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Mechanisms of Interaction of Electromagnetic Radiation with a Biosystem

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Abstract—Fine mechanisms of the interaction of weak electromagnetic radiation (EMR) with information structures of a living cell—nucleic acids, proteins, and membranes—are considered. Special attention is paid to the mechanisms of action of EMR of the millimeter range. Physicomathematical models of the EMR influence on a biosystem are proposed. Data on nonlinear dynamics of biomacromolecules are presented, in particular, the mechanism of the Davydov soliton for energy transfer in protein molecules is discussed. The processes of soliton formation in polynucleotides and of autosolitons in biosystems are considered. A crucial role of coherent effects in the EMR excitation of selected collective modes in biomacromolecules of proteins and DNA is revealed. Several ways of the excitation of levels of collective modes are considered, namely, a set of phased EMR pulses (an analog of the Veksler method of autophasing), periodic phase modulation of EMR, and amplitude–frequency modulation. A common feature of the suggested methods is the possibility of suppressing anharmonicity and, therefore, of the excitation of high quantum levels, which facilitates crossing of a potential barrier and transfer of a molecule to a new conformational state. A problem of the interaction of EMR with a biopolymer chain is considered; the resonances are shown to have a collective nature. The influence of EMR on the dynamics of biopolymers with an active site (antenna model) is studied.

CONTENTS

1. FORMULATION OF THE PROBLEM

1.1. Introduction

At present, a tremendous amount of experimental data on the action of coherent electromagnetic radiation (EMR) on biological objects of various levels of organization—from macromolecules to a living organism—has been accumulated. Construction of high-power sources of EMR, the possibility of concentration (focusing) of wave beams, synchronization of oscillations of many sources, and, finally, bulk data transfer through a single channel by means of these waves are the main advantages that determined successful application of coherent waves in different areas including medicine and biology. Nowadays, sources of coherent EMR of radio (EHF), optical, and UV ranges are applied in several areas of biology and medicine.

One may consider that the mechanisms of EMR action on biological objects already formed one of the most interesting interdisciplinary areas of electromagnetobiology.

For a long time, EMR interaction with living organisms attracts the attention of scientists and engineers by both realized and hypothetical, although insufficiently studied, possibilities of its application in medicine.

According to a general concept put forward by N. Devyatkov, academician of the Russian Academy of Sciences, and his colleagues [1] the areas of application of EMR can be rather clearly divided into two groups. The first group uses energy characteristics of coherent waves, whereas the second group employs information potentialities of coherent waves. Obviously, these two groups may overlap.

1.1.1. The application of energy properties of coherent waves in biology and medicine. It is customary to distinguish between ionizing and nonionizing radiation when evaluating the effects of interaction with different objects at the atomic–molecular level. Normally, electromagnetic oscillations (optical, vacuum-UV, X-ray, and gamma-ray) are classified as ionizing radiation if the energy quantum is large enough to cause, for example, breaking of intermolecular bonds or ionization of atoms, molecules, and radicals.[1] Electromagnetic oscillations with longer wavelengths and low energies of quanta, including radiation of the millimeter range, are related to nonionizing radiation.

Physiotherapy was one of the first areas of application of coherent short-wavelength radiation. Heating of tissues was always one of the main (radical) methods of physiotherapy. Chemical and biochemical reactions are accelerated by heating (proportional to an exponential factor $\exp(-E_A/T)$, where E_A is the activation energy and T is the temperature), which determines the physiological effect. The advantages of heating by coherent waves are associated with the fact that heat release takes place mainly in the tissues lying at a certain distance from the surface (diathermy). In this case, we diminish the undesirable heating of surface tissues, which is inevitable in the case when heat sources act on the surface of a body. The physical mechanism of diathermy is not clear yet. However, our studies shed some light on this problem. Specifically, it became clear that the so-called heat-shock effects are associated with reversible phase transitions of DNA liquid crystals in chromosomes during heating and cooling in the sublethal temperature ranges from 40 to 43°C [126].

The nature of EMR interaction with biological objects is determined by both parameters of radiation (frequency or wavelength, propagation speed, coherence of oscillations, and polarization) and the physical properties of a biological object as a medium in which an electromagnetic wave propagates (dielectric constant, electric conductivity, and nonlinear-dynamic parameters of information biopolymers, as well as parameters depending upon this quantities, namely, wavelength inside the tissue, penetration depth, and reflectance at the air–tissue interface). The decay of the amplitude of a wave during its penetration inside a tissue may be characterized by the penetration depth Λ, defined as the distance at which the amplitude of oscillations decreases $e \approx 2.72$ times. For example, the penetration depth in muscle and skin is $\Lambda = 15$ cm at $\lambda = 10$ cm ($\nu \approx 3$ GHz) and $\Lambda = 0.3$ mm at $\lambda = 8$ mm ($\nu \approx 37.4$ GHz).

The tendency of penetration depth Λ to decrease with the decrease of λ is traced while the wavelength inside the medium is much greater than the size of a cell or cellular organelles (cell nuclei, mitochondria, lysosomes, ribosomes, Goldgi organ, endoplasm net, etc.). Recall that the mean linear size of a cell is of the order of 10^{-2} μm [1], and the length of protein molecules ranges from 4 to 20 nm [3]. However, these estimates are arbitrary because the protein molecules may consist of many subunits and their sizes may change within a wide range, different from 4–20 nm. At very high frequencies, the transmissivity of tissues for EMR starts growing again. For example, hard X-ray and gamma-ray radiation penetrates through soft tissues virtually without attenuation.

As the penetration depth of waves depends upon the frequency, the corresponding physiotherapeutic devices make use of different ranges: 2375–2450, 915, 433–460 MHz, etc. [2].

Hyperthermia, a method of destruction of malignant tumors, became a very important step in the energetic application of coherent waves. The development of this method dates back to 1960–1970s, when it was demonstrated that the viability of tumor cells was strongly suppressed already at 40–42°C. The increase in the temperature influenced tumor cells stronger than the benign ones. The destructive action of ionizing radiation and chemotherapeutic drugs on tumor cells is enhanced by overheating up to a temperature of 43–45°C). Therefore,

[1] Note that the breaking of bonds of a microobject may be caused by EMR, the quantum of which does not exceed the binding energy. This is due to nonlinear effects, in particular, to multiphoton transitions.

nowadays, treatment of tumors uses, as a rule, a combination of hyperthermia and the mentioned factors. Coherent waves localize the heating and accelerate the process itself. In this case, both the limiting depth of the heated area and the ultimate possibilities of localization depend upon the selected frequency range: the lower the frequency of oscillations, the deeper the penetration of radiation. However, the possibility of localization of heated area is aggravated in this case. In the 1970s, academician N.D. Devyatkov and Dr. E.A. Gel'vich initiated and supervised pioneering works that resulted in the construction of appliances operating in different frequency ranges (2450, 915, and 460 MHz) and providing constant temperature during heating with an accuracy of 0.3°C.

At present substantial progress is being achieved in the field of laser application in surgery.

A real boom in laser medicine emerged relatively recently. It is explained, first of all, by the development of a series of novel highly effective and reliable lasers and by the development of flexible optical fibers for the delivery of laser radiation.

Let us enumerate only some of the main branches of laser medicine: ophthalmology (retina welding, treatment of glaucoma); cutting of biotissues (including biotissues with a developed net of blood vessels); ablation of sclerotic plaques, cutting, layer-by-layer evaporation, and coagulation of biotissues; laser dentistry; cardiosurgery (including recanalization of vessels clogged up by atherosclerotic tissue); laser surgery of cholelithiasis; laser microsurgery in gynecology; etc.

In practice, different types of gas and solid-state lasers, operating in pulse, cw, and pulse–periodic regimes, are widely applied, including ruby and neodymium pulse solid-state lasers, CO and CO_2 cw lasers (units that use pulse CO_2 lasers are also available), pulse–periodic copper-vapor lasers, and excimer lasers.

A possibility of the application of pulse lasers on yttrium aluminum garnet with neodymium in laser surgery is being studied at present. Unfortunately, the efficiency of these lasers is several percent only. The situation is the same with neodymium glass lasers. A relatively low efficiency of these lasers is associated with the fact that neodymium ions absorb only a small portion of radiation of a pumping lamp, all the rest is converted into heat. Researchers from the Institute of General Physics of the Russian Academy of Sciences headed by academician A.M. Prokhorov found the ways of increasing the efficiency of neodymium lasers. They suggested to use a crystal of gadolinium scandium gallium garnet (GSGG) with Nd and Cr as an active medium. Its efficiency is 2–3 times higher than that of widely applied yttrium aluminum garnet with Nd. A disadvantage of GSGG lies in its lower, compared to yttrium aluminum garnet, thermal conductivity. However, GSGG crystals have several advantages (apart from high efficiency): the rate of the growth of this crystal is 5 times higher and it has a higher radiation stability (the latter was proved by the scientists from the Institute of Nuclear Physics of the Republic of Uzbekistan). After that, new effective laser crystals were developed. Their application seems to be quite promising.

Summarizing we may state that the progress in laser medicine was achieved due to (1) the high level of studies of interaction of radiation with biotissues, (2) development of optical fibers with low losses and high radiation stability to high-power laser radiation, and (3) construction of a variety of original solid-state and gas-discharge pulse–periodic lasers.

1.1.2. Application of coherent resonance radiation of low power in biology and medicine. The second direction related to the application of coherent EMR in biology and medicine includes extensive works on the application of sources of low-intensity radiation in radio (EHF), IR, optical, and UV ranges. Interaction of such radiation with biotissues is not accompanied by any serious heating. The nature of radiation action in this case is not clearly determined yet. To some extent, we clarified the situation by publishing the results of our studies on nonlinear dynamic states of biomacromolecules that depend on EMR modeling these states (see, for example, [127]).

Upon the excitation of oscillations in bioobjects within different above-specified frequency ranges, the effects of radiation action have very much in common. The most substantial (unifying) feature is the manifestation of a sharply resonant response of a bioobject to the action of coherent radiation within all specified ranges.

Especially extensive studies of sharply resonant action on bioobjects were carried out by Russian and foreign researchers in the EHF range[2] (30–300 GHz) (see, for example, reviews [4–6], monograph [1], and papers [10–15] and [20–29]). Conditions under which the observation of sharply resonant action of these waves on an organism is possible were investigated in detail (see, for example, [7, 8]).

One encounters difficulties when reproducing a sharply resonant effect on different biological objects. The analysis of this complicated phenomenon is presented in [16]. This study developed methods allowing one not only to guarantee high reproducibility of the discussed effects but also to investigate the shape of resonance curves.

The experimental results clearly demonstrate the decisive role of a sharply resonant response of living bioobjects to EHF action in maintaining a homeostasis, which is a combination of adaptability reactions of living organisms [17–19]. The existence of multiple resonances is typical for biomembranes. These resonances are frequency-shifted relative to each other, and each of these resonance corresponds to its own type of biological action [18, 19]. It is assumed that EHF action mainly maintains and restores homeostasis, although

[2] The range of extremely high frequencies (EHF) from 30 to 300 GHz corresponds to the range of millimeter waves from 1 to 10 mm [9].

this approach is too simplified from the point of view of biochemistry and physiology. Radiation has virtually no influence on the functioning of normal cells that have no distortions [17]. In case of distortions, EHF action at the corresponding resonance frequencies speeds up recovery processes.

The potentialities of medicobiological action of EHF radiation are rather diversified. More than ten years have passed since both in our country and abroad EHF methods were applied for the treatment of ulcers of stomach and duodenum, trophic ulcers, traumas of soft and bone tissues, stenocardia and infarct of myocardium, hypertonia, ophthalmological diseases, osteochondropathia of the femur tip of children and youngsters, and burn diseases; for defending hemogenesis from harmful influences; and for regulating and recovery of enzyme activity of microorganisms [10–12, 20, 30, 31].

We emphasize that the principles of application of coherent millimeter waves ($\lambda = 1$–10 mm) of low intensity were tested both on microorganisms and on mammals already at the first stages of investigations in the late 1960s–early 1970s. Academician N.D. Devyatkov conducted general scientific supervision of the studies carried out in many scientific institutions. From the very beginning, the studies were aimed at elucidation of potentialities of application of these principles in medicine and biology. To get an idea of the extent of the works, note that the experiments were carried out with more than 10 thousand animals for comprehensive testing.

It is worthwhile to note that the therapeutic action of coherent millimeter waves of low intensity is optimal if certain resonance frequencies or their combinations used in experiments correspond to a given type of disease.

As soon as the possibility of application of coherent waves for the treatment of this or that disease is established, the introduction of the corresponding method into practical medicine occurs. The successful application of therapeutic methods based on the action of low-intensity waves at the resonance frequencies optimal for a given disease for the treatment of thousands of patients (although the number of working devices is not large, because their industrial production has not started yet) is the most important general result of the introduction of these methods into practical medicine. The period of treatment is reduced in comparison with the periods typical for treatment with medicines, whereas the efficiency of therapy is increased.

Here, it is worthwhile presenting some bright examples of the effective application of EHF methods.

In the recent years, a group headed by Professor I.M. Kurochkin and Dr. M.V. Poslavskii carried out fruitful studies and promotion in practical medicine of EHF methods of treatment of ulcers of stomach and duodenum. As a result, 95% of ulcers were cured without any medicine.

The results of the work performed at the Priorov Central Institute of Traumatology and Orthopedics showed that the action of coherent waves of millimeter range is highly effective in treatment of wounds and traumas, including infected ones, in specific cases when, because of various reasons, neither blood transfusion nor antibiotic therapy could be applied.

There are no doubts about the prospects for the application of the EHF method with sharply resonant radiation of low intensity. In this context, we briefly present the experimental results illustrating another approach to therapy with the application of low-intensity millimeter radiation (O.V. Betskii, M.B. Golant, N.D. Devyatkov, E.S. Zubenkova, and L.A. Sevost'yanova, 1987). In this experiment, the possibility of healing an animal after a lethal doze of ionizing radiation when marrow transplantation itself could not have any substantial influence on the recovery process was studied. The resources of an organism are already exhausted and the direct action of coherent waves on an affected organism may only speed up its death. However, such irradiation can be used for the activation of cells of transplanted marrow, thus increasing their activity after transplantation. Indeed, the transplantation of activated marrow made it possible to cure all the mortally irradiated animals. Their lives elongated approximately 40 times and became virtually normal for these animals.

A resonance character of biological action was detected also in the optical range [32]. Note that the study of the shape of resonance curves in this range is aggravated by the difficulty of continuous tuning of lasers within a wide spectral range and needs special approaches. Specifically, Karu *et al*. [33] demonstrated a rather narrow dependence of a biological effect on the frequency with the help of bandpass filters that cut out appropriate bands from the emission spectrum of an incandescent lamp.

Studies [34, 35] are mainly devoted to the emission of cells in the UV range. The authors also discuss sharply resonant irradiation and its relation to the disturbances of functioning. The existence of multiple resonances was stressed. Paper [34], devoted to the role of UV radiation, describes observations similar to the effects in the EHF range. It is stressed that any factors disturbing cell functioning cause changes of the emission of photons from the cell.

Wide application of helium–neon lasers in medicine gives evidence of the influence of low-intensity coherent radiation within the optical range at some resonance frequencies on the recovery processes in an organism. Radiation of both optical and millimeter ranges at proper resonance frequencies can be successfully applied in treatment of several diseases (ulcers of the stomach and duodenum, trophic ulcers, stenocardia, etc.). The similarity of the action of EMR in optical and millimeter ranges at appropriate resonance frequencies on biological tissues is traced even in some details of the phenomenon. In particular, in the course of medical treatment of ulcers of stomach and duodenum, rough cicatrices usually appear, which may cause illness relapses. The application of sources of coherent EHF radiation or

lasers of optical range in therapy of these diseases allows one to get rid of rough cicatrices. The same holds for the treatment of stenocardia.

The role of coherent waves of the IR range in metabolic processes was studied in [32, 36].

In Section 3, we consider the problem of the correlation of low-intensity resonant action in the EHF, IR, optical, and UV ranges within the framework of the hypothesis of information–control function of coherent radiation in the course of its interaction with bioobjects [28, 37].

1.2. The Influence of Low-Intensity Coherent Radiation of Millimeter Range on Biological Objects

The problem considered in this section is comprehensively discussed in monograph [1]. For the reasons of completeness of presentation, we reproduce here only the main points of this analysis.

1.2.1. Some general considerations. The spectrum of EMR ranges from the frequencies of 10^{23} Hz (the wavelength is 10^{-14} m), typical for γ-rays, to the frequencies lower than 10 Hz (the wavelength is greater than 10 m). The magnitude of a quantum of radiation determined the possibility of this or that transformation at the atomic–molecular level in a microobject being influenced by an electromagnetic field. According to Section 1 the entire spectrum may be divided into two parts: (1) the range of high frequencies, starting from the low-frequency bands of the visible range (with a frequency of 4×10^{14} Hz and wavelength of 7500 Å), when dissociation is possible, and low-frequency bands of the UV range ($\nu = 7.5 \times 10^{14}$ Hz and $\lambda = 4000$ Å) and higher, when ionization becomes possible (in this case, we consider ionizing radiation); (2) the range of low frequencies, where no breaks of bonds in an atom or a molecule occur (in this case, we consider nonionizing magnetic fields).

The second part of the spectrum includes far-IR, microwave, radio, and extremely low frequency ranges. According to the International classification [38], the low-frequency part may in turn be divided into narrower ranges (see Table 1).

For reference, we present the maximum permissible levels of radiation according to USSR standards [39] (see Table 2).

The idea of applying EMR within the EHF range for the specific action on biological structures and organisms was originally put forward by Soviet scientists (N.D. Devyatkov, M.B. Golant, *et al.*) in 1964–1965. The essence of this concept is as follows. Microwaves are strongly absorbed in the atmosphere of Earth. Therefore, living organisms could not have natural mechanisms of adaptation to the oscillations of significant intensity within this range coming from outside. However, they could adapt to similar oscillations of their own.

