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Control of the blood oxygenation process under the effect of THz radiation

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The possibility of controlling the process of the blood oxygenation under the effect of IR radiation modulated by THz frequency range from 1.25 to 3.25 THz was investigated. Experimental results of an increase in hemoglobin level on the one hand and a decrease in glucose level in the blood ot the studied patients, obtained by regulat blood sampling under the continuous irrasiation, on the other hand demonstrated the intersection of described characteristics values of the time constant. This result allowed us to assert the existence of the relationship between anabolic processes in the human body which exposed under the effect of THz-modulated radiation. Although the process of blood oxygenation is a fast-time process, the measured average time constant τ, equal to 22.5 min, indicates the important role of both collective excitations in biological systems and the tunnel factor accompanying the capture−emission processs of oxygen molecul during the oxygenation process, satisfyiing the general results of the proposed model.

Keywords: blood oxygenation process, THz modulation, tunnel factor, equilibrium thermodynamics.

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Introduction

The study of biological systems from the point of view of the laws of equilibrium thermodynamics, the field of which is the description of either equilibrium processes or processes that change rather slowly compared to the characteristic relaxation times of the system, turns out to be a difficult task. Unlike homogeneous inorganic objects, biological systems are highly heterogeneous not only spatially, but also in time. The latter is associated with the presence of a large number of seemingly different relaxation times of key biological processes. Given the finiteness of the rates of biological processes, the possibility of applying quasi-equilibrium concepts to biological systems, within which the system can be considered equilibrium, should be considered for each of the processes of interest separately.

Unfortunately, it is a common opinion that classical thermodynamics, and with it statistical physics, are inapplicable to biological systems due to the fact that the latter are open. This point of view is not plausible due to the fact that the difficulties in the classical description of biological systems are not at all related to their openness, but to the mentioned heterogeneity, which results in the fact that biological systems in general and living organisms in particular (humans are no exception) are non-equilibrium systems. This non-equilibrium, as is known, can be supported by energy presented in various forms and coming from the outside. The characteristic speeds of the most important processes, as well as the relationship between them, turn out to be extremely significant in the case of studying biological objects. Although, as is known from the course of general physics, the total entropy of any system, taking into account its environment, always increases, reaching its maximum when thermodynamic equilibrium occurs, the entropy of the system under study itself may decrease. Biological systems are no exception. The latter is ensured by a large increase of the entropy of the environment surrounding the system compared to the system itself. In this regard, all processes occurring in living organisms, generally speaking, belong to the category of irreversible processes [1].

It is known that non-equilibrium energy transfer processes in all its forms and manifestations are studied by the statistical thermodynamics of irreversible processes [1], formulated by the pioneer in this field L. Onzager in the first half of the 20th century [2,3] and further instantiated by the studies of Nobel laureate I. Prigozhin [4]. Using the methods of statistical physics, considering the equilibrium states of small systems exchanging energy under certain constant conditions [1,4], „classical" non-equilibrium thermodynamics, based on the concept of local equilibrium, allows describing the kinetics of chemical reactions in homogeneous media, i.e., the regularity of chemical reactions over time, depending on external conditions and factors stimulating this reaction and affecting the speed of both the entire process and all intermediate stages of the reaction.

The issue of the applicability of the results of non-equilibrium thermodynamics to biological processes and systems is still not only open, but also to a greater extent delicate. Nevertheless, some qualitative statements regarding this possibility can be made in this paper.

1. Content of the work and problem statement

There is always a hierarchy of relaxation times in the real studied systems: there are both fast „degrees of freedom“, relaxing on our time scale, and slow ones, the relaxation of which requires a relatively large amount of time. The possibility of isolating such weakly relaxing processes described by collective excitations, such as excitons, phonons and, for example, solitons, in inanimate nature has made it possible to explain a huge number of experimental observations in solids and other systems. This also applies to biological systems. Thus, many vital processes are associated with changes in the allocated collective degrees of freedom. The latter have long relaxation times due to their weak relationship with other degrees of freedom of the system [1]. It is precisely the change in such collective degrees of freedom that belongs to the category of non-equilibrium processes.

