In: Integrative Biopysics. Biophotonics. Eds. F.-A. Popp, L. Beloussov. Kluwer Academic Publishers. Dordrecht/Boston/London, 2003, Pp. 331-360.

Chapter

MITOGENETIC RADIATION, BIOPHOTONS AND NON-LINEAR OXIDATIVE PROCESSES IN AQUEOUS MEDIA

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Abstract: Mitogenetic radiation (MGR) discovered by A. G. Gurwitsch gave birth to the field of biophotonics that energetically develops now. However, most facts of unique properties of MGR and of processes in which they originate, of surprising discoveries made during several decades of intensive MGR research are practically forgotten. Present-day biophotonics may gain a lot for its further development from discoveries and insights made at that time. In particular, it was discovered that usual enzymatic reactions are followed with MGR, that MGR emission from aqueous solutions of simple amino acids is correlated with spontaneous polypeptide synthesis, that substances possessing specific enzymatic activities may self-reproduce in such solutions. All these processes crucially depend on oxygen (and in some cases on illumination with visible light). An extremely sensitive analytical method – MGR spectral analysis – helped to show that branched chain reactions with the participation of reactive oxygen species and other free radicals serve as energy source for the emergence of high energy mitogenetic photons. All these amazing phenomena are discussed, in particular here in relation to the growing understanding of the important role of reactive oxygen species and their reactions taking place in aqueous milieu for bioenergetics and bioinformatics.

Key words: Mitogenetic radiation, reactive oxygen species, water, biophotons.

1. INTRODUCTION

Mitogenetic radiation (MGR) discovered by Alexander Gurwitsch is met even until now with scepticism by many biochemists and biophysicists. There are several reasons of such an attitude. First, classical bioenergetics deals with biochemical reactions with the energy output not exceeding 0,5

eV, equivalent to the middle infrared region of the spectrum of electromagnetic waves. Photon emission having the mitogenetic properties belongs to the UV-region of the spectrum and energy of mitogenetic photons reaches as high as >5 eV. Second, many properties of MGR seem very strange not only from the position of classical physical chemistry on which current biochemistry is based, but also from the position of classical quantum physics.

Beginning from 1960-es with the development of very sensitive single photon detectors it has been demonstrated that all living systems are indeed emitters of low level photon fluxes, though it turned out that its intensity in the visible and near IR-range of the spectrum is enormously much stronger than in the UV range. Still the majority of investigators dealing with low-level photon measurements acknowledge the priority of Gurwitsch as the discoverer of electromagnetic radiation of living objects. At the same time Gurwitsch's evidence that that this emission plays any functional role is paradoxically rejected. Low-level photon emission phenomenon is generally looked upon in the frame of "Imperfection Theory". According to it photon emission originates from random metabolic aberrations due to uncontrolled free radical reactions [1, 2].

Nevertheless, there is another line of investigation of ultra-weak or low-level photon emission of living things, originated and persistently developed by F.-A. Popp, who bases in his studies on the coherence theory. This theory allows explaining many peculiar features of photon emission by living things and predicts also that this emission may play a significant informational role in living matter [3]. Such photon emission got the name of "Biophotons", and Gurwitsch's MGR is considered to be a particular case of biophoton emission. However, biophoton research is based mainly on registration of photons using photomultipliers, while MGR was registered due to its specific ability to induce cell mitosis. Both methods have their advantages and drawbacks, as they reveal different "faces" of biophotons. Unfortunately, most of the information collected by Gurwitsch and his school is unknown to the present-day scientists, and even to those who work in the field of biophotonics. But information obtained in these studies by no means is obsolete, on the contrary, it adds a new dimension to the fast developing field of biophotonics.

Here we'll present a digest of some forgotten discoveries in the field of MGR (biophotons) that were made as far as 50-70 years ago with our comments based on our own experience in biophoton research. We believe that taking into consideration old Gurwitsch's findings will provide a new impetus for the development of this frontier science.

2. PARADOXES OF MITOGENETIC RADIATION

2.1 Intensity and spectral properties of MGR.

A.G. Gurwitsch discovered MGR in 1923 in his famous and repeatedly described “onion experiments”. Very soon studies performed in Gurwitsch laboratory and multiple independent laboratories all over the world demonstrated that this radiation induces mitosis in all types of cells [4]. Major information of MGR properties was obtained in experiments with a more convenient and reliable biological detector – yeast culture grown on agar plates. A plate with yeast layer is cut into two parts and one of them is “irradiated” with a supposed source of MGR, while another serves for a control. Some time after irradiation the number of cells entering mitosis are counted on both plates and in the case of significant difference between experimental and control samples it is concluded that the tested object was indeed a source of MGR. Here we omit all other important experimental details and controls (including, e.g., double blinded evaluation of results) carefully described in many Gurwitsch’s publications. Their neglect practically always resulted in failure to detect MGR followed with the statements that MGR does not exist at all. Gurwitsch and his collaborates repeatedly discussed this strange situation [5].

Though the notion of most properties of MGR was obtained basing on its biological effects, in 1930-ies UV-radiation emitted by some biological objects and chemical reactions was successfully registered in several laboratories using physical detectors -- modified Geiger-Muller counters. Their photocathodes were made from materials having maximal light sensitivity in the range of 190-280 nm and practically insensitive to visible light – copper, magnesium, aluminium or their compounds. When such a material absorbs UV-photons it emits photoelectrons that trigger a gas discharge in a counter [6, 7, 8].

It was shown with such counters that intensity of UV-photon emission from developing frog eggs or a nerve-muscle preparation excited with an electrical current is very small -- 10-10000 photons ($10^{-10} – 10^{-8}$ erg) per 1 sec from 1 cm^2 of the emitting object. Figure 1 shows that counters detect UV-photons only in the moment of a nerve excitation and only if the nerve is alive. The same was demonstrated using biological detectors and nerve preparations as emitters of MGR.

The original conclusion that MGR is the flux of UV-photons was made basing on the experiments with glass and quartz filters: when a glass slide was put between an emitter and a detector, mitogenetic effect disappeared, while a quartz plate did not eliminate it. More rigorous evidence in favour of this conclusion was obtained using spectral analysis of

MGR with the help of precise spectrographs with quartz optics (Fig. 2). Emitting object was placed in front of the input slit and detectors – agar plates with yeast cultures – against the output slit.

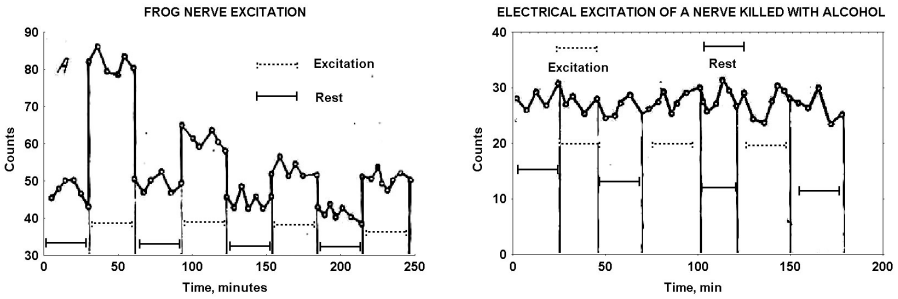


Figure 1. Registration of UV-radiation using modified Geiger-Muller counter with photocathode sensitive in the range of 215-240 nm from excited nerve of a frog leg. Left – alive nerve, right – nerve killed with alcohol.

