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THE BIOPHOTON EMISSION IN BIOTECHNOLOGICAL AND CHEMICAL RESEARCH: FROM META-EPISTEMOLOGY AND MEANING TO EXPERIMENT. Part 1

The review describes the rationale for the feasibility of assessing the biophoton emissions in chemical and biotechnological research and existing methods. In Part 1, we will present the analysis of Meta-Epistemology methods for assessing the biophoton emission. The following stages in the history of the development of methods are identified: First discoveries and formulation of the problem. Pre-paradigm phase. Pre-technical stage (80s of the 18th century – 30s of the 20th century); – Pre-paradigm phase. Technical stage (30s–60s of the XX century); Paradigm scientific phase. The stage of accumulation of scientific data (the 60s–00s of the XX century) is the paradigm scientific phase. Stage of digital technologies and systematic scientific analysis (XXI century). Part 2 will describe the technological features of the methodology and parameters for assessing biophotons, which will allow the use of biophoton emissions in experiments in biotechnological research.

Keywords: biophoton, biophoton emission, ultra-weak photon emission, biotechnological research.

1. Introduction

Basic science is constantly evolving. Therefore, for modern scientists, the issues of integrating new knowledge into the field of practical activity and the further development of science in general are relevant. What current and promising trends exist in the field of chemical and biological research and biotechnology? What new approaches and ideas can be used in science at the present stage of its development? How to bring the results of chemical experiments in vitro closer to the processes that occur *in vivo*? These are complex questions that require "small step tactics" from chemical scientists, since science cannot yet give clear and definitive answers to them. But scientific discussion in this direction is relevant. Therefore, this review makes the first attempt to solve the problem of how to combine physics and chemistry in studying the nanoscale metabolic processes in the body *in vivo*. The thing is that, over the past 50 years, there has been a fundamental change in views in fundamental science about the structure of matter at the nanoscale and deeper (<1 nm) [1–3]. The Standard Model of the structure of the atom [4, 5] and the

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principles of quantum physics [6–11] changed ideas of the structure of matter: it became clear that at, the nanolevel and deeper, atoms consist of wave electromagnetic processes of different energy parameters and that electromagnetic processes are the basis of all interactions between atoms and molecules, including all chemical reactions [12–15]. In other words, the occurrence of all biochemical reactions is determined by purely electrophysical phenomena at the nanoscale. Moreover, molecules *in vivo* differ from the same molecules *in vitro* in that they are under the additional influence of the physical fields of living cells of a biological organism. The passage of coherent energy flows through biological molecules makes them alive *in vivo* [15–22]. In *in vitro*, biological molecules are separated from the action of the physical fields of the body. Therefore, a chemical reaction *in vitro* may differ from the chemical interaction between molecules *in vivo*. This must be taken into account, and attempts must be made to overcome this limitation in research.

Because of this, the presence of quantum levels in the structure of living biological organisms (Fig. 1) [23] and the understanding of the fundamental importance of electromagnetic processes in ensuring the phenomenon of life [15–17, 19] cannot be ignored by biotechnological researchers at the present stage.

Of course, at present, this fundamentally different knowledge requires a further transformation of ideas of the structure and functioning of the human body's tissues *in vivo* from modern fundamental science. This knowledge about a quantum level of metabolism is a certain scientific challenge for biotechnological scientists. On the one hand, biotechnological scientists now need to ensure the following [23, 24]:

1. to develop the fundamentals of quantum pathogenesis of diseases of internal organs – that is, to ensure the further development of the paradigm of functioning of the living human body under normal conditions and in pathology at the nanolevel of the structure of matter and deeper;

2. to create the foundations of quantum pharmacology, – that is, to develop theoretical aspects of the implementation of the pharmacological effects of pharmacological agents at the nanolevel of the structure of matter and deeper;

3. to continue to work on improving the existing approaches to treating the patients, accounting for

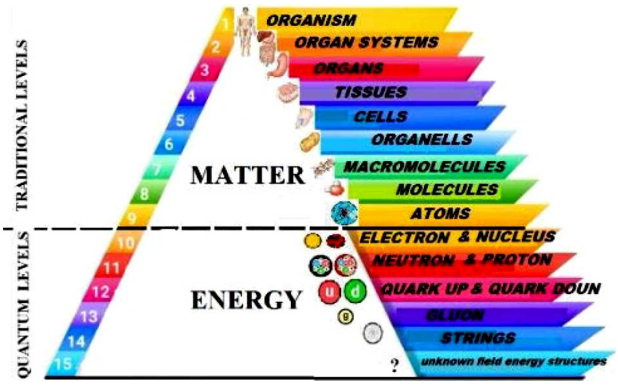

Fig. 1. Diagram of the levels of the human body structure [23]

the understanding of that the ultimate material goal of therapeutic effects in the tissues of the human body is the electromagnetic processes at the nanolevel. In science, it is generally accepted that the conditionally final carrier of electromagnetic energy is electrons. Therefore, we can talk about the development of the principles of bioelectronic medicine or the bioelectronic direction of biotechnological research.

On the other hand, this knowledge about the the existence of a quantum level of metabolism requires biotechnological chemists to develop new methods and methodologies in scientific experiments that can allow an objective assessment of the state of metabolic processes in living biological organisms at the nanolevel. This is a difficult task, since it requires a technique that would not violate the integrity of the body and would be objective, valid, and technically accessible for practical use. Therefore, searching for such a technique and developing a methodology for its use for studying the microlevel (nanolevel and deeper) is a relevant and important scientific task for fundamental science and chemistry, in particular.

2. Biophotons as a Substrate for Objectively Assessing Metabolic Processes in Tissues at the Nanoscale and Deeper.

To find an adequate method for assessing the metabolic processes in tissues at the nanolevel, it is first necessary to determine which indicator will need to be assessed. Let's look at the logic of searching for such an indicator.

