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THE PHYSICS OF LASER BIOSTIMULATION

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The book reviews mechanisms and effects of laser stimulation of biologic systems on the basis of quantum radiophysical and synergetic concepts. The interaction of laser radiation with biologic tissues is analyzed as a self-organizing process of non-adiabatic perturbation of quasi-participles – conformers, as well as a phenomenon of self-adjustment of distribution of laser radiation intensity to the cellular structure of the biologic tissue due to the Talbot effect. New experimental and theoretical evidence confirming the importance of a regular component of the electromagnetic field structures and perimembrane quasi-crystalline structures of biologic tissues during laser radiation interaction with the biotissue is discussed.

The book is oriented toward university students, postgraduate students and researchers in the fields of physics, biophysics, biology, medicine and radiophysics.

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1. Introduction

The phenomenon of laser biostimulation (LBS) is extensively used in medical practice, although its nature and mechanisms are far from being elucidated and understood (1). The available literature on LBS and laser therapy (1-3) and degrees of its clarity in explaining the effectiveness of laser treatment for biosystems resemble magic-astrologic and supersensory publications. Most of uncertainty relates to the fact that, first, laser radiation has a selective action on only "ill" cells and biosystems and, second, laser light with different wavelengths has similar therapeutic effects. Finally, it is not clear why electromagnetic perturbation of the subtle biochemical mechanism comprising more than 10,000 levels (enzymes and protein molecules) produces beneficial effects rather than impairment of the functioning of the sophisticated biologic "machinery" (4-6).

Biologic problems always drew attention of physicists. Definitions of the field theory that were effectively used in physics began to be actively adopted in theoretical biology back in the 1930s (8). The theory of incoherence of light fields as a holographic concept and several notions of quantum mechanics are finding use in the present-day genetic theory (9). The non-linear dynamic theory of solitons has been used for describing excited states of biologic molecules like DNA and RNA (4). Cybernetic and radiophysical approaches have proved fruitful in the development of the concept of extremely high frequency therapy (10).

Biologic research is specific in that vivid individuality and complexity of objects as a rule exclude a coincidence of their quantitative characteristics (1). Organization of experimental studies and interpretation of their results are interesting from a physical perspective, as they could help the development of new concepts and methodologies. One of promising approaches is to consider the biologic tissue as a special coherent state of substance (11, 12). Indeed, living objects show quantum properties; for instance, their characteristics have been found to depend on a measurement procedure and the non-linear dynamic behavior of biosystems (13).

The goal of this work is to formulate the process of interaction of laser radiation with biologic substance on the basis of physical concepts and to show that effects of LBS can be explained at least in the framework of present-day physical concepts.

2. Self-Organization and Non-equilibrium during LBS

Effects of laser biostimulation vary from their occurrence at molecular and biochemical levels to a systemic response of the organism on the one hand; on the other, the biosystems show an almost identical response to laser treatment in the range of wavelengths from the extremely high frequencies (30-300 GHz)) to infrared (up to 400 THz) and visible (400-800 THz) spectra. This diversity of effects inevitably warrants developing a single physical concept of interaction of coherent radiation with biologic objects.

Experimental studies have demonstrated that laser radiation acts on a separate cell (2) and not only on biologic cellular structures (3). Attempts to correlate energy levels of atoms or molecules to energy of a light quantum and the search for a photosensitive agent in the biotissue have been unsuccessful. This appears to be related to a lack of consideration for the degree of "openness" of biologic systems in terms of statistical physics. Unlike self-contained (isolated) systems, the open systems exchange with their environment their substance, energy and, importantly, information (14). Therefore, thermal degradation may coexist with self-organization processes during the interaction of the open systems, to which living systems belong, with coherent radiation emitted by the active laser medium that has an inverse population of energy levels. As a result, functions of an affected biosystem are restored. An important feature of LBS is equifinity: despite a broad variability of characteristics of laser radiation, final therapeutic effects prove identical.

Apart from being open, biologic systems consist of active small objects (quasi-particles), whose structure is complex and inadequately studied. Defining the elements of such active open systems appears to be largely dependent on task-setting with account for collective interactions in self-organization processes, which are phenomena examined by a new science - synergetics. The complex and non-linear dynamic behavior of specific systems in an ensemble makes the use of statistical description inevitable (14).

Biologic systems probably consist of a large number of "particles". However, the notions of the atom, molecule or macromolecule should not be used in modeling a biologic system. Adopting the definition of a special type of quasi-particles, conformers, appears to be appropriate. Examples of such quasi-particles are conformation states of macromolecules (5), Davydov solitons running in a DNA strand (4), excitons and biexcitons occurring in a quasi-liquid-crystalline environment, etc. Impossibility of using macromolecules as elementary units in the theory of LBS effects is confirmed by the finding that that the molecule's environment (for instance, hydrate envelopes) may play a significant role; also, there is the need to take into account the influence of boundary conditions (cell walls) on the spectrum of conformation states of a biomacromolecule. Thus a

possibility has been shown in statistical physics of polymers that properties of a macromolecule can be described when it is placed in a tube or a thin slit, as a system of blobs (15).

The presence of a hierarchy in the multi-level structural organization of biologic systems suggests a possibility of mutual transformations of the above-mentioned and other "quasi-particles". Such transformations can be described with account for the scale similarity of biologic structures (structural fractality).

The use of statistical description has shown that the interaction of laser radiation with biologic substance is non-adiabatic and determined by a narrow-band (monochromatic) character of the radiation spectrum (16). The laser radiation wavelength and other initial conditions such as the spatial pattern of the wave front are of secondary importance. Effects of usual radiation sources on a biologic system are similar to an adiabatic temperature increase in the entire system, while the action of monochromatic narrow-band laser radiation is comparable to the mechanical stirring of a biologic fluid.

Determination of physical parameters describing a system is of principal importance. The notion of entropy production, which was introduced in non-equilibrium thermodynamics on the basis of the Prigozhin principles, appears usable in evaluation of LBS effects. A major advantage of entropy characteristics is their relation to information and structural parameters, for instance, in the system of coherent radiation interacting with a biosystem. Therefore, LBS effects may be considered as c combination of non-equilibrium phase transitions forming the self-organization process, in which the coherent light-biologic substance system acts to decrease entropy production. It should be stated that the description of the self-organization process, which is formed by a temporal sequence of stationary states, does not uniformly correspond to real biologic stages (17), which may be related to reciprocal transformations of "quasi-particles".

Another aspect of LBS effects, which are a self-organization event, is adjustment of the spatial-temporal pattern of the radiation wave front to the structure of the biotissue (18). Importantly, the light field formed within the biotissue actually does not depend on the initial structure of incident laser radiation. The modal structure of the coherent radiation field spreading in cells may cause Talbot and Laue effects that result in image self-reproduction and "self-correction" of cell elements of the structure. The modal theory of images and the information theory might be a basis for determining differences between single-site and scanning tissue irradiation in laser therapy.

As its has been stated above, energy levels of atoms and molecules could not be correlated to energy of the light quantum because these attempts overlooked the openness of biologic systems. Elucidation of elements of the active open systems warrants account for collective interaction in the self-organization

process, unlike reliance on the definition of a macromolecule that connotes primarily chemical properties of substance.

A biologic object is a most complex system in optic and structural terms. All of the mentioned events and, in addition, dynamic characteristics of the organism appear to have a significant role in it. Dualism of biosystems presents as phenomena related only to properties of either separate microsystems or their internal structure or of macrosystems, with the provision that they act as an entity and are phenomena independent of the structure of macroscopic particles. The latter phenomena are determined by integral properties of a characteristic ensemble with an enormous number of "effaced" and independent participants, which is described in terms of thermodynamic and statistical physics. An obvious fundamental problem lies in the evolutionally granted presence of short-term, medium-term and long-term interactions in native conformations of biologic macromolecules (19). The situation in biosystems is compounded both by a lack of a distinct borderline between these phenomena and by openness and non-equilibrium of such systems.

By now characterization of developments in the cell is mosaic: the primary act of photon interaction with the macromolecule has to be depicted in a quantum mechanical way, while change in the conformation state is described in the framework of quantum chemistry and biochemistry (5). The macromolecular structure as a whole is described on the basis of the Flori theory, interactions of macromolecules evaluated in the determinist lock-key and hand-glove models, and the behavior of the cell as a whole is described using the theory of automates and systems (20). In addition, theories of phase transitions and self-organization are recruited if necessary (13, 15).

Effects of LBS are a non-trivial example of interaction between two non-equilibrium systems: the coherent field and the biologic system. It might seem the two systems need a wavelength "resonance" for their interaction to occur, but it always happens in the presence of monochromatic radiation. This appears to be related to discreteness of the energy spectrum of the biosystem and to change of its parameters in time - it "breathes" and thereby secures the resonance of structures. Major features of this interaction are the presence of self-organization and equifinity - independence of the final result of widely varying initial conditions (a wavelength, an illumination angle, intensity, etc.). This approach shows that the physical pictures like chaotization through bifurcations and heating by radiation, which seemingly stand far apart, can be reconciled in a single description (21).

3. Biologic Electrodynamics

A single cell as a study object is characterized by a complex spatial-geometric architecture (Fig.1), let alone the intricacy of its molecular dynamic organization (5, 6, 17). The impossibility of direct use of classical electrodynamics for description of the cell has determined the purely qualitative nature of the biologic field concept in theoretical biology. This is related to the fact that the situation occurs just in the cell where tools of the field theory cannot be used. Namely, a charge (or a system of charges) that is present in the field is exposed to effects of the field and in turn acts on the field, altering it. Nonetheless, definitions of classical electrodynamics can be used, with these limitations in mind, for analysis of biologic systems, at least as a language and not as numerical characteristics.

The dipole moment of the system of charges is introduced when the field is considered at distances from the system of charges that are significantly longer as compared to the system's size, an arrangement the cell actually does not meet. Nonetheless, there is evidence to indicate (22) that potential at the point $\vec{R}_0$ of the field created by the charge system q_i with the radius vector of each charge $\vec{r}_i$ is

$$\varphi = \sum_i q_i \Big/ \left(\left| \vec{R}_0 - \vec{r}_i \right| \right) \qquad (1)$$

and if $R_0 >> r_i$, the following expansion can be used:

$$\varphi = \varphi^{(0)} + \varphi^{(1)} = \sum_i \frac{q_i}{R_0} - grad \frac{1}{R_0} \sum_i q_i \vec{r}_i \,. \qquad (2)$$

On the basis of the latter expression, the notion of the dipole moment of the system $\vec{d}$ is introduced

$$\vec{d} = \sum_i q_i \vec{r}_i = \int q(\vec{r}) \left| \Psi(\vec{r}) \right|^2 \vec{r} dV \qquad (3)$$

where $\Psi(\vec{r})$ - wave function of the charge system that is determined in a quantum mechanical way. It is more correct mathematically to take into account all terms of the series during R_0 degree expansion

$$\varphi = \varphi^{(0)} + \varphi^{(1)} + \varphi^{(2)} + \ldots . \qquad (4)$$

where $\varphi^{(n)} \approx R_0^{-(n+1)}$. (5)

If the system is electrically neutral and has no dipole moment, i.e.

$$\sum_i q_i = 0 \qquad \text{и} \qquad \vec{d} = 0, \tag{6}$$

analysis of its field takes into account the third member of expansion into (4) - the quadrupole potential:

$$\varphi^{(2)} = \frac{D_{ik}}{6} \frac{d^2}{dx_i dx_k} \frac{1}{R_0}, \tag{7}$$

where D_{ik} - tensor of the quadrupole moment.

Fig.1. Schematic representation of the cell structure.
1 mcm=1,000 nm=10,000Å.
The 632.8 nm wavelength of the helium-neon laser=0.6228 mcm

It can be shown (22) that the *l*-th member of expansion (4) is determined by tensor 2^l -pole moment of the *l*-th rank that is symmetrical in all of its indices and turns into zero during the folding of any pair of indices. The quadrupole moment of the system does not depend on selection of the beginning of coordinates if all conditions are met (6). Unlike in classical electrodynamics, analysis of the field in the cell should take into account both quadrupole and higher moments of biomacromolecules, which certainly makes numerical calculation of field characteristics unrealistic.

A main feature of cellular biochemical processes is their electron conformation or matrix character (5). Changes in the conformation state of macromolecules, e.g. their "folding" or "unfolding" demand low energies, but they result in a significant variability of their catalytic activity. Known models of enzymatic catalysis, such as lock-key, hand-glove, rack and protein-machine, are based on the need to ensure complementarity of conformation states of the substrate and the enzyme. The conformation pattern of interaction between biochemical reagents determines the entopic type of these reactions, or in other words, their being designed to change and coordinate secondary, tertiary and other structures - conformations of biomacromolecules relative to each other. The limited macromolecular resource within the cell and the need to maintain a sufficient number of macromolecules in a certain conformation state for their functioning have led to the emergence in the evolution process of a special mechanism of selection of the molecules or induction of their necessary conformation states. In terms of laser physics, this mechanism may be considered as a "pumping" system that determined non-equilibrium of the whole biosystem. From the quantum mechanical standpoint, this non-equilibrium can be seen as a cause of the coherent state of biologic substance or biosystems (12, 14).

The mechanism of "pumping" or selection of macromolecular conformation states can be described by the electromagnetic field theory, at least at a definition level, as correct use of traditional mathematical formalism is difficult. The dipole (see equation 3) and/or multipole moment may be considered as a main physical characteristic of the biomacromolecule related to its conformation state. Biomacromolecules interact with the electric field of the light wave, changing their energetic states by readjusting their orientation and the dipole moment. Parameter α, which is a measure of potential energy $\vec{d}$ in the electric field with tension $\vec{E}$ can depict the effectiveness of such interaction:

$$\alpha = \vec{d}\vec{E} \qquad (8)$$

It should be stated that the dipole (multipole) moment of biomacromolecules or of their almost independent sites - blobs and domains - in a general case is different from zero because of temperature fluctuations (15, 17).

Since any physical system seeks minimization of its potential energy, it may be presumed that the end product of any biochemical reaction is bound to have a minimal dipole moment of its own because of the presence on the non-zero intracellular field alone. Therefore, reagents have different dipole moments during protein synthesis reactions, the cell's field can control their behavior, and they mutually compensate each other in a maximal possible degree after the and of the reaction. The dipole-dipole interaction of the reagents produces complementarity of the substrate and the enzyme and makes their interaction with the electromagnetic field of laser radiation more effective as compared to the end product. This leads to stimulation of different reactions of synthesis, for instance of DNA and RNA (2). These events may be presented as follows: as a result of dipole interaction of the macromolecule with its field, its energy increases, with intensification of different conformation states and the more rapid “finding” of a conformation state complementary to that of another reagent.

Impairment of cell function appears to cause accumulation of excess products of biologic reactions. For their faster elimination from the cell, the surface area of the cell membrane expands by producing prominences or processes and by plating of the membrane. A globe-like biomacromolecule getting in such "pocket" inevitably flattens, becoming a two-dimensional structure, which in turn leads to an increase in its own dipole moment (Fig.2).

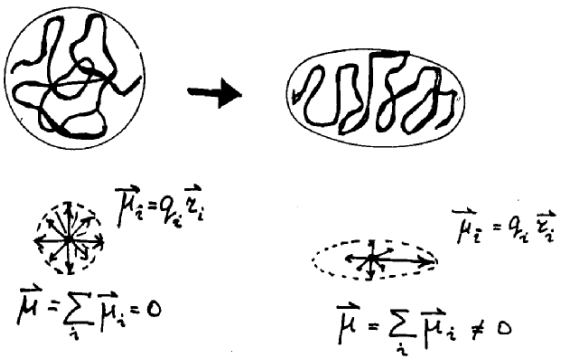


Fig.2. Increase in the dipole moment of the molecule during its planarization.