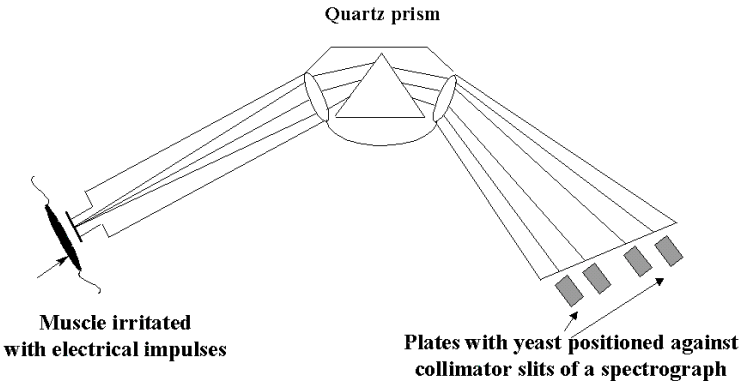


Figure 2. Outline of the MGR spectral analysis of a muscle preparation using an yeast culture as a detector.

Analysis of MGR spectra from different objects including such "simple ones" as enzymatic reactions performed *in vitro* (see below) revealed a lot of unusual facts. First, MGR spectra represented sets of spectral bands; some of them were as narrow as 1 nm wide. Second, sets of bands from different emitters differ very much in the number of lines, their width and position (Figure 3). Thus, MGR spectra are at variance from typical spectra of luminescence of aqueous solutions. In particular, spectra of fluorescence of aqueous solutions of luminofores at room temperature represent more or less wide "humps" with half-width usually exceeding 10 nm, which resolve into more narrow lines only at very low temperatures. Rather wide spectral bands (in visible range of the spectrum) are

characteristic also for bioluminescent and chemiluminescent systems in water. But one needs to note that first, MGR spectra are obtained using a biological detector, while luminescence spectra are obtained using physical detectors, and second, MGR intensity is several orders of magnitude lower, than that registered in most physical and chemical experiments. Taking into consideration such low intensity of MGR it is difficult to explain in terms of usual optic laws the very opportunity to register MGR spectra. If the total photon flux does not exceed several tens or thousands photons, while many spectra are represented by multiple bands, one needs to conclude that absorption of only few photons is enough to induce multiple mitoses in a cell culture containing many tens of thousand cells. Thus there should exist a mechanism with a tremendous coefficient of amplification which is switched on by UV-photons.

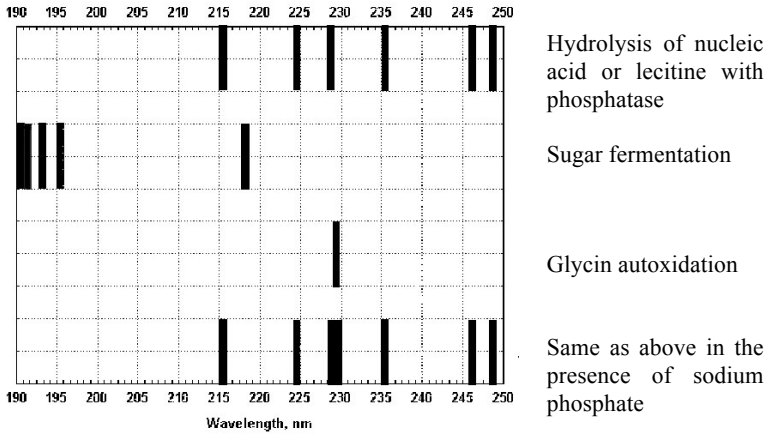


Figure 3. Mitogenetic spectra of different enzymatic reactions an of the reaction of glycin autoxidation induced with glycin solution irradiation with MGR (see below)

Mitogenetic effect may be induced also by physical sources of UV-light – arc discharges, hydrogen lamp strongly attenuated with grids or filters. But their efficiency in induction of mitoses was incomparably lower than that of "natural" sources of MGR. In other words, for effective commencing of mitogenetic effect emission should not only belong to a UV frequency range, but it should possess some other specific properties.

2.2 "Fractionation" of MGR

Efficiency of mitogenetic effect was measured basing on duration of irradiation period needed to trigger mitogenetic effect. Besides, too long irradiation from intense sources of MGR resulted in inhibition of mitotic

activity. Biological detector may be exposed to a MGR source either continuously of intermittently. To obtain an intermittent mode of irradiation a rotating disk with slits was installed between an emitter and a biological detector. It turned out that intermittence might significantly induce the efficiency of mitogenetic effect depending on width of slits, distance between them, and rate of disc rotation. For example, if two yeast cultures are positioned opposite to each other, they may induce mitogenetic effect in each other (mutual induction) only at a distance of less than 3 cm. Under these conditions threshold period at continuous irradiation was 6-8 min, while at the optimal parameters of intermittence it reduced 40-50-fold. At a larger distance without intermittence yeast cultures did not stimulate each other, but under the optimal parameters of intermittence they interacted even at a distance of 15 cm. This result seems extremely paradoxical: irradiation time might be reduced down to 1,5% of the total time of exposure and the effect was not lost but rather enhanced. Only due to intermittence it was possible to perform spectral analysis from many sources of MGR. Most important that intermittence increases efficiency of MGR only if it is performed in a rhythmic mode; at arrhythmical intermittence mitogenetic effects are usually lost.

2.3 Sensibilized fluorescence and selective MGR scattering.

It was found that practically all enzyme reactions *in vitro* are sources of MGR, and MGR spectra of different reactions are significantly different. Initially Gurwitsch suggested that the spectrum of a particular reaction, e.g., urea hydrolysis with urease is characteristic of this particular process, but later it turned out that addition of glucose to the urea-urease system resulted in appearance of same bands as in glycolytic process, that addition of phosphate to glycolytic system resulted in appearance of bands characteristic of a phospatase reaction, etc. This indicated that MGR spectral bands result from fluorescence of simple compounds and even of their chemical residues excited by energy released from some highly exothermic process. This phenomenon was named “sensitized fluorescence” (SF). SF was characteristic to small molecules and their residues, such as a peptide bond, phosphoric acid residue of a nucleic acid or a phospholipid, amino group of an amino acid, and even to such ions as Na^+ and Cl^-. On the contrary such big molecules, as nucleic acids or proteins did not produce SF. Thus there are many differences between SF and usual fluorescence, but conditions for their origination and observation also differ. For usual fluorescent analysis of solutions of flourophores they are irradiated with rather intense light sources and its own intensity is rather high. SF is excited by energy coming from a

reaction system itself – from reactions of free radicals (see below). Besides SF spectra were analysed using an extremely sensitive biological test systems, and until now there is no physical methods allowing registering and analysing this effect have been devised.