Conventionally, the final part of the material level of human tissue organization is the constituent parts of the atom – electron and nucleus. In a simplified

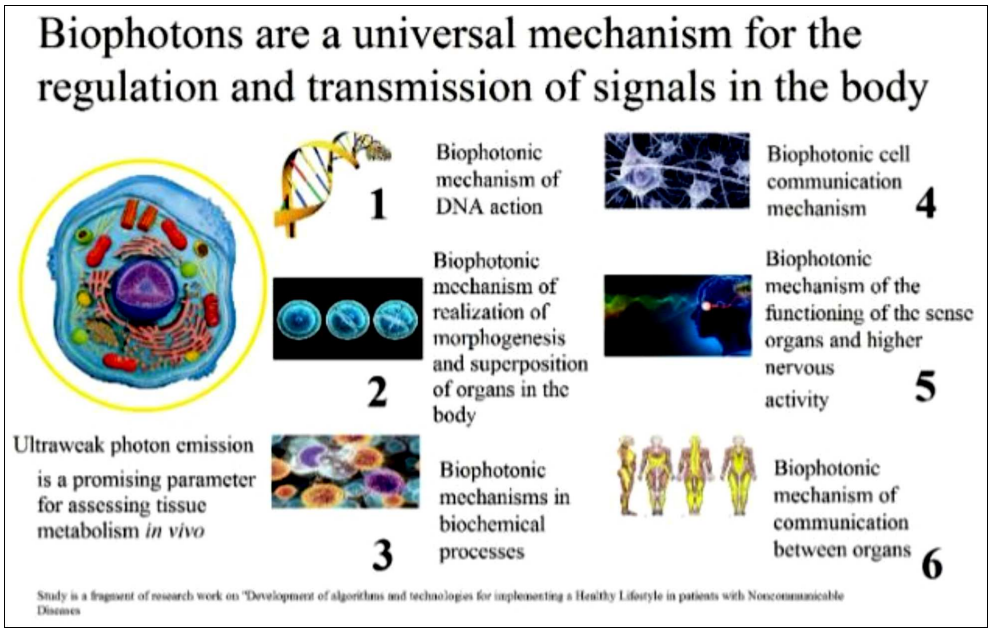

Fig. 2. Diagram of the key roles of biophotons in the human body [23]

view, it is the electron that can be considered the energetically active part of the atom, which determines its energy state. It is generally accepted that the energy state of an electron changes due to the intake or expenditure of an energy quantum – a photon. Photon (from ancient Greek $\varphi\tilde{\omega}\varsigma$, phos – light) is a fundamental particle, a quantum of electromagnetic radiation (in the narrow sense – light) in the form of transverse electromagnetic waves and a carrier of electromagnetic interaction. In the human body, energy interactions between electrons of atoms also occur with the participation of photons, since this is a generally accepted fundamental physical mechanism of energy exchange in the Nature [25–30].

The term "biophoton" was introduced by the German biophysicist F.-A. Popp [31].

The role of biophotons in the human body has already been sufficiently studied and continues to be studied. Electromagnetic radiation in the spectral region from 200 to 800 nm at a constant speed from several photons per cell per day to several hundred photons per organism per day is ultra-weak photon emission (UPE). UPE is recognized as a universal optical phenomenon for all living biological organisms [30, 32–42]. The biological role of biophotons was presented in detail in our previously published review [43].

It is worth to note that biophotons were initially considered as a by-product of biochemical reactions [44–48]. In this regard, to increase the information content of biotechnological research, it would be logical to conduct a correlation analysis between the results of biochemical reactions and photon emission. However, now science has more and more reasons to consider biophotons as a part of the complex process of intercellular electromagnetic communication – the so-called electromagnetic signaling [23, 31, 49]. This is so, because there is scientific evidence of the participation of biophoton mechanisms in key processes ensuring cell life (Fig. 2): 1) in the activity of deoxyribonucleic acid in the cell nucleus [23, 36, 50, 51]; 2) in the generation of a morphogenetic field, which determines the processes of deterministic self-organization of molecules, the functional and morphological association of cells into tissues [23, 28, 52, 53]; 3) in metabolic processes of the cell [53, 55]; 4) cellular communication, including processes of cellular regeneration, cellular activity [55–59]; 5) in the perception of light and higher nervous activity [23]; 6) in communication between organs [55, 60–63].

The biophoton emission is now being studied as a diagnostic parameter of the functional state of tissues of internal organs in normal and pathological conditions [64–73].

Based on the above, we propose to consider that the parameters of biophoton emission can characterize metabolic processes at the nanolevel. Moreover, the fact that their study is possible on samples in vitro and in vivo opens up new opportunities for science in studying the phenomenon of life of biological organisms and a human bodies. Therefore, the study of biophotons is certainly a promising scientific direction for biotechnological research. The inclusion of the biophoton emission parameters in chemical and biological studies can contribute to the further development of scientific ideas of the relationship of the body's biochemical reactions with electromagnetic processes and parameters of the internal physical fields of the human body.

3. Meta-Epistemology of the Discovery of Biophotons and the Phenomenon of Ultra-Weak Photon Emission

As a result of the study, the epistemological stages of the study of the emission of biophotons were established. We have identified five technological stages in the history of the study of biophotons and in the formation of methodological instrumental approaches to their study.

3.1. First discoveries and formulation of the problem. Pre-paradigm phase. Pre-technical stage (80s of the 18th century – 30s of the 20th century)

This stage began from the moment of the first registration of the electromagnetic field of living organisms. So in 1777, German scientist G. Lichtenberg first discovered and studied the phenomenon of a discharge glow around the human body and other objects placed in a high-voltage constant electric field. The study visualized the image using dust particles (Lichtenberg figures). At that time, science was not yet aware that this phenomenon in living organisms is due to the emission of photons. In the second half of the 19th century, these studies were continued by the Serbian scientist N. Tesla and the Belarussian scientist and doctor J. Narkevich-Yodko. Narkevich-Yodko invented the first device that made it possible to fix light radiation around people on a photographic plate. The invention became world famous, but did not receive a further development and implementation, possibly due to the lack of the proper level of development of physics at that time. In 1904, the Brazilian physicist R. Landell de Moura invented a device similar in principle, which had a similar fate [3, 39, 74].

