immunity
with an exceptional sensitivity to biologically signifi-
cant, routine influences of information nature.

It has been detected that the Bio-feedback-control of
a living cell by synchronizing the functional load with
the rhythms of its energetic is applicable to bio-feed-
back-control of the life performance of an organism
[6]. In both cases, the prerequisite for the effectiveness
of bio-feedback and the desired therapeutic effect on
the basis of bio-resonance is the synchronization of
external physical effects with the hierarchy of certain
energy rhythms. At the level of the organism, to en-
hance regenerative processes of biosynthesis, required
should be synchronization of external influences with
the rhythms of the blood filling in the tissue blood
vessel within the area affected by pathology. However,
the spectrum of the rhythms of blood microcircula-
tion in the pathology area, as Doppler flow metering
shows, is always found to be disturbed. According to
our research, it is possible to normalize the spectrum
of the rhythms of blood microcirculation in the zone
of pathology with the use of physiotherapy providing
the rhythms of the central blood circulation accord-
ing to signals from pulse and respiration sensors of
the patient.

The signals delivered by the pulse and respiration
sensors of the patient are multi-frequency signals
modulated by all range of the pulse and respiration frequencies. In our studies, we have used a range of rhythms of tremor with a variation within the range from 7 to 13 Hz as the carrier frequency to produce physiotherapeutic effects. These rhythms of the oscillations of muscle fibers play the role of peripheral hearts, which are intentionally orchestrated in coincidence with the spectrum of the rhythms of elongation (when amino acids are joining together in protein synthesis in the ribosome sites) and the Alpha rhythm of the brain. Those constant frequencies, which are widely used in conventional physiotherapy, are not in adequacy to the biological rhythms showing their varying periods. Synchronization and (or) modulation of the physiotherapeutic impacts with the phases of inhalation and systole enhances regenerative processes and restores the level and the spectrum of the rhythms of blood microcirculation in the zone affected by pathology. Synchronization with the phases of exhalation and diastole is suitable, when some tissue defects and tumors are removed with the use of surgical lasers, electric coagulators and some other destructive actions. In this case, when in the affected area the volume of blood filling is reduced, heat capacity and thermal conductivity of the tissue decrease, the pre-determined density of power exposure is falling. At the same time, an area of necrosis and thermal denaturation in the surrounding healthy tissue is minimized.

Laser equipment and some other types of physical therapy devices developed by us according to our specifications take into account the locations of the sensors with respect to the area to be treated by the therapy, the need to provide certain delays and reversal of the signals delivered by the pulse sensor, when exerting an influence on the myocardium. Used is a biological timer to read the pulse beats instead of seconds for standardization and tissue memory formation under various vegetative status conditions on different days of the treatment course. The ratio between the depths of modulation of the physiotherapy exposures according to pulse, respiration and tremor is selected, taking into account the nature of local pathologies (hypoxia, arterial or venous hyperemia).

The devices and techniques developed for the bio-controlled chronophysotherapy are capable of increasing effectiveness of basic therapy, reducing treatment times and providing its stability. In doing so, offered is a systems treatment avoiding undesired side effects for unaffected organs in the organism. It results in expanding of the therapeutic range of intensity of physical actions. Normalized is the spectrum of the rhythms of blood microcirculation in the area affected by pathology, cell immunity and vegetative status. It makes possible to eliminate an imbalance between the arterial and venous segments in the capillary bed and to exclude tissue hypoxia. It is the bio-controlled chronophysiotherapy only that provides not only an increase in the blood supply level in the pathology site, but also a restoration of the spectrum of the rhythms of blood microcirculation, thereby eliminating energy discrimination for some cell populations with respect to the other and increasing the quality of regeneration and stability of the required therapeutic effect. The method of the bio-controlled chronophysiotherapy allows obtaining the guaranteed curing effect for all patients, since it does not result in disordering homeostasis parameters, but it produces just a normalization of them. An advantage of the bio-controlled chronophysotherapy, as compared with the conventional methods of laser, light, ultrasound and electrotherapy, has been demonstrated by us in cooperation with leading experts from Moscow and Rostov-on-Don (Russia) in different fields of medicine [3.6].