Table 1

Name of the range	Frequency range
Extremely low frequencies (natural background)	300 Hz
Very low frequencies	300 Hz–10 kHz
Low frequencies	10 kHz–1 MHz
High frequencies	1–30 MHz
Very high frequencies	30–300 MHz
Ultrahigh frequencies	300 MHz–1 GHz
Microwave range	1–3000 GHz

Table 2

Frequency range	Maximum permissible level (field strength or intensity)
Long waves, 30–300 kHz	20 V/m
Medium waves, 0.3–3 MHz	10 V/m
Short waves, 3–30 MHz	4 V/m
Ultrashort waves, 30–300 MHz	2 V/m
Microwaves, 300 MHz–300 GHz (24-hour exposure)	5 μW/cm^2

In Section 1, we presented the effect of hyperthermia as a typical example of the energetic action of radiation on an organism, when a useful biological effect is achieved by the transfer of EMR energy into heat. However, such an influence of EMR on an organism is possible under which the temperature increase is insignificant ($\simeq 0.1$°C) and does not play the main role in bioeffect. In such cases, we usually speak about control or information action of EMR of low or nonthermal intensity. Numerous studies showed that this is the feature of EMR of the millimeter range (1–10 mm) at a low power density of several tenths of or several milliwatts per square centimeter of the irradiated surface.

The application of millimeter waves in biology and medicine is highly promising due to several peculiarities of coherent interaction of this EMR with bioobjects at different levels of organization—from biopolymer molecules to the whole body. At the initial steps of theoretical substantiation, the unique nature of the influence of EMR of millimeter range on the vital activity of organisms was inconsistent with standard concepts. It was assumed that only incoherent (thermal) oscillations can be generated in a living organism or in its cells and that the symptoms of external action are only of nonspecific thermal type, and an organism responds to them as to a stress factor. Note that the energy of a quantum within this range (at $\lambda = 1$ mm, $h\nu = 1.17 \times 10^{-3}$ eV) is lower than the energy of thermal motion (at $T = 300$ K,

Table 3

Type of energy	Typical values of energy, eV
Energy of electron transitions	1–20
Activation energy	0.2
Vibrational energy of molecules	10^{-2}–10^{-1}
Energy of hydrogen bonds	2×10^{-2}–10^{-1}
Energy of thermal motion	2.53×10^{-2}
Energy of a quantum for $\lambda = 1$ mm	1.17×10^{-3}
Energy of rotation of molecules around bonds	10^{-3}–10^{-4}
Energy of Cooper pairs in superconductivity	10^{-4}–10^{-6}
Energy of magnetic ordering	10^{-4}–10^{-8}

$kT = 2.53 \times 10^{-2}$ eV). In Table 3, we present for comparison the typical values of energies of other types.

It follows from the comparison of energies of different physical processes that millimeter radiation may influence substantially the vital activity only in the case of multiphoton processes typical for coherent oscillations.

Nevertheless, we should note some of the early hypotheses put forward before the implementation of correct experiments and important for understanding of the evolution of the concepts of mechanisms of interaction of radiation with biological objects.

One of the first mechanisms of generation of coherent oscillations by living organisms was proposed by English physicist H. Frölich [40, 41]. One may find further development of this idea in [15, 42–48].

The essence of the Frölich hypothesis is as follows. Biological systems may have polarization (dipole) oscillations within the frequency range from 100 to 1000 Hz ($\lambda = 3$–0.3 mm). Vital activity in biosystems is accompanied by energy transport through locally excited dipole oscillations (biological pumping). A transition of a system to a metastable state may take place due to nonlinear effects of interaction of dipole vibrations and due to nonlinear coupling of this vibrations with elastic vibrations of DNA, proteins, and membranes. In this transition, energy is transformed into vibrations of a certain type. Under the action of external EMR, a metastable state may turn into a ground state, which gives rise to a "giant dipole"—a specific case of coherent state in a biological object. Such perturbations of biosubstrates resemble low-temperature condensation of Bose gas (Bose condensation of phonons).

According to another version, a "protein machine" hypothesis of D.S. Chernavskii, Yu.I. Khurgin, and S.E. Shnol' is accepted [49]. In this case, we assume that the storage of electromagnetic energy is possible in the form of mechanical stress of a biomacromolecule, which is also a specific case of a coherent state.

The mentioned models differ mainly by the form of storage of energy. All of them are united by an idea that biological structures feature a selected degree of freedom of mechanical nature in which energy can be stored. This selected degree of freedom plays an important functional role in biological processes. In particular, this feature distinguishes living (thermodynamically nonequilibrium) systems from inorganic ones. The energy of external radiation transforms into the energy of polar molecules related to rotational degrees of freedom. Polar molecules of water with a dipole moment of 1.84 D may serve as such accumulators of energy.

The hypotheses put forward by the authors of [40, 49] are based on the assumption about the existence of coherent oscillations in living organisms. However, they do not account for the dependences and regularities characterizing interaction of microwave EMR with living organisms.

There is also a hypothesis [50] presuming the existence of an unidentified molecule that takes part in the intermediate stages of the development of biochemical reactions and resides in a triplet state where two nonpair electrons interact with each other through their magnetic fields. The molecule has three possible initial states, each of which corresponds to its own pathway of chemical reaction. It is assumed that the initial state may be influenced by EHF pumping, which regulates the course of biological processes.

1.2.2. The main regularities of the action of low-intensity electromagnetic radiation of millimeter range on biological objects. Let us present in brief the main regularities of the action of microwave EMR of low intensity on biosystems based, in particular, on the experimental data [1].

(1) The change of the power density within wide limits does not influence the reaction of organisms to the action of EMR as determined by a certain biological parameter. Starting from some minimal (threshold) value of the power density and up to its values causing pronounced (exceeding 0.1°C) heating of tissue, the biological effect of microwave EMR remains virtually the same [11, 51, 52]. In some cases, the effect related to the irradiation of microorganisms and determined by a certain biological parameter does not change with the variations in the power density up to 10^5 times.

(2) A variation in a certain biological parameter (e.g., of some particular enzyme activity) after the action of EMR on an organism occurs only within narrow bands of the acting frequencies that are normally 10^3–10^4 of the medium frequency. This phenomenon was called a sharply resonant effect of biological action. The number of such bands interchanging with the bands where no substantial changes of this parameter take place may be rather large [11, 51, 53, 54].

(3) The type of sharply resonant biological action depends on the frequency of coherent oscillations. At various resonance frequencies detected for one biological

reaction, the type of changes for another reaction may strongly differ from that for the first reaction.

(4) Effect of irradiation depends upon the initial state of the irradiated organisms.

(5) The results of action of microwave EMR may be memorized by organisms for a long time. This happens only in the case of prolonged (no less than half an hour) or, sometimes, multiple action of EMR [56].

(6) For animals, the biological effect of EMR is not related to the direct action of energy falling from the outside on the surface of a body or on an organ (or a system) controlling the function modified under the action of EMR. The distance from the irradiated area to the corresponding organs or systems may be a hundred or a thousand times longer than the distance at which the power density diminishes by an order of magnitude due to losses in tissues. At the same time, the effectiveness of EMR irradiation is different for different parts of the surface of a body. According to the experimental data [30], the action of EMR may be realized, in particular, in the case of irradiation of acupuncture points, which proved the hypothesis put forward earlier [27].

1.3. Information Aspects Associated with the Action of Resonance Electromagnetic Radiation of Low Intensity on Bioobjects

1.3.1. Information aspects associated with the action of radiation on a living organism. A very low energy of EMR necessary for substantially affecting the functioning of organisms, the specific features of this phenomenon, and a high reproducibility of the results—all of this pushed the researchers to a hypothesis [27, 28, 57, 58, 126] according to which EMR is not an accidental factor for organisms. Similar signals are produced and used for certain purposes by the organism itself. The external coherent radiation only imitates the signals produced by the organism.

The essence of the second hypothesis is as follows. The observed regularities in the action of coherent EHF EMR of nonthermal intensity are explained by the fact that, penetrating inside an organism, this radiation is transformed at certain (resonance) frequencies into information signals controlling and regulating recovery and adaptation processes in an organism. Both processes are referred to as an "adaptive growth" [59] or are treated, according to [126], as the wave epigenetic functions of chromosome apparatus, cytoskeleton, and extracellular matrix.

Here, we present some of the main facts that provide a background for these hypotheses.

(1) The minimal (threshold) power density of the incident radiation necessary for producing a substantial biological effect is negligibly low in comparison with heat power emitted by the organism itself into space. For human beings and animals, this power density is about 10^{-3}–10^{-4} of the heat power [51, 56, 60]. The power density is so low that radiation does not cause even local heating of tissues by more than 0.1°C. In any case, EMR cannot cause any disturbances in tissues because the energy of its quanta is two orders of magnitude lower than the energy of weak hydrogen bonds.

At the same time, the power of external radiation is quite sufficient for the formation of control signals. In any information system (including technical ones), the energy of such signals is several orders of magnitude lower than the energy of a system as a whole, which is determined by the power of actuators or appliances.

(2) It was noted in Section 2 that the action of EHF radiation, determined by a certain biological parameter, does not depend on its intensity within wide limits. Such a type of the dependence of the action on the intensity of an acting factor is quite natural for information systems and is due to the specific features of the control regulation process. Apparently, for energetic action (the effect of which is determined by energy), such a type of dependence has not been observed yet.

(3) Threshold type of the dependence of a biological effect on the intensity of radiation is an imperative condition for the operation of an information system. If this condition is not met, the operation of the system can be disturbed by any external interference or noise. A threshold type of action is possible for energetic action. However, in this case, a further increase in power changes biological effect, in contrast to the information action.

(4) The type of a biological response of an organism depends upon the frequency of the acting waves. Each specific action is possible only within a narrow frequency range. This action may be impossible at different frequencies or it may be qualitatively and quantitatively different (including the absence of any action [11, 51, 61]). In other words, the frequencies of oscillations determine the type of action of considered radiation on an organism, i.e., the frequency is the carrier of information.

(5) Resonance frequencies related to certain biological effects are strictly reproducible under reproducibility and control of the experimental conditions [8]. Such a distinct dependence of action on the numerical value of the information parameter (which is the frequency of oscillations in the case at hand) is typical for information systems designed for the processing of large amounts of data.

(6) All the above-listed features (2)–(5) are manifested only simultaneously. If an effect determined by a certain biological parameter is independent of the EMR power, then the bioeffect displays a resonance dependence on the frequency of oscillations [11, 51, 52, 62]. Thus, we deal rather than with a random set of factors, with a deep interrelation of factors which is due to specific features of operation of information systems.

(7) Information basis accounts well for the fact that the changes in living tissues resulting from irradiation are absent when the tissues are irradiated after

the termination of vital activity. Regulating systems do not work in dead tissues [10].

(8) We noted in Section 2 that the action of EMR depends crucially upon the initial state of an organism. Thus, if in the initial state some function is weakened several times compared to the normal state, then radiation may bring it back, whereas the same radiation has virtually no influence on the normal state of the organism [61, 63]. An important reason for that is the fact that one of the most important functions of information signals in the organism is the maintaining of homeostasis, i.e., the ability of biological systems to withstand mutations and to keep relative stability of composition and properties.

(9) If an organism is large enough, EMR may influence organs rather distant from the irradiated spot, which makes direct energetic effect impossible [62, 67]. However, this circumstance seems to be quite natural within the framework of the suggested hypothesis: the signals periodically amplified due to metabolic energy may spread over large distances along the communication channels within a single information system of a living organism. The amplification of weak signals does not require great energies and is comparable to the energetic resources of an organism.

(10) Living organisms under natural conditions do not experience the action of monochromatic EMR of millimeter wavelength range because of their absence in the environment. How did all the organisms, from bacteria to a human being, work out during the evolution a specific (depending upon the frequency of oscillations) reaction to this radiation? This fact does not contradict the information hypothesis because, according to this hypothesis, the efficiency of action of external coherent radiation is explained by the fact that, penetrating inside an organism, they are transformed into signals similar to information ones that are produced by the organism itself for the regulation of the process of recovery and adaptation to the environmental conditions. The existence of the same radiation in the environment could disturb the information system of the organism by introducing interference. Therefore, the use of the control signals that cannot be simulated by radiation from the outside in the inner system is not biologically expedient.

(11) It is rather important for substantiating the information nature of EMR action on living organisms that the information content (the ratio of the amount of the processed information to the energy consumption for this processing) for the millimeter range is extremely high. In particular, for living organisms, this information content substantially exceeds the corresponding value for optical and UHF ranges [1].

(12) The constitution of different living organisms, starting from bacteria up to a human being, the functioning of which can be influenced by in the millimeter range EMR is absolutely different. Irradiation may provoke the changes in various functions even for the same species. For example, in [60] the influence of EMR on the treatment of different human diseases and the regulation of functioning of microorganisms is described. One can hardly imagine that the mechanism of changes is the same for all the diversity of changes observed upon the irradiation of different and similar organisms. At the same time, the considerations mentioned above, which attribute the observed regularities of EMR action to the information function of this action, give quite a natural answer to this question: the general regularities of operation of information systems must be realized irrespective of the mechanisms implementing the regulating signals.

(13) Recently, new data that slightly fall out of the frames of the presented considerations have been obtained [126]. A notion of a "wave gene" was introduced for the most substantial part of "wave metabolism" of biosystems where the millimeter range (both exogenous and endogenous) is only a part of electromagnetic and acoustic symbol wave processes. Synthesis of soliton and holographic matrices performing transportation and reduction of strategic bioinformation, generated and accepted by organisms, is a particular case of conversion of wave processes into biosymbolic ones. DNA molecules included into chromosomes, cytoskeleton, ribosomes, membranes, and the system of extracellular matrices provide a substrate for the development of these processes.

1.3.2. Regulation of functioning in a living organism and generation of coherent waves by its cells. Living organisms, even elementary species, such as single cells, adequately adapt their functioning to continuous changes of habitat related to the changes both in the organism itself and in the environment. The number of possible changes and the corresponding reactions is tremendous. Hence, even a single cell must possess a complicated system regulating its reactions.

An average size of a cell is about 5 μm. How can such a regulating system fit such a small volume and how does it work? Priority studies carried out in our country during the last 25 years [1, 126] showed that cells regulate their functioning eliminating disbalances and adapting to the changing habitat with the help of coherent acoustoelectric waves. An alternate electric field of these waves, emitted into the surrounding space, allows interaction of neighboring cells and cells approaching each other. Spreading over an organism, they may promote organization of interrelation and regulation of the intracellular processes in the system as a whole.

The wavelength of acoustoelectric waves in an organism is roughly 10^6 times shorter than the wavelength of electromagnetic millimeter waves in free space ($\lambda = 1$ mm). Thus, the size of a cell is 5×10^3 times larger than the wavelength of acoustoelectric waves. Therefore, systems of large electric length may exist inside a cell. These systems are able to generate a large number of regulating signals and to influence in different ways the intracellular processes.

1.3.3. Mechanisms of generation of coherent waves by cells. The studies showed that the generation of coherent waves by cells is a systematic process in which cellular membranes, protein molecules, and metabolism are involved. The frequencies of generated oscillations are determined by resonances in membranes. The energy is fed to the membranes in cytoplasm and to protein molecules capable of vibrating at the same resonance frequencies. Protein molecules, in turn, acquire energy of intracellular metabolic processes. Adjoining are the processes of excimer and exciplex pumping of nitrous nucleotides of DNA according to laser principle. In this case, DNA attains a highly regular liquid-crystal structure and the ability of emitting an ultraweak coherent photon field within the range from 250 to 800 nm. The role of such a field may be associated, in particular, with read-out of quasi-holographic gratings of chromosome continuum and the recovery of symbol photon mark-up fields, which organize the spatial–temporal structure of biosystems [126].

In a normal cell, protein molecules are in thermal equilibrium with the medium, and the emission spectrum of the cell differs slightly from a thermal one, corresponding to the temperature of the environment. If the normal functioning is distorted and the shape of the cell is disturbed, the conditions are created for preferred excitation of cellular membranes at certain resonance frequencies. At these frequencies, the energy transfer from protein molecules to membranes is stimulated, which is promoted by the synchronization of the vibrations of bound protein molecules by membranes.

Thus generated oscillations reflect the existing malfunctioning, which, in accordance with the La Chatelier principle (and its analog in biology—the principle of conservation of homeostasis), results in the processes bringing the system back to the initial state.

It was revealed that the frequencies of vibrational process excited in a cell in the case of functional disorders remain the same until unbalances are removed. Such stability is provided by the formation of substructures consisting of protein conglomerates on the surface of the membranes under the action of excited acoustoelectric waves.

Note that the external irradiation of cells with coherent waves may lead to the formation of substructures on the membranes of healthy cells and induce the corresponding generation of coherent waves by cells themselves. A mechanically stable structure of membranes is not disturbed by the processes related to the generation. Radiation weakly influences the current functioning of the cells. In the case of the formation on membranes of sharp deformations (which corresponds to disturbance of functioning), the processes related to the generation of coherent waves at resonance frequencies result in relatively fast changes in the shape of membranes and easily detectable changes in cell functioning. The induced substructures gradually disappear as a result of Brownian movement upon the normalization of the state of cells.

The studies performed at the Institute of Radioelectronics of the USSR Academy of Sciences under the supervision of academician N.D. Devyatkov showed that the processes of heating of tissues and substances caused by coherent waves may influence substantially their functioning, in particular, information processes proceeding under the action of coherent waves. Of especial importance are the processes related to absorption of wave energy by water, playing an important role in the life of an organism. One should keep in mind that protein molecules and DNA polymers may function properly only inside highly organized water surroundings of intracellular and intercellular medium.

Absorptivity of water depends upon the type of intermolecular interactions. Therefore, the peculiarities of absorption of radiation by water molecules in biostructures may cause structural heating of water, phase transitions in biological membranes, etc. Even at low intensities of radiation of several tenths of or several milliwatts per square centimeter, large gradients of the electric field and related thermal gradients may arise in such layers. This may stimulate mixing of extracellular liquid, change transport of ions in water and of other substances through cellular membranes, and give rise to thermal and acoustic waves. However, these thermal phenomena themselves have no resonance character.

1.3.4. The interrelation of action of coherent low-intensity radiation of EHF, IR, optical, and UV ranges on living organisms. The application of coherent radiation of low power of the mentioned ranges in medicine and biology necessitates permanent specification of the concepts of the processes taking place in an organism under the action of this radiation. The development of the concept of information–control role of radiation within all indicated ranges in vital activity is the most important achievement in this way. Such a role is a direct consequence of the fact that the supercomplex systems of multicellular organisms may operate in a stable way only in the presence of a highly developed regulating system using a supply of rather low power (comparable with energetic potentialities of an organism) [37, 127].