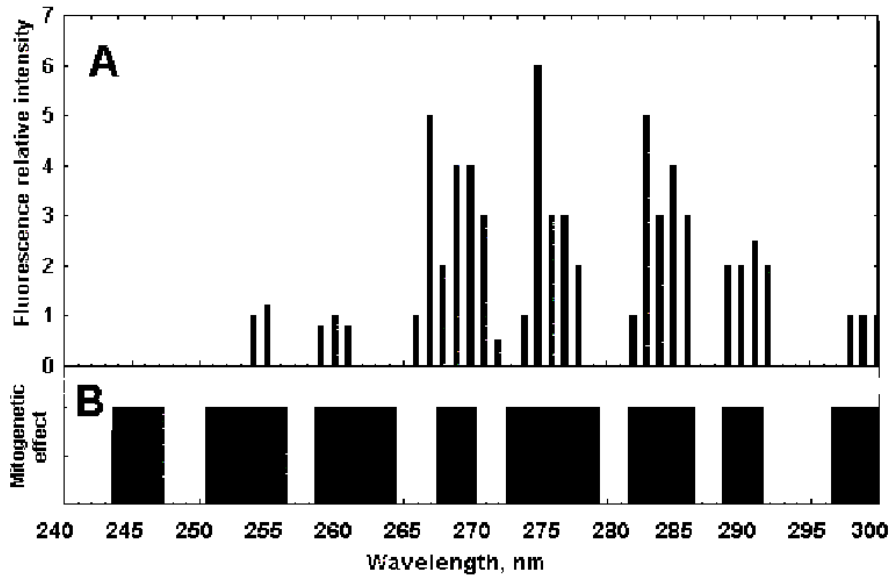


Figure 4. Comparison of fluorescence spectrum of benzol vapour (A) and MGR spectrum of glycin autoxidation reaction to which 1% of benzol water was added (see text)

Validity SF was directly demonstrated by comparison of benzol SF spectrum and usual fluorescence spectrum of benzol vapour. For this experiment a reaction system of glycin autoxidation in water (see below) having a very simple own spectrum (only one narrow line) was taken. To it 1% of water, being in contact with benzene and in which only traces of benzol are present was added. Fig. 4 compares MGR spectrum of this system with fluorescence spectrum of benzol vapour, which is resolved in many groups of narrow lines. It can be seen that all these groups are really present in MGR spectrum. This experiment shows an enormous sensitivity of SF that cannot be easily understood in frame of current knowledge. One needs to explain how energy from rare reactions of free energy recombination may be efficiently transferred to benzol present in reaction system in an extremely low concentration and remitted by them. It should be realised that from the point of view of purely stochastic processes the observed phenomenon is improbable. Precise mechanisms of such a transfer is not known, but it is interesting to speculate that water due to it unique properties should play a key role in this process.

SF may arise in aqueous solutions which are not irradiated from outside only if energy is supplied by highly exothermic reactions running in these solutions. Quanta of energy providing excitation followed with fluorescence in UV-range of the spectrum might come only from reactions of very active free radicals recombination. For example, recombination of two bi-radicals: ↓↓C=O + O↑↑ → CO_2 (arrows here symbolise unpaired electrons – see below) may supply a quantum of energy equivalent to a UV-photon with the wavelength of 170 nm sufficient to excite a certain fluorophore which remit a MGR photon with the shortest observed wavelength of 190 nm. Verification that free radicals with such high reactivity really arise in reaction systems is a very difficult task because of their extremely short lifetime. Nevertheless they were identified experimentally with the new method developed by Gurwitsch and collaborates – "selective scattering" (Figure 5).

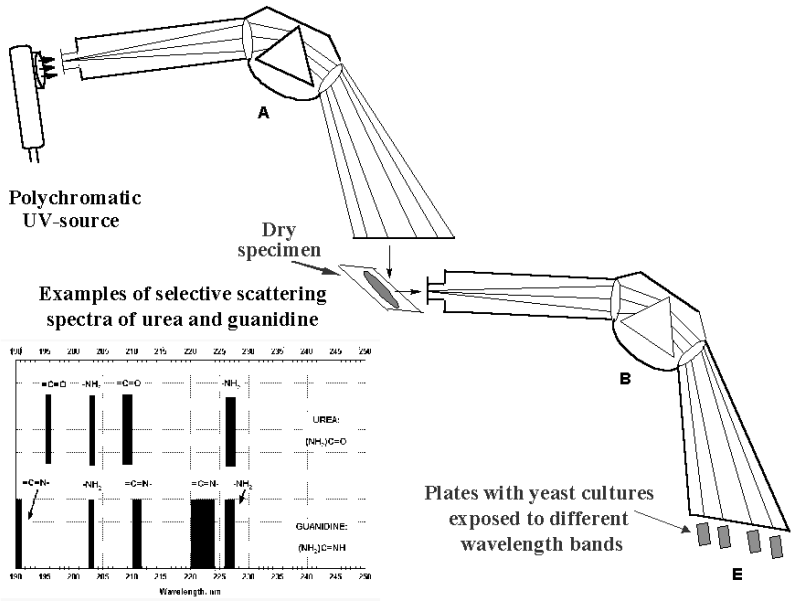


Figure 5. A set-up of an experiment for obtaining MGR spectra of a substance or a solution using a selective scatterin phenomenon. (A) and (B) – two quartz monochromators.

A tested substance (either a dry chemical or an aqueous solution) is irradiated with a monochromatic line, cut out by a spectrograph from a spectrum of a hydrogen lamp. Radiation scattered by a sample is dispersed by a second spectrograph and its MGR spectrum is obtained. It was demonstrated that mitogenetic effect was observed only in case when the wavelength of incoming light was exactly equal to the wavelength registered in the MGR spectrum. The latter was characteristic of particular chemical

groups or free particles, like ions or electronically excited free radicals present in irradiated solutions.

This extremely sensitive and informative method allowed confirming quite independently that MGR bands registered in the course of different enzymatic and non-enzymatic reactions result from SF of the substances and their chemical radicals present in a solution. In particular such free radicals, as ↑↑C=O, ↑NH_2, ↑OH, which emit photons with wavelengths of 202-204 nm, 253 nm, and 306-308 nm respectively could be identified. Selective scattering allowed also to detect particular fluorescent groups, such as R-OH, CH_2O, R=C—N=R, R=C=N—R and others. This precise method allowed understanding the intimate mechanisms of the processes accompanied with MGR.

2.4 Autocatalytic formation of enzyme-like substances and multiplication of low molecular weight substances in aqueous solutions of amino acids.

One of the most “shocking” discoveries made using the methods of mitogenetic analysis is the discovery of spontaneous polycondensation of amino acids into high molecular weight proteinatious compounds in aqueous solutions. Polycondensation is formation of a polymer from monomers with release of water. This reaction provides for the synthesis of all biopolymers: proteins, nucleic acid, polysaccarides in a cell.

A high barrier of energy of activation forbids spontaneous condensation of two amino acids producing a di-peptide and releasing a water molecule. To synthesize a peptide chain chemists use specially activated and “defended” amino acid derivatives and perform reactions in non-aqueous solutions. A very complex molecular «machine» performs protein synthesis in living cells, and amino acids that are attached to a growing peptide chain are also preliminarily activated. However, initial energy expenditure are nearly completely compensated when final products are formed and the overall reaction is nearly thermally neutral.