It is known that non-equilibrium states in biological systems arise when external disturbances [1], for example, physical fields or radiation, act on the system or any of its parts. Such effects results in qualitative biochemical changes, for example, occurrence of certain chemical reactions. Classical non-equilibrium thermodynamics asserts that, generally speaking, it is sufficient to know only the initial and final states of the system when evaluating the results of reactions. If these states are close to equilibrium, then the changes occurring will be determined by the expressions of classical equilibrium thermodynamics, regardless of the intermediate stages of the reaction. Unfortunately, within the framework of such assessments, the researcher will be deprived of the opportunity to say anything about the speed of changes and phenomena occurring, as well as about the mechanisms of the latter.

Let's return to the description of the non-equilibrium states of biological systems. It is known from general physics that in all irreversible processes taking place at constant temperature and pressure, the thermodynamic Gibbs potential decreases with the onset of thermodynamic equilibrium in order to achieve a minimum. This allows determining the direction of the studied process. However, the processes of synthesis of complex biological molecules from simple starting compounds are thermodynamically unprofitable: a change of the thermodynamic Gibbs potential is positive. Nevertheless, the occurrence of such reactions turns out to be possible in cases where the latter are accompanied by reactions with a large negative change in the thermodynamic potential [5,6]. It is possible to consider the hydrolysis reaction of adenosine triphosphate (ATP) as an example.

All biological molecules function in an aqueous environment, and therefore the corresponding chemical transformations of molecules should be considered taking into account their aquatic environment. Thus, the reaction of ATP hydrolysis, which results in the release of energy of the order of 0.54 eV, and such products as adenosine diphosphate (ADP) and separated inorganic phosphate (F):

$$\mathrm{ATP} + \mathrm{H_2O} \rightarrow \mathrm{ADP} + \mathrm{F},$$

accompanies most of the „unfavorable“ chemical reactions in a living organism. At first glance, the reverse recovery reaction turns out to be possible only due to energy consumption from an external source. This can be either chemical energy, or, for example, the energy of sunlight in the case of photosynthesis, or, in general, the energy of electromagnetic radiation coming from outside.

Although ATP hydrolysis is a thermodynamically advantageous reaction [5], ATP turns out to be necessary for the synthesis of guanosine triphosphate (GTP):

$$\mathrm{GDP} + \mathrm{ATP} \rightarrow \mathrm{ADP} + \mathrm{GTP}.$$

The presented reaction is significant because the presence of GTP in sufficient quantities ensures both intracellular protein transport between membranes and protein transport between cells [6,7]. It is important that the addition of a phosphate group to guanosine diphosphate in this reaction is stimulated by the action of one of the most important enzymes in the human body — insulin. In the case of insufficient insulin, protein transport becomes difficult, leading to the inability of sugar to penetrate cells with subsequent accumulation in the blood, which in medical practice is diagnosed as one of the signs of type II diabetes mellitus.

The process of blood oxygenation should also be attributed to anabolic processes in addition to the synthesis of GTP. Previous studies demonstrated [6] that irradiation of living organisms with IR radiation can not only activate these anabolic reactions due to the ability of cells to use the energy of radiation quanta instead of the energy of ATP hydrolysis, preserving adenosine triphosphate for subsequent synthesis of GTP, but also in the case of THz modulation, apparently, effectively affect the processes of ATP recovery. In this regard, it is proposed to use the results of a study of the effects of IR radiation modulated in the THz range on biological objects for demonstrating the relationship between seemingly different anabolic biological processes in the blood from the point of view of relaxation times.