The essence of homeostasis (relative stability) presumes that any changes in the organism and in its different systems, consisting of elements functionally related to each other, cannot be isolated. The changes in some of the functions must cause the changes in the others, compensating to this or that extent for the negative influence of the former on the functional systems. However, the compensation is probably incomplete and the action of each range has its own peculiarities. The assumption of the possibility of correlated excitation of oscillations within different frequency ranges seems to be highly probable if the most miniature organisms (cells) are considered. The elements of these organisms must take part in implementation of different functions because the

diversity of the latter is enormous. Radiation of all mentioned ranges influences primarily the cellular processes.

As the radiation generated by cells at different frequencies in different ranges may maintain homeostasis only in the case of concerted action, it is likely that the only way providing optimal recovery processes is the use of correlation of excitation of mentioned waves.[3]

Under correlated excitation of the oscillations of different frequency ranges in an organism, the biological results of action have very much in common: sharply resonant ($\Delta f/f \sim 10^{-3}$) biological response of the organism to the action of coherent radiation of all indicated ranges, existence of multiple frequency-shifted resonances of membranes, correspondence of each resonance frequency to its own type of biological action, and the absence of influence of radiation on the current functioning of normal cells having no disorders.

At the end of this section, we will point out an important fact. Since complex cellular systems include nonlinear elements, nonlinear conversion of frequencies is inevitable. In particular, Del Giudice *et al.* [68] considered the change of the dielectric permittivity in a strong electric field as a source of nonlinearity (for example, the dc component of the field of polarization for lipid membranes is of the order of 10^7 V/m, and the ac component of the field is proportional to the dc field). The main genetic molecule (DNA) is another important nonlinear element of the cell. Such a positively nonlinear effect as the formation of solitons is possible in this molecule. We proved it experimentally within the frames of phenomenon of Fermi, Pasta, and Ulam recurrence [126]. Holographic associative memory is another phenomenon of genetic apparatus, which is also related to a nonlinear effect of phase conjugation. The description of this effect involves the model of four-wave mixing [126].

According to the data presented in [32, 36], the original resonance frequencies (17910, 18420, 19560, 21150, 23970, 25080, 27960, and 28680 Hz) are converted in the course of metabolism into a long series of combination frequencies which are nothing but the second and the third harmonics of these frequencies and the frequencies of oscillations resulting from optical mixing and parametric generation. Only original frequencies are observed at the beginning of a cellular cycle. The spectrum is enriched in the course of metabolic processes with the bands of higher frequencies, which can be explained by the increase in the amplitude of generated oscillations and, consequently, of the amplitude of high-order harmonics. However, the spectral bands of higher frequencies related to the described frequency transformation do not exceed 9×10^4 GHz (3000 cm^{-1}), i.e., lie within the optical range where the lowest frequency bands are higher than 4×10^5 GHz. They obviously do not reach the range of UV spectrum, starting from 7.5×10^5 GHz. An effective frequency transformation into these ranges based on the principles mentioned above is hardly possible.

The generation of coherent waves in the IR range seems to be associated with metabolism [32] and the disturbance of electric symmetry of cells. However, metabolic processes are natural for cell functioning and, thus, they can hardly disturb the homeostasis. The excitation of coherent waves of EHF, optical, and UV ranges in cells results from the changes inside cells that disturb homeostasis. We may assume that, under the circumstances mentioned above, the coherent waves of the IR range, on the one hand, and of EHF, optical, and UV ranges, on the other hand, regulate different processes. This is the basis for the hypothesis about interrelation of excitation of coherent waves in different ranges. What is the physical and, so to say, intelligent nature of such regulating logical processes?

The length of the majority of protein molecules ranges from 4 to 20 nm [3]. As the speed of propagation of acoustic waves is several hundred meters per second, the resonance frequencies (the fundamental harmonic) of acoustic vibrations of the majority of these molecules belong to the EHF range. It determines [69, 70] the efficiency of participation of protein molecules in a system process of generation of acoustoelectric waves in cells. However, we should point out that the same molecules may serve as resonators for electromagnetic oscillations of substantially higher frequencies. Thus, in the case of wave propagation in vacuum, the wavelength in vacuum equal to the length of a molecule (1 nm) would correspond to the resonance frequency of 3×10^{16} Hz. However, if we take into account that an equivalent relative dielectric constant of a molecule is about several units and that the linear sizes of the resonators of complex shapes are often less than the wavelength by approximately an order of magnitude [71], then we may determine the excited frequencies as roughly 50 times lower than the indicated value, i.e., 5×10^{14} Hz. This value is close to the frequency boundary between UV and optical ranges and may account for the excitation of acoustic waves in both ranges. In particular, the excitation of acoustic vibrations of protein molecules may be related to the release of energy during its transformation in the course of metabolism. The same is valid for DNA molecules.

As the electrical charges are inhomogeneously distributed along the peptide bonds, acoustic vibrations of a protein molecule may give rise to oscillations of both types: acoustoelectric oscillations in the EHF range, which are determined by the total length of a given molecule, and oscillations in the UV and optical ranges, which are related to the excitation in a molecule of electromagnetic vibrations accompanied by the storage of energy of elastic deformations at the points of pronounced bendings of the molecule. As both types of oscillations are related to the same molecules, the simultaneous excitation of these oscillations seems to

[3] This idea does not contradict the earlier hypotheses [37] about the domination of EHF waves in the system of regulation of cellular processes aimed at maintaining and recovery of homeostasis.

be a natural process. One should note that the values of synchronously excited resonance frequencies of different ranges, their ratio, and the ratio of amplitudes of oscillations at these frequencies depend upon the topology of protein molecules. Apparently, the optimal type forms of proteins have been selected in the course of evolution not only according to optimal enzymatic functions of proteins but also with regard to adequate electromagnetic attributes of metabolism.

One cannot consider the sizes of cells (e.g., along the perimeter of the outer membrane) to be small in comparison with the wavelength of radiation in the UV and optical ranges. For cells (the mean diameter is 50 μm), the perimeter of the plasmatic membrane is close to 15 μm, i.e., it is approximately 30 times greater than the wavelength of an electromagnetic wave (even if we consider the wavelength in vacuum between the UV and optical ranges). That is why the "antenna systems" of cells [18], built up with the help of the waves of the EHF range, for the waves of optical and UV ranges can send a flux of radiation at significant distances with a rather high efficiency and admissible losses in the power density. There is virtually no evidence of almost complete (as in case of waves of the EHF range) stochastization and the loss of coherence of radiation. It was possibly due to this reason that, first, A.G. Gurvich [72] and then other authors [36, 73] revealed the influence of living organisms on each other by means of emitted waves in the UV range (reflection or absorption of these waves disturbed communication).

1.4. Possible Molecular Mechanisms of Interaction of Radiation of the Millimeter Range with Protein and Nucleic Acid (DNA) Macromolecules

The discovery of extremely sharp resonant effects is the most interesting subject of experiments on the interaction of low-intensity EHF EMR with biological objects (from "primitive" biomacromolecules to the whole organism). The elucidation of the molecular nature of the indicated resonance effects is a rather complex problem. The current situation is rather contradictory. In spite of successful clinical applications of EHF methods for the treatment of different pathologies (see Section 1), it is still not clear how one can account for the pronounced influence of the fields that cause local heating of tissues by no more than 0.1°C. It is not clear what is the level of reception of EMR and of "purely physical" primary acts of its bioinfluence. However, the universality of the action of weak microwave radiation on organisms puts forward a basic question a to whether the electromagnetic channel of interaction in the corresponding frequency range is a fundamental intrinsic way of information and regulation transfer in living nature.

1.4.1. Theoretical models of vibrations in proteins. In the case of globular proteins, the mechanisms that assume collective motions of the whole macromolecule or of its isolated large parts (domains), subunits, etc. are considered. The calculations of normal modes are based on X-ray data at the level of atomic resolution. One chooses initial coordinates in conformational space of macromolecules and uses different approximations to select, from the whole matrix of force constants, a part responsible for the lowest frequency modes with regard to possible nonlinear effects. To introduce the general tendencies in the development of these studies, we will briefly discuss some of the main results.

Brooks and Karplus [74] calculated low-frequency vibrational modes for a small globular protein–pancreatic trypsin inhibitor (PTI). Vibrational frequencies lower than 120 cm^{-1} correspond to a model of elastic vibrations of a protein molecule. Modes with frequencies lower than 50 cm^{-1} ($\lambda < 0.2$ mm) correspond to anharmonic vibrations.

Chon [75] developed a quasi-continuous model, which presumes that the dominant low-frequency mode in a protein molecule is determined by collective fluctuations of weak bonds, in particular, of hydrogen bonds and by internal displacement of massive atoms. On the basis of this model, low-frequency vibrations were calculated in α- and β-structures of proteins. It was demonstrated that accordion-type modes in β-sheet and breathing modes in β-barrels of immunoglobulin C and concavalin A corresponded to low-frequency modes with 20–30 cm^{-1} ($\lambda = 0.5$–0.3 mm).

Levy *et al.* [76] used the quasi-harmonic method for calculating normal modes. The effective force constants are derived from the molecular-dynamic estimations of root-mean-square changes of internal virtual coordinates with regard to harmonic effects. Amino acid residues of PTI are considered to be interaction centers. For 168 calculated normal modes, the highest frequency is 250 cm^{-1} and the lowest one is 0.32 cm^{-1} ($\lambda = 3$ mm). Thus, many of the predicted vibrations fall within the range of interest.

Go *et al*. [77] used an iteration method allowing one to extract eigenvectors from the full matrix of second derivatives of potential energy of the system. A hinge-bending mode (interdomain motion) of lysozyme with a frequency of 3.6 cm^{-1} ($\lambda = 2.8$ mm) was considered with the help of this method.

1.4.2. Theoretical models of DNA vibrations. In the case of DNA, theory also predicts the existence of vibrations manifesting themselves in the EHF range (the so-called "soft modes"). Here, we note the study carried out 25 years ago [78]. The model of related twisting vibrations of nitrous bases of DNA was considered. The frequencies of these vibrations were estimated to lie within a range from 10 to 100 cm^{-1}, i.e., $\lambda \simeq 1$–0.1 mm. The "solid-state" approach to DNA double helix was developed in a series of works [79–82]. According to the assumption used in these studies, long-range collective interactions exist in this helix. The lattice modes in the phonon spectrum of DNA are considered with the help of a model of valence and long-range electrostatic force field. On the basis of these models, the calculations of

the frequencies (20.3, 25, and 27 cm^{-1}) of modes active in Raman spectra were calculated [79].

Another model presumes the existence of both longitudinal and transverse acoustic waves in the DNA double helix. The frequencies of these vibrations are determined by the properties of DNA and depend upon the length of the DNA chain. Changing this length, one may cover a wide frequency range, including submillimeter, millimeter, and centimeter waves (see review in [126]).

Local vibrations of the type of "resonance on defects" of the DNA structure (end defects and fork-type defects) were also predicted in [81]. These vibrations were presumably detected in experiments at low frequencies of 600 MHz [83].

Note also a model of conformational motility of DNA proposed in [84], where "pendulum" motion of nucleotides was considered. The frequencies of vibrations determined with the help of this model (10 and 60 cm^{-1}) correspond to submillimeter waves.

The calculations of vibrations of nucleotides ($m \approx 200m_p$) of double-stranded DNA carried out on the basis of structural data for different conformations of macromolecules yield the values $\omega = 2\pi\nu \approx 10^{12}$ Hz, which correlates well with the data of Raman spectroscopy.

Our experimental data on the spectroscopy of correlation of photons of DNA, presented most completely in [127], prove the existence of acoustic vibrations with the frequencies ranging from 100 Hz to several millihertz. Typical are the repetitions of different and specific Fourier spectra of DNA dynamics, which is in line with the assumptions about soliton quasi-spontaneous excitations of DNA according to the Fermi–Pasta–Ulam return mechanism. Here, we face a problem of a new type of DNA memory and translation of "wave images" of sequences of nucleotides along DNA chains, which is important for understanding fundamental mechanisms of precise "piloting" of DNA transposons in a liquid-crystal multidimensional space of chromosomes.

1.4.3. Experimental results. The difficulty of experimental observation of vibrational states of DNA in the EHF range is explained by (1) the absence of sufficiently sensitive spectral apparatus in the range between IR and UHF areas and (2) very strong water absorption in this frequency range. Theoretical models (see Sections 4.1, 4.2) usually neglect the interaction with water solvent, which results in the shift of resonance frequencies and broadening of the spectra with the formation of broad bands [80, 86]. Van Zaldt [87] proposed a theory of resonance absorption of EHF EMR by solutions of plasmid DNA discovered by Edwards *et al.* [88]. It is assumed that a hydrate shell of DNA is a complex structure and that the interaction of the first water layer with DNA is free of energy losses.

The situation is more clear with Raman spectra of proteins with different water contents [89–92]. In the case of globular proteins, low-frequency modes are detected around 20–30 cm^{-1}. The frequencies depend slightly upon the size and shape of protein globules [89].

Similar Raman studies were carried out with DNA [91, 92]. For the A-form of DNA, the bands were observed at 85 and 21 cm^{-1}. With the increase of the water content in the sample, the low-frequency mode of the A-form shifts to 14 cm^{-1} and that of the B-form "softens" and disappears. This feature allowed the authors to attribute the indicated mode to an interhelical vibration.

Didenko *et al.* [93] used the method of gamma-resonance spectroscopy for recording changes in conformations of protein (lyophilized hemoglobin with ^{57}Fe tracer) under the influence of EMR in the range of 40–50 Hz. Very narrow peaks ($\Delta f/f \sim 10^{-4}$) of action were detected.

1.4.4. Some molecular mechanisms of interaction of EHF EMR with protein and DNA macromolecules. A major part of works aimed at theoretical consideration of effects of biological action of weak EMR, including that of the EHF range, are mainly of the phenomenological type. Rather general cooperative, to be more precise, synergetic models of biosystems are used. Many authors address, in particular, the well-known Frölich model [90]. However, synergetic approaches to this problem themselves can hardly clarify the nature of specific carriers of "unusual" properties of biosystems and give an answer to the question about primary mechanisms of biological action of EMR. For these purposes, a more detailed simulation taking into account quantitative parameters of the considered effects is necessary.

Information biopolymers of organisms realize their functions in many directions. Two of them are strategic; these are the levels of substance and field. The substance level for nucleic acids and proteins includes matrix and catalytic functions. The field (or wave) level is understood as an ability of DNA and proteins to emit electromagnetic and acoustic waves with biosignal purposes.

A property of molecular, in particular, conformational, isomerism is inherent in biopolymers. Conformation of biomolecules is of great importance for their functioning. Thus, the processes of replication and synthesis of proteins are accompanied by transformations of segments of the DNA double helix from "physiologically normal" B-conformation into A-conformation. Biochemically active states of enzymes correspond to certain conformations. The transitions between different conformational states of biomolecules separated by barriers of the height significantly larger than thermal energies kT normally require the use of energy of hydrolysis of ATP, which is a universal source of energy in biosystems.

All the aforesaid is also applicable to fragments of biological macromolecules, segments of DNA helix, active sites of enzymatics, etc.

One of the possible primary mechanisms of the influence of EMR on biosystems is the initiation with its help of the transitions between different isomer states of biomolecules (as applied to proteins, this idea was sug-

gested by Frölich). According to this assumption, the energy of absorbed radiation is spent on crossing the barrier separating conformers. The electrical activity of the corresponding degree of freedom of a biopolymer is necessary for the realization of this process.

Functioning of some biomacromolecules, including enzymes, is determined, to a great extent, by the processes in their active sites surrounded by biopolymer chains folded up into globules. It is reasonable to assume that resonance interaction with field results in the excitation of dipole-active vibrations of monomers, which, in turn, induce vibrations of an active site capable of bringing it into another conformational state (antenna effect [94]).

Excitation of dipole oscillations in separate groups (monomers) of a biopolymer may explain the influence of EMR on the form of a macromolecule (induced unfolding of a biopolymer). Considering a biopolymer chain as a long thread with bending rigidity a and curvature $\rho = r^{-1}$ (so that the density of free energy for small ρ is given by $\Phi = \Phi_0 + a\rho^2/2$) and using the expression $W \sim -\delta Phi/T$ for the probability of fluctuations "twisting" the molecular thread, we obtain the following expression for the mean square of scattering for distant points [96]:

$$\bar{R}^2 = 2(a/kT)^2(LkT/a) - 1 + e^{-LkT/2},$$

where L is the distance along the thread. Thus, a transformation of a linear form of molecule $\bar{R}^2 \sim L^2$ into a coil $\bar{R}^2/L^2 \simeq 0$ is determined by a ratio kT/a. The action of EMR exciting dipole-active oscillations leads to the repulsion of neighboring dipoles (and, consequently, to the increase in the rigidity of the chain), which influences the form of a macromolecule.

The efficiency of biological transport systems is provided, to a great extent, by the polymer properties of biomolecules. Resonance interaction of EMR with monomers of the chain may substantially influence charge transport, in particular, in transmembrane ion channels. Thus, here we speak about a possibility of regulation of charge transport through a membrane with the help of weak EHF EMR at rather high field intensities ($E_m \sim 10^5$ V/cm) on a membrane.

1.5. Solitons in Biomacromolecules

1.5.1. Introduction. The diversity of living organisms is determined by different combinations of the same atomic groups and compounds. Living organisms comprise six main chemical elements: nitrogen, oxygen, carbon, hydrogen, phosphorus, and sulfur. The content of calcium, potassium, sodium, magnesium, iron, copper, etc. is substantially smaller. Protein molecules are built of only 20 amino acids. The main elements of the genetic apparatus of a cell are formed by four types of nucleotides (elementary parts of DNA and RNA molecules that code a certain portion of genetic information). What is the difference between living organisms and inorganic objects? The main differences are as follows. Living organisms are, first of all, open systems with continuous exchange of energy. Living organisms are intrinsically heterogeneous, they possess a property of self-organization, and they are in a state far from thermodynamic equilibrium. Their evolution is one-directional and results in a state of "death," because, upon the achievement of complete thermodynamic equilibrium, all the proteins of a living organism disintegrate. Such physical notions as entropy, free energy, and other thermodynamic functions are arbitrarily applicable to biosystems.