Thus the discovery, that 10-15 min after a brief irradiation of a glycin (H_2N—CH_2—COOH) solution with MGR, the solution becomes a source of MGR, and compounds with peptide bonds (—CONH—) emerge in it was a surprise. The solution emits MGR for many hours, but concentration of a polypeptide stabilises at a certain and very low stationary level due to established equilibrium between its continuous formation and degradation.

The process could be initiated only with photons with $\lambda<326$ nm. Its caloric energy equivalent is >87 kcal/mol, that is equal to energy of a bond between hydrogen and nitrogen atoms of an amino acid. It was also shown that after the reaction initiation ammonia was accumulating in a reaction

system and that for its progress its illumination with visible or near IR-light (λ<1300 nm) was needed. From this the supposed scheme of the reaction could be described as following. Energy of MGR photons is somehow used to cleave a hydrogen atom from an amino acid with the formation of an amino acid free radical:

$$H_2N\text{-}CHR\text{-}COOH + h\nu \rightarrow H\uparrow + (HN\text{-}CHR\text{-}COOH)\downarrow \quad [1]$$

The radical condenses with an amino acid molecule, and a di-peptide plus a hydroxyl radical appear. This reaction needs energy of activation of 22 kcal/mol supplied by visible or near IR light:

$$H_2N\text{-}CHR\text{-}COOH + (HN\text{-}CHR\text{-}COOH)\downarrow + 22 \text{ kcal/mol} \rightarrow H_2N\text{-}CHR\text{-}CO\text{-}HN\text{-}CHR\text{-}COOH + OH\downarrow \quad [2]$$

Recombination of $H\uparrow + OH\downarrow \rightarrow H_2O$ [3] gives 110 kcal/mol, and as 110 kcal/mol - 22 kcal/mol = 88 kcal/mol – enough energy to start a new cycle of reactions 1 → 3. But this simple chain reaction should rapidly decay and can not produce any emission. The emergence of MGR in the contact with air indicates that additional and very high portions of energy come from oxidative deamination of an amino acid, which may be catalyzed by the proteinatious polymer emerging at the first stage, e.g.:

$$2H_2N\text{-}CHR\text{-}COOH + O_2 \rightarrow 2O{=}CR\text{-}COOH + NH_3 + \Delta E \quad [4]$$

Another peculiar property of this reaction is that it can be “multiplied”. Transfer of an aliquot of the solution already emitting MGR to a fresh amino acid solution initiates the same reaction in the latter: it becomes a MGR source and a proteinatious polymer possessing oxidase-deaminase activity appears in it. The procedure could be repeated many times with the same effect. These amazing experiments did not attract attention of a scientific community and were completely forgotten. Only recently we partially reproduced them and confirmed that after irradiation of aqueous solutions of different amino acids with very low intensity sources of UV-light high molecular weight substances possessing deaminase arise there [9].

In glycin aqueous solutions there may develop even more startling processes – “self-reproduction” of enzymes, or to be more precise, of compounds possessing specific enzymatic activities – “fermentoids” according to Gurwitsch’s terminology. If one makes a very dilute solution of, e.g. urease in glycin solution and incubate it in visible light with air access activity of urease measured by its ability to cleave urea increase after a lag period of 10-20 min. Same results were obtained with other tested enzymes, e.g., phosphatase and arginase. Enzyme activity increased not due

to some form of added enzyme activation, but due to self-reproduction of its "active principle". Gurwitsch never claimed that the process was a genuine protein self-reproduction, because specific activity of "fermentoids" was much lower that of template enzymes. It looked like it was reproduction of its rudiment with the properties of an active site. However, same specific inhibitors that suppressed activity of the respective natural enzymes suppressed activity of fermentoids, and if specific metals (e.g., manganese) were needed for a template enzyme, no fermentoid activity was observed without this metal. Though activity of fermentoids was very low, it could be registered by conventional biochemical methods [10]. Multiple consecutive transfers of portions of active solutions into large volumes fresh glycin solutions resulted in reinitiating of the same process there Besides performing their specific activities fermentoids catalyzed oxidative deamination of glycin, providing energy for their own reproduction and MGR emission from the solutions.

For the performance of specific catalytic functions fermentoids should contain different amino acids in addition to glycin, which could form an active center. Thus substances that are more complex than glycin should somehow arise in reaction systems. In fact, free radicals =CO, —CH_2—, —NH_2 и OH were detected there. These radicals arising from fragmentation of glycin molecules could serve as building blocks for substances having specific catalytic activities. Later Anna Gurwitsch, the daughter of A.G. Gurwitsch, demonstrated that complex specific substances might really quasi-spontaneously form from glycin [11]. After addition of tyrosine in a very small concentration (e.g., $5{,}5 \times 10^{-12}$ M) to glycin solution with diffuse visible light and being in contact with air tyrosine concentration increased 6 orders of magnitude. Selective scattering revealed the presence in this solution of the same free radicals as in solutions of fermentoids. Similar "self-reproduction" was shown under the same conditions for other natural aromatic and heterocyclic compounds (adenine, pirrol, indole). These revolutionary discoveries, demonstrating the new principle of matrix synthesis of complex compounds from the simplest one passed practically unnoticed though it was never disproved.

Nevertheless, recently there appeared some circumstantial evidence of unusual transformations of biomolecules in aqueous solutions without enzyme participation. For example, irradiation of an aqueous solution of phenylalanine and H_2O_2 with low intensity monochromatic UV-light (λ=253,7 nm) results in appearance in it of only four new compounds. All of them are amino acids: alanine, aspartate, lysine, and serine [12]. This set contains major functional amino acids to build different proteins. Notably that H_2O_2 is not consumed in this process, rather it behaves as a catalyst.

Besides, more and more attention is now attracted the so-called Maillard or amino-carbonyl reaction. This reaction starts from condensation

of simple sugars (ribose, glucose) or other carbonyl compounds and simple amino acids such as glycin. It proceeds in mild conditions (room temperature, slightly basic or even neutral pH), and in course of it much more complex compounds rapidly arise. They may become precursors of nucleic bases, other cyclic and heterocyclic molecules, complex polymers. Notably that in the course of all these reactions continuous generation and consumption of reactive oxygen species occur, and that the reactions are followed with very weak photon emission. Recently we have shown that such photon emission may proceed as a highly organized oscillatory process, indicating that self-organization is an essential feature of such reactions. Processes of this type may serve a contemporary adequate model of reactions discovered by Gurwitsch.

2.5 Role of visible light and oxygen in the development of Gurwitsch reactions.

As mentioned, MGR accompanies many enzymatic hydrolytic reactions, for example hydrolysis of urea by urease. According to thermodynamic calculations, such reactions are practically thermally neutral: energy needed to break down the substrates is nearly completely compensated by quantity of energy released when the final products are formed. Thus the major reaction process can not provide energy for emergence of such high-energy quanta as UV-photons. Where from than the additional energy come?