In a dipole approximation (24), the effectiveness of interaction with the magnetic field is described by equation 8. Therefore, the increase in the dipole moment of the molecule results in its higher photosensitivity. In other words, "illness" sensitizes the cell and makes laser biostimulation selective. This simple physical consideration, well known in the field of synthesis of organic photo detecting media (25), explains not only the improved effectiveness of LBS for

defective cells, but also some of causes underlying the variability of findings of in vivo and in vitro laser experiments in biophysics. Ample evidence of simulation of various enzymes by laser light also appears to be related to the flattening of the biomacromolecular spatial structure, as the catalytic center of many enzymes is located in a narrow "pocket" (15). Of note, photoreceptor cells are complete with flat structures such as discs and lamellae (Fig.3), which confirms the need for structural planarization of the molecule for enhancement of its photosensitivity (5).

The maximal amplitude of the electrical vector $\vec{E}_0$ (V/cm) of the light wave with intensity I (W/sq.cm) is determined by expressions for linearly polarized radiation (24):

$$E_0 = 27\sqrt{I} \qquad (9)$$

and for radiation with circular polarization

$$E_0 = 18\sqrt{I} \qquad (10)$$

It directly follows from these relations that LBS effects depend on the character of laser light polarization even without account for the orientation of the cell structure, but several researchers have questioned this (2).

These relations also suggest that a maximum intensity of laser radiation still causing LBS must be comparable to tension of the electric field surrounding a treated object (3). Real biosystems, including the human, function in conditions of the atmospheric electric field whose mean intensity is about 100 V/m and varies from +600 V/m to -600 V/m (26), and among fields produced by technogenic factors. Without dwelling on mechanisms of biologic process control by cellular electromagnetic fields, it may be presumed that the atmospheric electric field determines the magnitude of noises for such control systems. Therefore, the electric field of the light wave producing laser biostimulation should be more intensive than 10^{-4} W/sq.cm, according to expressions 9-10 (if dielectric permeability of the biotissue is accepted to be 50), which is a finding of many medical experimental studies. Whether adoption of this criterion is appropriate certainly remains to be confirmed by comparative analysis of LBS evidence and atmospheric electric field tension during laser therapy. Also, the figure of atmospheric electric field tension and dielectric properties of the biotissue should be used as a measure of laser light penetration into the tissue.

Fig.3. (a) schematic anatomy of the retina in vertebrates: EM - external member, CC - connective cilia, M- mitochondrion, N- nucleus.
(b) scheme of synaptic contacts between retinal cells. 1 - cone, 2 - rod, both consisting of disc organelles serving for photon entrapment, 3 - external synaptic layer, 4 - horizontal cell, 5 - bipolar cell, 6 - amacrine cell, 7 - internal synaptic layer, 8 - ganglionic cell, 9 - optic nerve axon (5).

It should be stated that the dipole approximation (8) is rough enough for the complex objects like biologic macromolecules and their associations; the field induced by them will have as sources so-called fractal currents. Characteristics of the latter are determined by distribution of spatial and temporal diffusion of primary photochemical reaction products, and they can be partially described by a fractal theory (27, 28).

4. The nature of Photosensitivity Centers

In terms of quantum mechanics, the radiation-substance interaction is a resonance phenomenon corresponding to the equality of photon energy and transition energy of a system. Therefore, in the presence of the interaction, it is always necessary to find a material system with the corresponding difference of energies. This often proves a non-trivial task. For example, such objects are simply non-existent (in a chemical sense) in the case of red laser biostimulation. Most likely this is related to the fact that chemically the molecule is not a minimal particle of live substance - it certainly retains chemical properties of a given compound, but it does not live its own life.

Intravenous laser irradiation of blood (ILIB) has proved one of early effective techniques of laser therapy. Blood cells have a high conformation liability. They may be able of cooperative interactions, as to move in capillary vessels, they must deform very much (29). The ability of cooperation appears to explain the "fine tuning" of blood to monochromatic radiation in a broad range of wavelengths (3, 29).

There is a long way from an elementary (primary) photochemical reaction and full characterization of interaction of radiation with an object where it concerns the development of concrete information or medical devices. Description of the field in scattering, biologic system-like and other intricately structured environments is especially difficult. If an environment in which radiation spreads proves "alive" or photosensitive (as in holography), the situation is almost hopeless or solvable only experimentally. Description and study of so-called singular wave fronts (spiral, speckle and dislocation radiation beams) also remains an elusive problem; attempts of fractal description of such wave structures so far have not yielded solutions to the problem of obtaining fields with predetermined parameters. From the standpoint of classical (and quantum) electrodynamics, radiation-substance interactions are related to the presence of the dipole or a higher moment of substance and to a sufficient radiation concentration at the same site. That said, the wave field structure has to be known in the interaction area on the one hand and causes of the presence of the dipole moment be elucidated on the other. We shall define local intensities of field concentration as singularities of radiation and locations of the dipole moment as singularities or photosensitivity centers (PSC) of substance.

For instance, an equal distribution of the entire volume of substance singularities or PSC is sought when a medium is designed for photographic or holographic registration of information. This proves possible if PSC are macromolecules or their sites, as is characteristic for colloid detecting holographic media and, in a certain degree, for biologic objects. A kind of PSC can also occur naturally due to boundary layers of fluid, as it takes place near biologic

membranes or near the substrate on which a photosensitive polymer emulsion is placed. It should be noted that it was once proposed to consider the membranes as a main step in the mechanism of interaction of extremely high frequency radiation with living organisms (10), but no adequate regard was given to the role of boundary structures.

The use of terms and approaches from the photographic process theory (74) is convenient and appropriate for description of radiation interaction with complex objects. Over more than one 150 years of its development, photography science has generated empirical but practicable formalism such as sensitometric description of photosensitive materials and processes that is quite usable not only in holography but in biologic optics.

Singularities of an Object as Photosensitivity Centers.

Boundary layers and film structures. Physical properties of films significantly differ from those of volumetric specimens of the same substance because of influence of both the free surface and the film-substrate border on the process of film formation (30). Surface and border layers often have a far order of locations of oriented molecules (31). This results in the formation of oriented quasi-crystalline macro structures (32). It was experimentally demonstrated back in the 1930s that the oriented border layers form when there is contact of surface-active substances with a solid body surface. This circumstance is widely used in the Langmuir-Blodget technique of forming monomolecular layers of polar molecules on inorganic substrates for super high performance nanolithography (33) and for obtaining multimolecular layers (Y-films) (31).

Another example of real use of oriented border layers of organic fluids is lubrication processes (31). Studies in this area have shown that the first layer of molecules does not screen the force field of a solid body. However, orientation of molecules in the polar fluid plays the role of a trigger that organizes the orientation of further layers. A mechanism of this effect may be interaction of molecular dipoles, with the formation of neutral "chains" perpendicular to the surface of the contact. These considerations were the basis for the empirical polarization theory of de Bur and Zwicker (31). It showed how a local short-term effect spreads in a fluid by inducing dipole moments in adjacent layers to produce long-acting forces that cause the ordering of large volumes of the substance. Therefore, the fluid structure in border layers changes as compared to the volumetric one, and the higher are polarity and sizes of molecules dissolved in its the substance the more prominent is the change. However, border layers become a volumetric fluid at a more remote distance from the solid substrate, a phenomenon that needs an adequate description.

5. The Theory of Boundary Structures

A. A classic approach based on the theory of fluids

The possibility of theoretical evaluation of the heterogeneous fluid structure near the surface is related to finding a solution to a joint system of equations for one-particle and two-particle distribution functions; moreover, there are several initial equivalent precise systems of equations (34). Their use even for simple systems of spherically symmetrical molecules requires huge efforts (35, 36). The task can be made simpler if the usual two-particle distribution function is used in the equation for the density profile instead of anisotropic two-particle function. Such a procedure is not uniform. Different initial systems of equations and simplification methods can produce different singlet equations for the density profile, preciseness of which can be assessed only by final results.

The most common approach is to review a two-component blend in which the size of one of components becomes as large as it may. In this case the function of distribution between the two components is considered at zero concentration of this component as a one-particle function of distribution of the non-zero component near the surface. Analysis of existing singlet approximations suggests that all singlet equations are satisfactory at small and medium densities (37). However, the situation changes at high densities. Physical solutions are available only for singlet equations obtained from the integral form of precise equations for one-particle and two-particle distribution functions (38).

Evaluation of the dipole system structure in a volumetric case and especially near the surface is difficult because of a complex orientation relationship to potential of interaction between molecules. Use of integral equations in a mean spherical approximation in studies of the volumetric structure of dipole solid spheres have yielded a semi-analytical solution in which the angular relationship of distribution functions is presented as certain combinations of trigonometric functions. This solution can be improved by using other versions of the Ornstein-Zernicke equation. Its presentation as a degree series of the dipole-dipole interaction parameter has been reported to be a convenient solution for analysis (39). It allows separating angular and radial variables on the one hand and obtaining a relationship of distribution functions to dipole moments on the other.

The presented approach, which also reviews dipole solid spheres near the solid surface (36, 40), differs in the following respects:

1. It relies on a singlet equation that follows from the integral form of the precise equation for one-particle distribution function (38, 39). However, this equation has a physical solution for dipole-free near-surface solid spheres at densities higher than $\rho = n\sigma^3 = 0.75$. (Here n=N/V is numerical density and σ - diameter of the sphere).

2. A solution for one-particle distribution function is sought as a series of dipole-dipole interaction, as it has been done for two-particle spatial distribution function (14).
3. Calculations were limited to the third-order in the dipole-dipole interaction parameter.

It should be stated that a major goal of theoretical analysis is obtaining solutions that are convenient for evaluation and description of peculiarities caused by effects of the solid surface on a dipole system. Apart from theoretical implications, evaluation of the systems with the dipole-dipole interaction is important for analysis of the structure of real fluids, as the presence of an orientation part of the interaction potential is characteristic of most of real molecular fluids. Similarly, evaluation of a heterogeneous system is important for an understanding of properties of fluids near solid body surfaces, the interaction of colloid particles and behavior of small volumes of fluids.

The presented approach in fact is one of versions of the thermodynamic theory of perturbations, and it certainly has all of its limitations, but it allows at least a qualitative assessment of structural and orientation effects. This approach is actually precise for weak dipole systems. This approach has a sufficient generality and is applicable in describing various bound-disperse systems in which phases cannot move freely, as they are structurally bound, for instance, in a gel system. This formalism is also usable for describing a broad class of structural-boundary events such as a phase transition of the melt crystal in a two-component system, calculation of quantum factors of pressure on phase equilibrium curves, Lennard-Johnson fluid crystallization and influence of the structure of the perimembrane water on laser biostimulation (40).

B. A Quantum-Mechanical Approach

In the physics of the condensed state, the intermolecular interaction is included in the Hamiltonian as scattering amplitude in the Born approximation. This leads to the need of interaction re-normalization. The method of temporal Green function allows calculating only a spectrum of elementary excitations through prescribed energy of the basic condition that determines initial conditions for the Green function series. The basic state energy is determined by diagonal matrix elements of the Hamiltonian. The intermolecular interaction enters the Hamiltonian as scattering amplitude in the Born approximation.

The Born approximation is not directly applicable for real potentials that are complete with intermolecular repulsion. Therefore, there is the need for interaction re-normalization in order to make the theory of perturbations usable. However, the physical sense of re-rating constants remains obscure. It is useful to proceed to a formulation that would initially contain an intermolecular interaction potential,

and not the scattering amplitude. Thermodynamic values could be thus calculated without resorting to the theory of perturbations.

Therefore, fluids have to be considered as quantum objects, with account for a strong intermolecular interaction. The system of strongly interactive fermions and bosons can be described using Wigner *l*-particle functions. The simplest of these is the two-particle function $F_{12}(\boldsymbol{r_1}, \boldsymbol{p_1}, \boldsymbol{r_2}, \boldsymbol{p_2})$, where $\boldsymbol{r_i}, \boldsymbol{p_i}$ are coordinates and impulses of particles. The particle impulse-averaged function $< F_{12}(\boldsymbol{r_1}, \boldsymbol{r_2}) >$ is the radial distribution function, i.e. the probability density of finding two particles at points with coordinates $\boldsymbol{r_1}, \boldsymbol{r_2}$. The set of *l*-particle Wigner functions is described by the infinite Bogolyubov equations. The development of methods for solving such equations still remains an important task. The difficulty of solution is related to the need for taking into account quantum and classical correlations. The latter subside with scattering much slower. For this reason analysis is usually limited to an ideal quantum gas, or the intermolecular interaction is considered using secondary quantization within the framework of the Born approximation. As the Born approximation is not applicable for systems with real intermolecular interaction potentials, there is the need for potential re-normalization.

The question is at which stage the re-re-normalization should be performed. The Wigner formulation of statistical mechanics provides such a possibility. Equations for Wigner distribution functions (particle matrices of density) contain the intermolecular interaction potential. The evolution of functions in time is described by an infinite chain of equations similar to the equation chain for Green functions. The equation for one-particle Wigner function has been long considered wrong, as it does not describe the quantum oscillator. For this reason the Wigner presentation has not found broad use. It was found out later that the equation for one-particle Wigner function should be supplemented by an "evolutional" equation that should correctly consider initial conditions. This circumstance is important for calculation of the elementary excitation spectrum. However, this is irrelevant for calculation of the basic state energy, as the energy is determined through equilibrium solutions. Therefore, we propose making a basis of the theory a chain of equations for thermodynamically equilibrated Wigner functions with particle density as an independent variable.

It has been accepted until now that the solution of equations for an equilibrium chain is of no interest (and it has not been described in the literature), as the basic state energy can be found only in the theory of the normal fermi fluid of Landau. However, the Born approximation is used in such calculations. Therefore, the offered approach will remove the limitations related to the Born approximation. Namely, we propose considering the equation for $< F_{12}(\boldsymbol{r_1}, \boldsymbol{r_2}) >$ in a pair collision approximation. In this case, there is a closed equation for $<F_{12}(\boldsymbol{r_1}, \boldsymbol{r_2}) >$ that is solvable analytically. Potential re-normalization should be carried out just in this solution. After this procedure, a generalization for systems with

arbitrary density is obtainable similarly to the classical equation of Ornstein-Zernicke.

As a result, classical and quantum systems can be described on the basis of single formalism using the radial distribution function giving the near order to fluids. This approach allows describing thermodynamic and structural parameters in quantum gases and fluids, including phase transitions, through prescribed the density, temperature and intermolecular interaction potential.

The Mechanism of Biologic System Photosensitivity.

Analysis of laser biostimulation in terms of modern physical concepts leads to the conclusion that, firstly, the process contains numerous different mechanisms of effects of coherent radiation on biological systems and, secondly, the laser biostimulation process should be considered as a self-organizing dynamic interaction of an open, statistically non-equilibrium biosystem with coherent radiation, which in turn warrants that the interplay of dynamic and informational aspects of the behavior of complex systems should be taken into account.

A major feature of biochemical processes in cells is their electron conformational or matrix nature (20). Changes in the conformational state of macromolecules, for instance, their "folding" or unfolding need little energies, but they lead to a significant variability of their catalytic activity. The known models of enzymatic catalysis, such as key-lock, rack and protein-machine, are based on the need for complementarity of conformation states of a substrate and an enzyme. The limited resource of biomacromolecules in a cell and the need for maintaining in a prescribed conformational state of a sufficient amount of macromolecules for life have resulted in the emergence in the evolution process of a special mechanism of selection or conversion of molecules to a necessary conformational state. In terms of laser physics, this mechanism may be considered as a "pumping" system determining statistical non-equilibrium of the entire biosystem. From the quantum mechanical point of view, this lack of equilibrium may be seen as a determinant of the coherent state of biological substance and systems (12, 24).