One of the main methods here is the method of system simulation, where only key processes determining the phenomenon under study are taken into account, whereas the secondary processes are ignored. The positive outcome of simulation depends, to a great extent, upon a correct choice of the simplified model and the methods of its description. Below, we consider the nonlinear processes playing an important role in bioenergetics. In particular, a process of vibrational energy transfer along a protein molecule is considered on the basis of a hypothesis of solitons, i.e., waves that satisfy nonlinear equations and that spread inside a living tissue virtually without losses and changes in their form.

A cell is an elementary structural unit with the size of about 10^{-3} cm. A bacterium is an example of the simplest unicellular organism. Inside a surface layer of a cell, cytoplasm and nucleus are located (for cells of higher animals and plants). Nuclei of cells contain chromosomes, carrying genetic information. In addition to the nucleus, some inclusions called organelles can be found inside a cell. These inclusions have their own membranes, similarly to the external shell of a cell. The most important function of organelles is the supply of a cell with energy due to synthesis of adenosine triphosphoric acid (ATP) in the course of hydrolysis (oxygenation of organic compounds). The first studies of the spatial structure of the cells by means of electron microscopes showed that all the inclusions are not free in their motion inside a cell but occupy certain places due to the fixation of organelles in a complex 3D structure of cytoskeleton. It determines the shape of a cell and participates in the transfer of energy and information.

Cellular membranes consist of molecules of lipids, proteins, and carbohydrates (small amounts). The main physicochemical properties of membranes are determined by the molecules of lipids, which, figuratively speaking, consist of a tail and a head. The head either carries an electric charge or possesses a rather large electric dipole moment. The tail of a lipid molecule consists of two parallel carbohydrate chains. Since a water molecule has a large dipole moment, the head of lipid is attracted to water molecules, i.e., it is hydrophilic. The tail of a lipid molecule is nonpolar and is repulsed by water. Thus, it is hydrophobic. At the water surface, these molecules are arranged in such a way that

the hydrophilic head is plunged into water and the hydrophobic tail is exposed from it. In aqueous solutions, lipid molecules tend to organize closed constructions of a bubble type. At the surface, a double layer is formed with the heads of lipids on the outer and inner sides. Protein molecules can be found at the exterior or interior surfaces of the lipid bilayer or they can even pierce the membrane. The latter proteins may be of two types. Stick-like proteins belong to the first type and the globular proteins belong to the second one. Long alpha-helical structure of fibrous proteins is located outside the membrane, whereas the globular structure belongs to the hydrophobic inner part of the membrane. A double layer of lipid molecules provides positive charge of the exterior surface of a living cell and negative charge of the interior surface. A potential drop appears in this case, and the resulting electric field inside the membrane may be as high as 10^2 kV/cm (for the membrane thickness of about 5 nm). About 50% of energy produced by a cell is required to maintain its normal functioning, potential drop, and difference of ion concentrations inside and outside the cell. Complexes of proteins with lipids perform transportation of substances and ions inside a cell thus providing its vital activity. Proteins play an important role in a living organism. However, they cannot synthesize themselves. The synthesis of protein molecules is performed by the molecules of genetic apparatus: desoxyribonucleic acid (DNA) and ribonucleic acid (RNA). Synthesis of one peptide bond between amino acids in cells of living organisms requires 0.14–0.21 eV of energy. However, the disintegration of a protein molecule is a rather slow process. For example, the half-life of the proteins of cardiac muscle equals approximately 30 days. That is why an organism must gradually replace the disintegrating protein molecules with new ones. Such a state of a system is classified in physics as a metastable one. A transition from a metastable state to stable thermodynamic equilibrium takes a long time because of a high potential barrier to be crossed in the course of a transition. Enzymes help to lower the potential energy barrier and accelerate this process. A repeated process of polymerization results in a formation of long chains of protein molecules (polypeptides) with equally spaced peptide groups. In 1951, Poling and Kory demonstrated that a polypeptide chain may form an ordered right-hand helix. Such helical molecules were called alpha-helices. Transverse hydrogen bonds of a polypeptide chain allow the existence of another elementary configuration suggested by Poling. This configuration is a zigzag folding of a polypeptide chain. It is called a beta-sheet. Generally, a polypeptide chain consists of interchanging alpha-helical and beta-sheet segments and is folded to form a globular structure.

1.5.2. Davydov soliton mechanism of energy transfer in protein molecules. Vital activity is associated with energy consumption and continuous metabolism. Energy in cells is stored due to synthesis of ATP molecules from ADP molecules. Thus produced ATP molecules diffuse to the places where the energy is consumed and release stored energy in the presence of enzymes in the course of back reaction. This energy is utilized by ion pumps and for the synthesis of proteins and other molecules.

Because of large sizes of organic molecules, the sites of energy storage (ATP synthesis) and energy consumption (ATP hydrolysis) are separated by the distances significantly larger than interatomic ones. Thus, a question arises about the mechanism of effective energy transfer along large protein molecules. As it was already mentioned, ATP hydrolysis results in the energy release of about 0.5 eV. This energy is sufficient for effective excitation of only vibrational degrees of freedom of the $c = 0$ atomic group, which is a constituent of peptide groups of all proteins. However, it is well known that, in molecular crystals, the lifetime of vibrational excitations is about 10^{-12} s. Therefore, the transfer of vibrational excitation from one peptide group to another must decay quickly at short distances, and the mechanism of effective energy transfer in a cell has no adequate physical interpretation. The question about energy transfer remained open up to a publication by A.S. Davydov and N.I. Kislukha [96]. It was demonstrated therein that waves of collective nature may propagate in helical protein molecules without energy losses and changes in the shape. Such waves are called solitons. Thus, the "crisis" in bioenergetics was overcome. Many studies carried out since that time in many countries of the world proved the feasibility of effective energy and, possibly, information transfer by solitons inside a cell and between the cells in biological systems. An extremely high stability of soliton is explained by the balance of nonlinearity and dispersion of a medium where the soliton was produced. Nonlinearity of the medium presumes the description of the processes on the basis of nonlinear dynamic and kinetic equations. Dispersion of the medium is treated as a dependence of the phase velocity of wave propagation upon the wavelength. A strong interaction of waves takes place in nonlinear media. If, in a wave packet consisting of a group of monochromatic waves, an energy transfer takes place from the slower waves to the faster ones, such a packet will not spread and will propagate as a single entity like a particle.

Thus, let an intrapeptide vibration amide-1 (with a vibrational energy of 0.21 eV) be excited at an end of alpha-helical protein molecule as a result of ATP hydrolysis. Peptide groups are bound to each other by the interactions of two types. The interactions of the first type are dipole–dipole interactions that are proportional to the square of the electric dipole moment (0.35 D) and are inversely proportional to the cube of the distance between peptide groups. The interactions of the second type are deformation interactions determined by displacements of peptide groups from their equilibrium states in the molecule.

The excitation of the first type is characterized by a uniform distribution of its probability along the entire protein molecule without violations of periodicity of peptide groups. These excitations are monochromatic waves of fixed energy, frequency, and phase velocity, and they are called excitons (physical analogy between a wave and a particle). Excitons determine the main properties of light absorption by protein molecules. Note that the efficiency of energy transportation by free excitons is low because of dispersion in a medium, which results in spreading of the wave packet of an exciton and, consequently, in a strong dispersion of energy.

Deformation interaction plays an important role in energy transfer along a protein molecule. Since the peptide groups are bound to each other by weak hydrogen bonds, their displacements from the equilibrium state in the molecule are large and the nonlinearity develops in interaction of this type to a full extent.

In reality, interactions of these two types develop in a protein molecule simultaneously and influence each other. The following model was proposed for the solution of this problem [97]. A one-dimensional chain consisting of carbonyl oscillators with dipole–dipole interaction between them was considered. In other words, the interaction between excitons described by means of quantum mechanics and acoustic phonons, i.e., collective vibrations of oscillators near their equilibrium states, was taken into account. In the approximation of a continuous system (when the distance between the oscillators is less than the typical width of a soliton) the model is described by a set of two coupled differential equations

$$i\frac{\partial\psi}{\partial t} = -\frac{1}{2m}\frac{\partial^2\psi}{\partial x^2} + \sigma\psi\frac{\partial L}{\partial x}, \quad \hbar = 1,$$
$$\left(\frac{\partial^2}{\partial t^2} - U_0^2\frac{\partial^2}{\partial x^2}\right)\frac{\partial L}{\partial x} = \frac{a\sigma}{M}\frac{\partial}{\partial x}|\psi|^2, \tag{1}$$

where ψ is the wave function of the exciton, m is its mass, a is a constant, L is the displacement of oscillators of mass M from equilibrium states, and σ is a parameter of correlation between excitons and phonons.

The solution of this set is a single wave (a bell-shape soliton) traveling along the chain by means of its deformation induced by the wave itself. It is customary to call this solution the Davydov soliton. Note that free excitons do not interact with each other and cannot produce a single wave of a stable form. The interaction between excitons takes place through the deformation of the chain due to the displacements of oscillators relative to the equilibrium state. It is due to the deformation of the chains, or phonons, that the interaction between excitons occurs. A similar situation is well known in the theory of superconductivity. Electrons, the main carriers of current, acquire an attracting force (in spite of the fact that they bear the same electric charge) due to electron–phonon interaction and form a self-organized state of superconductivity.

Depending upon the values of parameters in (1), the Davydov soliton can be considered as a result of dislocation motion with no regard to exciton. In this case, set (1) is reduced to the nonlinear sine-Gordon equation [98]:

$$\frac{\partial^2 f}{\partial t^2} = A^2\frac{\partial^2 f}{\partial x^2} + V_0\sin f. \tag{2}$$

On the other hand, the Davydov soliton may be treated as an autolocalized state of an exciton. In this case, the deformation of the chain manifests itself as a self-regulation of the exciton, whose motion is described by the well-known nonlinear Schrödinger equation [98]:

$$i\frac{\partial\psi}{\partial t} = -\frac{1}{2m}\frac{\partial^2\psi}{\partial x^2} \pm 2\sigma\psi|\psi|^2, \tag{3}$$

where σ is the parameter of self-action.

What does govern the efficiency of energy transfer by means of Davydov solitons? Firstly, the change from an exciton state to a soliton one gives an energy gain due to exciton coupling with a deformation grating. The softer the chain and the larger the coupling parameter σ, the more stable the soliton. Secondly, the speed of propagation of a soliton will always be less than the speed of sound in the chain because of the interaction of exciton with acoustic vibrations (phonons). It is due to this circumstance that exciton does not experience losses associated with the emission of phonons. Thirdly, according to the Franck–Condon principle [99], the absorption of light in this system of oscillators is not accompanied by the change of their coordinates at the moment of quantum transition. Thus, light excites a very small number of solitons, and solitons do not emit light. Solitons can emit light only at the ends of a molecule, which is a result of topological stability of solitons. Hence, solitons can appear in relatively short alpha-helical segments of protein molecules that are parts of majority of enzymes and proteins piercing cellular membranes.

1.5.3. Solitons in polynucleotides. The manifestations of nonlinear dynamics in different natural phenomena are quite diverse [99]. It is important to know when studying experimentally the biological objects which particular aspect of nonlinear dynamics is appropriate and how it shows up in experiment. In particular, evidence exists [100] that similar solitons can be excited in polymer nucleic acids. Here also dipole–dipole interaction exists between the chains of carbonyl oscillators, and they can be considered as two helical complexes of homopolynucleotide [101] or arbitrary nucleotide sequences [102]. Deformation of the grating can be expressed in terms of the change in distance between the planes of neighboring residues in a chain.

The weak bond in such a carbonyl chain is determined by the weakness of stacking interaction in the frames of duplex. In spite of the complexity of the dynamics of DNA, RNA, and nucleoproteids *in vitro* and *in vivo*, its study is urgent because such nonlinear dynamics in its essence is a new semiotic area generating acoustic and electromagnetic symbol structures utilized by biosystems for their own self-organization [127].

The model of DNA dynamics proposed in [103, 104] is close in its physical meaning to the Davydov soliton model. The authors of [103, 104] consider deformation vibrations of phosphodiester O–P–O bond as an exciton and the stretching and contraction of Watson–Crick hydrogen bonds as phonons (collective vibrations of a grating). Kashcheev [105, 106] developed the Davydov model and applied it to proton transfer along the chains of peptide hydrogen bonds under their interaction with a system of heavy ions. Classic Davydov solitons are considered also with regard to the interaction between excitons and optical and acoustic phonons.

Frölich [107] demonstrated that some biological molecules, in particular, proteins and DNA can be simulated by a chain of oscillating and interacting dipoles. Coherent external action on this system maintains its nonequilibrium state. One may state that polymers with high electric polarizability possess electron–phonon interaction, to be more precise, the interaction between electric and elastic degrees of freedom. If an external parameter exceeds a certain threshold, the low-frequency vibrational mode is excited in a coherent way with a formation of Bose condensate. One deals with a similar situation in laser systems that pass over the lasing threshold. Thus, it is suggested to consider biopolymers as structures with laser pumping.

We should note papers [108, 109] among the works devoted to DNA solitons describing conformational specific features of a double polynucleotide chain. In these works, a double helix is simulated by a chain of masses with elastic forces. Transverse displacements of masses from equilibrium points are also taken into account. The Hamiltonian of this model is presented as

$$H = \sum_{i=1}^{N}\left[\frac{m}{2}v_i^2 + \frac{L}{2}(y_i - y_{i-1})^2 + U(y_i)\right], \qquad v_i = \frac{dy_i}{dt}, \tag{4}$$

where m is the mass of a nucleotide particle, L is the constant of elastic interaction between the neighboring masses, and $U(y_i)$ is the potential energy of transverse displacement from the equilibrium of the element i.

The Hamilton equations in this case are written as

$$\dot{p}_i = -\frac{\partial H}{\partial y_i} \Rightarrow m\frac{dv_i}{dt} = L(y_{i+1} - 2y_i + y_{i+1}) - U'(y_i), \qquad \dot{y}_i = \frac{\partial H}{\partial p_i} \Rightarrow \frac{dy_i}{dt} = v_i, \tag{5}$$

where $p_i = mv_i$. The following system of nonlinear differential equations follows from (5):

$$m\frac{dy_i^2}{dt^2} = L(y_{i+1} - 2y_i + y_{i+1}) - U'(y_i). \tag{6}$$

If a soliton involves a large number of monomers, i.e., its typical size is much larger than the distance a between the neighboring monomers, then a transfer is possible to the continuous approximation or continuous description. Assuming that

$$\frac{dy^2}{dx^2} \underset{\Delta x = a}{\simeq} \frac{1}{\Delta x}\left[\frac{y_{i+1} - y_i}{\Delta x} - \frac{y_i - y_{i-1}}{\Delta x}\right] = \frac{y_{i+1} - 2y_i + y_{i+1}}{\Delta x^2},$$

where Δx^2 is a physically infinitely small quantity, we obtain

$$\frac{\partial^2 y}{\partial t^2} = C_0\frac{\partial^2 y}{\partial x^2} - \frac{1}{m}U'(y), \tag{7}$$

where $C_0 = La^2/m$.

Equation (7) is well known in physics of nonlinear phenomena. For $U'(y) \neq ky$, this equation is related to the class of the Klein–Gordon nonlinear differential equations [110]. Potential function $U(y)$ is determined by the anharmonicity range of displacements of monomers in the transverse (relative to the chain) direction. It can be seen that, in a particular case when $U = U_0\cos y$, this equation is reduced to the sine-Gordon equation. Analysis [108] of equation (7) with a potential containing nonlinear terms revealed the possibility of existence of nonlinear supersonic traveling waves in a molecular chain in the case of a physically reasonable choice of the parameters of the system. Any conformational transition in a monomer unit of a polynucleotide chain is described within the frames of this model by means of considering a two-well potential known as the Lifshitz band. If the ends of the chain are in energetically unfavorable state (in case of binding to biologically active molecules), then, within this model, a two-soliton solution is possible (kink + antikink), i.e., two solitary waves moving along a nucleotide chain may exist.

In addition to the works describing these or those features of biological processes in protein molecules on the basis of soliton theory, one may also find works doubting the stability of the soliton solutions. Perez [111] considered the interaction of Davydov solitons with grating solitons (grating distortions of large amplitude without interaction with excitons). Numerical simulation revealed the disappearance of Davydov solitons even in the case of collisions with grating solitons of low energy. This effect may be related to the simulation of interactions of neighboring units in a molecular chain with the Lennard–Jones potential. Note that such a chain is known in physics as the Toda chain [112].

In early DNA models [113–115], a DNA molecule was considered as a single thread or two equal threads rigidly bound to each other. The difficulties of explanation of experimental data necessitated the consideration of DNA as a duplex of two interacting threads (chains). The authors of [116, 117] suggest describing the main properties of the two-chain model with the help of a system of two coupled sine-Gordon equations:

$$\begin{aligned}\frac{\partial^2 u_1}{\partial t^2} &= \frac{\partial^2 u_1}{\partial x^2} - \sin u_1 - \alpha \sin(u_1 - u_2),\\ \frac{\partial^2 u_2}{\partial t^2} &= \frac{\partial^2 u_2}{\partial x^2} - \sin u_2 + \alpha \sin(u_1 - u_2).\end{aligned} \tag{8}$$

Kivshar [118] demonstrated that the solutions suggested earlier are special cases of (8) and that these solutions are unstable. Moreover, with regard to the fact that the system (8) is not integrable, collisions of solitons that satisfy this system are inelastic. Hence, the solitons of system (8) can emit transverse phonons and decay.

1.5.4. Autosolitons in biological systems. An important feature of Davydov solitons and solitary-wave solutions to the sine-Gordon and Klein–Gordon equations is the fact that all of them are obtained within the framework of the theory of conservative or Hamilton systems. These equations are invariant relative to the substitution of time $-t$ for t. In other words, Hamilton systems are unable to distinguish between "past" and "future," they are unable to describe the dynamics of transition to equilibrium state, i.e., they are non-Markovian systems. Indeed, there is no interaction of nucleic acids with their hydrate–ion shell in the theory of conservative systems. Taking into account the action of the environment on a biosystem, one could consider the latter as a highly organized object in a medium with low organization. The action of the environment on a biosystem determines its transition to thermal equilibrium. Far from the equilibrium state functions of distribution of the parameters may differ strongly from the equilibrium ones and describe metastable steady dissipative structures in a sense that the time of transition into the equilibrium state may be rather long due to the existence of high potential barriers.