It was stressed above, that contact of a solution with air was a necessary condition for the emergence of MGR and in many cases illumination with weak visible light was needed. Gurwitsch suggested that oxygen and water actively participate in processes. They should disintegrate together with substrate molecules into atoms and simple free radicals such as =CO, —CH_2—, —NH_2, =O, —OH. Than additional energy may be supplied by reactions of radical recombination in which electron excited products arise. For example for urease reaction MGR spectral analysis and selective scattering spectra confirmed presence of the predicted radicals and products of their recombination in the reaction system. From calculation of energy balance it followed also that for dissociation of O_2 into atoms extra 118 kcal/mol were needed. Gurwitsch suggested that energy of two photons of visible light were added constructively to reach this energy quantum. Than the reaction system should emit MGR only if it was irradiated with photons of $\lambda<473$ nm (equivalent to energy of 60 kcal/mol x 2=120 kcal/mol). In fact when it was irradiated with monochromatic light with $\lambda>500$ nm no MGR from the reaction system could be registered, and it appeared only under illumination of light with $\lambda<(=)470$ nm. Similar predictions made basing on

the calculation of energy balance for other enzymatic reactions also were completely confirmed experimentally.

Thus, two crucial facts were found out. First, oxygen participates in all chemical reactions followed with MGR emission though it does not follow from chemical equations of these reactions derived from their analysis by less sensitive methods. Second, constructive adding up of two photons was discovered. This phenomenon seemed unbelievable until recently when it was demonstrated, that constructive two- and even three photons adding up may be observed in physical experiments. In particular, irradiation of a solution of a tyrosine derivative with a picosecond Ti-saphire laser (λ=780 and 855 nm) may excite it and provide its fluorescence in UV spectral range [13]. However, even now it is not easy to realize that similar processes may occur in systems where the processes accompanied with MGR emission proceed under illumination with non-coherent light sources.

The role of visible light in MGR emergence was impressively demonstrated in an another type of experiment. A 10 cm long tube was filled with a solution of a highly diluted extract of cancer tissue or liver which contains a low molecular weight substance. When the tube was irradiated from one side with monochromatic light (λ=<480 nm) MGR photons of λ=218-220 nm were emitted from another side. No effect was observed if a tube was illuminated with light λ>500 nm. In this case energy of MGR photon exceed even the double energy of photons of visible light by 0,5 eV, indicating that some energy donating processes takes place in this solution.

3. BRANCHING CHAIN REACTIONS AND PUMPING OF ENERGY INTO NON-EQUILIBRIUM AQUEOUS SYSTEMS.

3.1 Basics of branching chain reaction chemistry

Gurwitsch noted that many features of reactions accompanied with MGR are characteristic for branching chain reactions (BCR), which were discovered at the end of 1920s by Nikolai Semyonov [14] and Cyrill Hinshelwood [15]. BCR may be initiated by an introduction of only few active particles (free radicals, atoms) into a reaction mixture or emergence of such species in it, for example, due to photodissociation. Under certain conditions each active centre may give birth to more than a single new one and the reaction rate accelerates in these processes exponentially. Accordingly free energy of a reaction system spontaneously increases. However, the active centres being very short-lived intermediate products

completely disappear from the reaction mixture when the process comes to its end. The final result of BCR is the same as for any other chemical and physical process proceeding in closed systems: absolute reduction of free energy and entropy growth. However, the essence of BCR is manifested in its dynamics rather than in its overall balance.

Chemical BCR in gaseous and organic liquid phase, physical BCR taking place in an atomic bomb or a nuclear reactor (known also as "run-away reactions") are extensively studied. However, Gurwitsch's claim that reactions of such type may proceed in aqueous systems under mild physiological conditions was neglected: it contradicted to traditional views on the mechanisms of chemical processes running in water. Nevertheless, contemporary studies indicate that BCR may occur in aqueous systems though in a very peculiar form. Before we pass to discussing special properties of BCR in aqueous systems, general features of such reactions should be considered by the classical example: idealized BCR of oxidation of hydrogen with oxygen. We'll discuss it basing on a "polycyclic" model for the first time suggested by us (Figure 6).

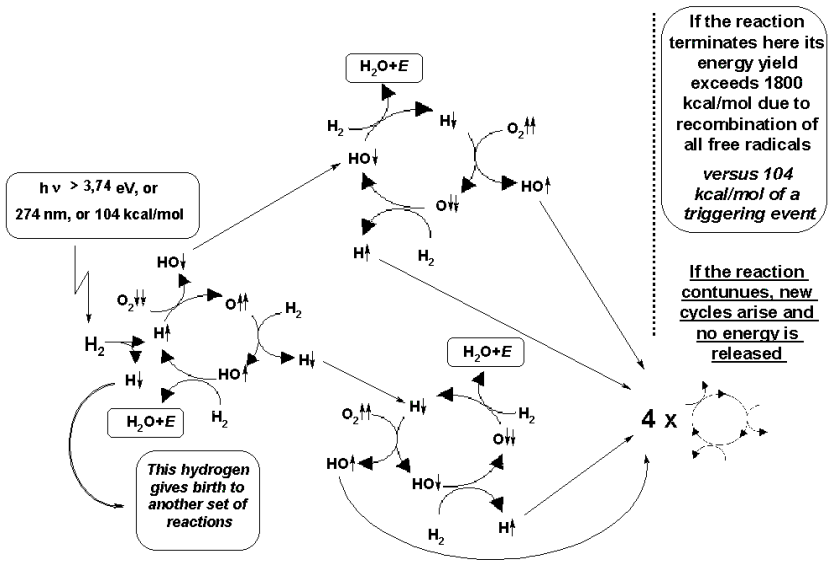


Figure 6. «Polycyclic» scheme of BCR of detonating gas ($H_2 + O_2$ --> H_2O). Arrows at atoms and molecules symbolize unpaired electrons.

A mixture of oxygen and hydrogen may stay for a long time without any visible changes until an active particle such as hydrogen atom emerges in it. It may appear as a result of breaking down of H_2 by a UV-photon of the proper energy. Under the appropriate conditions a hydrogen atom may react with an oxygen molecule producing hydroxyl radical and oxygen atom. The

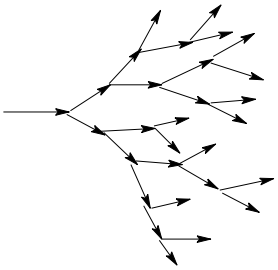
former reacts with hydrogen molecule producing a new hydroxyl radical, and the latter oxidizes hydrogen molecule to water and regenerating a hydrogen atom, which a new turn of the cycle.

Thus two active particles – a hydroxyl radical and a hydrogen atom, are released when the first cycle makes one turn, and they may give birth to new cycles. Notably that when all radicals either "rotate" in cycles or generate new ones no energy is practically released from the system. But it is well known that the reaction of hydrogen oxidation with oxygen is the explosive "detonating gas" reaction, releasing an enormous quantity of energy. This happens when chains break off due to radicals' recombination, which occur near the boundaries of the vessel or on other defects of the system. On the other hand, the system may hold substantial quantity of free energy which many times exceeds the quantity of energy needed to initiate and to support the process after only three cycles arise.