In 1912, the biologist A. Gurwitsch used the method of biological detection, registered the presence of electromagnetic radiation in an onion cell culture, and, for the first time, applied the physical term "field" to a living biological system (Fig. 3) [39, 75–77].

Therefore, 1912 is considered to be the date of the birth of ideas of UPE, which then began to be called "mitotic radiation". During that period, many scientific studies were carried out that were debatable and subjected to scientific doubts. Research of that period was based on the registration of changes visible under the microscope in living cells under the influence of the external "mitotic radiation"/UPE [39].

3.2. Pre-paradigm phase. Technical stage (30s–60s of the XX century)

1. This stage was based on the use of modified Geiger–Muller detectors. Rajewsky was the first to detect UPE with a physical device in 1930. The operating principle of Rajewsky's photosensitive modification of the Geiger–Müller counter is illustrated in Fig. 4 [78, 79].

A metal cylinder with a window and a photosensitive inner surface was the metal cathode of the modified counter. A thin wire with a semiconductor coating was an anode, localized in the center of the cylinder and connected to a resistor of $\sim$1010 Ω. The voltage difference between the cathode and anode reached 1.5 kV. This design was in a quartz shell with an inert gas. The source of mitogenetic radiation was localized opposite the cathode window and UPE passed through the window to the photosensitive layer. The photon hit the photolayer and knocked out an electron accelerated by the electric field. This caused the avalanche ionization of the gas. The voltage between the anode and cathode was lower than necessary for self-sustaining the discharge. The electrometer registered an electrical discharge (Fig. 4) [78, 79].

Thanks to the use of modified Geiger–Muller detectors, a number of scientists scientifically proved the reality of the existence of mitogenetic radiation/UPE [16–18]. This gave rise to the increased scientific in-

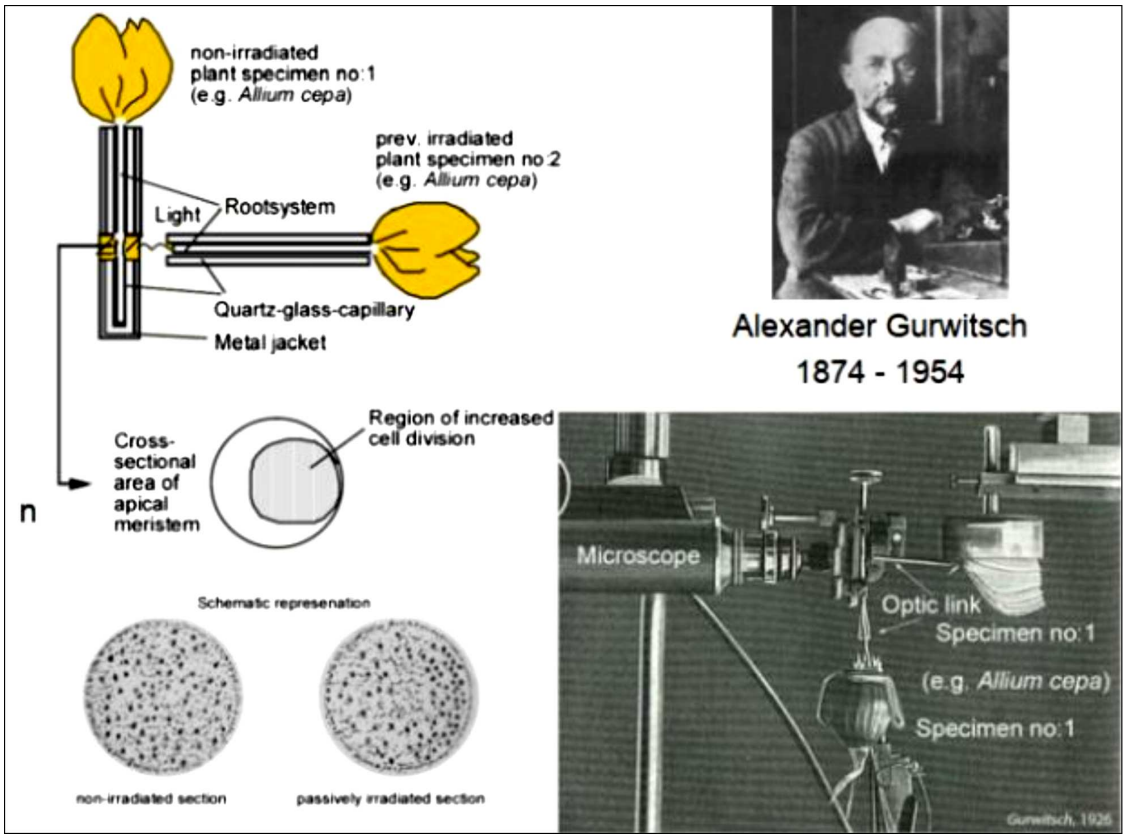

Fig. 3. Scheme of the experiment and photograph of A. Gurwitsch's original setup for the induction of mitosis from a donor to a perpendicularly oriented recipient species of onion cells [39]

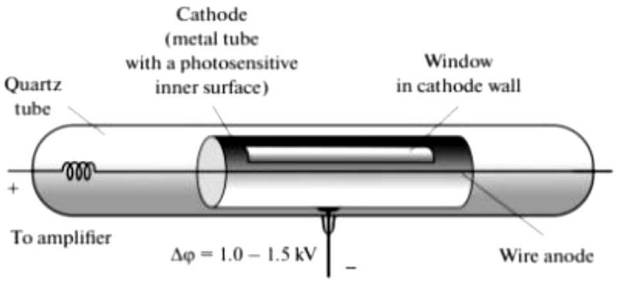

Fig. 4. The operating principle of Rajewsky's photosensitive modification of the Geiger–Müller counter [78]

terest in this issue and an increase in the number of studies. Then the "electrodynamic theory of life" was formulated for the first time. [19]. However, by the 1950s, research in this area using modified Geiger–Muller detectors had almost completely ceased. This was due to the fact that dozens of reviews and publications disproved the existence of "mitotic radiation"/UPE. For some time, this discredited the idea of "mitotic radiation". The fundamental science of that time could not develop a theoretical basis to give a full scientific explanation for this phenomenon [39, 74].