Thus, taking into account the action of fluctuating stochastic environment on a biosystem requires the application of nonlinear kinetic equations similar to that used in the studies of nonequilibrium processes in semiconductors for the description of the dynamics of information biopolymers [119, 120]. The construction of nonlinear kinetic equations is the main difficulty in such formulation of the problem. However, a substantial simplification can be achieved by means of analysis of the first several moments of kinetic equations. In physics, equations of gas dynamics and magnetic hydrodynamics may be examples of such moment equations. These equations follow from the Boltzmann equation and are valid within certain time intervals upon the achievement of the equilibrium state. It was demonstrated in [119, 120] that emergence and evolution of ordered states (both spatial and temporal) can be simulated by means of a system of nonlinear diffusion equations:

$$\frac{\partial x_i}{\partial t} = \sum_j \nabla(L_{ij}\Delta x_j) - g_i(x_1, \ldots, x_N), \tag{9}$$

where L_{ij} is the matrix of transport coefficients and g_i are the nonlinear terms taking into account interrelation of the parameters of the biosystem.

An important feature of system (9) is its ability to give rise to traveling solitary waves (autosolitons) as a response to an external local disturbance [120, 121]. The simplest mechanism of formation of an autosoliton can be described on the basis of a system of two nonlinear diffusion equations. Because biological objects are intrinsically nonequilibrium systems, the approach to their analysis on the basis of equations (9) seems to be preferable as compared with that making use of the equations of conservative dynamics.

Solitons and autosolitons are known to be the solutions of nonlinear equations. Nowadays, there are no general methods of the construction of their solutions. It is worthwhile to note the method of inverse problem [122, 123] is one of the most well-developed methods of analysis of a certain class of nonlinear equations. The essence of the method lies in reducing the solution of a nonlinear equation of a certain type to the solution of an auxiliary linear integral equation. The simplest method of construction of the solution to a nonlinear equation is its presentation in the form of a wave traveling at a certain speed v. Let us demonstrate the construction of the solution to, e.g., the sine-Gordon equation:

$$\frac{\partial^2 u}{\partial t^2} = \frac{\partial^2 u}{\partial x^2} + \sin u. \tag{10}$$

Let us look for a solution in the form of a traveling wave: $u = u(z)$, $z = x - vt$. Then, we arrive at

$$(v^2 - 1)\frac{d^2 u}{dz^2} = \sin u.$$

To reduce the rank of this equation, we make a substitution $du/dz = P(u)$. As a result, we obtain an ordinary differential equation with separable variables:

$$(v^2 - 1)P\frac{dP}{du} = \sin u.$$

Its solution is given by

$$\frac{du}{dz} = \pm\sqrt{\frac{2}{(1 - v^2)}\cos u + C}, \tag{11}$$

where C is an arbitrary constant.

The variables in (11) are also separable and its solution is presented as an implicit dependence of z on u:

$$z = \pm\int \frac{du}{\sqrt{2(1 - v^2)^{-1}\cos u + C}} + C_1. \tag{12}$$

Taking into account that u is a physical and, consequently, positive variable, by an appropriate choice of the integration constant, one can build up a solution in the form of a wave traveling at a speed v of a solitary wave. However, within this scheme, we cannot answer the question as to whether we have found all the solutions to equation (10) or not.

Apparently, such a simplet method can be applied to find a solution to two coupled nonlinear equations (9) for an autosoliton. The general methods of analysis of system (9) are not developed yet. The method of integration of the system of linear differential equations (9) is well developed. If the system of linear equations (9) is presented in the matrix form,

$$\frac{\partial x}{\partial t} = \hat{L}x, \quad \hat{L}_{ij} = \frac{\partial}{\partial x_i} L_{ij} \frac{\partial}{\partial x_j}, \quad x = \begin{pmatrix} x_1 \\ \vdots \\ x_N \end{pmatrix}, \qquad (13)$$

its solution can be presented as an expansion in a series in eigenvalues and eigenfunctions of self-conjugate operator $\hat{L}$ that has a positive spectrum of eigenvalues:

$$x = \sum_{i=0}^{\infty} c^{(i)} \psi(i) \exp(-\lambda_i t), \quad \hat{L}\psi(i) = -\lambda_i \psi(i), \quad (14)$$

where λ_i and $\psi(i)$ are the eigenvalues and the eigenvectors of operator $\hat{L}$ determined by the boundary conditions and $c^{(i)}$ are the vectors taking into account initial conditions.

Reshetnyak *et al.* [124, 125] demonstrated that, for time-independent coefficients L_{ij}, the series (14) is equivalent to the solution in the form of a series in the powers of operator $\hat{E} = \hat{L}^{-1}\partial/\partial t$,

$$x = x_e + \hat{E}x_e + \hat{E}^2 x_e + \ldots, \qquad (15)$$

where $\hat{L}^{-1}$ is the operator inverse of the operator $\hat{L}$ and x_e is the solution to the homogeneous equation $\hat{L}x_e = 0$ containing integration constants that generally depend on time.

Applying operator $\hat{L}$ to both sides of (15), we may verify that expansion (15) is really a solution of equation (14):

$$\hat{L}x = \hat{L}(x_e + \hat{E}x_e + \hat{E}^2 x_e + \ldots) = \frac{\partial x}{\partial t}.$$

The vector x_e can be considered as a state that the system approaches in the course of transition to thermodynamic equilibrium, i.e., for $t \longrightarrow \infty$, all the terms in the series, except the first one, disappear. To describe the stage when the system approaches the equilibrium state, one can consider the first several terms of expansion (15). The further the analyzed state from the equilibrium state, the larger the number of terms in (15) should be taken into account. Solution (15) makes a full use of the intrinsic property of a biological system—the Markovian character, the or erasure of memory with time and, as a consequence, the simplification of its description.

Apparently, the symptotic in time approach to the analysis of linear equations (13) is applicable to the construction to the nonlinear equations (9) provided x_e is considered as a solution of nonlinear homogeneous equation $\hat{L}x_e = g$ and an iteration scheme is used for approaching the equilibrium state. Within this scheme, the deviations of the distribution function for the parameters of a biosystem from their equilibrium values can be significant.

Thus, in spite of the complexity of the structure of biological objects and diversity of the processes therein one may state that nowadays sufficient evidence is available in the form of experimental data, theoretical concepts of functioning of biosystems, simulation of different processes in biopolymers for adequate comprehension of fundamental attributes of living systems, namely, synthesis of energy and information and their transportation in time and space of organisms.

2. THE ROLE OF COLLECTIVE AND COHERENT EFFECTS

2.1. The Role of Coherent Effects in the EMR Excitation of Induced Collective Modes of Proteins and DNA

In simulation of dynamics of protein and DNA macromolecules, the latter are presented as chains of monomers involved in local nonlinearly related dipole-active vibrations. Combinations of these vibrations are treated as the so-called collective modes, which characterize an ensemble as a whole from the energetic point of view. According to modern concepts, these collective (cooperative) modes play an important role in the dynamics of protein and DNA macromolecules. Therefore, it is interesting to study the resonance action of EMR on these collective modes.

The considerations below are carried out within the framework of a model of a selected cooperative mode.

2.1.1. Approximation of harmonic oscillator. Let us consider an elementary system—harmonic oscillator with a quantum $\hbar\omega_0$ excited by a resonance electric field $E = E_0 \cos\omega t$. Then, the Hamiltonian is presented as

$$\hat{H} = \hbar\omega_0 \hat{\varepsilon} - E(t)\hat{\mu},$$

where $\hat{\mu}$ is the operator of projection of the dipole moment of a molecule on the direction of the field, $\hbar\omega_0\hat{\varepsilon}$ is the Hamiltonian of an isolated harmonic oscillator, the matrix with elements $\varepsilon_{ik} = (i-1)\delta_{ik}$ $(i, k = 1, 2, \ldots)$ corresponds to the operator $\hat{\varepsilon}$, and $\hbar$ is the Planck constant. It is assumed that the field induces a high-frequency polarization only between neighboring pairs of quantum levels.

Using a standard procedure [128], we arrive at the equation for the operator of the induced dipole moment:

$$\frac{d^2\hat{\mu}}{dt^2} + \frac{2}{T_2}\frac{d\hat{\mu}}{dt} + \left(\omega_0^2 + \frac{1}{T_2^2}\right)\hat{\mu} = \frac{\omega_0}{\hbar}E(t)[[\hat{\mu}\hat{\varepsilon}]\hat{\mu}],$$

where T_2 is the phase relaxation time and square brackets correspond to commutation operation. Taking into account the relation between the squares of matrix elements $\mu_{k+1,k}^2 = k\mu_{21}^2$ and the relationship

$$\mathrm{Sp}(\hat{\rho}[[\hat{\mu}\hat{\varepsilon}]\hat{\mu}]) = 2\mu_{21}^2$$

($\hat{\rho}$ is density matrix with elements ρ_{ik}), we can find the observed value of the dipole moment

$$p = \mathrm{Sp}(\hat{\rho}\hat{\mu}) = \sum_{m=1}^{\infty}(\mu_{m+1,m}\rho_{m,m+1} + \mu_{m,m+1}\rho_{m+1,m})$$

from the equation

$$\ddot{p} + \frac{2}{T_2}\dot{p} + \left(\omega_0^2 + \frac{1}{T_2^2}\right)p = 2\mu_{21}\omega_0\Omega\cos\omega t, \qquad (1)$$

where $\Omega = \mu_{21}E/\hbar$ is the Rabi frequency. It is easy to derive an equation for operator $\hat{\varepsilon}$,

$$\frac{d\hat{\varepsilon}}{dt} + \frac{\hat{\varepsilon}}{T_1} = \frac{E(t)}{\hbar\omega_0}\left(\frac{d\hat{\mu}}{dt} + \frac{\hat{\mu}}{T_2}\right),$$

so that the average number of quanta $\varepsilon = \mathrm{Sp}(\hat{\rho}\hat{\varepsilon})$ is governed by

$$\dot{\varepsilon} + \frac{\varepsilon}{T_1} = \frac{E_0}{\hbar\omega_0}\cos\omega t\left(\dot{p} + \frac{p}{T_2}\right), \qquad (2)$$

where T_2 is the energy relaxation time.

For small detunings $|\Delta|/\omega_0 \ll 1$ with $T_2^2\omega_0|\Delta| \gg 1$, we obtain from (1) and (2) [$\varepsilon(0) = 0$]:

$$\varepsilon = \frac{\Omega^2}{2(\Delta^2 + T_2^{-2})}\left\{\frac{T_1}{T_2}(1 - e^{-t/T_1}) + \frac{\Delta^2 + (T_2\tau_{12})^{-1}}{\Delta^2 + \tau_{12}^{-2}}e^{-t/T_1}\right. \qquad (3)$$

$$\left. - \frac{(\Delta^2 + (T_2\tau_{12})^{-1})\cos\Delta t + \Delta(T_2^{-1} - \tau_{12}^{-1})\sin\Delta t}{\Delta^2 + \tau_{12}^{-2}}e^{-t/T_2}\right\},$$

where $\Delta = \omega_0 - \omega$ and $\tau_{12}^{-1} = T_1^{-1} - T_2^{-1}$.

In a particular case when $T_2 \ll t$ and $T_2 \ll T_1$, the expression for the energy has the same form as that obtained without taking into account coherent effects [129],

$$\varepsilon = \frac{T_1}{2T_2}\frac{\Omega^2}{\Delta^2 + T_2^{-2}}(1 - e^{-t/T_1}).$$

It is seen that the energy approaches a stationary level with time; for small t, we have $\varepsilon \sim t$. In the opposite limiting case (T_1^{-1} and $T_2^{-1} \longrightarrow 0$), we have from (3)

$$\varepsilon = \frac{\Omega^2}{2\Delta^2}(1 - \cos\Delta t),$$

i.e., the stored energy pulsates with a frequency of optical beats (see [130]). For small t we have $\varepsilon \sim t^2$.[4]

2.1.2. Excitation of an anharmonic oscillator by a series of phased pulses. A method based on the known principle of phase stability can be used for the excitation of high levels of an anharmonic oscillator by a resonance field. Veksler [132] was the first to suggest the principle of autophasing for infinite maintaining of a resonance between charged particles and a high-frequency field in a cyclotron-type accelerator.

This method is modified in our case in the following way. If the frequency of an EMR pulse $E = E_0\cos\omega t$ equals the transition frequency of the lowest pair of levels 1 and 2 ($\omega = \omega_{21}$), then, in the absence of relaxation, the population of each of these levels will change periodically in time with the Rabi frequency $\Omega_{21} = E\mu_{21}/\hbar$ [128]. At time instants $t = \tau_1$ determined by $\Omega_{21}\tau_1 = (2n + 1)\pi$ ($n = 0, 1, 2, \ldots$), all the particles reside at the upper level.

Assume now that, at the instant τ_1, the frequency of radiation changed in a jumpwise manner and became equal to the frequency ω_{32} of the higher lying pair of levels. The particles "trapped" in resonance by a pulse will start oscillating again but now between the levels 3 and 2 with the frequency $\Omega_{32} = E_0\mu_{32}/\hbar$. The choice of the phase of the next pulse according to the condition $\Omega_{32}\tau_2 = (2n + 1)\pi$ brings a particle even higher, etc. Thus, a series of phased pulses with the frequencies ω_{21}, ω_{32}, ω_{43}, … theoretically allows one to excite high levels of an anharmonic oscillator.

Let us determine the portion of the particles that can go to high levels of a collective mode. Suppose that external action consists of a series of sequential pulses. For the kth pulse of the duration $\tau_{k+1,k}$, we have

$$E_k(t) = E_{k0}\cos\omega_{k+1,k}t, \quad k = 1, 2, \ldots,$$

$$t_{k-1} < t < t_k, \quad t_k = \sum_{i=0}^{k}\tau_i, \quad \tau_0 = t_0 = 0.$$

Within the interval $t_{k-1} < t < t_k$, the difference of populations is $W_k = \rho_{k+1,k+1} - \rho_{k,k}$, and the sum of populations $V_k = \rho_{k+1,k+1} + \rho_{k,k}$ satisfy, correspondingly, the equations

$$\ddot{W}_k + \frac{2}{T_{12}}\dot{W}_k + \left(\Omega_k^2 + \frac{1}{T_1T_2}\right)W_k + \frac{1}{T_1T_2}\delta_{1k} = 0,$$

$$\dot{V}_k + \frac{1}{T_1}V_k = \frac{1}{T_1}\delta_{1k} = 0, \quad k = 1, 2, 3\ldots,$$

[4] The idea of this method was proposed by Prof. A.N. Oraevskii.

$$W_k(t_{k-1}) = -\rho_{kk}(t_{k-1}), \quad \dot{W}_k(t_{k-1}) = 0,$$
$$V_k(t_{k-1}) = \rho_{kk}(t_{k-1}),$$
$$\Omega_k = \frac{E_{0k}\mu_{k+1,k}}{\hbar}, \quad \frac{1}{T_{12}} = \frac{1}{2}\left(\frac{1}{T_1} + \frac{1}{T_2}\right).$$

It is assumed that an inequality

$$2\sqrt{\left(\Omega_k^2 + \frac{1}{T_1 T_2}\right)} > \frac{1}{T_1} + \frac{1}{T_2}$$

is fulfilled.

The conditions of coherent phasing of EMR pulses allow one to determine their durations:

$$\Omega_k'\tau_k = 2\arctan(T_{12}\Omega_k') + 2\pi n_k, \quad n_k = 1, 2, \ldots,$$
$$\Omega_k'^2 = \Omega_k^2 - \frac{1}{4}\left(\frac{1}{T_1} - \frac{1}{T_2}\right)^2.$$

For a portion of particles occupying the kth excited level at the instant of time

$$t_{k-1} = \sum_{j=1}^{k-1}\tau_j,$$

we have

$$\rho_{kk} = \frac{2^{1-k}T_1T_2\Omega_{21}^2}{1 + T_1T_2\Omega_{21}^2}[1 + \exp(-\tau_1/T_{12})] \times \exp\left(-\sum_{i=2}^{k-1}\tau_i/2T_1\right) \times \prod_{j=2}^{k-1}[\exp(-\tau_j/2T_1) + \exp(-\tau_j/2T_2)].$$

In a particular case when $T_1 = T_2 = T$ and $\Omega_j \equiv \Omega$, this expression is reduced to ($n_k = 0$)

$$\rho_{kk} = \frac{x^2}{1 + x^2}\cosh y \exp(-(2k-3)y), \quad k \geq 2,$$
$$t_{k-1} = 2T(k-1)y, \quad x = \Omega T, \quad y = \arctan x/x.$$

For $x = 10^2$, a typical time of population of, e.g., the tenth level is about $0.3T$, and the portion of excited molecules at this level is about $e^{-0.25}$.

2.1.3. Periodic phase modulation as a method of cascade excitation. Let us consider the second way of excitation of particles by EMR allowing one to neutralize anharmonicity.

Let us enumerate levels 1, 2, 3, …, N, $N + 1$. The energy of level ($N + 1$) corresponds to the activation energy. The frequencies of one-quantum transitions of an anharmonic oscillator can be presented as

$$\omega_{m+1,m} = \omega_{21} - (m-1)\Delta\omega \quad (m = 1, 2, \ldots, N), \quad (4)$$

where ω_{21} is the frequency of transition $2 \longrightarrow 1$, $\Delta\omega$ is the anharmonic shift, and $\Delta\omega/\omega_{21} \ll 1$. A typical feature of an anharmonic oscillator under the assumption (4) lies in the fact that the difference of frequencies of transitions between neighboring pairs of levels does not depend upon the number of the pair and equals the frequency of the anharmonic shift,

$$\omega_{m,m-1} - \omega_{m+1,m} = \Delta\omega.$$

An expression for periods is valid with the same accuracy:

$$T_{m+1,m} - T_{m,m-1} = \Delta T = \frac{2\pi}{\Delta\omega}. \quad (5)$$

Note that the Veksler's idea is actually based on relationship (5), where $T_{m+1,m}$ is treated in [132] as the period of the mth cycle of rotation of a charged relativistic particle around the magnetic field. Thus, the difference of times of two subsequent cycles remains constant irrespective of the energy of a particle, i.e., of m, which is the physical meaning of (5).