What is the source of this energy? It was initially "locked" in oxygen molecule (O_2) which is unique among other molecules in the environment. O_2 has two electrons with parallel spins (unpaired electrons) on its valence molecular orbitals **(M↑↑,** where ↑ represents an electron with a certain spin). Such constitution of an outer electron shell is termed a triplet state. Particles in a triplet state are paramagnetic (attracted into the magnetic field) and possess an excess of energy over their singlet state **[M↑↓]**, in which all their electrons are paired. Triplet O_2 is a vast energy store, able to release more than 180 kcal/mole upon its reduction to two water molecules after gaining 4 electrons (together with their carriers – protons). But it is rather inert by itself, because according to Wigner spin conservation rules it cannot directly interact with singlet state molecules. On the other hand, a free radical – a particle with an unpaired electron (in our case it is hydrogen atom) rather easily reacts with oxygen. This reaction represents a chain branching because it produces two free radicals, which can easily react with other molecules generating two new chains.

Polycyclic scheme of BCR (Fig. 6) gives an idea why energy may accumulate in the reaction system before its dissipation. It can be also seen that energy from reaction systems where BCR run may release in form of light, rather than heat (the so called "cold flame"), and often strong luminescence may be observed while the temperature of the reaction system is relatively low. Under certain conditions regular flashes (oscillations) of luminescence appear. From the presented sketch one can presume that the conditions for oscillatory release of photonic energy may be in principle provided by electron currents in closed circles of free radical transformations. It can not be excluded that these currents may interact with each other providing stability of the process as a whole, and beget oscillations with longer and longer relaxation times.

BCR similar to the reaction of detonating gas are termed “throughout branched chain reaction” and are schematically presented like this:



Here the arrows indicate reproduction of active centers (free radicals). But from Fig. 6 it can be seen, that the cycles generating free radicals themselves consist of free radicals (O↑↑, H↑, and OH↑). The cycles sustain due to continuous consumption of hydrogen and oxygen molecules. It is easy to conceive that any perturbations in the reaction system hindering supply of “fuel” impede cycles “rotation”, and in this case radicals creating the cycle may recombine. If triple recombination of radicals occur H_2O_2 molecule is produced with the release of an energy quantum equivalent to a photon ~ 200 nm; if only oxygen and hydrogen atoms recombine, an excited hydroxyl radical together with another one can initiate new chains.

In other words, in a system where BCR flows metastable objects may exist which retain a lot of labile high density energy. This is a most general property of BCR and when it is pronounced the reactions are termed “degenerate BCR”, or more precisely – “chain reactions with delayed branching” (CRDB). Delayed branching is typical even of nuclear run-away reactions. After a nucleus of a splitting atom absorbs a neutron and breaks down releasing more than 1 new neutron, metastable fragments of the nucleus also appear. They decay later, when the major chain has already run away or has been terminated. But when these fragments desintegrate they release neutrons that initiate new chains. The property of delayed branching provides for a long life of the process as a whole, while its participants (active sites and individual chains) may be very short-lived.

BCR running in a liquid phase are practically always CRDB. They develop much more slowly than reactions in gaseous phase and do not look like explosions though kinetically they have all the features of explosions. CRDB are always oxygen-dependent oxidative reactions, and branching in them is provided basically due to a un-pairing of electrons of triplet molecular oxygen. Branching generally occurs due to the appearance of metastable by-products in the course of the development of major chains, e.g., peroxides.

For a delayed branching to come about, a peroxide should decompose in to free radicals that launch two new chains (Figure 7). Oxygen present in the

system provides for production of excess of peroxide free radicals. When they recombine, extremely unstable and energy rich compounds – tetroxides appear. Tetroxide decompose generating electronically excited products which either relax, or their energy may be non-radiatively transferred to other substances present in the system. Such energy quanta either perform photochemical work or is remitted with the wavelength typical to a fluorophore.

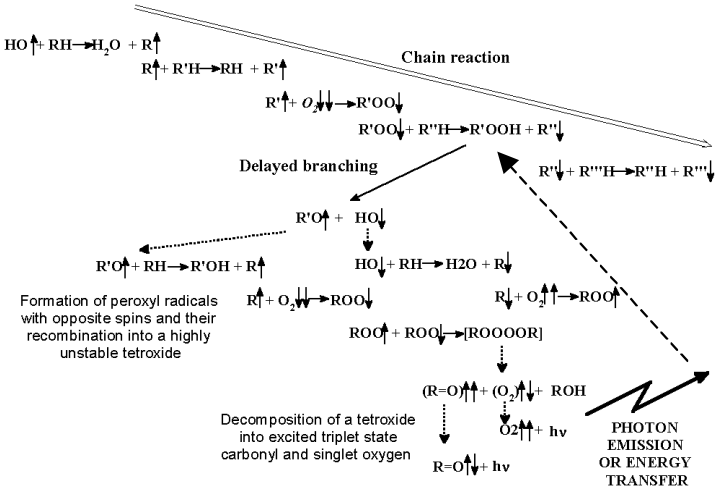


Figure 7. An outline of a chain reaction with delayed branching. A dashed arrow indicates that energy of electron excitation may be used for the decomposition of a metastable intermediate product into two radicals thus providing a chain branching.

This reasoning is true for the description of mechanisms of CRDB running in liquid organic phase [16]. But from the first sight it cannot be applied to the processes taking place in aqueous solutions at room temperature because energy of activation needed for peroxides to decompose into radicals reaches several tens of kilocalories per mole. If so, the probability of such reactions in water at usual temperatures seems to be very small. However, the results of many experiments performed by Gurwitsch and his colleagues (some of them have been described above) as well as the results of our studies of oxygen-dependent oxidative reactions in aqueous systems accompanied with photon emission [17, 18, 19, 20], as well as many properties of oxidative reactions occurring in biological systems, such as blood, need to admit that BCR may proceed in aqueous milieu [21].

The possibility of disintegration of peroxide and other metastable compounds in the course of the reactions under consideration may be provided by high non-equilibrium state of reaction systems which may be

looked upon as the active medium. Its stable non-equilibrium state is sustained by the continuous inflow of energy due to oxidative processes (and in some cases – due to illumination with visible light) and by the special properties of the aqueous milieu, that provide energy circulation over the common electron levels of system components before its dissipation. The latter statement is based on the phenomenon of "degradative radiation" discovered by Gurwitsch and repeatedly observed by other authors.

3.2 Degradative radiation and non-equilibrium molecular constellations.

Properties of MGR discussed above had been established mainly in the studies of enzyme and other reactions going by in homogenous systems. Yeast and bacterial cultures, eggs at early stages of their development and other biological systems where intensive cell division takes place, blood, nervous and contracting muscle cells also spontaneously emitted MGR. It was a surprise that liver, kidney and most other tissues of adult animals do not emit MGR in a resting state, though intensity of oxidative metabolic processes in them is undoubtedly high. However, it turned out that all biological systems regardless of their capability to emit MGR spontaneously responded on different injuries or physiological irritants – rapid cooling, mechanical compression, passage of an electrical current even of very low power, narcotics, and even glucose with an intensive flash of MGR. The flash lasts for many minutes and until it completely relaxes irritants cannot induce a new one. Spectra of degradative MGR are very different from that of homogenous systems. For example, bands characteristic of specific fluorophores may be identified in spectra of spontaneous MGR from yeast cultures and they are relatively constant. Spectra of degradative MGR of yeast differ not only from that obtained in a resting state, but they differ significantly for different strains of yeast, they change depending on the nature of a factor inducing degradative MGR, on the physiological state of the living system, on the state of its development.