Boundary layers and structures in laser biostimulation. Sandwich structures of dipole fluids near biologic membranes are spatially coordinated with the self-organized Talbot field of laser radiation in the biotissue (43). Integral equations for the water density profile near the membrane surface can be obtained from the Bogolyubov-Born-Green-Kirkwood-Yvonne equations. The structure of the dipole system of a heterogeneous fluid near the surface can be described in the presence of a complex orientation relationship of the intermolecular interaction potential. The alternation of dipoles with different predominant orientations near the membrane exerts an influence on both folding-unfolding of protein molecules and

on their sensitization to electromagnetic radiation. This structural organization of the perimembrane fluid does not allow considering laser biostimulation as a thermodynamically equilibrated process, but warrants the use of the open system theory of statistical physics. For this reason the interaction of laser radiation with biostructures in general is a self-organizing process of non-adiabatic perturbation of the membrane - bound water - biomacromolecule system, and it influences primarily the effectiveness of synthesis of new biomolecules (44).

6. The Structure of Perimembrane Water

If the cell is considered as an elementary biological object, natural receivers of radiation are cell membranes whose function is determined by their role of "boundary structures" ensuring selective permeability of cells to substances and the cellular response to milieu conditions. Bioregulatory functions of membranes are reception of external impacts at some local site and transmission of such impulses to the entire membrane surface. After this, an intracellular mechanism of response to the external influence is activated.

The structural bulk of membranes is a lipid bilayer that consists mostly of phospholipids (70-80% of all membrane lipids). The phospholipid molecule looks as follows: a polar part - a radical – and an incomplete two-chain hydrocarbon tail.

Fig. 4. Schematic representation of the phospholipid molecule: a polar radical and a terminal double hydrocarbon chain.

In the water environment, such molecules form thermodynamically stable structures where non-polar hydrocarbon chains are not in contact with the water environment and form a hydrophobic area, while polar ends make a hydrophilic surface interacting with the water.

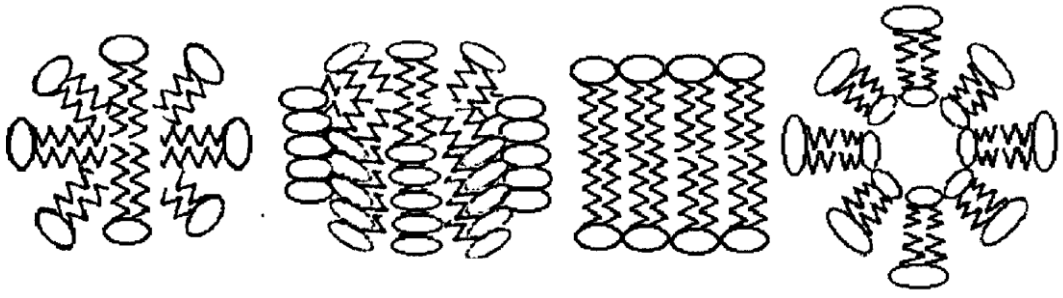


Fig.5. Some structures formed by phospholipid molecules in the water environment as a result of hydrophobic interaction.

Lipid molecules are able of rotating around their axes, moving into the bilayer (at a linear velocity of 5-10 mcm/s) and coming from one monolayer to another (the time of semi-transition is a few hours). Therefore, the bilayer is dynamic and maintaining short-range interactions between lipid molecules.

However, the membrane is on the whole characterized by stability and remote action, when a local external perturbation is transmitted to a significant distance along the membrane surface (46).

For this reason a membrane model has been proposed, in which the regulatory role of the membrane is determined by coexistence of two structurally separate, but functionally related matrices: of a dynamic two-dimensional lipid bilayer and a stable three-dimensional protein carcass ensuring long-range interactions.

This model provides an explanation for the vector pattern of membrane processes, the formation of short-lived complexes and the prominent features of cooperation of membrane elements, which is very important in biologic control processes.

It is accepted that a primary event in biologic regulation is interaction of an external impulse (a photon, a signal molecule) with a specialized protein receptor on the membrane surface. In the formed complex, protein makes a conformational transition at the level of a tertiary structure (a second-order transition), i.e. a local structural change of the membrane occurs.

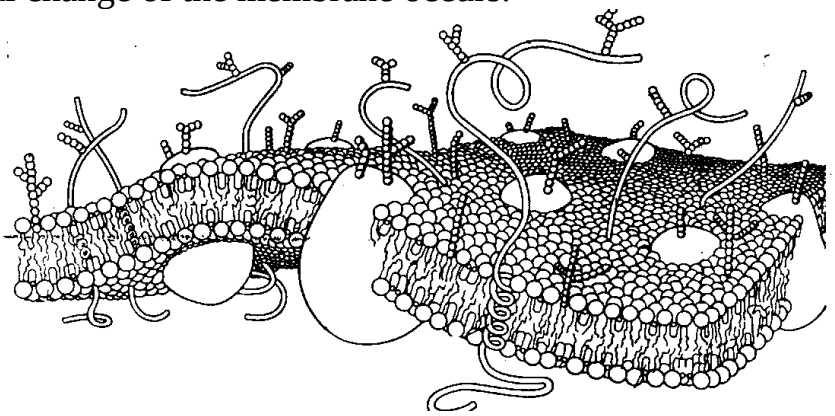


Fig.6. The lipid bilayer with inbuilt globular protein complexes producing a rigid membrane carcass as a result of interaction.

Perturbation is generalized on the whole membrane that is considered as a cooperative system maintained by protein-protein, lipid-lipid and protein-lipid interactions with participation of the water. After the cooperative readjustment of the membrane, its functional activity and, as a consequence, the state of the cell abruptly changes (43).

The spread of the structural perturbation over the membrane surface is probably related to the presence of the structured water that has a quasi-crystalline or ice-like structure strongly dependent on surrounding biomolecules. The water can structure itself in two ways in perimembrane areas - by binding near the lipid bilayer surface as a boundary surface and by structuring along the macromolecule's chain. If the molecular system has an internal cavity (which is possible in the case of globular protein), the water can structure within the cavity (45).

A statistical consideration based on Bogolyubov-Born-Green-Kirkwood-Yvonne equations can be used for description of fluid behavior near the boundary surface (36). Two distribution functions are introduced for a spatially heterogeneous system: $G_1(z)$, which depicts the profile of local fluid density, and $G_{12}(r_{12}\ z_1\ z_2)$, which describes correlations between particles and between particles and the surface, where r_{ij} is the distance between centers of particles i and j, and z_i the distance from the i-th particle to the surface. The boundary condition is an off-wall transition to the voluminous fluid:

$$z_1\to\infty,\ z_2\to\infty\ \lim G_{12}(r_{12}\ z_1\ z_2)= G^0_{12}(r_{12}).$$

Two terms are used for calculation simplification:

1) the term of the thermodynamic limit (concentration constancy with $N\to\infty$, $V\to\infty$ $n_v=N/V=\text{const}$.

2) the term of singlet approximation when not anisotropic function $G_{12}(r_{12}\ z_1\ z_2)$, but its boundary value for a volumetric fluid $G^0_{12}(r_{12})$ is used.

This yields a solution for local density distribution function which is parametrically related to the concentration and which allows expressing macroscopic characteristics like surface tension and adsorption.

A statistical consideration of thin films can be used for describing water structuring along the macromolecule chain (36). The thermodynamic boundary condition is not fulfilled for them, and density is $n=N/SH$, where S and H are respectively the surface area and film thickness. The singlet approximation does not work in this case either, but a generalized singlet approximation is introduced (an assumption that solid surfaces do not influence two-particle correlations in the fluid). The function $G_{12}(r_{12})$ is used to describe a certain hypothetical volume fluid with a density coinciding with film density. Resultant ratios allow calculating all structural characteristics of thin films. The ratios yield correct boundary transitions to a spatial fluid off the wall ($H\to\infty$) and to a two-dimensional fluid in the presence of the disappearing film thickness ($H\to0$).

It should be stated that the local structure of the water near the chain of macromolecules is strongly dependent on their forms. In addition, the dipole moment of the fluid should be taken into account. Therefore, consideration of water structuring only in the framework of this description is insufficiently correct. Studies of near-surface structuring of dipole fluids and of structuring

specific for the shape of an object are available, and their results are expected to be used in the evaluation of water structuring near biomembranes.

As concerns the role of the water in biologic regulation processes, it provides for near-membrane phase transitions with layering (45). Elementary carcasses of water molecules are categorized into two radically different types - ice and clatrates.

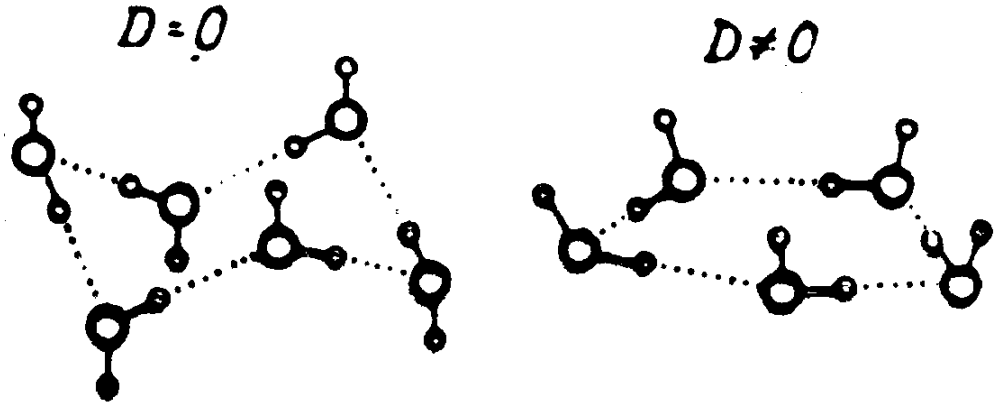
Fig. 7. Protein structures: (I) - the monomer sequence of protein (amino acids); (II) - in this case alpha is a helix produced by the "twisting" of the amino acid sequence; the tertiary structure (III) - spatial conformation (linear or globular) of the alpha helix.

Specific carcass shapes can be quite diversified within each type, and this makes phase transitions with layering possible. Such transitions in the perimembrane area occur with a radical change in the pattern of water molecule links with biomacromolecules, i.e. they are related to near-range restructuring. In general, water binding to macromolecules results in change of the configuration, effective size and properties of particles. Therefore, any variability of the structure of the hydrate membrane modifies the state of the biomolecule.

A flexible behavior of layering solutions, their high sensitivity to external effects and a significant influence of some substances on stability of the water bound to biomolecules have been reported. (Stabilization of such complexes occurs as an increase in the temperature of their degradation.)

For this reason, it has been proposed that a phase transition with layering may be considered as one of mechanisms of the perturbation transfer along the membrane surface (45). The phase transition with layering in the bound water - biomolecule system can produce two situations. First, layering in this complex means abolition of the biomolecule from the solution, i.e. a stop to the biochemical reaction with participation of this substance. Second, the water structures itself on the biomolecule surface so as to maximally compensate for local charges and dipole moments of the macromolecule. Therefore, layering means the onset of an extreme non-equilibrium state of protein. As it returns to equilibrium, the nearest environment of protein can locally alter, which is perceived by the membrane as a structural perturbation. Perturbation along the membrane becomes generalized, initiating a similar conformation transition that triggers a chain of biochemical reactions in the cell.

Therefore, the interpretation of the water as a structured dipole fluid is rewarding it terms of description of biologic regulation processes in the cell. The phase transition with layering may be viewed either as a process of reception of an external influence or as a mechanism of impulse generalization spreading from one site to another due to cooperative features of biologic membrane elements.



1- ice 2 - clatrate

Fig.8. Two major forms of structured water carcasses

7. Sensitometric Criteria of Blood Photomodification Degrees

Effects of biostimulation by intravenous laser irradiation of blood (ILIB) have been delineated, and this methodology has found extensive use, but mechanisms of its action remain uncertain. On the one hand, laser radiation is known to alter the conformation state of hemoglobin molecules, enhancing the effectiveness of oxygen metabolism in the body. On the other, laser radiation stimulates the intensity of capillary circulation, which cannot be explained by change in the state of macromolecules alone, since cooperative interaction of erythrocytes and vessel walls is essential (it is known that sizes of non-deformed erythrocytes are larger than diameters of capillaries) (29).

One of important and unsolved problems in the medical use of lasers is dosimetry of light energy absorbed by the biotissue and quantitation of laser effects, desirably in terms of physically measurable values. At present, results of ILIB are evaluated in practical health care by biochemical blood tests before and after irradiation. Proceeding from results, an energy schedule of the laser therapy course is determined for an individual patient. The literature presents numerous guidelines of this kind, but their physical and methodological validity is doubtful, at least where they concern metrological accuracy of the absorbed light energy dose, and they do not give even a minimal quantitative description of the time dynamics of ILIB. Besides, published evidence is very difficult to interpret because biochemical parameters of blood are related to numerous individual factors and test methodologies vary with researchers.

Properties and Composition of Blood. Blood is a liquid body tissue in which cells are freely suspended in a liquid environment. The liquid portion of blood – plasma - has relations with all organs and tissues, and it shows biochemical and biophysical processes occurring in them. The quantity of blood in the human body is normally 1/13 to 1/20 of the bodyweight (3-5 liters). The blood color depends on the oxyhemoglobin content: arterial blood is bright red (rich is oxyhemoglobin), while venous blood is dark red (poor in oxyhemoglobin). Blood viscosity is five times higher than water viscosity. Blood has 80% of the water, 1% of inorganic substances (sodium, chlorine, calcium) and 19% of organic substances. Blood plasma contains 90% of the water. Its specific weight is 1030, which is lower as compared to that of blood (1056-1060). Blood as a colloid system has colloid-osmotic pressure, i.e. it can retain a certain amount of the water. This pressure is determined by protein dispersity, salt concentration and the presence of other admixtures. Colloid-osmotic pressure is normally about 30 mmHg (2940 P) (50).

Formed elements of blood are erythrocytes, leukocytes and thrombocytes. The formed elements make an average 45% of blood. The proportion of plasma in it is 55%. Erythrocytes are enucleated bodies made up of membranes, liquid hemoglobin, protein and nucleoproteins. Erythrocyte membranes consist of lipids (cholesterol and lecithin). The red blood cells have a significant deformability. They probably can elongate as they squeeze through capillaries and regain initial shapes. On leaving capillaries, venous blood contains blood cells of larger volumes (because of their swelling rather than an increase in numbers). Hemoglobin normally makes about 95% of the solid mass of an erythrocyte and 13% of the total weight of blood. Normal hemoglobin values vary with nutrition patterns, weather conditions and places of residence.

Leukocytes are colorless nucleated cells. The number of leukocytes is usually 800 smaller than that of erythrocytes. Body areas have different numbers of leukocytes. Dilated vessels contain more leukocytes as compared to constricted ones because the blood flow is slower in such vessels. Leukocytes move mostly near walls of blood vessels (51).

Functions of Blood. Blood comes in touch with body tissues through capillaries and supplies them with oxygen, nutrients, water and even heat, and carries away metabolic waste, CO_2, lactic acid, etc. Red blood cells carry gases; with the help of hemoglobin the erythrocytes take oxygen from the alveolar air and transport it in blood vessels (50, 51).