In 1949, the Soviet scientist S. Kirlian rediscovered the phenomenon of the glow of living biological objects placed in a high-voltage constant electric field and invented a device for its photo registration. The method was called Kirlianography and did not have an adequate physical explanation of its mechanism at that time. This discovery was kept secret in the USSR till the 1970s. This slowed down the development and popularization of the method [74, 80].

3.3. Paradigm scientific phase. Stage of acccumulation of scientific data (60s–00s of the XX century)

In the 1960s, the use of photomultipliers for UPE registration became a revolutionary breakthrough for this scientific direction. Direct registration of biophotons was carried out, and the existence of UPE was

finally proved. L. Kubetsky invented the first photomultiplier in 1930 [39, 78]. The operating principle of photomultiplier tubes is illustrated in Fig. 5.

The first modifications of photomultipliers had low radiation intensity and high thermal noise. Therefore, the detection of UPE using them became possible only after the advent of improved instruments. Therefore, it was photomultipliers without spatial and spectral resolution in the range of 370–1270 nm that were used in most UPE studies [78]. The operating principle of photomultiplier tubes without spatial and spectral resolution is illustrated in Fig. 6.

Such a device consists of an amplifier (or a preamplifier and an amplifier); discriminator, pulse shaper, pulse counter, interface. The biological object and the photomultiplier are localized in separate light-protected chambers, which sometimes maintain significantly different constant temperatures [78].

Through the use of photomultipliers, scientists were able to directly measure very small amounts (up to one photon) of emitted light in the visible range of the seed germination spectrum [81, 82]. During this period, a series of experiments were carried out by a number of scientists, and the fact was finally established that, from different biological substrates in the course of their life and activity, light is emitted – the emission of photons. In fact, a significant revolution was made in this matter, since the presence of radiation in the visible range was proved. Initially, it was believed that mitogenic radiation comes from cells only during their replication phase and that the spectrum of this radiation belongs to a part of the spectrum of ultraviolet radiation, invisible to the human eye. The study of other spectral ranges of radiation from living biological systems also continued [26–29, 39].

The 70s of the 20th century are the "period of the birth of biophotons" as a scientific concept. The German biophysicist F-A. Popp introduced the term "biophoton" and subsequently made a fundamental contribution to developing this direction. He theorized all the scientific material in this direction and created and summarized scientific information about the electromagnetic fields of living biological systems, bringing it to adequate scientific evidence [51, 83–85].

In parallel, techniques for electrical imaging of biophotons were developed. In the 1970s, scientists began to develop Kirlian cameras of their own design. Research was started by N. Milhomens (Brazil),

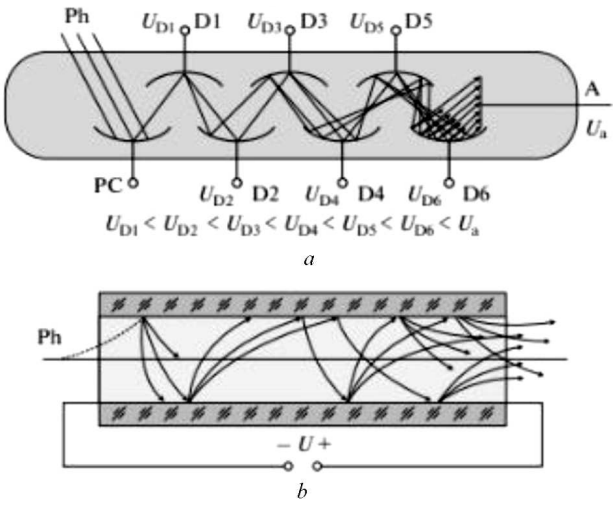

Fig. 5. The operating principle of photomultiplier tubes with different variants of electronic multiplication: (*a*) a system of dynodes and (*b*) channel multiplication. Photons (Ph) fall onto a photocathode (*a*) or photosensitive (*b*) wall of the channel and knock out primary electrons as a result of the external photoelectric effect. The electrons are accelerated by the voltage difference (*a*) between the dynodes (D) or (*b*) along the channel walls and knock out secondary electrons upon every collision with the surface. The resulting avalanche of secondary electrons comes to the anode (A) to produce an electric pulse [78]

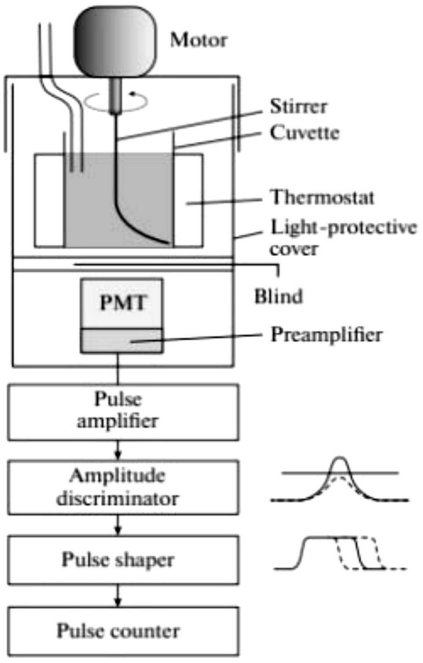

Fig. 6. The operating principle of photomultiplier tubes without spatial and spectral resolutionis (a device to measure UPE from liquid samples) [78]