The latter is well illustrated by A.A. Gurwitsh [22]. She studied the properties of MGR of the naked baby rabbit muscle *in vivo* in different times of postnatal development. Spontaneous MGR was measured at a body temperature and degradative after the muscle was doused with cold physiological solution. Evolution of intensity of both kinds of MGR and of the spectrum of MGR are presented in Figure 8.

It can be seen that in the course of postnatal development intensity of spontaneous MGR decreases, while that of degradative MGR increases. During this period the processes related to muscle tissue functioning become progressively consolidated so that by the 15-th day intensity of degradative

MGR reaches its maximum. Exactly by this time the posture and coordination of movements of an animal stabilizes indicating that the processes related to muscle tissue functioning reached maximal interrelation. Spectrum of MGR also changes in a specific way. At the early stage of development it looks like spectra of spontaneous MGR from systems containing many different flourophores. Later the number of spectral lines decreases, they widen, until only one wide line is left which has no correlation with flourophores known from selective scattering data.

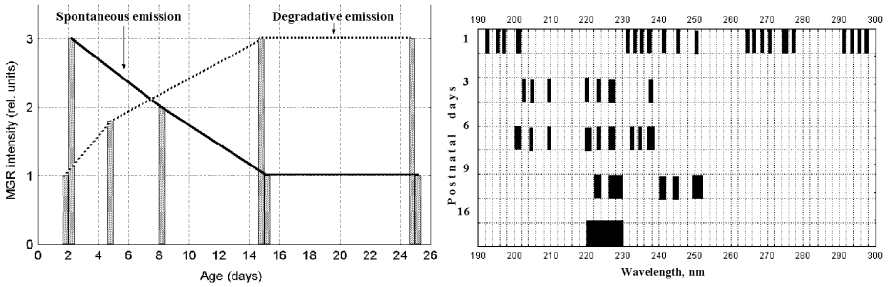


Figure 8. Left: evolution of intensity of spontaneous and degradative MGR of a baby rabbit muscle in vivo in different terms after birth (intensity was evaluated as a reverse of threshold period of irradiation by a muscle of yeast culture for obtaining a mitogenetic effect). Right: MGR spectra of a muscle (recorded at normal temperature).

All the properties of degradative MGR indicate that it differs in its origin from that of spontaneous one from homogenous systems. As already mentioned the latter most probably originates due to remission of energy originating in reactions of radical recombination by fluorophores present in reaction systems. The properties of degradative MGR suggest that it arises due to disintegration of some preexisting objects retaining a lot of easily mobilizing energy, in particular of energy of electron excitation. Gurwitsch named these presumed objects “non-equilibrium molecular constellations”. He supposed that they represent groups of excited macromolecules kept together due to constant energy circulation along their common energy levels. “Constellations” are fundamentally different from usual molecular associations and clusters. Components of the latter are kept together with different types of chemical bonds; energy is released when bonds lock, and sufficient energy inflow is needed for their dissociation. On the contrary, molecular constellations are sustained due to constant energy inflow, and any variations of energy supply let alone its blockade results in dispersion of constellations with release of energy retained by them. Lability of constellations precludes their revealing in fixed and even faulty biological material, and only the methods of studies of living cells and cellular systems

similar to mitogenetic analysis may provide an insight of the existence of such dynamic structures.

Components of constellations – excited molecules – are prone to continuous exchange, because as soon as a molecule relaxes to a ground state it leaves a constellation. But at any given moment closely arranged excited molecules mutually orient, consequently blending in constellations as systems. In other words, there are weak orientation interactions between the elements of constellations, but free energy of the constellation as a whole is higher than that of its elements in time preceding a constellation formation and after its desintegration due to the reasons mentioned above.

It is natural that if a constellation is disturbed by any means and loses its potential energy, the next distortion would not bring about a flash of degradative MGR until new constellations are formed. From the biological point of view there is nothing extraordinary of such a behavior of a constellation. Existence of refractory periods for excitable (more precise – irritable) tissues is well known. There are many ways to trigger a nervous impulse (discharge), and until the critical value of membrane potential is restored, next irritation would not induce new impulse.

Gurwitsch applied to constellations the notion of Nobelist Albert Szent-Gyorgyi of migration of energy along the common electronic levels of protein molecules [23]. But he broadened it to the possibility of migration of excitation energy along the constellations consisting of different molecules and also considered the possibility of energy quanta summation in different localities to the levels enough to emit UV-photons. Developing this concept he stressed that because of univocacy of energetic and spatial parameters of constellations fluctuations in energy migration should result in spatial realignments of constellations. That is why he stated that at the molecular level of living systems "… it is wrong to oppose the notion of a structure to the notion of a process. The only correct approach to living systems is an approach to them as to the structured processes, flowing in molecular complexes widely different in the degree of their lability" [24].

The possibility of high density energy transfer to macroscopic distances has been experimentally demonstrated using mitogenetic analysis by A.A. Gurwitsch. She has shown that if to fill a narrow capillary with a dilute protein solution and expose it to MGR from one end, no emission may be registered from the opposite end under usual conditions. However, if the capillary is placed in the longitudinal (parallel to its axis) electrical field (50 v/m), it becomes a MGR conductor. Same effect is observed if the protein solution flows in a capillary at a rate of 1 m/sec. This phenomenon may be explained by a thread-like form of protein molecules, and their alignment along the capillary axis under the action of electrical field or a fluid flow, that increases the probability of energy transfer from one molecule to the

next one. It is interesting, that the rate of photon "diffusion" in this experimental system was around 30-32 m/sec, which is very close to the rate of a nerve impulse travelling along an axon.

It also follows from this experiment that pumping of constellations with energy is a necessary but not the sufficient condition of their emergence. As the elements of constellations can not mutually orient in them due to usual chemical bonding there should exist an external vectorial factor that imposes a certain spatial arrangement to the elements of constellations. In an example with protein solution able to conduct MGR the role of such factor was played by an electrical field or a fluid flow.

As constellations are postulated to be the most fundamental necessary condition for the existence of living matter ("structured processes") the uninterrupted existence such vectorial factor of dynamic nature is also to be postulated. That is why Gurwitsch's theory of a biological and cellular fields – an imprescriptible property of all living systems – can not be considered without referring to his experimental work in "mitogenetic biology". However, Gurwitsch's theory of biological field cannot be considered here, and the reader may inquire other sources for more information on it [25, 26].