2. Source of THz-modulated IR radiation

A silicon nanosandwich structure (SNS) was used as a source of IR radiation modulated in the required THz range (Fig. 1). It was shown that the presence of trigonal boron dipole centers with negative correlation energy leads to an

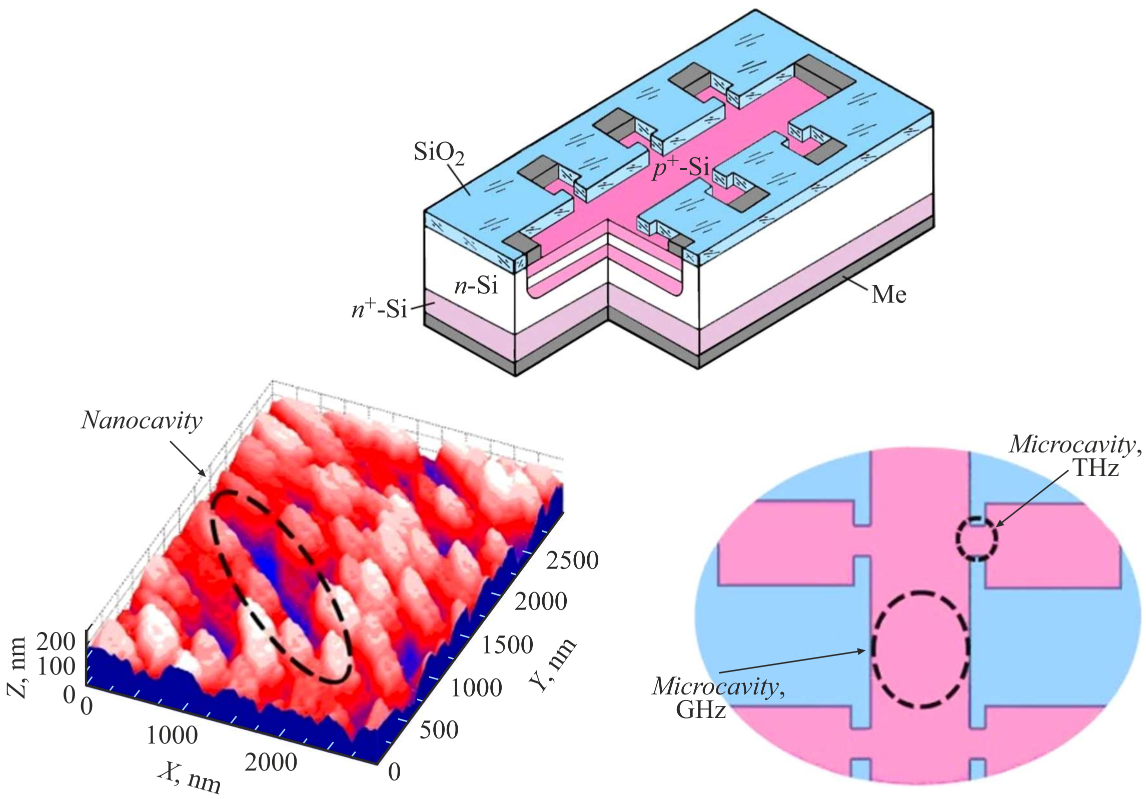

Figure 1. A silicon nanosandwich structure possessing nano- (on the surface of p^+-Si) and microresonators tuned to selected wavelengths of the spectral range, and used as an IR emitter with THz modulation. The image of the surface p^+-Si was obtained by scanning tunneling microscopy (STM).

effective decrease in the electron-electron interaction between the current carriers located inside the edge channels of the SNS [8]. The latter form chains of quantum harmonic oscillators that generate THz and GHz radiation [8]. The value of the correlation gap $2\Delta = 44$ meV corresponds to the modulation frequency 10.64 THz.