Oxygen is bound to hemoglobin in the form of unstable oxyhemoglobin. Passing through tissues, hemoglobin loses the ability to bind oxygen in the presence of carbon dioxide entering the blood from tissues. Oxygen leaves

erythrocytes and dissolves in plasma to be absorbed by body tissues. Carbon dioxide partially binds to plasma bases and is partially carried by blood to lungs to be eliminated there.

The vascular system is a transport network of the body connecting all its parts and supplying them with blood. It includes the heart - a muscle pump propagating blood through multiple tubes that are called blood vessels, and arteries that are vessels through which blood flows from the heart to tissues and organs. Veins are vessels by which blood returns to the heart. Blood flows from arteries and veins through tiny vessels called capillaries. Properties of blood vessels are almost entirely determined by the structure of their walls. Arteries have elastic muscle walls, while walls of veins are more flaccid, and their diameters are larger. Capillary walls are very thin and made up of one cell layer.

Dynamics of Blood. Blood of large vessels may be considered as a Newtonian fluid, i.e. a fluid subordinate to hydrodynamic laws of movement (51). The blood flow is accepted to be laminar and homogeneous. However, ramification of large vessels into smaller vessels can produce gaps and boundary fields, and the blood flow becomes turbulent. In physical terms, blood is a mixture of fluids with different viscosity coefficients. The viscosity coefficient of the whole mixture is related to percentages of its components. On the other hand, blood moving in round channels may be defined as a suspension, a fluid with suspended particles whose sizes are much smaller as compared to the diameter of the tube. The flow of such a suspension has a remarkable property: the suspended particles are absent from a narrow area near tube walls. This phenomenon is called a parietal effect (52). The flow of the mixture with a random distribution of the concentration of a more viscous fluid can meet physical laws of preservation, but a flow with the parietal effect establishes after all. The concentration of the fluid with a higher viscosity is actually zero near walls of the tube and maximal around its axis. The parietal effect explains a decrease in blood viscosity that is observable during intravenous laser irradiation of blood simultaneously with an increase in geometric sizes of cells due to their more effective oxygen uptake. This circumstance confirms the need for laser irradiation of just larger vessels, as a decrease in blood viscosity in capillaries is not achievable. However, it is a key factor in the treatment of diseases like myocardial infarction.

The Capillary System. Diameters of capillaries vary from 4 to 5 mcm, and their total length is an estimated 100,000 kilometers. Therefore, the capillaries make a huge area in which transport metabolism occurs. The capillaries form an orderly system of microcirculatory pathways ensuring the incessant movement of blood near cells and tissues, where metabolic mechanisms take place, without which the life of tissues would be impossible.

Studies of capillaries have shown that the organization of the microvascular network rests on the collective functioning of capillaries, in which the blood flow follows different laws than in large vessels. Therefore, specificity of many rheologic phenomena in capillaries is determined by the fact that their sizes are comparable with sizes of blood cells that move in them. This prompts the need for analysis of properties and the behavior of cells in capillaries.

The effect of abnormally low friction of blood in capillaries during periodical impacts of pulsed tension is determined by the formation of so-called wave packages of blood cells. In particular, this effect occurs because of a larger gap between the structural block during their "physical pendulum" movement and the appearance of superficial deformation waves of a soliton type on surfaces of blood cells. Characteristics of the soliton waves conform to the relief of surfaces interacting within a wave package of blocks. Pulsed tension induces the packing of these packages into a structure similar to the spiral flow at the funnel inlet. This suggests that apart from the blood flow, the presence of pulsed tension is a necessary mechanism preventing the turbulent flow of blood in vessels (29).

Histologically and physiologically, the circulatory bed is made up of compartments (modules) that are relatively separate in structural and functional terms, which provides equal conditions for blood delivery to numerous capillaries of an organ. This produces functional cooperation of the capillaries not only with adjacent tissues but also with adjacent minor vessels that determine the regime of capillary hemodynamics (29).

It may be presumed, therefore, that if the system ensures equal conditions for blood delivery to capillaries, it can be described as a polymeric macro crystalline structure. The structural organization of cellular aggregates rests on a certain probabilistic principle, which is minimization of potential energy of structural units. A principle of hierarchic subjugation, or interaction of regulating systems, thus works. Cells maintain interactions in two ways: with the help of hormones that act at a distance and by contact, mostly based on the phenomenon of cellular polarization (29).

The boundary between macro- and microcirculation appears to have a key role in the mechanism of the blood supply in the body. Capillary walls consist of one layer of cells and have no smooth muscle cells. There are narrow gaps between the cells in the layer. Owing to this structure, capillary walls are highly permeable to the transport of gases, water and substances. Surfaces of many cells are covered by microvilli, whose breadths vary from 50 to 100 nm and lengths from 90 to 1,000 nm. The blood flow produces undulating movements of the microvilli. They capture plasma droplets and give rise to vacuoles and micro vesicles that are submerged in the cytoplasm. The microvilli substantially enlarge the total exchange surface of the endothelium and thereby are actively involved in the transport of substances (29).

The transport of substances is based on two processes: transcapillary diffusion exchange of molecules induced by the difference of concentrations of substances across the capillary walls, and the movement of the fluid (convective transfer of substances) induced by hydrostatic and oncotic pressure. The rate of exchange through the capillary wall by diffusion is about 200 times higher as compared to exchange by filtration. Blood gases and partially the water freely diffuse through endothelial cells, but most of the water and substances dissolved in it go through endothelial gaps (29).

The exchange process occurs as follows. Heart muscle contraction produces blood pressure; as a result, the water and nutrient substances dissolved in blood pass through the gaps. However, the size of a blood cell like the erythrocyte (8-10 mcm) is about two times the diameter of the capillary. For this reason there is no conclusive evidence of mechanisms of erythrocyte passage through capillaries. According to one of hypotheses, erythrocytes make stacks like coins and propel though capillaries like a plunger.

Causes of Photosensitivity During Intravenous Laser Irradiation of Blood (ILIB). Spectral studies have demonstrated that at the macromolecular level, blood components have no prominent absorption maximums at wavelengths that are used in ILIB (17). The approach accepted in physics of polymeric holographic detecting media (53) suggests that apart from iron ions of hemoglobin, biologic macromolecules and their ensembles with a dipole moment different from zero, or with a spherically asymmetric conformation state, can act as centers of photosensitivity during ILIB (42). Different types of interaction of blood elements with each other and with capillaries and larger vessels can determine the latter. Therefore, its may be said that photosensitivity during ILIB is related to systemic factors, and has a fractal or hierarchically organized structure both in terms of the mechanism of interaction with coherent radiation and the amount of energy and spectral photosensitivity.

Structural elements may be categorized in the order of diminishing photosensitivity (which is inversely proportional to threshold energy of stimulation of the entire vascular system of the body. An approximate spectral sensitivity range presented below is parenthesized.

- Aquatic complexes of blood cells and vascular walls (the extremely high frequency and far infrared spectrum) (10);
- Collective water modules and aquatic complexes of protein macromolecules (medium and near infrared) (47);
- Shapes of membranes of erythrocytes and other blood cells with a quaternary structure of protein macromolecules (the infrared and visible spectrum) (17);
- Tertiary and secondary structures of protein macromolecules like hemoglobin (the visible spectrum) (17);

- Iron ions in hemoglobin (blue-green visible);
- The primary structure of protein macromolecules (ultraviolet).

This categorization certainly is not all-embracing, but it is consistent with a classification of structural types of protein macromolecules known in biophysics (17).

ILIB Sensitometry. Having outlined the mechanism of vascular wall photosensitivity, it is logical to use a sensitometric system of presenting blood interaction with laser radiation that is broadly adopted in the theory of the photographic process (74).

One of studies has examined effects of laser photomodification of blood using spectrometry of patient blood samples obtained before and during ILIB at different intervals, with the presumption that curative effects of ILIB were not related to the action of light on vessel walls (49).

The results of this study provide an initial glimpse into dynamics of the ILIB process.

The methodology of pretreatment spectral examination. The absorption spectrum of whole venous heparinized blood was examined before and after ILIB. A 2-3 ml blood sample was obtained from a peripheral vein with a heparinized syringe, and a single-fiber light guide with an irradiating cone was introduced into the blood flow. The venous blood samples were diluted with 1 ml of blood; 5 ml of an isotonic sodium chloride solution was added and then 54 ml of distilled water. The resultant 1:60 sample was placed in the cuvette of a Specord spectrophotometer and absorption spectra were recorded at 400 to 800 nm. After an ILIB treatment, 2-3 ml of venous blood was repeatedly obtained with a heparinized syringe, a 1:60 sample was made and absorption spectra were recorded (49).

Sensitometric surfaces. Changes of spectral characteristics of blood during ILIB using a helium-neon laser with an optic fiber output power of 2 mW during one treatment demonstrate the pattern of laser photomodification of blood shown in Figures 9 and 10. These graphs describe changes in blood sample spectral transmission at different radiation wavelengths in relation to irradiation energy. Irradiation energy is defined as a product of radiation intensity (2 mW) and the exposure duration.

Absorption values at a 633 nm wavelength did not alter much in samples from normal subjects and patients, as can be seen in Figs. 9 and 10 (a,b). On the whole, ILIB changed the functional type of the blood transmission spectrum - an initial spectrum with two absorption maximums (Fig. 9). It should be noted that the pre-ILIB spectral transmission surface in Fig. 19 (a,b) shows a smoother configuration.

Since wavelengths correspond to different energies in blood absorption spectrums, which in turn may be related to energies of reactions in blood macromolecules, the following conclusions can be made:

1) Laser blood photomodification using λ=0.63 mcm wavelength does not induce chemical reactions, but leads only to conformational changes of molecules;

2) Blood photomodification occurs as photo transfer of the electron, as it does in layers of dichrome gelatin (53). In other words, a light quantum with the wavelength of 0.63 mcm knocks the electron from a molecule by an internal photo effect, e.g. from a hemoglobin molecule, which results in a change of the charge architecture of protein of the whole macromolecule. The latter entails the transfer of the conformational state of the macromolecule. With an increase in absorption energy, this enhances the motility of the entire macromolecular chain and facilitates, after the end of ILIB, the return of the molecule to a native normal state during relaxation (Fig. 10);

3) the ILIB process should be monitored at a 725 nm wavelength at which absorption changes are most conspicuous.

In summary, the proposed new way of presenting ILIB data as sensitometric surfaces in coordinates (T-λ-lgE (0.65) allows interpreting the phenomenon of laser blood photomodification as a combination of conformational changes of hemoglobin macromolecules resulting from a primary electron photo transfer reaction.

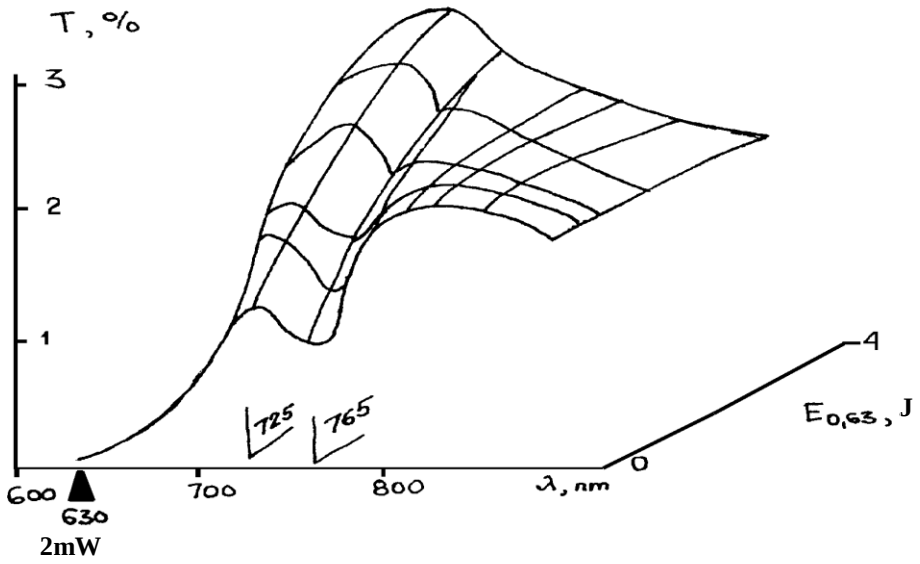
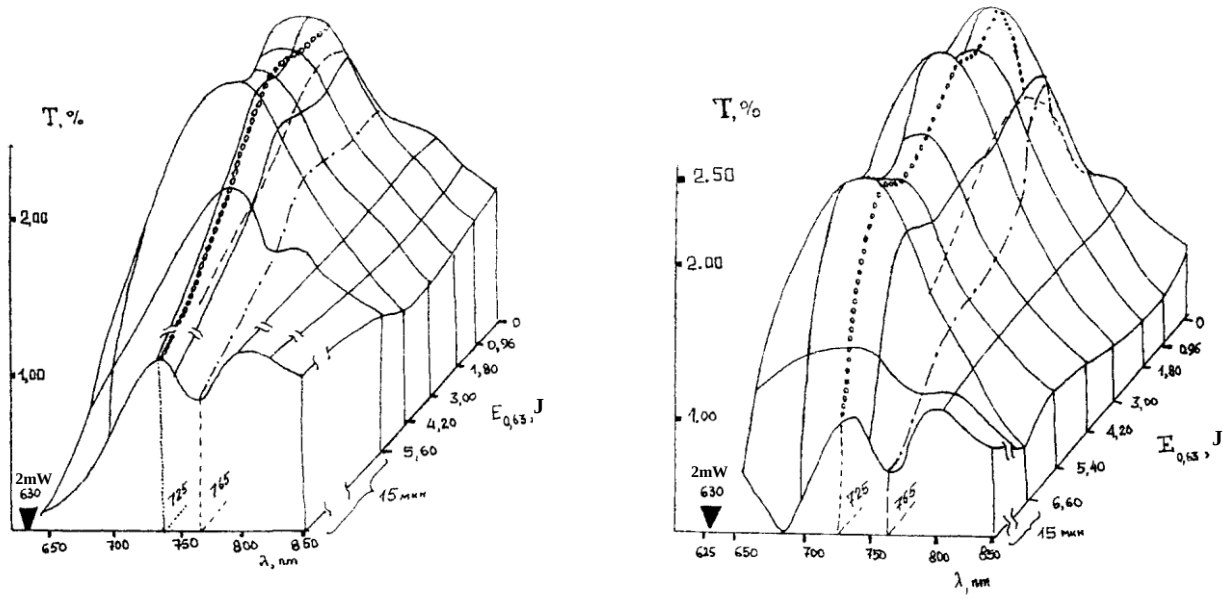


Fig. 9. Change of spectral transmission at different wavelengths in blood samples from normal subjects in relation to irradiation energy.



a) b)

Fig. 10. Change of spectral transmission at different wavelengths in blood samples from a) patients with the ischemic heart disease, b) diabetes in relation to irradiation energy.

8. Statistical Physics of Biologic Systems

A common property of living systems is their non-equilibrium and being not closed to the environment. This determines their negentropy that is described in terms of non-equilibrium thermodynamics (5). The basis of living organisms are biopolymers, proteins and nucleic acids - biologically functional substances with a high conformational flexibility providing for a broad range of conformational states of macromolecules and their transitions at low energy costs (5, 54-56).