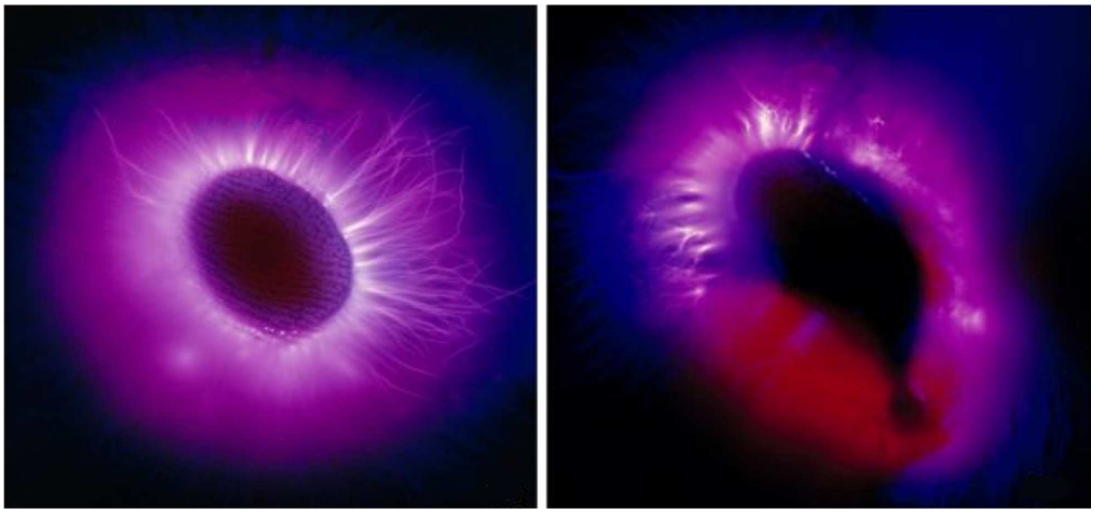

Fig. 7. Color photograph of electrophoton emission from a human fingertip using the method I. Ignatov [94]

P. Mandel (Germany), S. Knirner (USA), T. Moss (USA), S. Romaniy (USSR-Ukraine), K. Korotkov (USSR-Russia), V. Inyushin (Kazakhstan), A. Antonov, I. Ignatov (Bulgaria), M. Kurik, O. Minser, L. Pesotskaya, N. Glukhova (Ukraine) and other scientists. F. Bell (USA) made a significant scientific contribution to the development of the method. He proved the method's validity for assessing the body's physiological state in the research programs Apollo and Saturn of the National Aeronautics and Space Administration/NASA. As a result of the research activity of many scientists worldwide, the method was called "Bioelectrography". [3, 74, 80, 86–90].

In 1976, Pehek *et al.* demonstrated that the size of the gas-discharge corona is inversely proportional to the resistance of the circuit. The circuit is formed by power supply, the electrode with the with the film, and the object for investigation. No effect on corona glow was observed from the resistance of the skin [91].

A. Antonov at the Bulgarian Academy of Sciences investigated the physical parameters of the corona gas discharge effect. He found the formulas for the dependence on the dielectric permeability of the object [92, 93]. In 2007, I. Ignatov registered the color spectrum of color coronal discharge. The spectrum ranges between 380–495 and 570–750 nm [87, 88, 94].

At the coronal gas electrical discharge, the color of the emitted light depends solely on the gas itself. The electrodes of the device does not affect the color spectrum. The color coronal glow carries biological information from the studied biological object. The observed phenomenon cannot be described and explained by modern physical theories of the color light in a gas discharge. The fact that different colors are observed confirms the possibility of a selective biological influence on the researched object. Figure 7 illustrates the results from two individuals. It has a violet spectrum with an average energy of $E = 3.03$ eV. Figure 7 on the left shows the red spectrum region with an average energy of $E = 1.82$ eV. In Fig. 7 on the right, the average energy is $E = 2.58$ eV. The studies were conducted under identical conditions of electrical parameters of the device, temperature, and air humidity.

In the 20th century, the physical principles of the method were not yet fully understood, and they were not associated with the process of emission of biophotons. However, during this period, the German scientist P. Mandel empirically developed a scheme for sectoral analysis of the results of the electrophoton emission from human fingertips, which allows linking the physical parameters of the glow with the functional state of the body's organs [61, 80, 86]. This logically allows us to connect the results of the electrophoton emission with the movement of biophotons through the Primary Vascular System [3, 43, 60-63, 95]. Of course, this requires further study at the present stage with the use of modern technologies and with a systematic analysis of existing scientific results on this topic.

In 1978, Pohl indirectly confirmed the presence of an electromagnetic field in living biological objects – he used the method of dielectrophoresis [96]. In this method, the electromagnetic field was detected by the action of an inhomogeneous electric field on a neutral particle through the polarization force. Based on these experiments, Pohl calculated that the frequencies of cellular electrical oscillations were in the radio range (5–9 MHz). Other researchers have reported similar results for various cell types, including human leukocytes [12, 97, 98]. This was important for the further development of electromagnetic ideas of the phenomenon of life and the idea of biophotons.

In the 80s and 90s of the 20th century, the existence of UPE in cells was repeatedly confirmed by many scientists worldwide using photomultipliers [85, 99, 100]. During this period, the dependence and connection of UPE with chronobiologic processes and the influence of near space was noticed [101–103]. Many scientists were engaged in detecting cellular vibrational states by spectroscopic methods during this period. Detecting non-thermal fluctuations in the terahertz range using Raman shifts has been done for biological systems. A model was created to interpret the Raman spectrum of metabolically active cells, based on the close interaction between coherent electrical oscillations and solitons [104–106]. All this accumulated data for system analysis and understanding of the role of UPE in the 21st century.

During this period, the development of the method of bioelectrography also continued. In 1983, Brazil began mass production of the Newton Milhomena Standard device for the use in practical medicine in accordance with The Official Brazilian Standard of Kirliangraphy, based on the results of Newton Milhomen's research. In 1989, the Soviet scientist Romaniy developed and patented a prototype device for psychophysiological research based on the Kirlian gas discharge corona effect, in which the image was recorded on X-ray film and photographic paper. In Ukraine, this device was used and now continues to be used as an experimental device for research. K. Korotkov made the greatest contribution to the development of the method. He devoted his scientific activity to the development of various devices based on the method and the study of the mechanisms of the method. The scientific achievements of K. Korotkov led to the fact that knowledge about the method gradually deepened. Thanks to him, the method received the next new name, "gas-discharge visualization". During this period, K. Korotkov gradually created a line of devices – GRV-cameras, which were gradually improved, certified, and put into mass production as measuring devices [3, 39, 74, 80].