During the process of obtaining such quantum-dimensional structures using planar silicon nanotechnology, it is possible to form a system of fractal microresonators embedded in the nanostructure [9]. A system of microresonators tuned to frequencies characteristic of the IR range of electromagnetic waves makes it possible to enhance the intensity of their radiation [9]. The proven nanotechnology of boron doping, which leads to the formation of delta barriers limiting the previously mentioned ultra-narrow silicon quantum wells arising in the presented nanostructures, allows these structures to be used as generators of electromagnetic radiation in the terahertz (THz) and gigahertz (GHz) ranges [8,9].

3. Experimental results

Experimental results are presented (Fig. 2) demonstrating a decrease in sugar levels and an increase in hemoglobin levels in the blood of three patients during irradiation with IR radiation modulated in the THz frequency range 1.25−3.25 THz. These frequencies cover the spectral range of optical stimulation of both the GTP synthesis reaction and blood oxygenation. A regular blood sampling of patients was performed during the irradiation process for measuring sugar and hemoglobin levels.

The dependence of sugar (glucose) levels in the blood of the studied patients on the time of irradiation can be described by analytical expressions of the form:

$$G(t) = G_0 - \Delta G(1 - e^{-\beta t}),$$

where $\Delta G = G_0 - G_{res}$ — there is a difference between the initial (G_0) measured before irradiation and the steady-state (G_{res}) blood sugar levels of each patient, and $\tau = 1/\beta$ — characteristic time constant of the sugar reduction process.

Moreover, the time dependence of the hemoglobin level of each of the patients, obtained under the same conditions, has a similar appearance:

$$H(t) = H_0 - \Delta H(1 - e^{-\beta t}),$$

where $\Delta H = H_0 - H_{res}$ — corresponds to the difference between the initial (H_0) and steady-state (H_{res}) hemoglobin levels in the blood of patients.

The results of processing the above experimental dependencies allowed us to determine the characteristic time constants for both the process of lowering sugar levels,