In theory, a biologic macromolecule can have a very large number of configuration states without changing its primary chemical nature. However, being within a cell, the macromolecule does not have such a broad range of configuration states because of several restrictions (15). Firstly, these are topological restrictions - for instance, self-intersections of a polymer chain must be absent, as one of its stretches cannot cross another. Secondly, there are spatial restrictions, such as the presence of the cell membrane. Since a particular macromolecule is involved in a variety of biochemical and biophysical processes in vivo, restrictions are imposed on its possible configuration states by adjacent macromolecules and by interactions between its own polymer constituents. Finally, there are restrictions on resources of biochemical reactions within the cell or the organism, resulting in important feedbacks in the temporal organization of

biologic processes (57). These restrictions determine discretization of the energy spectrum of the macromolecule or quantization of its states, an event occurring at energies of in vitro conformation transitions in the range of 10 to 100 kJ/mol (3). Comparison of these values to radiation energy at 0.63 mcm, which is equivalent to 194 kJ/mol, or at 0.87 mcm, which corresponds to 136 kJ/mol, suggests that laser initiation of these conformational transitions is possible. In reality, in vivo energy required for a conformational transition may be still lower because of the above-mentioned restrictions. A change in the conformational state of the macromolecule can alter its biologic activity and, therefore, the course of biochemical reactions in cells and in the organism (55, 56).

In the framework of the statistical physical approach, a larger length of a macromolecular polymer chain makes it presentable as a cloud of quasi-monomers (15), as each segment is in a "standard" surrounding of others, mostly of adjacent polymers. This standard environment causes change of properties (the mass, charge, etc.) of each segment, to re-emerge in the theory of the spatial macromolecular interaction as an independent quasi-particle whose characteristics differ from those of the real initial polymer segment. According to the scaling concept (15, 18), finding a polymer macromolecule in a spatially limited area, for instance in the cell, provides a possibility of adopting the notion of the macromolecule's blobs or domains that also have properties of quasi-particles (17) (Fig. 11). Physically, the definition of the blob spells that polymer segments do not "feel" the restrictions imposed on the whole polymer chain when they are in an environment that is smaller than, for example, the diameter of a tube in which a macromolecule is placed, and these segments remain in an unperturbed, native state.

Fig. 11. The macromolecular polymer chain as a system of blobs (a) and domains (b), and an example of the domain structure of a dimer fragment of gluthatione reductase (c) /17/. Each subunit consists of three domains: one attaches FAD (flavine adenine nucleotide), the other NADP (nicotinamide adenine dinucleotide), and the third makes the interface. The dotted line shows the general course of the polypeptide chain. The FAD and NADP cofactors are attached in elongate configurations. The substrate glutathione (GSSG) is located between subunits. Four domains form each active center.

The above considerations show a possibility of including in analysis of laser biostimulation (LBS) the notion of quasi-particles whose properties may radically differ from real, native biomacromolecules. This circumstance also explains the variability of LBS results in vivo and in vitro.

Furthermore, conformational states of macromolecules may have a different structure of their water environment. In physical terms, such systems have a liquid crystalline structure showing a wide range of conformations of biomacromolecules and hydrate envelopes associated with them. Therefore, effects of laser radiation on a biologic system are related to photo initiation of microstructural readjustments in such liquid biologic environments (3), the mechanism of which is described as an electronic conformational interaction (5). In this case, the mechanism of laser treatment may be interpreted as consisting of a primary photochemical reaction with electron transfer (59) in a macromolecule with a subsequent conformational change of the associate that is made up of the macromolecule and its hydrate environment.

Another name for these events and their consequences is the syndrome of structural alteration of biologic fluids defined as transformation of body tissues and liquid media, stable structural changes of body fluids occurring both locally at the site of laser irradiation and in fluids that are not exposed to direct irradiation (60).

The conformer will be further referred to as a certain conformational state of an associate consisting of one or several biomacromolecules or of their parts in combination with water molecules interrelated with them. It should be stated that the definition of such associate, which retains properties of the whole organism at a micro level and is a "true molecule" or quasi-particle of the biologic system, is a non-trivial physical problem. Properties and parameters of such an associate are in particular determined by the environment of the biologic system - boundary conditions of the considered task, which is confirmed by results of in vivo and in vitro studies. Also, developing a general dynamic theory of LBS effects is complicated by a possibility of mutual conversions of different quasi-particles, the conformers, and of their conversion to solitons, excitons, polarons and other quasi-particles. Nevertheless, a general description of the LBS process can be given using results of the open system statistical theory (14).

As it has been stated, the matrix and stereochemical pattern of biochemical reactions requires a mechanism of "selection" of necessary conformational states of molecules. The mechanism may be considered as the formation of population inversion of energy levels and as an analogue of laser pumping system. Formal theoretical similarity of organisms with another open quantum-radiophysical system, which is the laser, has been reported (61). A defect or "disease" of the cell results in a decline in the effectiveness of such "pumping" to subthreshold values, an event describable as thermolysis - a molecule transition to a Boltzmann equilibrium of thermal energy distribution. If the definition of the negative effective temperature is used for describing inverse conditions (62), the cell "disease" is consistent with a transition from "high negative figures" of the temperature to "low" ones that are described by standard statistical physics of equilibrium systems.

The equilibrium system statistical theory is not suitable for describing biosystems because the number of controllable freedom degrees in the equilibrium Gibbs ensemble is very small and uncertainty of definition of micro conditions in separate systems of the ensemble is therefore very high. The classical description has a high degree of randomness or, in other words, incoherence of elementary subsystem states. In the case of biosystems, the presence of feedbacks leads to a steady state of a system that is different from the equilibrium state and a from a quasi-particle - conformers are in a coherent state, providing for cooperative effects. In this sense, the situation in biosystems is similar, at least in formal mathematical terms, to other cooperative phenomena known in physics -

superfluidity and superconductivity. Just coherence of the ensemble of conformers, coordination of their wave functions ensures the functioning of living systems, i.e. biological substance is coherent (12). Apart from the openness of the biosystem, an important circumstance is its activity: individual elements are small active objects.

The equation of a reaction diffuse type is a basic equation in the statistical theory of active media and the self-organization theory (synergetics)

$$\frac{dX(R,t)}{dt} = F[X(R,t)] + \frac{d}{dR_i}[D_{ij}(X)\frac{dX}{dR_j}], \qquad (11)$$

called Fischer-Kolmogorov-Petrovsky-Piskunov equation (14). In this equation *X(R,t)* - a set (vector) of characteristics of a concentration-like system, a velocity field and so forth; *R* - spatial coordinate; *t* - time. Non-linear functions F are determined by the structure of subsystem elements and D_{ij} values by the spatial diffusion coefficient of system elements. The real application of equation (11) for description of systems like the biologic cell is limited even with the use of computers because of complexity of its spatial structure. This task is similar to delineating characteristics of a rough surface in non-contact optic diagnosis, where statistical parameters are used instead of a detailed description of the spatial geometry, while correlation analysis is used in experimental studies (63).

A priority task is making precise the definition of elements of an open active system; the conformers discussed above can act as such elements. To describe biosystems and the LBS process, it is necessary to use the kinetic equation for conformer energy distribution function *f(X,R,t)*.

Since any biologic system is orderly, the characteristic of the order, entropy, should be used as a main parameter. An advantage of the entropy state lies in that entropy can be defined for an arbitrary non-equilibrium state if a relevant distribution function is known (14). The latter can be ascertained both by mathematical modeling and from experimental data such as temporal realizations, spectra and spatial distributions.

If the system is characterized by Hamilton function *H(X)* and conformer state distribution $f_N^{(0)}(X)$ in an equilibrium state is determined by a canonical Gibbs distribution, then, according to the Gibbs theorem, entropy of the equilibrium state is higher than entropy of an arbitrary state, provided that average energy is equal to average energy of the equilibrium state (14) (See also p.43). In the case of the biosystem, the condition of average energy equality is

$$\int H(X) f_N^{(0)}(X) dX = \int H(X) f_N(X) dX, \qquad (12)$$

where $f_N(X)$ - conformer distribution function for the non-equilibrium state - is met, as for considerations of heat loss minimization, average energy of biosystem elements is equal to average thermal energy of environment elements or is close to the latter. Since conditions of the Gibbs theorem are met for difference of entropies of equilibrium *S(0)* and non-equilibrium *S(T)* states, inequality takes place.

Fig.12. Change of statistical distribution functions of the biosystem and coherent field during laser biostimulation:
a - before interaction of systems;
b - after interaction of systems;
c - "exchange" of coherence states between photon and conformer ensembles.

$$S(0) - S(T) = k_Б \int \ln \frac{f_N(X,T)}{f_N^0(X)} f_N(X,T) dX \geq 0. \qquad (13)$$

It can be said that a restriction on the mode of conformer distribution function follows from the Gibbs theorem according to equation (12).

Let entropy of the cell ensemble + light system before laser irradiation be

$$S(0) = S_0(1) + S_0(2) + S_0(3), \qquad (14)$$

where $S_0(1)$ - entropy of normal cells, $S_0(2)$ - entropy of "ill" cells and $S_0(3)$ - entropy of the coherent electromagnetic field. According to the physical sense, Gibbs distribution with a temperature of the biosystem (close for heat loss minimization to the temperature of the environment) corresponds to entropy $S_0(2)$, while non-equilibrium distributions correspond to entropies $S_0(1)$ ands $S_0(3)$, as these systems are coherent (Fig. 12a). After laser irradiation, numbers of "ill" cells decrease, radiation coherence diminishes, and its distribution by elastic and non-elastic scattering in the interaction process evolves toward a thermal pattern (Fig. 12b). The Gibbs theorem (13) and the Prigozhin principle show that the system minimizes the entropy production $\sigma = dS/dT$ in the steady state during non-equilibrium phase transitions that form the self-organization process; for the state «*0*» before LBS and the state «*T*» after irradiation, inequalities take place:

$$S(0) - S(T) \geq 0$$
$$\sigma(0) - \sigma(T) \geq 0 \qquad (15)$$

In terms of conformer distribution function, the LBS process is described as in (14), but distribution function is defined as a function of distribution of conformers and the electromagnetic field (12b). Then equations (12) and (15) can be considered as a restriction to the class of "arbitrary" conformer distributions.

Therefore, LBS effects may be interpreted as an "exchange" of coherent properties between the biologic substance and the electromagnetic field; the laser light is scattered and absorbed as a result of the interaction, while the decorrelated non-equilibrium system returns to a fully coherent state. The general physical mechanisms of this self-organization have been considered above. The LBL process may be also interpreted as a kind of "heat exchange" between two systems that have a negative absolute temperature - the biosystem and the coherent magnetic field.

In experimental terms, it is more convenient to use temporal spectra of electric parameters of biologic objects or scattering spectra of radiation probing the object, and not temporal realization, for determining the relative degree of order (entropy) of open systems before and after laser treatment (14). Certainly, the choice of a probing signal for evaluation of LBS effects poses a serious scientific problem. Studies of bio-like self-expressing detecting media based on gelatin-glycerin compositions, which are sensitive to blue light, offer some possibilities of modeling LBS effects. The helium-neon laser may be used as a probe. Conformers as a tool for describing the work of such media (64, 65) and gelatin holographic detecting media as possible models of biologic systems have been discussed (9).

9. Non-Linear Dynamics of Laser Biostimulation

The biologic system, in particular the cell, is a non-linear system. Therefore, it can be described in the framework of non-linear dynamics (66-68). Dynamics of a native, or "healthy", cell is a steady state with numerous variables x, in which the state of the system does not change with time. In the most general form of the basic model of non-linear dynamics - one-dimensional representation, it can be written

$$x_{n+1} = f(x_n, \alpha), \qquad (16)$$

where x_n corresponds to a set of variables of the state at a moment of time, t_n, f - continuous function describing biochemical processes in the cell and α - a generalized parameter depicting the system itself, the environment and interaction between them. Since the evolution of the system behavior is significantly dependent on parameter α, it is sometimes called a controlling parameter.

The steady "healthy" state of the cell corresponds to the stationary point x^*

$$x^* = f(x^*, \alpha), \qquad (17)$$

which shows a lack of relationship of dynamic processes to the beginning of time reading t_n. Dynamics of the system's behavior changes according to a so-called Feugenbaum scenario for general functions that correspond to reactions of a diffuse-chemical type during the change of parameter α - there is a transition to chaos as a result of an infinite cascade of doubling period bifurcations (66, 67). Figure 13a presents a generally accepted bifurcation chart showing the distribution of values of stationary points from parameter α. With the above-presented considerations in mind, the controlling parameter α (see equation (8)) is defined as energy of the dipole and/or multipole moment of the macromolecule in the cell's own field $\vec{E}$ (3).

Figure 13b is a schematic representation of the Darwin origin of species (5). The apparent similarity of these charts suggests that the controlling parameter in evolutional development was the environmental resource recruited by all populations for their life activity. There are no reasons to presume that the dynamic developmental scenario of the tiny biosystems like cells and biomacromolecules radically differs from philogenesis.

Fig. 13. Transition to chaos as a result of a cascade of doubling period bifurcations in a non-linear dynamic system:
a - Feugenbaum chart fir stationary representation points $f(x)= \lambda x(l-x)$ (66);
b - schematic representation of the Darwin origin of species. A, B,...L - species of an extensive genus. The dotted lines leaving A and I - changing descendants of these species. Spaces between horizontal lines indicate 1,000 or a greater number of generations; a^1, m^1 etc - clearly emerging diversities; a^{10}, f^{10}, m^{10} etc - new species, F^{14} - a species that remained without change (5).

If it is accepted that the normal functioning of a certain biomacromole corresponds to the controlling parameter $\alpha<A_1$ (Fig.13a), an impairment of its function enhances the dipole moment $\vec{d}$ or field $\vec{E}$ within the cell, which causes an increase in parameter α and corresponds to a bifurcation of thee doubling period. If the ensemble of "ill" cells is considered, such evolution leads to chaotization of the ensemble (the right margin of Fig.13b) and in physical terms corresponds to thermolysis of the ensemble (a transition from the coherent state of substance to an equilibrium thermal state); in biological terms, it is described as the process of death of the cell and its elimination by the phagocytosis processes. This can be presented in an enzyme catalysis model as gaining by the "key" or "hand" of energies that destroy the structure of the "lock" or "glove" at an attempt of approximation i.e. complementary approximation of reagents becomes impossible, and excess energy is released as heat.

The presence in a biosystem of the electromagnetic field of laser radiation also causes an increase in the controlling parameter α, but this time through value $\vec{E}$ in equation (8). Higher dipole moments of "ill" biomacromolecules (cells) result in their faster progress to a chaotic state and death; in "healthy" cells, processes of synthesis are accelerated, namely steps where reagents have relatively high dipole moments. If the electromagnetic field is of such an intensity that parameter α grows above A_1 at one of stages of synthesis, this becomes manifest as inhibition, and not stimulation, of biologic processes. It appears that critical maximum electric field intensity $\vec{E}$, which makes the mechanism of the biologic negative feedback ($\alpha<A_1$) inoperative, can be assessed by the degree of maximum cell heating during exposure to laser radiation (69).

Theoretical concretization of the concept of LBS effects is difficult enough because of complexity of describing interactions of biomacromolecules in a certain conformation state with the electromagnetic field which depends on the analyzed molecule, boundary conditions related to the cell structure and the cytoplasm substance. As a minimum, such models require tensor analysis and the attempt to take into consideration changes of the conformational state of the macromolecule appears to make the task trans-calculational. Therefore, the value A_1 should be determined experimentally for the controlling parameter as a dose of absorbed laser radiation that inhibits biologic processes. It may be presumed that variability of experimentally found threshold intensities of laser light for LBS is related to the mathematically complex structure of the controlling parameter α.