Let us consider the vibrations of an anharmonic oscillator in the electric field

$$E(t) = \frac{E_0}{2}(e^{i(\omega t + \Phi(t))} + \text{c.c.}), \quad (6)$$

where the carrier frequency ω equals the frequency of one of the transitions (e.g., for the lowest pair $2 \longrightarrow 1$) and the phase $\Phi(t)$ changes periodically in time with the frequency equal to the frequency of the anharmonic shift $\Delta\omega$. Then, the spectrum of oscillations of the field will evidently contain the frequencies of all one-quantum transitions of the cooperative mode. Thus, a periodic phase modulation with the frequency of anharmonicity allows one to realize a cascade mechanism of population of the levels of an anharmonic oscillator (6) in the Fourier representation:

$$E(t) = \frac{E_0}{2}\left(\sum_{n=-\infty}^{\infty} c_n e^{i(\omega + n\Delta\omega)t} + \text{c.c.}\right),$$
$$c_n = \frac{\Delta\omega}{2\pi}\int_0^{2\pi} dt \exp[i(\Phi(t) - n\Delta\omega)t)]. \quad (7)$$

In a particular case of sine modulation, i.e., when $\Phi(t) = \delta\sin\Delta\omega t$, we have for spectral components

$$c_n = J_n(\delta),$$

where J_n is the Bessel function.

A process of excitation of an oscillator by coherent EMR is described by an equation for the density matrix (the Boltzmann equation)

$$i\hbar\left(\frac{\partial\hat{\rho}}{\partial t} + \frac{\hat{\rho} - \hat{\rho}_0}{T}\right) = [\hat{H}\hat{\rho}], \quad (8)$$

where the Hamiltonian in the dipole approximation is given by

$$\hat{H} = \hat{H}_0 - E(t)\hat{\mu}.$$

The eigenvalues of Hamiltonian $\hat{H}_0$ are the energies of levels of the anharmonic oscillator, $\hat{\rho}_0$ is the equilibrium density matrix, T is the phenomenological time of relaxation (for diagonal elements $T = T_1$, for nondiagonal, $T = T_2$). For simplicity, we assume that only one resonance spectral component from expansion (7) acts on each separate period ($m + 1 \rightleftarrows m$):

$$E_{m+1,m}(t) = \frac{E_0}{2} c_m [\exp(i\omega_{m+1,m}t) + \text{c.c.}].$$

Then, the following system of equations will correspond to Boltzmann equation (8) (we consider only one-quantum transitions):

$$\begin{aligned}
&i\hbar\left(\dot{\rho}_{mm} + \frac{\rho_{mm} - \delta_{1m}}{T_1}\right) \\
&= E_{m+1,m}(t)A_{m+1,m} - E_{m,m-1}(t)A_{m,m-1}(1 - \delta_{1m}), \\
&i\hbar\left(\dot{\rho}_{m,m+1} + \frac{\rho_{m,m+1}}{T_2}\right) = -\hbar\omega_{m+1,m}\rho_{m,m+1} \\
&\quad - E_{m+1,m}(t)\mu_{m,m+1}(\rho_{m+1,m+1} - \rho_{mm}), \\
&i\hbar\left(\dot{\rho}_{m+1,m} + \frac{\rho_{m+1,m}}{T_2}\right) = \hbar\omega_{m+1,m}\rho_{m+1,m} \\
&\quad + E_{m+1,m}(t)\mu_{m+1,m}(\rho_{m+1,m+1} - \rho_{mm}), \\
&A_{m+1,m} = \mu_{m+1,m}\rho_{m,m+1} - \mu_{m,m+1}\rho_{m+1,m}, \\
&\sum_{m=1}^{N+1} \rho_{mm} = 1, \quad m = 1, 2, \ldots.
\end{aligned} \tag{9}$$

System (9) is of the order of $2N$. It is assumed that the equilibrium value of the diagonal element of density matrix ρ_{11} (the lowest quantum state) is equal to unity and the equilibrium values of other elements are equal to zero.

If we set $E_{m+1,m}(t) = E_0(t)$ in (9), then this system describes, in particular, the excitation of a truncated harmonic oscillator.

It is convenient to perform further analysis for a renormalized density matrix. Let us introduce the variables

$$y_m = 1 - \sum_{j=1}^{m} \rho_{jj}(t), \quad m = 1, 2, \ldots, N.$$

The quantity y_m has a simple physical meaning: this is a portion of particles populating the levels from $(m+1)$ to $(N+1)$ (i.e., to the level of the activation energy).

It is easy to demonstrate that the system (9) may be reduced to the following system [in calculations, we neglected the second harmonics $\exp(2i\omega_{m+1,m}t)$]:

$$\begin{aligned}
&\ddot{y}_m + \left(\frac{1}{T_1} + \frac{1}{T_2}\right)\dot{y}_m + \frac{1}{T_1 T_2} y_m \\
&= \frac{\Omega_m^2}{2}(\delta_{1m} + y_{m-1} - 2y_m + y_{m+1}), \\
&m = 1, 2, \ldots, N \quad y_m(0) = \dot{y}_m(0) = 0, \\
&y_0 = y_{N+1} = 0, \quad \Omega_m = \frac{E_0 c_m \mu_{m+1,m}}{\hbar}.
\end{aligned} \tag{10}$$

Here, we restrict ourselves to the case $\Omega_m \equiv \Omega_0$. Let us introduce collective coordinates

$$z_k = \sqrt{\frac{2}{N+1}} \sum_{m=1}^{N} y_m \sin\frac{mk\pi}{N+1}, \quad k = 1, 2, \ldots, N, \tag{11}$$

where

$$y_m = \sqrt{\frac{2}{N+1}} \sum_{k=1}^{N} z_k \sin\frac{mk\pi}{N+1}, \quad m = 1, 2, \ldots, N. \tag{12}$$

Then, we obtain a system of uncoupled equations for z_k,

$$\begin{aligned}
&\ddot{z}_k + \left(\frac{1}{T_1} + \frac{1}{T_2}\right)\dot{z}_k + \left(\nu_k^2 + \frac{1}{T_1 T_2}\right) z_k = \frac{\Omega_0^2}{2} f_k, \\
&z_k(0) = \dot{z}_k(0) = 0, \quad k = 1, 2, \ldots, N.
\end{aligned} \tag{13}$$

Here, the notations

$$\nu_k = \sqrt{2}\Omega_0 \sin\frac{k\pi}{2(N+1)}, \quad f_k = \sqrt{\frac{2}{N+1}} \sin\frac{k\pi}{2(N+1)} \tag{14}$$

are introduced.

Solving (13) and substituting the result into (12), we obtain

$$\begin{aligned}
&y_m = \frac{1}{N+1} \sum_{k=1}^{N} \sin\frac{mk\pi}{N+1} \sin\frac{k\pi}{N+1} \left(\frac{\Omega_0}{\omega_k'}\right)^2 F_k(t), \\
&F_k(t) = 1 - \frac{\omega_k'}{\omega_k} \exp\left[\frac{-t}{2}\left(\frac{1}{T_1} + \frac{1}{T_2}\right)\right] \cos(\omega_k t + \phi_k), \\
&\omega_k^2 = \nu_k^2 - \frac{1}{4}\left(\frac{1}{T_1} - \frac{1}{T_2}\right)^2; \quad \omega_k'^2 = \nu_k^2 + \frac{1}{T_1 T_2}; \\
&\cos\phi_k = \frac{\omega_k}{\omega_k'}; \quad k = 1, 2, \ldots, N.
\end{aligned} \tag{15}$$

Diagonal matrix elements ρ_{mm} are determined by the relationships

$$\rho_{mm} = y_{m-1} - y_m = \frac{1}{N+1}\sum_{k=1}^{N}\left[\sin\frac{(m-1)k\pi}{N+1} - \sin\frac{mk\pi}{N+1}\right] \times \sin\frac{k\pi}{N+1}\left(\frac{\Omega_0}{\omega_k'}\right)^2 F_k(t), \quad m = 1, 2, \ldots, N+1. \tag{16}$$

For the average number of quanta in an oscillator we have

$$\varepsilon = \sum_{m=1}^{N+1}(m-1)\rho_{mm} = \sum_{m=1}^{N} y_m = \frac{1}{N+1}\sum_{k=1}^{N}[1-(-1)^k]\cos\frac{k\pi}{2(N+1)}\left(\frac{\Omega_0}{\omega_k'}\right)^2 F_k(t). \tag{17}$$

The physical structure of these relations is evident: formulas (15)–(17) are the superposition of the solutions of the problem. If the condition $\omega_k > (T_1^{-1} + t_2^{-1})/2$ is met, the solutions describe damped oscillations. The latter are determined by a coherent mechanism of interaction of the field and a medium. The spectrum of pulsations is given by the formula for ω_k ($k = 1, 2, \ldots, N$). In a particular case when $T_1 = T_2$, the frequencies are $\omega_k = \nu_k$.

For $t \longrightarrow \infty$, the amplitudes of pulsations go down, and the solutions approach the stationary level. Using standard methods of operational calculus, one can demonstrate that the stationary values of the corresponding variables are

$$y_{m,0} = \frac{\cosh(N+1-m)\alpha}{\sinh(N+1)\alpha}, \quad \rho_{mm,0} = 2\frac{\sinh(\alpha/2)}{\sinh(N+1)\alpha}\cosh(N+3/2-m)\alpha, \quad m = 1, 2, \ldots, N+1, \quad \varepsilon = \frac{1}{2}\frac{\sinh(N\alpha/2)}{\sinh(\alpha/2)\cosh[(N+1)\alpha/2]}, \quad \cosh\alpha = 1 + \frac{1}{\Omega_0^2 T_1 T_2}. \tag{18}$$

For strong fields, $\beta = \Omega_0^2 T_1 T_2 \gg 1$ ($\alpha \longrightarrow 0$), we have

$$y_{m,0} = \frac{N+1-m}{N+1}, \quad \rho_{mm,0} = \frac{1}{N+1}, \quad \varepsilon = \frac{N}{2}, \tag{19}$$

i.e., the saturation regime is realized where the population probabilities of levels of anharmonic oscillators are equal.

For weak fields ($\beta \ll 1$), the dependences are of the power type:

$$y_{m,0} \approx (\beta/2)^m, \quad \rho_{mm,0} \approx (\beta/2)^{m-1}, \quad \varepsilon \approx \beta/2.$$

In a purely coherent regime ($\nu_k^2 \gg 1/T_1T_2$), for small times $t \ll T_2 < T_1$ (the times of phase relaxation and field are long), the population probabilities of the levels of oscillator and the average number of quanta in it are given by

$$\Delta\rho_{mm} = \sum_{k=1}^{N} U_{mk}\cos\nu_k t, \quad \Delta\varepsilon = \sum_{k=1}^{N} V_k\cos\nu_k t, \tag{20}$$

where the notations are introduced:

$$\Delta\rho_{mm} = \rho_{mm}(t) - (N+1)^{-1}, \quad \Delta\varepsilon = \varepsilon(t) - N/2, \quad U_{mk} = \frac{1}{N+1}\left[\cos\frac{mk\pi}{N+1} - \cos\frac{(m-1)k\pi}{N+1}\right], \quad V_k = \frac{1}{2(N+1)}[(-1)^k - 1]\coth\frac{k\pi}{2(N+1)}. \tag{21}$$

The first relationship in (20) generalizes the known relationship for a trivial two-level medium [128] (exact resonance) to an arbitrary finite number of quantum levels. It follows from (20) and (21) that the probabilities ρ_{mm} oscillate near the values $(N+1)^{-1}$, and the number of quanta oscillates near the value $N/2$. Note that the spectrum of pulsations of the average number of quanta stored contains only the frequencies with odd indices.

In the opposite case

$$4(T_2^2\nu_k^2 + T_2/T_1) \ll 1, \quad T_2 \ll 1, \tag{22}$$

the role of coherent effects is insignificant. The function $F_k(t)$ in (15)–(17) becomes

$$F_k(t) = 1 - \exp[-T_1^{-1}t(1 + T_1T_2\nu_k^2)]. \tag{23}$$

In the next section, we demonstrate that relationship (23) can be obtained directly from standard balance equations for diagonal matrix elements of the density matrix. Hence, conditions (22) define the range of applicability of the latter equations (for a constant field amplitude).

2.1.4. An approach based on equations of balance type. A standard representation for balance equations for population probabilities of the levels of an oscillator $\rho_m = \rho_{mm}$ is

$$\dot\rho_m + \frac{\rho_m - \delta_{m1}}{T_1} = \sigma_m I_m(\rho_{m+1} - \rho_m) - \sigma_{m-1}I_{m-1}(\rho_m - \rho_{m-1}), \quad \sum_{m=1}^{N+1}\rho_m = 1, \quad \rho_m(0) = \delta_{m1}. \tag{24}$$

For the cross sections of induced transitions $\sigma_m = \sigma_{m+1,m}$ (exact resonance) and the spectral intensities $I_m = I_{m+1,m}$, we have

$$\sigma_m = 4\pi T_2 \omega_{m+1,m} \frac{\mu_{m+1,m}^2}{\hbar c},$$

$$I_m = \frac{c}{8\pi\hbar\omega_{m+1,m}} E_{m+1,m}^2, \quad \sigma_m I_m = \frac{T_2}{2}\left(\frac{E_{m+1,m}\mu_{m+1,m}}{\hbar}\right)^2.$$

Let us solve the system (24) in general case, when the spectral amplitudes of the field are time-dependent, i.e.,

$$E_{m+1,m} = E_{m0} g(t).$$

Introducing, similarly to Section 2.3, variables y_m, we obtain from (24) a system of equations:

$$\dot{y}_m + \frac{1}{T_1} y_m = \frac{\Omega_m^2}{2} T_2 g^2(t)(\delta_{1m} + y_{m-1} - 2y_m + y_{m+1}),$$
$$m = 1, 2, \ldots, N. \tag{25}$$

Let us consider only the case $\Omega_m = E_0\mu_{m+1,m}/\hbar \equiv \Omega_0$. Then, the solution of the system (25) is formally determined by (12), and the collective coordinates z_k obey the equations

$$\dot{z}_k + \frac{z_k}{T_1}[1 + \nu_k^2 T_1 T_2 g^2(t)] = \frac{\Omega_0^2 T_2}{2} f_k g^2(t),$$
$$z_k(0) = 0, \quad k = 1, 2, \ldots, N. \tag{26}$$

Recall that ν_k and f_k are determined in (14). Equations (26) are easily integrable. Substituting $z_k(t)$ in (12), we find the dependence of y_m on time. This dependence has the form of (15) where $F_k(t)$ is given by

$$F_k(t) = T_1^{-1}(1 + \nu_k^2 T_1 T_2) e^{-\psi_k(t)} \int_0^t dt' g^2(t') e^{\psi_k(t')},$$
$$\psi_k(t) = T_1^{-1}(t + \nu_k^2 T_1 T_2) \int_0^t g^2(t') dt'. \tag{27}$$

The form of presentation for probabilities ρ_{mm} and the average number of quanta of an oscillator ε is similar to (16), (17), but $F_k(t)$ is defined by (27).

In a particular case $g(t) = 1$, (27) coincides with expression (23), which was obtained earlier for the incoherent regime.

If the spectral amplitudes of the field change periodically in time, $g(t) = \cos\nu t$, then, in the absence of collisional relaxation ($T_1 \longrightarrow \infty$), we obtain

$$\Delta\rho_{mm} = \sum_{k=1}^{N} U_{mk} \exp(-\gamma_k(t)),$$
$$\Delta\varepsilon = \sum_{k=1}^{N} V_k \exp(-\gamma_k(t)), \tag{28}$$

$$\gamma_k(t) = \frac{1}{2}\nu_k^2 T_2 t\left(1 + \frac{\sin 2\nu t}{2\nu t}\right).$$

It follows from the second relationship in (28) that, neglecting coherent effects gives the number of vibrational quanta stored $\varepsilon < N/2$ because $V_k < 0$. It means that, at any instant, the population probability of the lower half of all levels in the collective mode exceeds that of the upper half.

In the next section, we will demonstrate that, in the case of periodic modulation of the amplitude, the coherent mechanism of interaction can play an important role even for long time intervals $t \gg T_1, T_2$. In this case effects that cannot be described within the framework of rate equations arise.

2.1.5. Coherent effect of conversion of distribution over the levels of an anharmonic oscillator (parametric excitation). It follows from considerations of Section 2.3 that, in the case of interaction of an anharmonic oscillator with the field whose frequency is periodically modulated in time [see (7)], the maximal possible number of quanta stored equals $N/2$. In the coherent regime, this is an average around which the energy of an oscillator is pulsating. If coherent effects are not substantial, then $\varepsilon \longrightarrow N/2$ for strong fields (the saturation regime).

An important question arises whether it is possible, in principle, to implement conditions under which the number of quanta exceeds $N/2$. In this case, we consider an overexcited state of a quantum oscillator; an inverted distribution over its levels corresponds to such a state. It is *a priori* clear that a coherent mechanism of resonance interaction of the electromagnetic field with an anharmonic oscillator must be a basis for a method used to realize the corresponding conditions.

Coherent effects involve, in particular, pulsating changes in the population probability of levels. In case of a two-level oscillator, the frequency of pulsations coincides with the Rabi frequency for a given transition. In a multilevel system, we should analyze the spectrum of pulsations. Assume that the amplitude of the field (7) changes periodically in time with the frequency ν:

$$E(t) = \frac{E_0}{2} g(t)\left(\sum_{n=-\infty}^{\infty} c_n e^{i(\omega + n\Delta\omega)t} + \text{c.c.}\right). \tag{29}$$

Then, the Rabi frequencies corresponding to different transitions of an anharmonic oscillator will be modulated with the same frequency. Selecting properly the frequency and the modulation depth, one can implement parametric excitation of the oscillator. Here, the situation is similar to the oscillation of a pendulum with a pulsating point of support (Kapitsa pendulum [131]). A proper choice of modulation frequencies stabilizes a new (dynamic) equilibrium state of a pendulum. An overexcited state is an analog in the case of coherent excitation of an oscillator by a field. In the presence of amplitude

modulation (29), a system of equations similar to (10) is given by

$$\ddot{y}_m + \left(\frac{1}{T_1} + \frac{1}{T_2} - \frac{\dot{g}(t)}{g(t)}\right)\dot{y}_m + \frac{1}{T_1}\left(\frac{1}{T_2} - \frac{\dot{g}(t)}{g(t)}\right)y_m = \frac{\Omega_0^2}{2}g^2(t)(\delta_{1m} + y_{m-1} - 2y_m + y_{m+1}). \quad (30)$$

Note that the change in the field amplitude results not only in the modulation of the Rabi frequency but also in the modulation of the "friction coefficient." Such an effect is intrinsically impossible within the framework of the classical approach.