4. GENERAL CONCLUSIONS

We depicted only a small fragment of Gurwitsch's heritage concerning the problems of "mitogenetic biology". We practically did not touch an enormous amount of data obtained in application of mitogenetic methods of analysis to cell biology, general physiology and physiology of the central nervous system, oncology, plant physiology, etc. Taken as a whole the results obtained in these studies and conclusions from them should have drastically change the very foundations of biology. However, mitogenetic biology until now is practically unknown to the great majority of biologists, and most of those who have heard of it do not consider it a serious science. One of the major reasons for this – is the apparent absence of serious physical-chemical background for phenomena related to MGR.

Here we concentrated on the most "simple" model systems, which are able to emit MGR – aqueous solutions of amino acids where very peculiar processes develop. It should be stressed again that the very term – mitogenetic radiation – means that these systems "act at a distance" upon populations of cells inducing in them a definite response, a burst of cell divisions. Thus, from the biological point of view MGR should be

considered as a signaling (triggering) factor, and it may display biological activity only if it acts on a responsive biological system·.

On the other hand, these signals should have a very definite physical nature. Gurwitsch claimed that MGR are UV-photons. After a long debate it is currently accepted that living systems may emit photons in UV range (e.g., [27]). But why it took so much time to accept this though in the last 50 years it was indisputable that both living things and some chemical reactions (such as lipid peroxidation) may be sources of weak photon emission in the visible and near IR-range of electromagnetic spectrum? There are both technical and psychological reasons for this paradox.

Ultra-weak photon emission from living things is currently registered with sensitive photomultipliers (PMT), while Gurwitsch used biological test systems. Even if PMT sensitive to UV-range of EM-spectrum were used, researches had a lot of problems to detect UV-photons, though it had been claimed in 1930-ies that MGR intensity could reach tens-thousands photons per second per 1 cm^2. But a very important thing stressed above was neglected: in most cases the ability of an experimental system to emit MGR depends upon its illumination with visible light. In the darkness MGR is either drastically reduced or disappear and precisely under these conditions photon emission is registered with PMT.

Another reason for misunderstanding of many peculiarities of MGR is in a certain sense psychological. In order to get reliable information about the system a researcher tries to obtain a good "signal-to-noise ratio" and prefers to deal with more or less intense signals. So, *a priori* there is a tendency to consider that informative part of the signal should be "loud", while a "whisper" is insignificant. As the intensity of radiation measured with PMTs in a visible and IR-part of the spectrum is much usually higher than that in the UV-region, and may be additionally amplified by addition to a natural system of chemiluminescent and fluorescent compounds (e.g., luminol, lucigenin, Rhodamin), most researches judged about the properties of systems under study taking into consideration only intensity of radiation and not its other properties. As a matter of fact, in our studies of photon emission from the chain reaction with delayed branching running in solution of glycin in the presence of H_2O_2 we could barely register any photons in UV-region, but on addition to the reaction mixture of tiny quantities of fluorophors that could be excited only by UV-photons (or equivalent energy quanta) and remit in the visible range photon emission intensity increased enormously.

· In fact, in one of the papers with alleged refutation of the existence of MGR (Hollaender A., Klaus W. Bull. Nat. Res. Council 1937, 100:3-96), which is sited until now to claim that the whole problem of MGR is an example of "pathological science" (Langmuir I. Physics Today, 1989, 36: 47.) this very mistake was made: an yeast culture taken as a detector of MGR was used at a stage when it is unresponsive to it.

But is intensity of photon emission really so important? Let us return to a very significant Gurwitsch's observation: supply of MGR (which is very weak by itself) to a biological detector in the intermittent mode, when the overall intensity of incident photons is reduced drastically significantly increases its biological efficiency. This does not happen when intermittence is chaotic. Therefore not intensity of radiation, but rather its orderliness is of primary importance for considering this radiation "biophotonic"! Besides, we should realize that radiation from a living system registered by us is energy, which lost by it, and very "expensive" high density energy. And the phenomenon of "degradative radiation" discovered by Gurwitsch shows, that a living system may store a vast amount of it which may be easily mobilised as photonic energy under perturbations of its stationary state.

And here we come to a controversial term of "biophotons". This term was first suggested by Friz-Albert Popp to designate photons belonging to very low level of photon emission from living organisms (not to be mixed up with "bioluminescence" – high intensity radiation of many organisms due to specific enzymatic reactions) [28]. Popp discovered that statistical and temporal properties of this radiation are very different from those expected from stochastic emission of usual chemiluminescent reactions. He proved that at least the so-called delayed luminescence induced by irradiation of living organisms with a flash of light results from the relaxation of an intrinsic coherent electromagnetic field [3]. As far as in 1983 Nagl and Popp suggested that there is a negative feedback-loop in living cells which couples together states of a coherent ultra-weak photon or biophoton field and the conformational state of the cellular DNA. They assume photon transfer or non-radiation chemical pumping from the metabolism which results in changes of the DNA conformation via exciplex/excimer formation [29]. Recently energy transfer to tremendous (in molecular scale) distances without its dissipation has been demonstrated for DNA molecules and for helical regions of proteins [30, 31].

It should be taken into consideration that when Szent-Gyorgyi and Gurwitsch formulated concepts of "energy circulation along the common electronic levels" no corresponding physical notions were yet formulated and no physical evidence for such phenomena existed. Apparently the time has come to consider the properties of biological systems starting from the molecular level from the position of soliton and exciton physics, from the notion of active medium in laser physics.

However, even if special properties of "biophotons" emitted by living organisms are acknowledged and explained due to special structural properties of macromolecules present in living matter, there stays a need to explain the origin of biophoton fields in living matter. We believe that processes developing in "simple" aqueous solutions of amino acids followed

with emission of ultra-weak radiation of high energy photons are the foundation of all other processes related to generation and relaxation of electronic excitation, which may or may not follow with photon emission from living systems [32]. Very recently we have demonstrated that in such initially simple reaction systems real self-organisation takes place under the conditions when oxygen-dependent chain reactions with delayed branching develop: temporal, spatial and even chemical complexity of these solutions increase, and they behave as the active medium [33, 34]. Diverse external mild stimuli induce intense flashes of photons from these solutions, indicating that they accumulate a huge amount of easily mobilised high density energy – in close analogy to "degradative" radiation. Of special interest is that photons may be emitted from solutions where the named processes develop in an oscillatory manner, sometimes highly ordered and displaying wide range of frequencies and amplitudes. We registered emission mainly in the region of 400-500 nm, but there are all reasons to believe that these systems are radiating also in other spectral regions (though at much lower intensity) and that this radiation is also well-ordered.

Thus "biophotonic-like fields" may emerge even in initially very "plain" systems, such as aqueous solutions of simple organic molecules under soft but specified conditions which imply the development of oxidative chain reactions with delayed branching in aqueous milieu. Water should be regarded as an active participant of these processes rather than a passive medium for them [35] due to its unique dynamic organization. Thus, aqueous systems where there develop processes first discovered by Gurwitsch gain ability to emit "biophotons" – electromagnetic radiation of very low intensity, in a very wide spectral range, and possessing specific orderliness. That provides them capability to trigger realignment and modulate reorganization of own biophotonic fields in living organisms accompanied with specifically patterned biophoton emission from them, and followed with an array of responses including cell division, differentiation, dedifferentiation, apoptosis, shifts in metabolic activity, locomotion and other manifestations of their vitality.

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