10. A Mode Concept for Description of LBS Effects

One of important tasks is to develop an adequate interpretation of laser radiation-biologic substance interaction and of the mechanism of wave field structuring in the biologic tissue that prepare physical conditions for the photochemical reaction proper. The mathematical modeling of LBS effects could yield recommendations of experimental methodologies, computation and prognosis of various aspects of medical use of lasers.

Substantial results in determination of the spatial distribution of light energy within biologic structures have been obtained on the basis of the radiation transfer theory, the multiflow theory and the Monte Carlo statistical modeling method (70,71). In optic terms, these methods are modifications of the Bouguer law. Allowing the calculation of intensity distribution within the biotissue, they do not provide information about the fine structure of the tissue light field that is determined both by the cell microstructure and the degree of coherent radiation intensity. Averaged figures of coherent radiation intensity distribution in the tissue depth cannot provide an explanation of effects apparently related to spatial structural heterogeneity of the external light field, such as enhancement of the blood flow and activation of transport of substances through vessel walls (3). It follows from general considerations that a primary cause of such effects of continuous laser light biostimulation may be only regular spatial heterogeneity of light treatment. The appearance of such regular heterogeneity is in turn explainable only by the influence of the biotissue and cellular structure, namely diffraction of coherent radiation on it. On the other hand, it is known from the photographic process theory and from studies of holographic detecting media that effectiveness of a primary photochemical reaction depends on the spatial structure of exposing illumination (72-74). In case of laser biostimulation, such relationship should prove stronger, as diffusion processes in biotissues are more intensive than in photo emulsions.

Peculiarities of the field structure during diffraction of coherent light on cellular structure can be determined using a traditional quasi-optic approach (75, 76) without controlling for the scattering component that produces speckle structures, and is described with statistical methods (70, 71).

Like in the diffraction theory, two characteristic areas, a quasi-optic ($d>>\lambda$) and a resonance ($d\sim\lambda$) ones, can be singled out during the interaction of infrared and visible-range laser light with biologic cell structures that have a characteristic size of regular heterogeneity - the linear size of the cell (d) ranging from 100 to 1 mcm. So-called natural electromagnetic oscillations excited in a volume of heterogeneity (in the cell) by the incident wave play a significant role in the resonance area (77). Since each final physical body has a discrete set of its own

oscillations (modes), emission of an oscillating mode whose frequency, polarization and than spatial form are closer to those of the incident wave makes a main contribution to the scattered field that spreads into the depth of the biotissue. Given that cells are a multilayer system, it may be concluded that a radiation intensity distribution corresponding to "averaged" parameters of the cell will asymptotically establish after radiation passes through a sufficiently large number of layers. On other words, there are resonance conditions for passage of monochromatic radiation through the cell structure. This process may be also interpreted as "self-tuning" of characteristics of incident radiation to optic features of the system, as most of transmission occurs in the presence of spatial-temporal modes that are contained in the incident wave and correspond to the lowest mode of the elementary component of the structure - the cell.

Local structural non-homogeneities, i.e. cell boundaries, exert a main influence in the quasi-optic area ($d >> \lambda$). It is accepted that a relative contribution of oscillation modes of a separate heterogeneity is small. In this case, diffraction phenomena near caustics, focuses and in the semi-shadow area are taken into account as effects of ray amplitude diffusion into adjacent ray tubes, i.e. into wave fronts of spreading radiation (76-78), and are described by the parabolic equation of Leontovich.

The cellular structure is a periodic quasi-optic system consisting of repetitive structural elements, i.e. cells; therefore, the transverse structure of the radiation wave front should recur, because of symmetry, after the same period d, which can be written as conditions of the Flocke theorem (75):

$$u(x,y,z+d) = u(x,y,z)e^{-j\varphi} \qquad (18)$$

where $u(x,y,z)$ – the amplitude of the coherent field, φ - the phase shift gained by the wave front during passage of one layer with the depth d, $j = \sqrt{-1}$. Its is well known (75, 76) that radiation propagation in periodic structures like "lens" or "diaphragm" lines (which are physical analogues of open laser resonators) are described by the homogeneous second-order integral equation of Fredholm

$$\hat{L}\{u\} = \mu u, \qquad (19)$$

where $\hat{L}$ - integral operator that has, for example in case of the "lens" line form

$$\hat{L}\{u(x,y,z)\} = \frac{jk_0}{2\pi L}\int_{Q(\xi,\eta)} U(\xi,\eta,z)\exp\left\{-j\left[k_0\frac{(x-\xi)^2+(y-\eta)^2}{2L}+\Psi\right]\right\} d\xi d\eta \qquad (20)$$

where $\Psi = k_0(L + \frac{r^2}{2f}) + \varphi_0$; $Q(\xi,\eta)$ - integration area determined by the aperture of the solitary lens; φ_o - field phase in the plane Q_o, f - focal length of the lens, $k_o=2\pi/\lambda$ - wave number. The rest designations are presented in Fig.7 showing the scheme of only one "lens" line cascade.

Equation (19) has a countable set of eigenvalues $\{\mu_n\}$ and a corresponding set of eigenfunctions $\{U_n(x,y)\}$, called modes in the resonator theory. Eigenvalue μ_i,, which may be also composite, determines energy losses in the amount of $(1-|\mu_i|^2)$, because radiation partially goes beyond the boundaries of the lens and a phase incursion on $arg\ \mu_i$ occurs during wave front passage from one lens to another (75, 76).

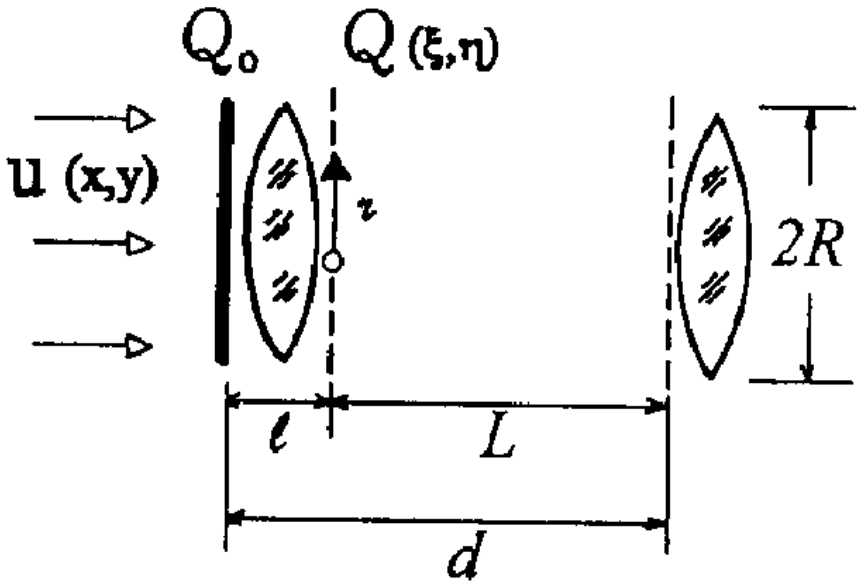


Fig.14. Parameters of the elementary unit of a cellular structure.

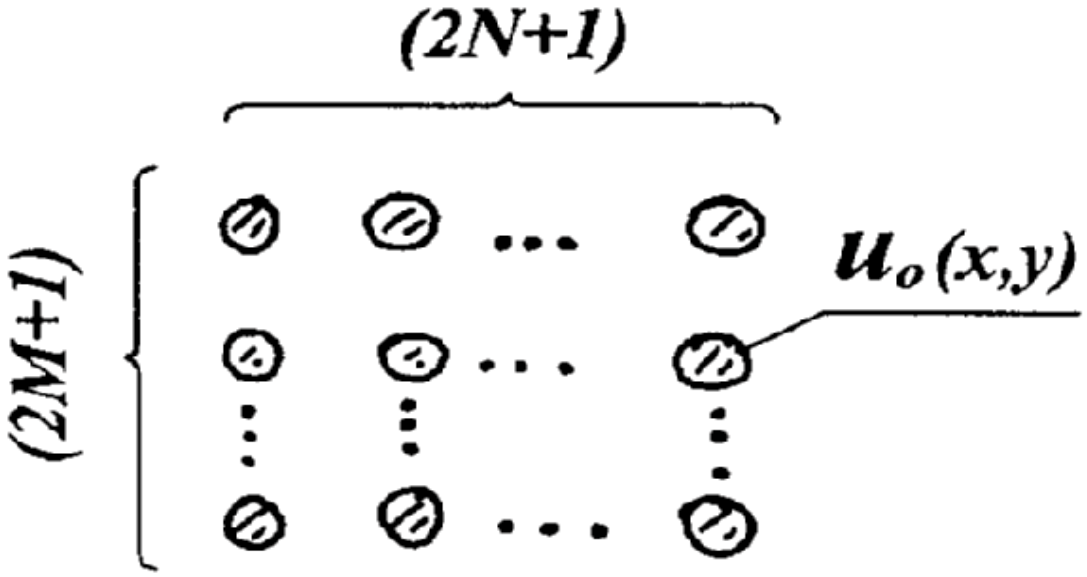


Fig.15. Schematic structure of an established wave front in the cellular structure.

In a sufficiently long lens line, a natural wave with minimal losses $(1-|\mu_o|^2)$ and a mode - an amplitude distribution $u_o(x,y)$ establishes. The narrowest beam running along the optic axis of the system corresponds to the mode. When inequality $R^2>>\lambda d$ is not met, each subsequent lens cannot "intercept" the light beam of energy coming from a preceding lens, and radiation transfer will be accompanied by high radiation losses - the spread of radiation beyond the boundaries of the lens line. Since $R\sim d$ in this case, and the $d\sim\lambda$ situation will also correspond to the resonance area of diffraction discussed above.

Since equation (19) includes wavelength λ as a parameter, the presented analysis also applies to monochromatic radiation. In other words, monochromatic radiation interaction with the cell structure has a wavelength-resonant pattern, as the established mode $u_o(x,y)$ depends on the wavelength λ as a parameter.

If radiation is delivered as a flat wave front in real biologic structures, the mode $u_o(x,y)$ is formed by the first layer of cells on the way of radiation because of their prominent optical non-homogeneity. An optimal way of maximizing light energy delivery into a cell structure is to apply coherent radiation with a flat wave front to the first cell layers collimated along the optical axis of the lens line. Since all body organs have curvatures, laser therapeutic devices should be complete with adaptive optical elements making phase correction of an incident wave front adjusted to the curvature of an irradiated site.

The modal pattern of radiation propagation in the lens or diaphragm line is formally similar to modes of light guides that are used in fiber optics. Since periodical optic and cellular systems may be considered as wave-guide media with characteristic quantization of propagation constants along all three coordinate axes, modes are definable as steady wave fields during propagation in such media (79). The modes do not change the spatial structure as they spread in their medium, but only gain a phase incursion proportional to the passed distance according to equations (19) and (20).

After radiation goes through several cell layers and the regime becomes established (80), steadiness of the mode $u_o(x,y)$ occurs at any distance passed by radiation. Therefore, if the cell area sized $(2M+1)(2N+1)$ is irradiated, where $M,N>>1$, the whole wave front (Fig.15) can be described with the expression:

$$u_c(x,y) = \sum_{m=-M}^{+M} \sum_{n=-N}^{+N} u_o(x-md,y-nd), \qquad (21)$$

where the elementary mode $u_o(x,y)$ is defined as eigenfunction of equation (19) if $d>>\lambda$, or as a field distribution corresponding to the mode of natural oscillation of a separate cell with $d\sim\lambda$.

For biostimulation of the tissue by laser radiation to occur regardless of the presumed character of a primary photochemical reaction, the fine spatial structure of radiation must correspond to the entire cellular structure. Since radiation interaction with the cellular structure has a resonance pattern, as has been shown above, the spatial structure of the scattered field should have a maximal contrast, which is achieved during high monochromatic and spatial coherence of incident radiation (81).

To ensure a maximum coordination of the entire field consisting of elementary modes with an irradiated biologic structure, which is achieved be selection of modes in cellular lens or diaphragm lines, it is desirable to simultaneously irradiate the whole cell mass $(2M+1)(2N+1)$. Indeed, if a cell structure is irradiated with a scanning laser beam, intensity distribution will be not the module square of expression (21), but

$$I_S(x,y)=|u_S(x,y)|^2 = \sum_{m=-M}^{+M} \sum_{n=-N}^{+N} |u_o(x-md,y-nd)|^2 \qquad (22)$$

and biostimulation of each cell will occur regardless of other cells, even through biologically all cells function in a coordinated way. In case of simultaneous

irradiation of the entire cell mass *(2M+1)(2N+1)*, intensity distribution is written as

$$I_c(x,y)=|u_c(x,y)| = \left| \sum_{m=-M}^{+M} \sum_{n=-N}^{+N} u_o(x-md,y-nd) \right|^2 \qquad (23)$$

and contains in its right part interference components, making the field (23) more diversified structurally and more topologically cohesive as compared to field (22).

The complexity of the coherent field structure can be evaluated using the theory of degrees of optic image freedom (82), where the total number of freedom degrees of the radiation field is defined as the number of effective values necessary for a full description of it. In this case it can be seen that *(2M+1)(2N+1)* of real values are necessary for describing the field (22) and two times more for field (23) because of the combined character of terms of a series that is wholly under the module sign.

It follows from the theory of control of complex systems (83) that exerting an information influence on them requires a sufficient diversity of an external signal (the Ashby principle of necessary diversity), which in this case is the established field in the cell structure. The degree of diversity can be assessed through the amount of Shannon information contained in the signal, which is in turn related to the total number of degrees of freedom of the optic field (82). For this reason the influence of non-scanning field influence on a biosystem is more effective for biostimulation in an information sense as compared to spot scanning, if energy considerations are not taken into account. Besides, like in the case of coherent imaging systems, the distribution of degrees of freedom of the wave field during non-scanning irradiation has a threshold character, and not a descending one as during the scanning regime similar to incoherent imaging systems (82). Nonetheless, the situation with scanning biostimulation may prove complex if temporal changes in a real biosystem are taken into consideration. With this in mind, periods of natural oscillations, movements of cells and the whole structure, as well as the time of diffusion of primary photochemical reaction products should be taken unto account in selecting scanning parameters. In principle, the mode of scanning will be identical to continuous irradiation if the time of beam sweep is much less than a minimal time characteristic for biologic processes.

Therefore, the quasi-optic approach to diffraction of coherent radiation in cellular structures has shown that the interaction has a largely resonant character relative to the spectral composition of light in a sense that spatially inhomogeneous and structurally diverse distribution of radiation intensity in the biotissue occurs during monochromatic illumination having a high spatial coherence. In this connection, medical studies comparing effects of LBS processes

in tissues with cells sized about 5 mcm would be of interest. Comparison of helium-neon laser radiation (when $d>>\lambda$, i.e., a quasi-optic diffraction area occurs) and CO_2-laser radiation with a 10.6 mcm wavelength (when $d\sim\lambda$, i.e. there is a resonance area of diffraction) would have given a glimpse into the mechanism of laser light interaction with biologic matter.