No effective medical drugs without side effects and addiction are known. The used physiotherapy methods cannot replace conventional medication therapy. At the same time, it should be mentioned that the existing physiotherapy techniques are not capable of taking into account fluctuations in sensitivity of the organs in an organism, which are associated with the phase of the circohoralian rhythms of the vegetative status in a patient, time of the day, moon phases and a season in the year. Devices applied for the conventional physiotherapy employ constant frequencies, which are not adequate to variable rhythms of the patient. Therefore, often we have to deal with some undesired side effects, and the therapeutic effect is sometimes of temporary character, since it is based on a placebo effect. Similar to the best medication, the conventional physiotherapy addresses rather symptoms, ignoring desynchronization as the cause of the disease. Chronodiagnostics identifies a functional desynchronization as predictors of early preclinical stage of a disease. This is important for the further successful development of preventive medicine. The bio-controlled chronophysiotherapy, normalizing the spectrum of the biological rhythms in the area affected by pathology, is targeted
not only at the removal of symptoms of the disease, but also desynchronoses themselves as the cause of these diseases. This should be considered as an important component of the future personalized medicine.

Statement on ethical issues
Research involving people and/or animals is in full compliance with current national and international ethical standards.

Conflict of interest
None declared.

Author contributions
The author read the ICMJE criteria for authorship and approved the final manuscript.

References
1. Anokhin P.K. Biology and neurophysiology of a conditioned reflex. -M.: Medicine, 1968. 547p. [in Russian].
2. Bauer E. C. Physical basis in biology. M.: Mosobilpolkom. 1930, 101p. [in Russian].
3. Zaguskin S.I. Rhythms cells and human health. Rostov-na-Donu, SFU 2010. 292p. [in Russian].
4. Zaguskin S.I. Biofeedback life based on bioresonance hierarchy rhythms of sol-gel transitions in body cells. Space and Time. 2016, 3-4, (25-26), 261-269. [in Russian].
5. Zaguskin S.L., Gurov J.V. Chronodiagnostic and devices of biocontrolled physiotherapy. //Proceedings of SFU. Technical science. 2009. 9. 78-83. [in Russian].
6. Zaguskin S.L., Zaguskina S.S. Laser and biocontrolled quantum therapy. M.: "Quantum medicine", 2005. 220p. [in Russian].
7. Zaguskin S.L., Prokhorov A.M., Savransky V.V. Way enhance the biosynthesis in normal or its oppression in pathologically altered cells. A.S. USSR N1481920 "t" from 22.01.89. Priority 14.11.86. [in Russian].
8. Zaslavskaya R.M. Chronodiagnostic and chronotherapy diseases of the cardiovascular system. M.: Medicine, 1991. 320p. [in Russian].
9. Makarov L.M. Holter monitoring. Medpraktika, 2000, 216p. [in Russian].
10. Molchanov A.M. Possible role of oscillating processes in evolution. Oscillatory processes in biological and chemical systems. M.: Nauka, 1967. 274-291. [in Russian].
11. Rudenko А. P. Self-development theory open catalytic systems. M. MSU. 1969. 183p. [in Russian].
12. Selkov E.E. Temporary organization of energy metabolism and cellular clock. Regulation of energy metabolism and physiological state of an organism. M.: Nauka.1978:15-32. [in Russian].
13. Halberg F. Temporal coordination of physiological functions. The biological clock. M.: Mir, 1964. 475-509. [in Russian].
14. Chislenko L.L. Structure of the fauna and flora due to the sizes of organisms. M., MGU. 1981.206p. [in Russian].
15. Goldberger A. Is the normal heart beat chaotic or homeostatic? News Physiol. Sci. 1991;6:87–91.
16. Goldberger A, West B. Applications of nonlinear dynamics to clinical cardiology. Ann. N Y Acad. Sci. 1987;504:195–213.
17. Guzzetti S, Mezzetti S, Magatelli R., et al. Symbolic dynamics of heart rate variability: a probe to investigate cardiac autonomic modulation. Circulation. 2005;112:465-70.
18. Halberg F, Lagogiyney M, Reinberg A. Human circannual rhythms over a broad spectrum of physiological processes. Int.J. Chronobiol. 1983;8(4):225-68.
19. Ivanov P, Amaral L, Goldberger A., et al. Multifract. in hum. heart beat dyn. Nat. (Lond.). 1999;399:461-5.
20. Voss A, Schulz S, Schroeder I R, Baumert M, Caminal P. Methods derived from nonlinear dynamics for analyzing heart rate variability. Phil. Trans. R. Soc. A. 2009;28(367):277-96.