The solution of system (30) is presented in the form of (12) where z_k satisfies the equations

$$\ddot{z}_k + \left(\frac{1}{T_1} + \frac{1}{T_2} - \frac{\dot{g}(t)}{g(t)}\right)\dot{z}_k + \left(\frac{1}{T_1}\frac{1}{T_2} - \frac{\dot{g}}{g}\right)z_k = \frac{\Omega_0^2}{2}f_k g^2(t). \quad (31)$$

Below, we consider the case $T_1 = T_2 = T$. One can show that the system (31) allows exact solution for an arbitrary function $g(t)$:

$$z_k = \alpha_k[1 - G_k(t)], \quad k = 1, 2, \ldots, N,$$
$$G_k(t) = e^{-t/T}\cos\tau_k(t) + \frac{1}{T}e^{-t/T}\int_0^t \cos[\tau_k(t) - \tau_k(t')]e^{-t'/T}dt', \quad (32)$$
$$\tau_k(t) = \nu_k\int_0^t g(t')dt', \quad \alpha_k = \frac{1}{2}\sqrt{\frac{2}{N+1}}\cot\frac{\pi k}{2(N+1)}.$$

Having determined $z_k(t)$, we find $y_m(t)$ from (12), so that for $\Delta\rho_{mm}$ and $\Delta\varepsilon$ we have

$$\Delta\rho_{mm} = \sum_{k=1}^{N} U_{mk}G_k(t), \qquad \Delta\varepsilon = \sum_{k=1}^{N} V_k G_k(t). \quad (33)$$

Let us consider now the case of periodic modulation of the of field amplitude,

$$g(t) = \cos\nu t.$$

If the modulation period is shorter than the relaxation time, $T_\nu \ll T$, then, for time intervals $T_\nu \ll t \ll T$, averaging of (33) over the period T_ν yields

$$\langle\rho_{mm}\rangle = \frac{1}{N+1} + \sum_{k=1}^{N} U_{mk}\left(\frac{\nu_k}{\nu}\right), \qquad \langle\varepsilon\rangle = \frac{N}{2} + \sum_{k=1}^{N} V_k J_0\left(\frac{\nu_k}{\nu}\right). \quad (34)$$

In particular, for a two-level system ($N = 1$) we have

$$\langle\rho_{11}\rangle = \frac{1}{2}\left[1 + J_0\left(\frac{\Omega_0}{\nu}\right)\right], \quad \langle\rho_{22}\rangle = \frac{1}{2}\left[1 - J_0\left(\frac{\Omega_0}{\nu}\right)\right].$$

Hence, the probability of population of the upper state exceeds 1/2 in certain ranges of frequencies of amplitude modulation where the Bessel function J_0 is negative.

For long time intervals ($t \gg T$), functions $G_k(t)$ in (33) and (34) are given by

$$G_k(t) = P_k(t)\cos\left(\frac{\nu_k}{\nu}\sin\nu t\right) + Q_k(t)\sin\left(\frac{\nu_k}{\nu}\sin\nu t\right),$$
$$P_k(t) = \sum_{n=-\infty}^{\infty}\frac{J_{2n}(\nu_k/\nu)}{1 + (2n\nu T)^2}(\cos 2n\nu t + 2n\nu T\sin 2\nu T),$$
$$Q_k(t) = 2\sum_{n=-\infty}^{\infty}\frac{J_{2n+1}(\nu_k/\nu)}{1 + ((2n+1)\nu T)^2} \times [\sin(2n+1)\nu t - (2n+1)\nu T\cos(2n+1)\nu t]. \quad (35)$$

Thus a coherent mechanism of interaction determines undamped oscillations of diagonal elements of the density matrix for times t longer than the relaxation time of the system, and the frequencies of pulsations are aliquot to the modulation frequency ν.

Averaging (35) over the period T_ν, we obtain

$$\langle G_k(t)\rangle = \sum_{n=-\infty}^{\infty}\frac{J_n(\nu_k/\nu)}{1 + (n\nu T)^2} = \frac{\pi x}{\sinh\pi x}J_{ix}(\nu_k/\nu)J_{-ix}(\nu_k/\nu), \quad (36)$$

where $x = (\nu_k T)^{-1}$ and i is imaginary unit. In a particular case $x \ll 1$, (33) is reduced to

$$\langle\rho_{mm}(\infty)\rangle = \frac{1}{N+1} + \sum_{k=1}^{N} U_{mk}J_0^2(\nu_k/\nu), \qquad \langle\varepsilon(\infty)\rangle = \frac{N}{2} + \sum_{k=1}^{N} V_k J_0^2(\nu_k/\nu). \quad (37)$$

It follows from (37) that $\langle\varepsilon(\infty)\rangle < N/2$.

If the modulation law is given by the relationship $g(t) = 1 + \gamma\cos\nu t$, then, for the functions $G_k(t)$ in (33), one can easily get ($T_\nu = 2\pi/\nu \ll t \ll T$)

$$G_k(t) = \sum_{n=-\infty}^{\infty} J_n\left(\gamma\frac{\nu_k}{\nu}\right)\cos(\nu_k - n\nu)t. \quad (38)$$

Thus, the pulsation spectrum consists of combination frequencies

$$\nu_{kn} = \nu_k \pm n\nu \quad (k = 1, \ldots, N, \quad n = 0, 1, 2, \ldots).$$

Suppose, that for certain n and k, a condition $\nu_k = n\nu$ is met, i.e.,

$$q_{nk}^{-1} = \frac{\nu}{\Omega_0} = \frac{\sqrt{2}}{n}\sin\frac{\pi k}{2(N+1)}. \quad (39)$$

Then, it follows from (38) that constant component of the probability ρ_{mm} and the number of quanta ε shift. The following values correspond to the dynamic equilibrium state in this case:

$$\bar{\rho}_{mm} = \frac{1}{N+1}\left[1 + J_n(n\gamma)\left(\cos\frac{mk\pi}{N+1} + \cos\frac{(m-1)k\pi}{N+1}\right)\right],$$
$$\bar{\varepsilon} = \frac{N}{2} + \frac{1}{2(N+1)}((-1)^k - 1)J_n(n\gamma)\cot^2\frac{k\pi}{2(N+1)}. \quad (40)$$

It follows from the second relationship in (40) that, for even k, the number of quanta is $\bar{\varepsilon} = N/2$. If

$$k = 1, 3, 5, \ldots (k \le N)$$

and the parameter of modulation depth γ lies within the ranges where the Bessel function $J_n(n\gamma)$ is negative, then $\bar{\varepsilon} > N/2$, and, thus, an overexcited state is realized.

2.1.6. Conclusion. In this section, we considered important methods of excitation of high quantum fields of a collective anharmonic mode using a series of phased pulses (analog of the Veksler autophasing method), a periodic modulation of the EMR frequency, and amplitude–frequency modulation (AFM). Under certain conditions, coherent effects of interaction of the field with an oscillator in all of these cases may play an important role. In particular, the AFM method allows one to employ the coherent mechanism to create an anomalous state of an anharmonic oscillator, when the distribution over its levels is inverted as a whole (an overexcited state). A common feature of all proposed methods is the possibility of neutralizing anharmonism and, consequently, of excitation of high quantum levels.

2.2. Interaction of EMR with Biopolymer Macromolecules

2.2.1. Introduction. Functioning of biological macromolecules (enzymes and other types of proteins, nucleic acids, etc.) is determined, to a great extent, by biochemical processes in their elements. One of possible primary mechanisms of EMR action on biosystems is an induction with the help of transitions between different isomeric states of biomolecules (as applied to enzymes, this idea was proposed, in particular, by Frölich [40, 42]). The absorbed energy is spent according to this hypothesis on crossing (complete or partial) of a barrier between the conformers. It is natural that electric (or magnetic) activity of the corresponding degrees of freedom of a biopolymer molecule is necessary for realization of such a process. The information on protein and nucleic acid spectra may be considered as a certain substantiation of this method of consideration of primary mechanisms as applied to experiments in the microwave range (see Section 4).

An elementary model illustrating the change of conformational states of macromolecules by means of EMR corresponds to the problem of the motion of a particle in a potential well $U(x)$ with two minima separated by a potential barrier. An alternating force $F(t) = eE(t)$ (where e is the charge of a particle and $E(t)$ is the strength of the electric component of the electromagnetic wave) induces oscillations of a particle initially localized on one of the sides of the potential barrier. The amplitudes of these oscillations become close to the coordinate of the maximum, so that thermal fluctuations become sufficient for direct crossing of the barrier (during the time of action of the electromagnetic field).

The applicability of classical (nonquantum) description of oscillations of a particle in the EHF range is guaranteed by a low value of the ratio $h\nu/kT$, where $h\nu$ is the energy of a quantum and kT is the thermal energy. For the frequencies $\nu \sim 10^{11}$ s^{-1} ($\omega = 2\pi\nu \sim 10^{12}$ rad), this value is about 0.01. However, the height of the potential barrier exceeds the thermal energy ($kT \ll U_{max}$), which allows one to avoid direct introduction into consideration of random forces giving rise to thermal fluctuations (insignificant for high-energy vibrations). Thus, the multiparticle nature of the problem is reduced to the introduction of friction forces, and we arrive at the equation

$$m(\ddot{x} + 2\lambda\dot{x}) + \frac{\partial U(x)}{\partial x} = F(t). \quad (1)$$

With regard to the anharmonicity of the interaction potential, equation (1) is reduced to

$$\ddot{x} + 2\lambda\dot{x} + \omega_0^2 x = \frac{f}{m}\cos\omega t - \alpha x^2 - \beta x^3. \quad (2)$$

In (2), the electric field strength is presented as $F(t) = f\cos\omega t$. In the linear approximation, we have

$$\ddot{x} + 2\lambda\dot{x} + \omega_0^2 x = \frac{f}{m}\cos\omega t. \quad (3)$$

The solution of (3) is trivial:

$$x = Ae^{-\lambda t}\cos(\sqrt{\omega_0^2 - \lambda^2}t + \phi) + B\cos(\omega t + \phi).$$

The first term decays exponentially so that, after a rather long period of time, only one term survives. This term corresponds to induced oscillations:

$$x = B\cos(\omega t + \phi).$$

It is not difficult to determine their amplitude and phase:

$$B = \frac{f}{m\sqrt{(\omega^2 - \omega_0^2)^2 + 4\lambda^2\omega^2}}, \quad (5)$$
$$\tan\phi = \frac{2\lambda\omega}{\omega_0^2 - \omega^2}.$$

In the case of exact resonance, we have

$$B = \frac{f}{2m\lambda\omega_0}, \quad \phi = \frac{\pi}{2}. \tag{6}$$

Thus, the maximal amplitude of induced oscillations is

$$x_{\max} = \frac{eE}{2m\lambda\omega_0}. \tag{7}$$

The amplitude of free oscillations of a harmonic oscillator with the potential energy $U(x) = m\omega_0^2 x^2/2$ can be expressed through the energy ε as follows: $x_0 = \sqrt{2\varepsilon/m\omega^2}$. Equating x_0 to (7) we obtain

$$E = 2\sqrt{2m\varepsilon}\omega_0\lambda/e = q\sqrt{2m\varepsilon}\omega_0/\pi e,$$

where $q = \lambda/\nu_0 = 2\pi\lambda/\omega_0$ is the logarithmic decrement of damping (the inverse of the oscillator quality factor).

Assuming that $\varepsilon \simeq 10kT$ (which is a rather large value compared to the energy of thermal oscillations and, at the same time, is comparable with the energy of ATP hydrolysis, providing conformational transitions in the course of functioning of biomolecules) and taking the values typical for local vibrations of biomolecules in the EHF range,

$$\omega_0 = 10^{12}\ \mathrm{s}^{-1}, \quad m = 200m_p, \quad e = \bar{e},$$

for $E = 1$ W/cm (which corresponds to the EHF EMR intensity of 1 mW/cm^2), we obtain an estimate $q \sim 3 \times 10^{-7}$. The corresponding Q factor (about 3×10^6) is several orders of magnitude higher than the Q factors (10^3–10^4) characteristic of resonances in typical experiments on the interaction of low-intensity EHF EMR with biological objects.

Therefore, the interaction of EMR with isolated local vibrations of biomolecules cannot be a sufficiently effective primary mechanism providing experimentally observed biological action of EHF fields.

2.2.2. Biopolymer chain in a resonance field. Let us consider an elementary one-dimensional chain of monomers. It is assumed that the interaction with the field of radiation results in excitation of dipole-active oscillations of monomers that form the chain. The oscillations of monomers are interrelated, in turn, by means of dipole–dipole interaction. Note that a model of this type is used, as a rule, for the study of dynamics of such biomacromolecules as nucleic acids (DNA).

Assume also that local dipole-active vibrations of each monomer characterized by x_k coordinates have the same natural frequency ω_0 and damping λ and interact with each other by means of the electric field of dipole moments $d_k = ex_k$. In the considered case of a one-dimensional structure, we can restrict ourselves to the consideration of the interaction of only neighboring dipoles (the so-called short-range interaction).

The potential function of a biopolymer chain in the simplest case is given by

$$U = \sum_k \frac{\omega_0 x_k^2}{2} + \sum_k \frac{\xi_x}{3} x_k^3 + \sum_k \frac{\Omega_0^4}{4}[(x_k - x_{k-1})^2 + (x_k - x_{k+1})^2] + \sum_k \frac{\xi_{xx}}{3}[(x_k - x_{k-1})^3 + (x_k - x_{k+1})^3] + \ldots. \tag{8}$$

Let us present the equations of motion for coordinates x_k under the action of an external isotropic monochromatic field as

$$\ddot{x}_k + 2\lambda\dot{x}_k + \omega_0^2 x_k = \frac{\Omega_0^2}{2}(x_{k-1} - 2x_k + x_{k+1}) + f_0\cos\omega t + \Phi(x_{k-1}, x_k, x_{k+1}), \tag{9}$$

where

$$\Phi = -\xi_k x_k^2 - \xi_{xx}[(x_k - x_{k-1})^2 + (x_k - x_{k+1})^2].$$

In the linear approximation, the system of equations is reduced to

$$\ddot{x}_k + 2\lambda\dot{x}_k + \omega_0^2 x_k = \frac{\Omega_0^2}{2}(x_{k-1} - 2x_k + x_{k+1}) + f_0\cos\omega t. \tag{10}$$

Let us introduce collective variables:

$$z_m = \sqrt{\frac{2}{N+1}}\sum_{k=1}^{N} x_k \sin\frac{mk\pi}{N+1}, \quad m = 1, 2, \ldots, N, \tag{11}$$

while

$$x_k = \sqrt{\frac{2}{N+1}}\sum_{m=1}^{N} z_m \sin\frac{mk\pi}{N+1}, \quad k = 1, 2, \ldots, N. \tag{12}$$

Then, for the variables z_m, we obtain a system of uncoupled equations,

$$\ddot{z}_m + \lambda\dot{z}_m + \nu_m^2 z_m = s_m f_0\cos\omega t, \quad m = 1, 2, \ldots, N, \tag{13}$$

where the frequencies of collective modes are introduced,

$$\nu_m^2 = \omega_0^2 + \Omega_0^2 \sin^2\frac{m\pi}{2(N+1)}, \quad m = 1, 2, \ldots, N, \tag{14}$$

and the partial coefficients are defined by

$$s_m = \sqrt{\frac{2}{N+1}}\sum_{k=1}^{N}\sin\frac{mk\pi}{N+1} = \sqrt{\frac{2}{N+1}}\frac{\sin\frac{\pi}{2}m\sin\frac{\pi}{2}\frac{N}{N+1}}{\sin\frac{\pi}{2}\frac{m}{N+1}}. \tag{15}$$

Induced oscillations are of the main interest. The solution of (13) is trivial. Let us present it as

$$z_m = \frac{s_m f_0}{\sqrt{(\omega^2 - \nu_m^2)^2 + \lambda^2\omega^2}}\cos(\omega t + \phi_m),$$

$$\tan\phi_m = \frac{2\lambda\omega}{\omega^2 - \nu_m^2}.$$

The maximal value of z_m is achieved for $\omega = \sqrt{\nu_m^2 - \lambda^2/2}$. Dynamics of induced oscillations of coordinates x_k is determined according to (12) as

$$x_k = \sqrt{\frac{2}{N+1}} f_0 \sum_{k=1}^{N} \frac{s_m \sin\dfrac{mk\pi}{N+1}}{\sqrt{(\omega^2 - \nu_m^2)^2 + \lambda^2\omega^2}}\cos(\omega t + \phi_m). \tag{16}$$

In (16) the resonances at the collective frequencies (14) are clearly seen. It is evident that resonance action of an external electromagnetic field exactly at these frequencies ensures the highest efficiency.

It follows from (15) that variables s_m equal zero for even m. Therefore, the number of resonances is $r = [N/2]$, i.e., it is twice less than the number of oscillators in the system. This circumstance is directly related to the symmetry of the problem.

It is interesting to determine the distances between the frequencies of the collective modes:

$$\nu_{m+2}^2 - \nu_m^2 = \Omega_0^2\left[\sin\frac{(m+2)\pi}{2(N+1)} - \sin^2\frac{m\pi}{2(N+1)}\right] = \Omega_0^2 \sin\frac{\pi}{N+1}\sin\frac{\pi(m+1)}{N+1}. \tag{17}$$

It follows from (17) that, for m close to unity, the spectrum becomes more concentrated, near $m \approx N/2$ it is rarefied, and for $m \approx N$ it is concentrated again. Hence, the most pronounced resonances can be expected for m close to $N/2$.

Assume that the external signal is modulated in its amplitude,

$$f = f_0(1 + 2\gamma\cos\Omega t)\cos\omega t, \tag{18}$$

where 2γ is the modulation depth and Ω is the modulation frequency. Then the expansion in (18) yields

$$f = f_0[\gamma\cos\omega t + \gamma(\cos(\omega - \Omega)t + \cos(\omega + \Omega)t)].$$

Thus, amplitude modulation provides additional potentialities of implementing resonance action on biomacromolecules:

$$\nu_m = \begin{cases} \omega, \text{ standard situation} \\ \omega - \Omega, \text{ Stokes resonances} \\ \omega + \Omega, \text{ anti-Stokes resonances.} \end{cases} \tag{19}$$

Thus, is the case of amplitude modulation of the external field, the number of possible resonance realizations increases (in comparison with a purely monochromatic field) up to $3[N/2]$, where N is the number of monomers.