Biotissue periodicity in three spatial coordinates results in longitudinal periodicity of the light field because of structural changes of the field in a plane perpendicular to the propagation direction. In traditional optics, such processes are known as self-reproduction or self-imaging of the light field structure and are qualified as Laue effects (for incoherent illumination) and Talbot effects (for coherent illumination) (84). The low intensity of incoherent light sources allows ignoring the Laue effects during analysis of light propagation in biotissues and limiting the description to events to the Bouguer law. The situation is different in case of laser light sources providing high intensity of monochromatic spatially coherent illumination, when horizontal periodicity of the radiation field causes periodicity in a longitudinal direction. During analysis of the Talbot effect in optics, objects like one or several diffraction gratings are usually considered (84-86). In the case of the biotissue, a more complex problem appears to arise. It is related to coherent light wave propagation in an environment periodical in three dimensions, and requires further research. Nevertheless, findings of theoretical and experimental studies of coherent radiation diffraction in periodical structures for image multiplication (85) and non-contact metrology (86) can be used as a starting ground for elucidating the structure of the light field in biosystems.
For the wave equation

$$\nabla^2 U + k^2 U = 0 \qquad (24)$$

where $k = 2\pi/\lambda$, λ - wavelength, $U(x,y,z)$ - three-dimensional function of the wave field. If the field $U(x,y,z)$ has the capability of self-imaging along the axis z, it is periodical along the direction of propagation (axis z) with the period Δz, and it can be presented as a Fourier series

$$U(x,y,z) = \sum_m v_m(x,y) \exp(j2\pi mz/\Delta z) \qquad (25)$$

with the boundary condition

$$U(x,y,0) = \sum_m v_m(x,y) = t(x,y), \qquad (26)$$

where *t(x,y)* - amplitude transmission of an object. If such wave field *U(x,y,z)* corresponds to the wave equation, differential relations must be met

$$\frac{d^2 v_m}{dx^2} + \frac{d^2 v_m}{dy^2} + k^2 \left[1 - \left(\frac{m\lambda}{\Delta z} \right)^2 \right] v_m = 0. \qquad (27)$$

To determine requirements for an object that forms its self-images, we shall review the case

$$1 - \left(\frac{m\lambda}{\Delta z} \right)^2 > 0$$

or (28)

$$\Delta z/\lambda > m \geq 1.$$

By using the Fourier transform

$$U_m(x,y) = \int_{-\infty}^{+\infty} \int \tilde{v}_m(f_x, f_y) \exp\left[j2\pi(xf_x + yf_y) \right] df_x df_y, \qquad (29)$$

where $\tilde{v}_m$ is the fourier image of function v_m, we shall present a differential equation for $v_m(x,y)$ in the spatial frequency area as

$$\int_{-\infty}^{+\infty} \int \tilde{v}_m(f_x, f_y) \exp\left[j2\pi\left(f_x x + f_y y \right) \right] \left\{ -(2\pi)^2 (f_x^2 + f_y^2) + k^2 \left[1 - \left(\frac{m\lambda}{\Delta z} \right)^2 \right] \right\} df_x df_y = 0. \quad (30)$$

The latter equation is fulfilled if $\tilde{v}_m(f_x, f_y) = 0$ or the expression in the brackets is zero. Therefore, a periodical object's having a range of spatial frequencies meeting the Montgomery condition is an adequate requirement for self-reproduction of horizontal structures of the optic field along the direction of its spread (84) (Fig.16):

$$f_x^2 + f_y^2 = \frac{1}{\lambda^2} - \frac{m^2}{\Delta z^2} = \rho_m^2, \qquad (31)$$

where m - limited entity; $0 \leq m \leq m_{max} \leq \Delta z/\lambda$ (value m_{max} is determined by the condition of appearance of damped waves); f_x , f_y – spatial frequencies of the spectrum of the periodic object with the period d_x and d_y, $f_x = d_x^{-1}$, $f_y = d_y^{-1}$),

λ - radiation wavelength. If the object is a diffraction grating with the period d, planes of precise self-imaging are located at distances that are multiples of the value

$$\Delta z = 2d^2/\lambda \qquad (32)$$

from the plane of the periodic object (86). Half-way between these planes, light intensity also reproduces the initial image which is, however, shifted on the transverse coordinate by a half-period.

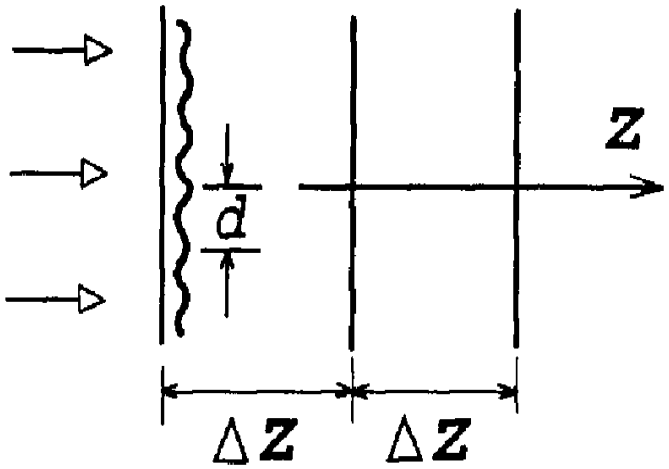


Fig.16. Location of self-imaging planes – Talbot planes for the periodic object.

Since such shift is insignificant in most cases, it may be accepted that Talbot images are observable at equidistant distances

$$z_k = m\frac{d_x^2}{\lambda} \qquad (33)$$

from the plane of the object. The self-reproduction phenomenon is related to interferences of coherent waves that have diffracted on the object; therefore, the number of really observed Talbot planes significantly depends on the aperture size; it has been found out experimentally that a minimum 17-25 periodic changes are necessary within the aperture of the object (84).

If the object has complex amplitude transmission (in a one-dimensional case):

$$t(x) = \left[C + A\cos\left(2\pi\frac{x}{d}\right)\right]\exp\left\{j\left[B\cos\left(2\pi\frac{x}{d}\right) + \psi\right]\right\} \qquad (34)$$

then, according to (84)

1. light intensity corresponds in planes determined by equation (33) to the image in plane $z=0$; moreover, an image of the absorbing part of complex transmission is observed, and there are no planes, where the image of only the phase part is seen;
2. the location of the plane of an image with best contrast depends on initial contrast A/C and the value of phase modulation B;
3. The behavior of intensity distribution in the Talbot plane in the presence of modulation $B>\pi/4$ is determined mostly by a phase component of complex transmission.

It should be stated that it is practically impossible to carry out full analysis of the self-imaging phenomenon and for this reason computer modeling methods are usually used, in particular when a self-image is considered in a non-paramaximal approximation at large diffraction angles.

If a lattice of transparent strips with the breadth a and period d ($\varepsilon=a/d$ lattice porosity) is used as a periodical object, contrast K of the self-image depends on z according to the graph presented in Fig.17 (86). It can be seen that the breadth of the contrast peak near the self-reproduction planes on axis z is approximately $\varepsilon\Delta z$, where Δz is determined with equation (32). In other words, the area of the most contrast distribution of intensity near the Talbot planes narrows with increasing structural fineness of the object near (which is determined by porosity ε) (86). A similar relationship is seen for the phase lattice, which is a model of the cellular structure of the biotissue, where the magnitude of phase modulation is significant because of the presence of cell walls.

Proceeding from the structure of the coherent field with a periodical spatial structure, differences between optic conditions of intravenous irradiation of blood using transcutaneous and invasive techniques can stated (Fig.18). When the invasive method is used (Fig.18a), laser radiation forms a light cone as it leaves the light guide introduced through a hollow needle into circulation. With non-invasive transcutaneous irradiation (Fig.18b), light is periodically modulated by circulation-adjacent cellular structures of the tissue to form in the fluid a set of Talbot planes resembling “gill plates”.

Fig.17. Contrast K of the periodical image in relation to the distance along the optic axis – (b), for an object in the form of the amplitude lattice with transmission – (a).

Fig.18. The structure of the coherent field during intravenous irradiation of blood using invasive (a) and transcutaneous (b) techniques.

Theoretically, a total number of planes is $m_{\max} \approx D / d$, where D – diameter of the illuminating beam. Most of spatial modulation of light intensity occurs near Talbot planes, where the flowing fluid produces intensive diffusion of photochemical reaction products into non-irradiated areas of blood. It follows from general considerations that the mode of blood irradiation with the formation of such gill-like light planes allows biostimulation of larger areas as compared to irradiation with the whole light cone.

Another significant effect related to radiation distribution in the cell structure is self-restoration of the image of the periodical object that has malfunctions or

defects occurring as a lack of its small structural elements. Theoretical and experimental analysis shows that the essence of this effect is as follows. The mass *(2M+1)* × *(2N+1)* of identical images, each of which has amplitude transmission $t_e(x,y)$ and which are located on the rectangular two-dimensional lattice with periods d_x , d_y , can be described using the expression

$$t(x,y) = \sum_{m=-M}^{+M} \sum_{n=-N}^{+N} t_e\left(x - md_x, y - nd_y\right) = t_e(x,y) \otimes \sum_{m=-M}^{+M} \sum_{n=-N}^{+N} \delta\left(x - md_x, y - nd_y\right), \qquad (35)$$

where ⊗ means convolution and $\delta(x,y)$ is delta function. The Fourier image of such an object is

$$\hat{F}\left\{t\left(x,y\right)\right\} \approx \hat{F}\left\{t_e\right\} \frac{\sin\left(2\pi f_x (M+1/2) d_x\right)}{\sin\left(\pi f_x d_x\right)} \frac{\sin\left(2\pi f_y (N+1/2) d_y\right)}{\sin\left(\pi f_y d_y\right)} \approx (M+1/2)(N+1/2)\hat{F}\left\{t_e\right\}, \quad (36)$$

If defects in the form of vacancies are introduced into the object (35), i.e. several components of elementary images with transmission $t_e(x,y)$ are eliminated, expression (35) should be replaced by

$$t_r\left(x,y\right) = t\left(x,y\right) - t_e\left(x,y\right) \otimes \sum_{k=-K}^{+K} \sum_{l=-L}^{+L} \delta\left(x - kd_x, y - ld_y\right), \qquad (37)$$

where the second component corresponds to a mass of empty cells with sizes *(2M+1)*×*(2N+1)*. It can be demonstrated (85) that the Fourier image in this case looks like

$$\hat{F}\left\{t_r\right\} \approx \hat{F}\left\{t_e\right\} \frac{\sin\left(2\pi f_x (M-K) d_x\right)}{\sin\left(\pi f_x d_x\right)} \frac{\cos\left(2\pi f_x (M+K+1) d_x\right)}{\sin\left(\pi f_x d_x\right)} \cdot$$
$$\cdot \frac{\sin\left(2\pi f_y (N-L) d_y\right) \cos\left(2\pi f_y (N+L+1) d_y\right)}{\sin\left(\pi f_y d_y\right) \cos\left(\pi f_y d_y\right)} \qquad (38)$$

Comparison of this expression to equation (36) shows that the Fourier spectrum of the periodical object with vacancies is the spectrum with a changed number of elementary images, namely *[(M+1/2)-(K+1/2)]*×*[(N+1/2)-(L+1/2)]*, modulated by a cosinusoidal factor. It is seen from (38) that with *K*<<*M* and *L*<<*N*, the defective periodical object produces the same image as an intact one. This is related to the fact that during self-reproduction, a solitary image is formed

by the light field that has diffracted on all elementary images making up the object (84, 85).

This capacity of periodical fields of self-restoration explains one of causes of a lack of effects of laser radiation on the functioning of normal biologic tissues, an occurrence well known in laser therapy. Light radiation passing through a cell layer is little influenced by “deformed” cells if they are scarce (up to 5%) (85). If non-deformed cells make up a field corresponding to an intact cellular structure, biologic processes designed to minimize a departure of a “deformed” cell from the “right” field can be photostimulated in the “deformed” cells in some way.

Experimental Results

An experimental study of diffraction in biologic objects used an LG-222 helium-neon laser with a λ=0.63 mcm wavelength, power up to 50mW, a beam 2 mm in diameter and coherence length not less than 15 cm.

Biologic preparations were made using the following techniques. Plant tissues were stored in a solution containing active chlorine (for destroying chlorophyll, a strongly absorbent pigment) until complete bleaching. The preparations were accurately washed and placed on a slide. After excess water evaporated, the preparations were embedded in an immersion fluid and laminated with a cover glass, and the glass sandwich preparations were placed in an optic circuit.

Distance ℓ between the biologic preparation and the plane of the image (a matted screen) was much larger compared to the size of an illuminated area of the preparation.

Fig.19a presents a photograph of intensity distribution of radiation that has passed through a section of the onion tissue in an area of Fraunhofer diffraction. The photograph shows apparent diffraction orders. Calculation of the period of the cell structure using this diffraction image has shown that an averaged transverse period of the onion cell lattice structure was 0.07 mm, which was consistent with direct measurements using an IMT-10 microscope. An averaged transverse period of the visually measured lattice was d=0,067±0,004 mm.

Fig.19a. Fraunhofer diffraction in onion tissues. A linear lattice.

Fig.19b. Fraunhofer diffraction in a maple leaf. A combination of rings.

Fig.19b presents the pattern of laser radiation diffraction in tissues of the maple leaf. In this case, the diffraction picture is a ring-like structure with a bright zero-order spot. Such diffraction patterns occur when an elementary object with a periodical structure has similar sizes on axes x and y, and a rounded shape similar to an image that formed during laser radiation diffraction on matrices of round openings.

Since the spatial spectrum of biologic objects studied by us meets the Montgomery criterion, it has proved possible to obtain self-images of biologic objects in Talbot planes. Focusing on different planes was accomplished by moving a micro lens along the optic axis of the system. A magnified image was projected with the micro lens on the screen and photographed with a mirror camera.

Distances from the onion tissue preparation to planes of the self-image, which proved a multiple of 1.4 cm, were calculated from the period of the cell structure of onion tissues.

Fig.20 presents a photograph registered in the self-image plane located at the distance $z=d^2/\lambda=1{,}4$ cm. It is known that an image of the periodical object shifted in phase by π is observable at this distance. This particular image shows that borders of cells are darker than their cores.

Fig.20. A self-image of the cellular structure of onion tissues in the plane $z=d^2/\lambda$. The panel shows a defective site.

A total of seven self-reproduction planes have been obtained. This indirectly confirms the conclusions of the previous section that the regular structure of the electromagnetic field can influence effects of biostimulation despite scattering.

To directly corroborate this concept, experiments have been conducted to stimulate the formation of somatic embryoids in a cell culture.

The experiments used plants of L-229 line of Solanum melongena L., West Asian subspecies (ssp.ocidentale Has.), as well as a L-271 line, South Asian subspecies (ssp.meridionale Fil) and hybrid F1 L-271 x L-229. The plants were grown in controlled medium conditions: the photo period, 16 hours; the temperature, 25±2 degree centigrade; illuminance, 3500-400 lux. Murashige and Scoog media without hormonal additives were used.

The seeds were pretreated with 15% calcium chloride during 20 minutes and subsequently flushed five times with sterile distilled water. Effects of the physiologic conditions were studied in the same plants transferred to a cold chamber for growing at a temperature of 15-18 degree centigrade, a photo period of 12 hours and illuminance 3,000-3500 lux.

Experimental repetitiveness was 5 to 20 explants per variant. Dynamics of somatic embryoid formation were registered.

Hybridization was carried out by a conventional isolation methodology. Hybridity of F1 was examined using a dominant marker trait – the presence of antocyan coloration of the hypocotyls.

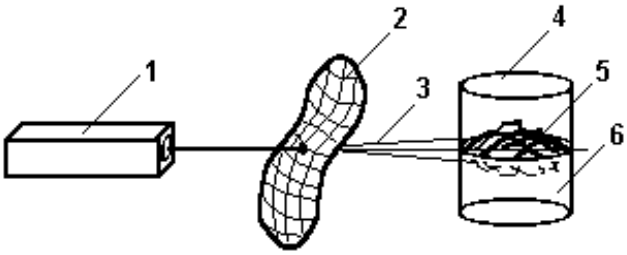


Fig.21a. An optic scheme of biologic stimulation of cell cultures. 1 – laser, 2 – leaf modulating electromagnetic radiation, 3 – modulated laser radiation, 4 – glass flask, 5 – cell culture, 6 – nutrient medium.