3.4. Paradigm scientific phase. Stage of digital technologies and systemic scientific analysis (XXI century)

The 21st century is a period of scientific breakthrough, systematization of scientific knowledge of the world and development of digital technologies. The fundamental science of the world has accumulated a large amount of new knowledge, which was systematized in the 21st century and became the basis for the formation of new concepts and paradigms of scientific views. So, with the improvement of detection methods, the direct detection of cellular electromagnetic signals has been technically improved. The researchers were able to once again verify the existence of cellular electromagnetic fields in the process of cell mitosis in the MHz range [29, 47, 104]. In 2014, R. van Wijk successfully repeated the experience of A. Gurwitsch on modern equipment [39, 105, 106]. Thus, the electromagnetic mechanisms of life have become categorically scientifically proven and undoubted. The physical and biological parameters of UPE and the role of UPE as a non-invasive spectroscopic tool for diagnosing a person's internal states were studied [64]. At the present stage, it is already clear that the study of the emission of biophotons is a promising area of quantum information biophysics, which studies the stochastic wave properties of biological objects using the methods of information theory, large systems theory, synergetics, and other mathematical and physical scientific areas in application to systems biology and biomedicine.

The development of computer technologies in the 21st century has brought progress to the technical possibilities of studying the emission of biophotons. Research processes have been computerized. There is also a new possibility to register UPE using a charged-coupled device – a CCD camera. A CCD camera is a video camera containing a charged-coupled device, a transistorized light sensor on an integrated circuit. CCD devices convert or manipulate an electrical signal into some kind of output, including digital values. In cameras, CCD enables them to take in visual

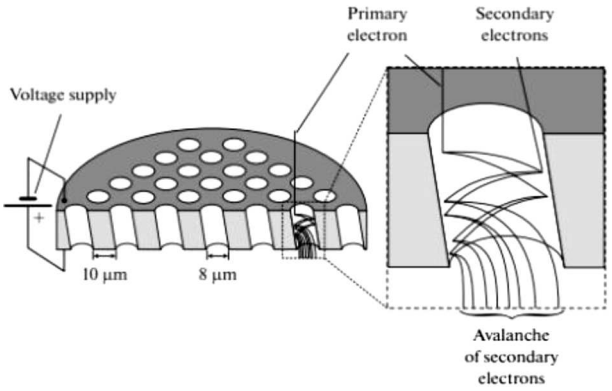

Fig. 8. The operating principle of position-sensitive photomultiplier tubes [107]

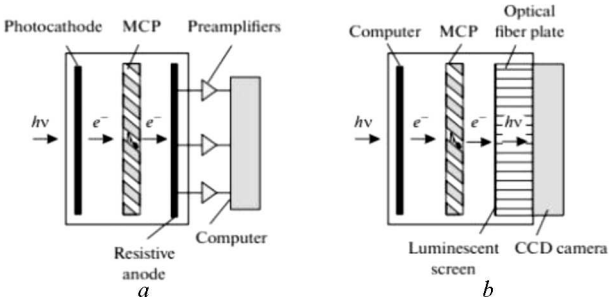

Fig. 9. Schemes of 2D photon counters: (*a*) with a position-sensitive anode and (*b*) with a luminescence screen and an optical camera, that is, electrooptical conversion [107]

information and convert it into an image or video [39, 78, 107].

Now, photomultipliers are used only for studying UPE biological objects in the photon counting mode, and the current mode, where the total current is determined, is not used. A computer interface is used in modern systems. Modern photomultiplier tubes have a quantum yield of 15–50% in the range of the maximal spectral sensitivity, a dark count of 10^0–10^4 photons cm^{-2} s^{-1}. Devices with noise $<10^0$ photons cm^{-2} s^{-1} are used to detect UPE. The parameters are electron flow multiplication factor of 10^6–10^9, and temporal resolution ranging from several nanoseconds to tens of picoseconds. A new method of visualization using vacuum electronic devices has appeared. In this case, position-sensitive photomultipliers are used, in which information about the location of the incident photon is stored during the process of electron multiplication. This allows a higher spatial resolution to be achieved. Dynode systems, made in the form of grids or metal channels, or microchannel boards are used in them to store position data also [107–109]. The operating principle of position-sensitive photomultiplier tubes is illustrated in Fig. 8.

Microchannel plates are designed to multiply an electron flow with spatial resolution. A photomultiplier tube can be considered as an array of short single-channel multiplying tubes of a small diameter. However, in position-sensitive photomultiplier tubes, some of the photoelectrons are lost, because these electrons do not enter the microchannels. This leads to a loss of 30% of the useful signal [107, 110].

Two main types of 2D photon counters are used for the UPE imaging, and they are illustrated in Fig. 9.

In first type (Fig. 9, *a*), a position-sensitive anode (a resistive anode most commonly) receives an electronic image in the form of avalanches localized in microchannels. A 2D distribution of incident photons is calculated from the signals from the anode, and an image forms as enough counts per pixel accumulate. In the second type (Fig. 9, *b*), an avalanche leaving a microchannel bombards a luminescent screen and causes a bright flare. This creates a variety of UPE images with increased intensity in the spectral range of the phosphor emission. Conventional cameras are used to record images. Digital photographic images make it possible to study the features of the UPE spectrum as well. However, according to the literature, the photomethod was used only in a few studies. [107, 110]. Functional design of a microchannel plate attached to a CCD is illustrated in Fig. 10.

Cooled CCD cameras with long-term charge accumulation are used to acquire the 2D imaging of UPE. They are semiconductor devices without electron multiplication in a vacuum. These devices still cannot provide a signal-to-noise ratio and continue to improve. They also use the summation of signals from neighboring pixels (binning). Compared to vacuum electronic devices, CCD cameras have a higher quantum yield and usually higher spatial resolution, but a lower temporal image resolution. CCD cameras outperform position-sensitive cooled photomultipliers [44, 46, 110, 111].