If the solution (16) to a linear system is assumed to be a zeroth-order approximation, it is not difficult to find the first approximation taking anharmonicity into account [see also (9)]. For this purpose, one has to substitute the solution (16) into the right-hand side of (9) and integrate the resulting equation. This procedure is not difficult. However, the final results are rather cumbersome, and we do not present them here.

Note an important fact that the nonlinearity in the right-hand side of (9) is a quadratic nonlinearity. Consequently, the right-hand side involves a constant term, which is independent of time, and the terms proportional to the second harmonic. Therefore, new resonance potentialities emerge,

$$\nu_m = 2\omega,$$

associated with the second harmonic. The latter widens the potentialities of active resonance action on biopolymer systems. One should keep in mind that the resonances at the second harmonic may be realized due to both anharmonicity of the monomers themselves and the cubic nonlinearity in the potential of interaction between the monomers of a macromolecule.

Finally, for the most interesting case of amplitude modulation (18), it can be easily demonstrated that a substantial broadening of resonances takes place:

$$\nu_m = \begin{cases} \Omega \\ 2\omega \\ 2\omega \pm \Omega \\ 2(\omega \pm \Omega). \end{cases} \tag{20}$$

With regard to (19) and (20), the number of possible realizations of resonance excitation is equal to $(3 + 5)[N/2] = 4[N]$.

Thus, the above consideration demonstrates that the resonances in the interaction of EMR with biopolymer chains are of collective nature. The number of resonances in the interaction of a monochromatic field with a macromolecule is twice less than the number of oscillators (the spectrum is not equidistant). Amplitude modulation increases the number of possible resonance realizations due to Stokes and anti-Stokes frequencies. The number of resonance realizations increases substantially when nonlinearity is taken into account, in particular, a two-quantum resonance becomes possible.

2.3. Interaction of EMR with Biopolymer Macromolecules and Its Influence on the Dynamics of the Active Site (Antenna Model)

2.3.1. Introduction. As it was mentioned several times, functioning of several biological macromolecules (in particular, enzymes) and other biological compounds is determined, to a great extent, by the processes in the active sites surrounded by biopolymer

chains folded into globules. Based on such a notion of the structure of a biomolecule, one may assume that the interaction with the field of radiation results in the excitation of dipole-active vibrations of monomers constituting the chain which, in turn, induces oscillations in the active site (antenna model). Thus excited oscillations may cause biomacromolecule transition into another conformational state.[5]

This concept is completely adequate to several biomacromolecules, e.g., chlorophyll, hemoglobin, myoglobin, etc. These macromolecules have two common structural properties: (1) an ion is situated in their geometrical centers (a magnesium ion in chlorophyll and iron ion in hemoglobin); (2) the ion is arranged at the center of symmetry of a tetrapyrrole ring (pseudoplane structure).

Recall that chlorophyll (along with the multitude of its derivatives) is a pigment playing an important role in photosynthesis, hemoglobin is a well-known protein of blood that enters into erythrocytes and that is a carrier of oxygen, and myoglobin is a muscle protein (of sperm whales) that is an analog of hemoglobin in biological function (it is an oxygen carrier).

Note also that the third class of biomacromolecules corresponding to the antenna model is based on the chemistry of macrocycle compounds.

Pointing out three classes of biomolecular systems, we specify once again the notion of an antenna model. An external energy (in particular, associated with resonance interaction of EHF EMR with bioobjects or with biochemical reactions, etc.) is transferred to the periphery of the system, i.e., to an ensemble of subunits (which are not necessarily identical in their structure). An associating center (a metal ion in the case under consideration) actively interacts via biochemical bonds with peripheral acceptors that receive encoded energy. Thus, the former acquires the information, which causes biological action. Reaction ability of biomacromolecules substantially depends on the level of excitation of central subunits.

Swiss scientist L. Ruzhechka was the first to perform in 1926 the synthesis of macrocyclic compounds. He obtained cyclic ketones with a 10–30-link ring after dry vacuum distillation of thorium salts of dicarboxylic acids. Nowadays, synthesized and studied are such macrocyclic compounds as crown ethers, cryptands, annulens, cyclophans, catenans, and rotaxans.

Macroheterocyclic compounds, such as crown ethers, cryptands, and their heteroanalogs are of special interest in the chemistry of macrocycles. The study of these substances is closely related to the discovery of natural macroheterocycles, namely, cyclic peptides, depsipeptides, and depsides. Natural macroheterocyclic compounds are able to form stable complexes with ions of alkaline and alkaline-earth metals and to transport ions through natural and artificial membranes. They were called membrane-active complexes or ionophores.

In 1955, valinomycin was extracted from fungous culture. This antibiotic is a 36-link cyclododecadepside. Soon a remarkably high selectivity of valinomycin in the complex formation with certain metal ions was discovered. This compound binds potassium ions ten thousand times more effectively than sodium ions. According to the X-ray data on the complex salt of valinomycin with potassium ion, the latter is located in the central hollow of the ring and interacts with carbonyl oxygen of the ester group. Other similar natural macroheterocycles were discovered: valinomycin analogs, nonactins, enniatins, and other ionophores. Complexons (in particular, crown ethers) with ions of alkaline metals (lithium, sodium, potassium, rubidium, and cesium); with ions of alkaline-earth metals (magnesium, calcium, strontium, and barium); and with copper, silver, mercury, lanthanum, thallium, lead, cobalt, and nickel ions are synthesized already.

2.3.2. Antenna model. As an elementary model that illustrates the antenna effect, we consider a one-dimensional closed (circular) chain of monomers. An active site is located at the center of the ring. It is coupled with monomers of the chain by means of dipole–dipole interaction.

Let us denote the coordinate displacements of monomers as $x_1, \ldots, x_N$ and the displacements of the active site as y. For the potential function, we have

$$\begin{aligned} U(x_1, \ldots, x_N, y) &= \sum_{k=1}^{N}\left[\frac{1}{2}\omega_x^2 x_k^2 + \frac{1}{3}\xi_x x_k^3\right] \\ &+ \frac{1}{2}\omega_y^2 y^2 + \frac{1}{3}\xi_y y^3 + \sum_{k=1}^{N}\left[\frac{1}{2}\omega_{xy}^2 (y - x_k)^2 + \frac{1}{3}\xi_{xy}(y - x_k)^3\right] \\ &+ \sum_{k=1}^{N}\frac{1}{2}\omega_{xx}^2[(x_k - x_{k-1})^2 + (x_k - x_{k+1})^2] \\ &+ \sum_{k=1}^{N}\frac{\xi_{xx}}{3}[(x_k - x_{k-1})^3 + (x_k - x_{k+1})^3] - \sum_{k=1}^{N} x_k f_0 \cos\omega t. \end{aligned} \tag{1}$$

The first two terms in (1) correspond to the oscillations of monomers (the second term takes anharmonicity into account), and the last two terms correspond to the bonds between monomers. The other terms correspond to the coupling of monomers with the active site. Equations of motion are given by

$$\begin{aligned} \ddot{x}_k + \lambda\dot{x}_k &= -\frac{\partial U(x_k)}{\partial x_k} + f(t), \\ \ddot{y} + \lambda\dot{y} &= -\frac{\partial U}{\partial y}, \end{aligned} \tag{2}$$

[5] Antenna effect is known to be realized in photosynthetic systems (a photosynthetic subunit includes a light-collecting antenna and a photoreaction center coupled with this antenna).

where $f(t) = f_0\cos\omega t$ is an external monochromatic force acting only on monomers and λ is the damping coefficient introduced phenomenologically (for simplicity, this coefficient is assumed to be the same for both monomers and the active site). With regard to (1), equation (2) is reduced to

$$\begin{aligned}\ddot{x}_k + \lambda\dot{x}_k &= -\omega_x^2 x_k - \xi_x x_k^2 - \omega_{xx}^2(2x_k - x_{k-1} - x_{k+1}) \\ &+ \omega_{xy}^2(y - x_k) + \xi_{xy}(y - x_k)^2 + f(t) \\ &+ \xi_{xx}[(x_k - x_{k-1})^2 + (x_k - x_{k+1})^2], \\ \ddot{y} + \lambda\dot{y} &= -\omega_y^2 y - \xi_y y^2 \\ &- \omega_{xy}^2\sum_{k=1}^{N}(y - x_k) - \xi_{xy}\sum_{k=1}^{N}(y - x_k)^2,\end{aligned} \tag{3}$$

or

$$\begin{aligned}&\ddot{x}_k + \lambda\dot{x}_k + (\omega_x^2 + \omega_{xy}^2)x_k - \omega_{xy}^2 y \\ &= \omega_{xx}^2(x_{k-1} - 2x_k + x_{k+1}) - \xi_x x_k^2 + \xi_{xy}(y - x_k)^2 \\ &+ f(t) + \xi_{xx}[(x_k - x_{k-1})^2 + (x_k - x_{k+1})^2], \\ &\ddot{y} + \lambda\dot{y} + (\omega_y^2 + N\omega_{xy}^2)y - \omega_{xy}^2\sum_{k=1}^{N}x_k \\ &= -\xi_y y^2 - \xi_{xy}\sum_{k=1}^{N}(y - x_k)^2.\end{aligned} \tag{4}$$

Let us introduce a common coordinate for the ensemble of monomers,

$$x = \sum_{k=1}^{N} x_k. \tag{5}$$

Then, the system of equations (4) in the linear approximation is

$$\begin{aligned}&\ddot{x}_k + \lambda\dot{x}_k + \omega_1^2 x_k - \omega_0^2 y \\ &= \frac{\Omega_0^2}{2}(x_{k-1} - 2x_k + x_{k+1}) - \xi_x x_k^2 + f(t), \\ &\ddot{y} + \lambda\dot{y} + \omega_2^2 y - \omega_0^2 x = 0,\end{aligned} \tag{6}$$

where

$$\begin{aligned}\omega_1^2 &= \omega_x^2 + \omega_{xy}^2, \\ \omega_2^2 &= \omega_y^2 + N\omega_{xy}^2, \\ \omega_0^2 &= \omega_{xy}^2, \\ \Omega_0^2 &= 2\omega_{xx}^2.\end{aligned}$$

N is the number of monomers.

With regard to (5), we have

$$\ddot{x} + \lambda\dot{x} + \omega_1^2 x - N\omega_0^2 y = Nf(t), \tag{7.1}$$

$$\ddot{y} + \lambda\dot{y} + \omega_2^2 y - \omega_0^2 x = 0. \tag{7.2}$$

It follows from (7.2) that

$$x = \frac{1}{\omega_0^2}(\ddot{y} + \lambda\dot{y} + \omega_2^2 y). \tag{8}$$

Substitution of (8) into (7.1) yields

$$\begin{aligned}&y^{(4)} + 2\lambda y^{(3)} + (\omega_1^2 + \omega_2^2 + \lambda^2)y^{(2)} \\ &+ \lambda(\omega_1^2 + \omega_2^2)y^{(1)} + (\omega_1^2\omega_2^2 - N\omega_0^4)y = N\omega_0^4 f(t).\end{aligned} \tag{9}$$

The corresponding characteristic equation obtained after the substitution of $y \sim e^{kt}$ into a homogeneous equation is

$$(k^2 + \lambda k + \omega_1^2)(k^2 + \lambda k + \omega_2^2) = N\omega_0^4. \tag{10}$$

Denoting $z_k = k^2 + \lambda k$, we obtain

$$z^2 + (\omega_1^2 + \omega_2^2)z + \omega_1^2\omega_2^2 - N\omega_0^4 = 0,$$

so that

$$z_{1,2} = -\frac{1}{2}(\omega_1^2 + \omega_2^2) \pm \sqrt{\frac{1}{4}(\omega_1^2 + \omega_2^2)^2 - \omega_1^2\omega_2^2 + N\omega_0^4}. \tag{11}$$

It is assumed below that the following inequalities are fulfilled:

$$\omega_0^2 < \frac{\omega_1\omega_2}{\sqrt{N}}, \quad \lambda < \sqrt{\omega_1^2 + \omega_2^2}. \tag{12}$$

The first inequality corresponds to a weak coupling of monomers with the active site, and the second one corresponds to weak damping of monomer oscillators.

For eigenvalues, we have

$$k_{1,2} = -\frac{\lambda}{2} \pm i\sqrt{\Omega_1^2 - \frac{\lambda^2}{4}}, \quad k_{3,4} = -\frac{\lambda}{2} \pm i\sqrt{\Omega_2^2 - \frac{\lambda^2}{4}}, \tag{13}$$

where the collective frequencies are introduced:

$$\begin{aligned}\Omega_1 &= \left\{\frac{1}{2}(\omega_1^2 + \omega_2^2) + \left[\frac{1}{4}(\omega_1^2 - \omega_2^2)^2 + N\omega_0^4\right]^{1/2}\right\}^{1/2}, \\ \Omega_2 &= \left\{\frac{1}{2}(\omega_1^2 + \omega_2^2) - \left[\frac{1}{4}(\omega_1^2 - \omega_2^2)^2 + N\omega_0^4\right]^{1/2}\right\}^{1/2}.\end{aligned} \tag{14}$$

We consider the induced oscillations (for an external force $f_0\cos\omega t$):

$$y = A\cos\omega t + B\sin\omega t. \tag{15}$$

Substituting (15) into (9) and equalizing the corresponding coefficients of $\cos\omega t$ and $\sin\omega t$ yield a system of algebraic equations:

$$\begin{cases} A(\omega^4 - \alpha_2\omega^2 + \alpha_0) - B(2\lambda\omega^3 - \alpha_1\omega) = F_0 \\ A(2\lambda\omega^3 - \alpha_1\omega) + B(\omega^4 - \alpha_2\omega^2 + \alpha_0) = 0, \end{cases}$$

where

$$\alpha_0 = \omega_1^2\omega_2^2 + N\omega_0^4, \quad \alpha_1 = \lambda(\omega_1^2 + \omega_2^2),$$

$$\alpha_2 = \omega_1^2 + \omega_2^2 + \lambda^2, \quad F_0 = N\omega_0^2 f_0.$$

Finally, we obtain

$$y = \frac{F_0}{\sqrt{p^2 + q^2}}\cos(\omega t + \phi),$$

where

$$p = (\omega^2 - \omega_1^2)(\omega^2 - \omega_2^2) - \omega^2\lambda^2 + N\omega_0^4,$$

$$q = \lambda\omega(2\omega^2 - \omega_1^2 - \omega_2^2),$$

$$\tan\phi = \frac{q}{p}.$$

After simple but cumbersome transformations, we obtain the expression for the induced oscillations of the active site:

$$y = N\omega_0^2 f_0 \cos(\omega t + \phi)[(\omega^2 - \Omega_1^2)^2(\omega^2 - \Omega_2^2)^2 + \omega^2\lambda^2[\omega^2\lambda^2 + (\omega^2 - \Omega_1^2)^2 + (\omega^2 - \Omega_2^2)^2]]^{-1/2}. \quad (16)$$

It follows from (16) that the maximal amplitude of the induced oscillations of the active site is achieved under the conditions of collective resonance:

$$\text{either } \omega = \Omega_1$$

$$\text{or } \omega = \Omega_2.$$

In any of these cases, the amplitude of the induced oscillations is given by

$$y_0 = \frac{N\omega_0^2 f_0}{\omega\lambda\sqrt{\omega^2\lambda^2 + (\Omega_2^2 - \Omega_1^2)^2}}. \quad (17)$$

It follows from (17) that the maximal effect of resonance excitation of the active site is achieved for a large number of peripheral "antenna" subunits, high coefficients of coupling of the active site with monomers, minimal damping coefficient, and minimal detuning of the collective modes.

It is not difficult to determine the "choreography" (dynamics of the induced oscillations) of separate monomers. According to (6), the equation for the kth monomer is

$$\ddot{x}_k + 2\lambda\dot{x}_k + \omega_1^2 x_k = \frac{1}{2}\Omega_0^2(x_{k-1} - 2x_k + x_{k+1}) + \omega_0^2 y + f(t). \quad (18)$$

Introducing collective coordinates

$$z_m = \sqrt{\frac{2}{N+1}}\sum_{k=1}^{N} x_k \sin\frac{mk\pi}{N+1},$$

and applying the methods of linear algebra (already used in Section 1), we obtain for the induced oscillations of monomers:

$$x_k = \sqrt{\frac{2}{N+1}}\sum_{m=1}^{N}\frac{s_m \sin\dfrac{mk\pi}{N+1}}{\sqrt{(\omega^2 - \nu_m^2)^2 + \lambda^2\omega^2}} \times [f_0\cos(\omega t + \delta_{m1}) + y_0\cos(\omega t + \delta_{m2})], \quad (19)$$

where

$$\nu_m^2 = \omega_1^2 + \Omega_0^2 \sin\frac{m\pi}{2(N+1)},$$

$$s_m = \frac{\sin(m\pi)\sin\dfrac{m\pi N}{N+1}}{\sin\dfrac{m\pi}{2(N+1)}},$$

and y_0 is determined from (16).

Thus, within the framework of the antenna model, the maximal effect of external action of a monochromatic field $f = f_0\cos\omega t$ is achieved under the conditions of collective resonance:

$$\Omega_1 = \omega, \quad \Omega_2 = \omega.$$

Repeating the considerations of Section 2, we can make the following conclusions:

(1) Amplitude modulation of an external signal provides additional potentialities of resonance action on biomacromolecules at the frequencies

$$\Omega_{1,2} = \begin{cases} \omega \\ \omega - \Omega \\ \omega + \Omega. \end{cases}$$

(2) Nonlinearity of quadratic coupling for a monochromatic signal gives rise to an additional resonance at the second harmonic,

$$\Omega_{1,2} = 2\omega.$$

(3) Taking into account nonlinearity of amplitude modulation, we obtain additional series of resonances,

$$\Omega_{1,2} = \begin{cases} \Omega \\ 2\omega \\ 2\omega \pm \Omega \\ 2(\omega \pm \Omega). \end{cases}$$

Thus, collective effects play a rather important role in the interaction of resonance EMR with biomacromolecules with incorporated active sites. The properties of radiation itself determine extensive potentialities of

active control of the dynamics of a biomacromolecule as a whole and, consequently, of biochemical processes that involve such molecules. Hence, the required biological action is implemented either directly or indirectly.

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