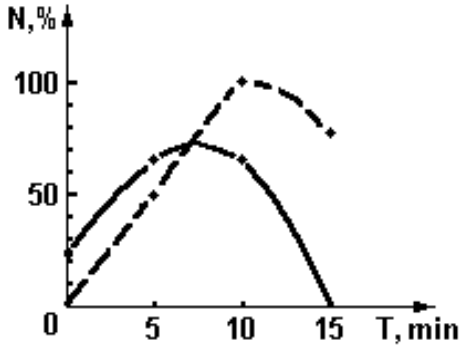


Fig.21b. A graph of relationship between the numbers of formed embryoids to the time of exposure to the helium-neon laser with an intensity of 2.5 mW/cm2 modulated by the plant leaf.
—— for hypocotyls,
------ for stem tissues.

The experiment was conducted using the scheme shown in Fig.21a. A control trait was the ability of the plant cell culture to form normal somatic embryoids. Cultures were illuminated through leaves of a different plant with an undiluted beam of the helium-neon laser. It was presumed that spatial modulation of electromagnetic radiation occurred as the above-described mechanism. Power intensity after the passage through the leaf was 2.5 mW/cm^2. A leaf of a plant whose trait was manifest without stimulation was used in the experiments.

The graph in Fig.21b presenting a relationship of numbers of forming embryoids to the exposure time shows extremes. Thus an exposure of callus tissues longer than 15 min appeared to inhibit and to completely or completely inactivate the embryoid formation process. Moreover, the graph shows that the controlled trait has expressed after modulated irradiation of the cell culture from the plant stem. However, this tissue culture did not form embryoids of plants without irradiation and after non-modulated irradiation.

Therefore, the experiments have confirmed the presumed influence of the electromagnetic field on the efficacy of laser biostimulation, with the provision that the field structure is consistent with the structure of the biologic object.

11. The Optics of Biologic Structures

Propagation of coherent radiation in a three-dimensional biologic structure results in modulated and axis-located distributions of light intensity. It should be stressed that the Talbot effect is not associated with the presence of any focusing

properties of an object. Besides, it is known that the Talbot effect is most prominent in the presence of spatial coherence of incident radiation (84) that is achievable with the use of lasers. This underlines another important aspect of coherence of radiation for laser biostimualtion. The Talbot and Loue effects occur only during simultaneous illumination of the whole periodical object, and not during its scanning with a sweeping laser beam – this may be a reason of the difference between scanning and total modes of therapeutic laser irradiation.

Therefore, a general conclusion may be made that established distribution of radiation intensity in a cell structure is little sensitive to geometric parameters of the illuminating beam. The structure of such beam is determined by parameters of the cellular structure and a radiation wavelength, and is little dependent on cellular structural defects. Therefore, one should seek energy loss minimization during the development of optic systems for biomedical laser devices, while control of stimulating effects should rely on temporal parameters of laser radiation (pulsed and scanning radiation, temporal modulation).

The Role of Non-Linear Optic Processes. Getting on the living tissue, laser radiation passes a structurally complex medium with a quasi-liquid crystalline structure. This causes a strong change in spatial distribution of light intensity, occurring as the appearance of bright caustic lines and a "spotty" field structure on the beam cross-section – a speckle structure. An average size of speckles depends on characteristics of the medium through which light goes. It turns out that the longer optic path light travels in the biotissue the more its structural characteristics – speckles and caustics – correspond to those of the tissue. This feedback mechanism determines the inevitable tuning of the light wave front to the structure of the irradiated tissue and explains the biologic effectiveness of laser biostimulation.

High coherence of laser radiation and the phased pattern of interaction with the biotissue lead to a fast change, on a small stretch of the optic path, of various spatial and temporal distributions of light intensity. Energetically significant in terms of a maximal effect on the biotissue prove intensity distributions that are microstructurally well consistent with the site of the irradiated biotissue. As a result of such consistency, there occurs effective excitation of biomacromolecule ensembles or molecule receptors that transfer their excitation to molecules of nucleic acids. In mathematical terms, such processes can be described within the framework of fractal geometry (27, 28), all the more so that biologic tissues also allow fractal description. Fractality of tissues is defined as their similar geometric structure at different scales of magnification that can have fractional (fractal) dimensionality and not be only two- or three-dimensional. In terms of fractal geometry it may be said that change in the structure of the light front must be going on until its fractal dimensionality becomes equal to fractal dimensionality of

the irradiated tissue, which will ensure the best conditions for excitation of biologic structures and macromolecules (42).

The self-similar (fractal) spatial and temporal structures of tissues for difference scales of review determine a mechanism of coordination of electromagnetic field characteristics with biologic substance. “Indifference” of the organism to natural light is related to selectivity of the response of complex biomolecules or cells to effects of light with different wavelengths. The lack of biologic effects of natural light is related to the fact that the amount of energy of this radiation per frequency, to which some freedom degree of the molecule responds, is too small to create a significant probability of excitation of a mode that could trigger some or another biologic mechanism, even though spatial density of energy in natural light can be significant (42).

Therefore, getting in biologic substance, coherent radiation changes its spatial intensity distribution because of optic anisotropy of the living tissue. Caustics and speckles occur in space when power density of laser radiation is high. It can be demonstrated that the degree of radiation focusing – the magnitude of maximal power density – increases with the degree of radiation coherence. High power density of radiation in these areas, which are also structurally consistent with the irradiated tissue, provides for the appearance of a set of radiation components with combination frequencies due to non-linear effects characteristics of biologic substance having a quasi-liquid crystalline structure. Since the resultant biologic effect is determined by interaction of radiation with a combination frequency, which in turns is related to non-linear characteristics of the tissue, there is no critical relationship to the frequency of incident radiation. It is only important that arising combination frequencies have a discrete and not a continuous spectrum. In brief, the process of interaction of laser radiation with the living tissue is self-organizing: the tissue itself changes spatial and frequency characteristics of initial radiation which in turn alters optic properties of the tissue through excitable biologic processes. Such an approach to describing the mechanisms of laser biostimulation reconciles the seemingly conflicting demands of coherence, independence of therapeutic effects from coherent radiation wavelengths and a lack of effects of natural white light. Studies of the team of Academician N.D.Devyatkov (10) also have addressed extremely high combination frequencies. It was stated that optic-range frequencies of radiation were not achievable because of combination events. When near infrared and visible spectrum lasers are used, a “descent” down the scale from optic frequencies to extremely high frequencies is most likely to occur, with no ban on the onset of events that have been well studied in medicine for extremely high frequencies. Such dynamics must include as one of its aspects soliton mechanisms of transfer of charge energy. The formation of a spectrum of coherent radiation combination frequencies due to fractal properties of biologic substance allows a

new approach to describing therapeutic effects of combined (for instance, two-wave) laser irradiation of biologic objects, in particular determining an optimal proportion of intensities during such irradiation. Change of optic properties of the living object also appears to provide for a certain conformity of radiation with the structure of biologic tissues. This probability is being more or less fully used in the evaluation of the biologic activity of plant objects by analysis of temporal decorrelation of speckle structures formed by laser radiation during its scattering on the object surface (87).

12. Generalization of the Local Process of Laser Biostimulation

The reviewed physical concepts encompass, in our view, all known aspects of the laser biostimulation (LBS) process during its therapeutic uses. Major properties of LBS and results of studies of laser radiation interaction with biologic objects (88, 93) may be summed up as follows:

1. selectivity of laser treatment: changes are induced only in "ill" biosystems, while there is no effect on "healthy" cells;
2. treatment effects are different in vivo and in vitro;
3. LBS effects are seen in non-cellular objects like plant pollen;
4. the stimulation effect has not been found during irradiation with white light;
5. therapeutic effects of LBS are practically identical for laser radiation with any wavelength in the range of 0.4 to 1.5 mcm;
6. protein molecules do not have in vitro absorption bands for radiation in the wavelength range of 0.4 to 1.5 mcm;
7. LBS effects are seen during the use of 1.5 mW/cm^2 or lower intensities and of small energy doses calculated even without account for reflected light or light that has traveled through a phase object (88). If the dose is calculated by the above-presented criteria, stimulation of sperm cells requires 4.9 mJ/cm^2. LBS effects reported in medical practice include a decrease in blood viscosity, stimulation of microcirculation, pain relief, enhancement of motility of cell receptors and some cells (e.g. sperm cells), stimulation of the immune and nervous systems.

It is important to take into account the following properties of laser radiation during analysis of LBS effects:

- the radiation spectrum is a narrow peak or a "comb"combination of such peaks, which is a monochromatic property of laser radiation;
- laser radiation has high spatial and temporal degrees of coherence;
- laser radiation, except for semiconductor lasers, has a high spatial directivity;
- intensity and brightness of laser light are higher as compared to traditional sources of light.

The need for evaluation of the LBS process in the organism as a whole is prompted by the increasingly broader use of laser acupuncture and intravenous irradiation of blood. It is accepted at present that regardless of primary mechanisms of laser radiation absorption, therapeutic effects are achieved with the help of integrating systems of the organism – the nervous, blood and immune systems (89, 90). The sole concrete explanation for therapeutic effects so far is that the striving of these systems to preserve homeostasis results in correction of disease processes. The development of an integral concept is in particular hampered by a lack of a scientific theory of acupuncture.

Generalization of local effects of LBS can be explained within the framework of the Gurvich concept of cell fields (8), with the addition that a source of the cell field is not only chromatin but also oscillations and movements of blobs, domains and biomacromolecules. Effects of laser treatment are transferred to biotissues on a relay principle, from cell to cell. Configurations of the electromagnetic field that correspond to a major mode of the cell have minimal energy losses. It is clear from general consideration that these configurations must correspond to soliton solutions of wave equations for a cellular environment. The energy-information exchange between molecules (cells) mediated by electromagnetic solitons means that the latter, being solitary waves, are modulated by all natural frequencies of the biologic biomacromolecule (cell) – naturally, with different weights. Thereby the "reading" by the soliton of energy-information characteristics from non-defective elementary biologic structures (macromolecules, cells, etc.) secures their steady transfer to "extinct" elementary structures, providing for their "triggering", destruction of defective elements and probably the synthesis of new, non-defective ones. The role of this mechanism of information transfer has been convincingly demonstrated in a book devoted to the millimeter wave range (10).

Since any system seeks a minimum of energy losses, a biologic system radiates into its environment the least possible amount of energy in the form of the electromagnetic field. This is why formally functional native cells have smooth surfaces. As it has been stated above, functional disorders lead to an increase of a field gradient near impaired smoothness of the cell membrane. This initiates an activation of metabolic reactions in these areas, helping "dissolution" or recovery of a "defective" cell.

As coherent radiation gets into biologic substance, it forms an unfolding set of combination frequencies that are separated in time and space, and sooner or later some or another molecular or conformation transition will get "its own frequency" (91). There is no critical relationship with a frequency of incident radiation; only separate appearance of combination frequencies in time (with sufficient resolution) is important. It is apparent that also important is the presence of initial radiation coherence. Even though the structure of one macromolecule can have vary (spiral, fractal conformation), the spectrum will be too complex. An

absorbed electromagnetic quantum of incident radiation will be sequentially "exchanged" according to the molecule's energy structure (which is determined, among other things, by its conformation structure), thereby triggering various mechanisms of energy-information exchange.

Apart from the mentioned mechanism of the transfer of information about non-defective structures by modulation of the electromagnetic field "wandering" in the biologic environment, its may be presumed that the structured water, in which molecules of biologic substance are "dissolved", has an important role. Indeed, the structures of the macromolecule and the structure of the water surrounding this macromolecule coincide in a sense of meeting equilibrium conditions (92). Locally, the defective macromolecule structure is reflected in its water environment. The laser-stimulated appearance of a set of combination frequencies carrying information about non-defective structures (which are immeasurably more numerous than defective ones) can occur as wave-like impulses in the water environment. The latter reach locally defective sites of the tissue and properly readjust the water environment of the defective molecule. Readjustment of the macromolecule itself then occurs due to conditions of equilibrium for the structured water plus macromolecule system.

Studies of effects of total laser irradiation of the organism are expected to provide additional information about mechanisms of laser biostimulation. Total laser irradiation is defined as treatment of body areas larger than 10 square centimeters (93, iss.5, p.114). This methodology has been called "laser tan" because of its similarity with the artificial tan procedure. The "laser tan" principle is in some degree used in the laser hydro system (93), in which laser radiation is delivered through a fiber with a usual shower, the flow of which acts as a light guide irradiating the body of the patient. It is apparent that the energy irradiation dose cannot be controlled in such a system.

Finally, the concept of generalization of the local treatment due to intercellular electromagnetic field relation is applicable not only to LBS but also to effects of traditional drugs and homeopathic remedies. Indeed, the purely diffusion mechanism of drug distribution in the entire cellular structure is unlikely to be dominant, at least at an initial stage. This stage can be described in terms of quasi-particles – conformers. It is plausible that just a part of the intercellular electromagnetic field that is external relatively to the organism accounts for the phenomena of "gene brotherhood" and "kin selection" (94).

Quantum Aspects of LBS. It has been stated above that the present-day quantum-mechanical approach dictates the need to take into account the information openness of biologic systems involved in the LBS process; it makes quantum processes non-local and causes a collapse of wave functions as a result of

"self-measurements" (95). The biosystem has a so-called tangled wave function describing a coherent state of substance. This results in a non-linear behavior of the entire open system through which energy and information flows can travel (negentropy). For this reason the whole process is able for self-organization. Due to this property, effects of LBS can be explained and modeled within usual physical concepts with recruitment of synergetic notions. The hierarchy in multi-level structural organization of biologic systems suggests a possibility of describing LBS effects within the framework of the non-linear dynamic model of M. Feugenbaum. Energy of the dipole or multipole moment of biomacromolecules in the electromagnetic field of laser radiation acts in this model as a controling parameter. This mechanism accounts for acceleration of synthesis, for example of DNA and RNA, in which macromolecules with relatively high dipole moments take part. On the other hand, the living organism and lasers are known to have an similarity in that the organism, like the laser, is a non-linear, ordered, open system comprising analogues of the active environment, a pumping source and a resonator (61), and this promises effective use of formalism of quantum radiophysics in describing effects of laser biostimulation.

13. Summary

A main practical conclusion that should be made is that monochromaticity, coherence and good directivity of low-energy laser radiation are extremely important for LBS. For this reason the use of helium-neon lasers proves more effective as compared to semiconductor ones.

Effects of LBS are a non-trivial example of interaction of two non-equilibrium systems: the coherent field and the biologic system. Despite the seeming need for wavelength "resonance" for the two systems to interact, their interaction always occurs in the presence of radiation monochromaticity, which appears to be related to the discrete energy spectrum of the biosystem and to change of its parameters in time – it "breathes", thereby securing resonance of structures. Major features of this interaction are the presence of self-organization and equifinity – independence of the final results from broadly varying initial conditions (a wavelength, an illumination angle, intensity, etc.). In our opinion, these considerations explain, at least at the level of analogies, causes of such "mono direction" of the whole process of laser biologic stimulation toward positive therapeutic results. Without rejecting the preexisting notions of LMS mechanisms, the approach proposed in this book is a generalization demonstrating that the physical pictures like chaotization through bifurcations and heating by radiation, seemingly standing far apart, can be synthesized in one description.

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