This is a very complex technology, and therefore, it has been used in anecdotal studies. Spontaneous/unstimulated UPE must be registered in a specially equipped photo laboratory – a dark room with an approximate size of 2 m/2 m/1 m. The walls and ceiling of this photo lab should be covered with black matte

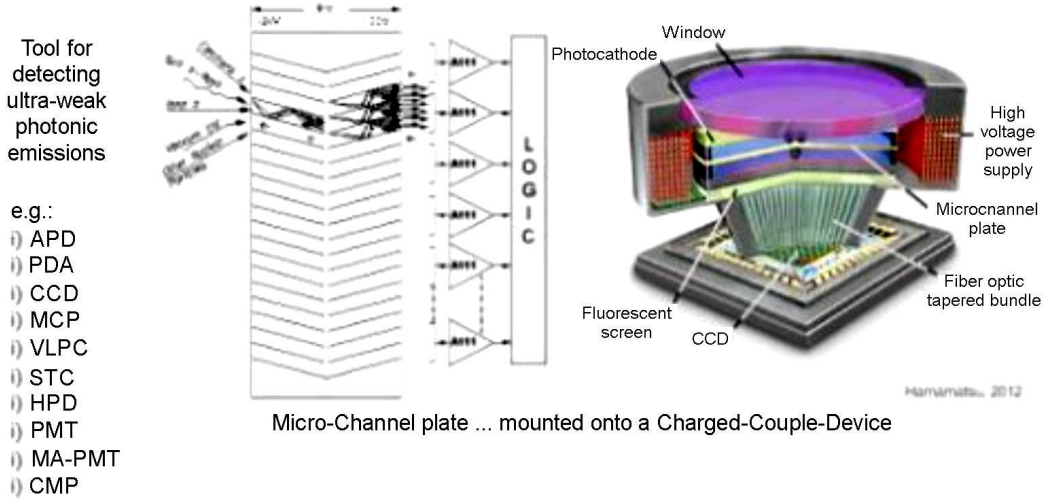

Fig. 10. Functional design of a microchannel plate attached to a CCD [39]

paint. The dark room should be built inside a windowless control room and separated by a tight door so that no light is leaking into the dark room. It should be provided with adequate sanitary and hygienic conditions and a bed for the patient/respondent to stay comfortably during the examination. Measurement equipment and computer system must be located in the control room. The control room should be illuminated with red light, *etc.* Measuring instruments are not mobile. All this creates additional difficulties for the widespread use for research purposes.

In the 21st century, thanks to the scientific activities of a number of scientists, and primarily K. Korotkov, the views on the physical essence of the bioelectrography/gas-discharge visualization method were improved. It was scientifically substantiated that the physical mechanism of this method is the emission of biophotons, enhanced by an electromagnetic field/gas discharge with the visualization of this biological radiation due to digital video recording and computer data processing. Therefore, new names of the methods "electrophotonic imaging technology" and "analysis of electrophoton emission" began to be used in the scientific literature (AEPE) [49, 68, 70, 72, 112–119]. The operating principle of device for AEPE is illustrated in Fig. 11.

There are many technical solutions for AEPE registration, but they share a common technical principle. The essence of the AEPE visualization process is digital video registration of the optical phenomenon of biophoton emission, which arises from a biological

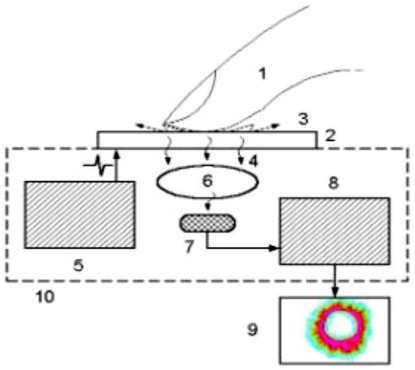

Fig. 11. The operating principle of device for AEPE/GRV-camera: object of study (*1*); transparent electrode (*2*); gas discharge (*3*); optical radiation (*4*); generator (*5*); optical system (*6*); video converter (*7, 8*); computer (*9*); instrument case [118] (*10*)

object (for example, a section of the skin of a human finger) due to the occurrence of a gas discharge when exposed to an electromagnetic field. When performing an AEPE study, the object of study (for example, a section of the skin of a human finger) is placed on a dielectric plate, on the reverse side of which, a transparent conductive coating is applied. A series of bipolar voltage pulses from an electromagnetic field generator is applied to the plate. The integral value of the current in the pulse does not exceed 50 mA. With each pulse, a corresponding phase of the discharge occurs, and a superposition of images of the photon emission from positive and negative discharges (consideriing the electric field distor-

tion by the positive surface charge remaining after the previous discharges) occurs. The biophoton emission images are stored as AVI files by a memory unit associated with a computer processing processor. The processing processor is a specialized software package that allows one to calculate a set of parameters and, based on them, make certain diagnostic conclusions about the features of an AEPE image or a series of AEPE images [118, 119]. Devices of different authors and manufacturers may differ in design, materials used, have different technical parameters. Availability of technical certification and corresponding software and hardware systems for the automated processing and analysis of video images of the biophoton emission is an important component in the UPE registration methodology for modern devices. The AEPE registration process takes place inside the darkened body of the instrument. Therefore, this method is affordable, mobile, and can be widely used in scientific research under almost any condition. This opened up the possibility of studying the influence of external natural factors (forest, water, contact with animals and other people, etc.) on the physiological state of a person [120, 121]. The possibility of the dynamic monitoring of AEPE parameters during certain periods of time also appeared thanks to these devices. A significant database of results of the use of devices for AEPE has been accumulated in various branches of science and in clinical medicine [69, 121–126]. The scientific schools of P. Mandel and K. Korotkov developed aspects of visual and clinical analysis of the results of AEPE video recording, which also opens up new prospects for research in the field of complex medicine [61, 118, 119, 127–129].