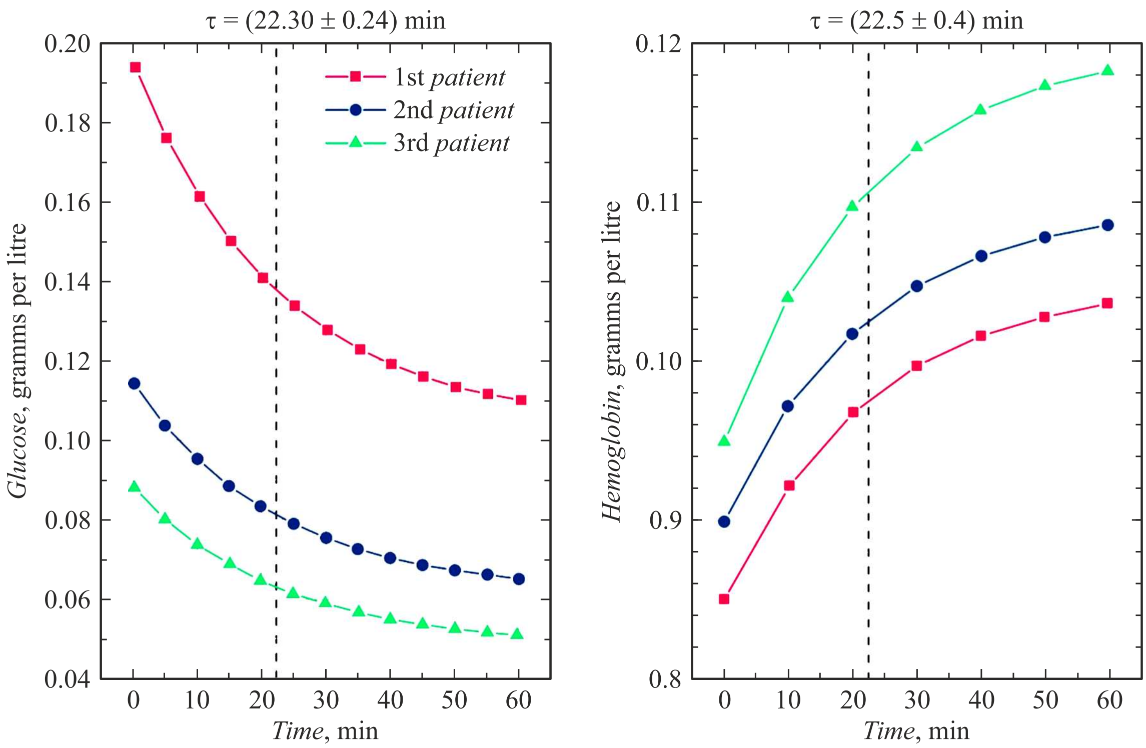

Figure 2. Kinetic dependences of glucose and hemoglobin levels in the blood of three studied patients during irradiation of the forearm of the right hand with IR radiation modulated in the MHz frequency range 1.25–3.25 MHz.

$\tau = (22.3 \pm 0.3)$ min, and in the process of increasing hemoglobin levels, $\tau = (22.5 \pm 0.4)$ min, obtained with a confidence probability of 68%.

As is known, blood oxygenation is a temporary and reversible addition of an oxygen molecule O_2 to an iron ion Fe^{2+} in hemoglobin and myoglobin at an average process energy of 55 MeV. The detected enhancement of the oxygenation process is observed during the average irradiation time of 22.5 min. It turned out that a similar value of the time constant τ, taking into account the error, corresponds to a decrease in blood sugar levels during the noted irradiation, which suggests that there is a certain relationship between the corresponding anabolic processes of blood oxygenation and sugar reduction under continuous exposure to THz radiation. Nevertheless, the answer to the question of the duration of life of such collective excitations requires a more detailed consideration.

The time constant of the oxygenation process can be estimated using the energy ratio $\Delta E/\Delta\Phi = e/\tau_0$ which is an equivalent of Faraday's law of electromagnetic induction, where ΔE — the average energy of the oxygen capture process, and $\Delta\Phi = B\Delta S$ — the magnetic flux penetrating the cross section of a red blood cell with an area of $\sim 50\,\mu\mathrm{m}^2$ in the Earth's magnetic field. This ratio is directly related to the Heisenberg ratio $\tau_0 \sim h/\Delta E$. Taking into account the values of the parameters used, oxygenation is a fast-time process occurring at times of the order 10^{-13} s, corresponding to the generally accepted tunneling through the energy barrier of the reaction.

Nevertheless, the registered long-time oxygenation process indicates the important role of the tunneling factor accompanying the capture and emission of an oxygen molecule during interaction with an iron ion: $K = \tau/\tau_0 \approx 2.7 \cdot 10^{16}$. However, these concepts of generally accepted tunneling and the reduced tunneling factor should be separated. The latter is directly related to the characteristic time parameter 22.5 min, reflects the probabilistic nature of the oxygenation process associated with the influence of local phonon modes on the capture of an oxygen molecule on an iron ion, accompanied by a change in the spin state of the latter with subsequent structural adjustment of the environment. The conducted assessment of the tunneling factor in the presence of an appropriate energy barrier in the Earth's magnetic field satisfies the general results.

Conclusion

The obtained values of the time constants τ of the sugar level reduction and hemoglobin level increasing processes seem to suggest the important role of collective excitations in biological systems: a soliton occurring in the adenosine ring, on the one hand, and, on the other hand, an exciton excited by external irradiation inside the porphyrin ring of heme with the subsequent emergence of a similar soliton.

The registered long-time oxygenation process indicates the important role of the tunneling factor accompanying the capture and emission of an oxygen molecule during interaction with an iron ion, and therefore the long-time component of the blood oxygenation process may presumably be associated with interference in hemoglobin chains, reflecting the probabilistic nature of the oxygenation process.

Conflict of interest

The authors declare that they have no conflict of interest.

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