4. Discussion of the Results

The results of a theoretical study presented by us in the form of a review demonstrate a long period of more than a century of development of engineering and technical thought and the scientific idea of studying UPE as a universal basic mechanism of intercellular signaling and the flow of energy processes at the microlevel of the functioning of living biological tissues and organisms. Light and matter are closely related. Indeed, light and living matter have such a special relationship that is now being advanced to the most advanced frontiers of modern research in the field of quantum computing, optics and other nonlinear optical phenomena in condensed matter physics [130]. In our opinion, strengthening scientific activity in this field of knowledge is very important for the further progress of medicine. Our previous theoretical studies have once again confirmed the importance of understanding and studying aspects of the energy functioning of tissues and organs at the micro level of their structure. As a result, we started working on conceptualizing the Magnetoelectrochemical theory of metabolism [15, 19]. The review of the results of the theoretical study presented in the publication continues this study. We also understand the importance of conducting further experimental and clinical studies to investigate the energy at the micro level of the structure of living tissues and UPE in the human body in vivo. Therefore, the review we presented describes those instrumental methods that we and other scientists can use to achieve these goals.

In our study, we identified five historical stages in the development of engineering and technical capabilities for studying the emission of biophotons, and we began counting the time from 1777. However, several scientists who studied the history of the study of biophotons before us suggested that the 60s of the 20th century should be considered as a "start" after the invention of photomultipliers. So, J. Ives *et al.* proposed to distinguish between such five stages as the historical development of this field can be subdivided in five main areas: (1) the initiation of research of UPE with photomultiplier tubes in USSR and its connection to radical oxygen species (ROS) and lipid peroxidation, (2) the recognition of UPE worldwide and globalization of this research, (3) the use of UPE as a non-invasive diagnostic marker, (4) the extension of time measurement into spatial patterns, and (5) the use of photon count distributions (PCD) and statistics (PCS) (based on fluctuations in the number of photons in successive counting in contiguous measurement times) for detecting a 'light language' that is connected with the system's organization of the living biological state [33]. Since our epistemological study considered the study's engineering and technical capabilities as the main criterion, the historical stages we propose do not contradict, but complement the work of J. Ives *et al.* In this review, we covered the technical stages of development, and J. Ives *et al.* devoted their review to pure aspects of the study of scientific evidence UPE as a non-invasive health assessment [33].

What devices and methods can modern researchers use for the UPE registration and clinical research? Everything depends on the set scientific goals. According to the scientific literature, a significant part of modern studies of spontaneous emission of biological objects (plants, seeds, food, *etc.*) was carried out using a CCD camera cooled [33, 46]. For example, CCD cameras made it possible to image endogenous UPE from bioluminescence-free insects during their metamorphosis [53], a growing mouse tumor (grafted cancer) [66], and a mouse with induced rheumatoid arthritis [48]. Human UPE images were examined in several studies with cooled CCD cameras [48, 67, 110, 131, 132]. Devices for AEPE have already received practical application in the work of psychologists and holistic medicine doctors worldwide. They have been used in many scientific studies around the world as well [72, 133].

Thus, the analysis of the biophoton emission can be an important addition to biotechnology research techniques. Biophotonics is a rapidly developing scientific field that includes quantum physics, biophysics, optics and related experimental research, engineering technology, systems biology, and so on. Scientific achievements in biophotonics and analysis of biophoton emissions can be of great importance for the development of fundamental science, especially its biological branches. They can make a significant contribution to the understanding of tissue functioning at the nanoscale and for the further development of quantum medicine/bioelectronic medicine.

5. Conclusions

1) Biophotons are an objective parameter of the metabolism of biological organisms at the nanolevel, and the study of biophoton emission by various methods can be an important addition to biotechnological research methods.

2) Four technological stages in the history of the study of biophotons and in the formation of methodological instrumental approaches can be distinguished:

• First discoveries and formulation of the problem. Pre-paradigm phase. Pre-technical stage (80s of the 18th century – 30s of the 20th century);

• Pre-paradigm phase. Technical stage (30s–60s of the XX century);

• Paradigm scientific phase. Stage of accumulation of scientific data (60s–00s of the XX century);

• Paradigm scientific phase. Stage of digital technologies and systemic scientific analysis (XXI century).

3) A significant part of the modern studies of spontaneous emission of biological objects (plants, seeds, food, *etc.*) was conducted using a cooled CCD camera.

4) Devices for AEPE are the current valid and most accessible measurement method.

We, as modern scientists, cannot but admire the scientific genius of our predecessors, who, lacking modern technical capabilities and digital technologies, were able to register and start researching the UPE phenomenon. Therefore, our team of authors in this review wanted to once again draw the attention of their colleagues to the existence of the UPE phenomenon, to its significant study, and to show the availability of relatively accessible methods for its study with different possibilities and endpoints of results.

Part 2 will describe, in detail, the basic principles of the methodology and parameters for assessing biophoton emission using various techniques.

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ЕМІСІЯ БІОФОТОНІВ
У БІОТЕХНОЛОГІЧНИХ ДОСЛІДЖЕННЯХ:
ВІД ГНОСЕОЛОГІЇ ТА ЗНАЧЕННЯ
ДО ЕКСПЕРИМЕНТУ. Частина 1

В огляді представлено обґрунтування доцільності оцінки біофотонної емісії в хіміко-біотехнологічних дослідженнях та існуючі для цього методи. У частині 1 також здійснено гносеологічний аналіз методів оцінки випромінювання біофотонів. Виділено наступні етапи в історії розвитку методів: перші відкриття та постановка проблеми – допарадигмальна фаза – дотехнічний етап (80-ті рр. XVIII ст. – 30-ті рр. XX ст.); допарадигмальна фаза – технічний етап (30–60-ті рр. XX ст.); парадигмальний науковий етап – етап накопичення наукових даних (60-ті–00-ві рр. XX ст.); парадигмальний науковий етап – етап цифрових технологій і системного наукового аналізу (XXI ст.). У частині 2 будуть описані технологічні особливості методології та параметрів оцінки біофотонів, що дозволить використовувати біофотонне випромінювання в експериментах у біотехнологічних дослідженнях.

Ключові слова: біофотон, біофотонне випромінювання, надслабке випромінювання фотонів, біотехнологічні дослідження.