Physical aspects of biological activity and cancer

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Mitochondria are organelles at the boundary between chemical–genetic and physical processes in living cells. Mitochondria supply energy and provide conditions for physical mechanisms. Protons transferred across the inner mitochondrial membrane diffuse into cytosol and form a zone of a strong static electric field changing water into quasi-elastic medium that loses viscosity damping properties. Mitochondria and microtubules form a unique cooperating system in the cell. Microtubules are electrical polar structures that make possible non-linear transformation of random excitations into coherent oscillations and generation of coherent electrodynamic field. Mitochondria supply energy, may condition non-linear properties and low damping of oscillations. Electrodynamic activity might have essential significance for material transport, organization, intra- and inter-cellular interactions, and information transfer. Physical processes in cancer cell are disturbed due to suppression of oxidative metabolism in mitochodria (Warburg effect). Water ordering level in the cell is decreased, excitation of microtubule electric polar oscilations diminished, damping increased, and non-linear energy transformation shifted towards the linear region. Power and coherence of the generated electrodynamic field are reduced. Electromagnetic activity of healthy and cancer cells may display essential differences. Local invasion and metastastatic growth may strongly depend on disturbed electrodynamic activity. Nanotechnological measurements may disclose yet unknown properties and parameters of electrodynamic oscillations and other physical processes in healthy and cancer cells. *Copyright 2012 Author(s). All article content, except where otherwise noted, is licensed under a Creative Commons Attribution 3.0 Unported license.*
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I. INTRODUCTION

In the twenties of the last century Warburg *et al.*[1] disclosed suppression of oxidative metabolism in living cells caused by mitochondrial dysfunction and suggested its connection with diminished order in the cell (Warburg[2]). In 1967 M. Marois organized the first Versailles meeting entitled "Theoretical Physics and Biology" where H. Fröhlich[3] presented the idea of correlation over macroscopic regions and creation of macroscopic wave function in biological systems. Non-linear interactions between elastic and electric polarization fields and non-linear spectral energy channeling may lead to establishment of coherent oscillation states in systems with energy supply.[4–6] Cooperative phenomena in systems far from thermodynamic equilibrium (synergetics) were analyzed by Haken.[7] Pohl,[8] Hölzel and Lamprecht,[9] and Hölzel[10] observed attraction of dielectric particles to living cells. The dielectric particle may move to and from the cell in dependence on the difference of the permittivity of the particle and the medium. The amount of attracted particles depends on their permittivity, conductivity of the suspending liquid, shape of the cell (enhanced attraction to the tips of elongated cells), and on the cell cycle (increased attraction in the M phase of the cell cycle). It was not clear, what cellular structures are responsible for the measured electrodynamic activity. Microtubules fulfill conditions for generation of the oscillating electromagnetic field (Pokorný *et al.*[11,12]). The field was measured at the membrane in the frequency range 8–9 MHz (Pokorný *et al.*[13]). Sahu *et al.*[14] claims

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that microtubules in vitro display resonance at the frequency of about 10 MHz. It might be important discovery of microtubule properties. Kirson *et al.*[15,16] proved that microtubule polymerization may be interrupted by external electromagnetic field in the frequency range 100–300 kHz with intensity of the electric field 1–2 V/m. The forces exerted by the external field on tubulin heterodimers prevent their correct orientation and attraction to the close vicinity of the tip and disturb transport of tubulin heterodimers to the growing microtubule end. Vedruccio and Meessen[17] observed increased damping of the external electromagnetic field in cancers at the frequency of about 465 MHz and its first and second harmonics if the radiating antenna is placed in the vicinity of the tumor. The effect corresponds to microtubule energy oscillation losses in cancer cells (Pokorný *et al.*[18]). Oscillation of microtubules seems to be a fundamental mechanism for generation of the cellular electrodynamic field. Cooperation between mitochondria and microtubules may form convenient conditions for excitation (Pokorný *et al.*[19]). The generated field might play a role in organization, transport, interactions (Pokorný,[20,21] Pokorný *et al.*[22]), and information transfer. Dysfunction of mitochondria in cancer cells may disturb internal cellular electrodynamic field with consequences to biological functions based on physical processes (Pokorný *et al.*[19] and Pokorný[23,24]). Conditions for excitation of the cellular electrodynamic field are described in this paper.

II. INTERFACIAL WATER ORDERING

For a long time organization of water was a controversial issue. Hydration was assumed to be limited to several water layers. Bulk water (i.e. water without ordering) was assumed to be in living cells. But ordering of the intracellular water is a crucial phenomenon affecting its elasto-electrical properties. Experimental results have gradually brought essential evidence for this phenomenon. Significant increase of the NMR (nuclear magnetic resonance) spin–lattice relaxation time (T_1) in cancer cells was explained by decrease in water ordering of the intracellular water (Damadian[25]). Zones without solutes were observed around microtubules. These clear zones were assumed to be occupied by a coating of proteins that prevent large particles approaching the microtubule surface (Amos[26]). Stebbings and Hunt[27] connected formation of clear zones with the negative charge at the microtubule surface. The biomolecules and structures carry electric charge at their surfaces, and, therefore, the ordering of water should be a general phenomenon. Ling[28] formulated theory of ordering of water molecules caused by electrostatic field of the surface charge at the interface. Zheng and Pollack[29] and Zheng *et al.*[30] observed clear (exclusion) zones that excluded solutes up to a distance of the order of magnitude of 0.1 mm. The electric potential across the exclusion zone is dependent on the ion concentration in the solution. The measured potential difference across the exclusion zone is of about 100 mV. Thermal motion in the exclusion zone is lowered as follows from suppressed infrared radiation (in the range 3.8–4.6μm) from the zone extending from the sample surface up to a distance of 0.3–0.5 mm. UV absorbance at 270 nm is increased. Molecules of the ordered water are organized in plane layers parallel with the surface in the case of a flat interface.

Ordered water has different physical properties in comparison with the bulk water, in particular higher viscosity (Pollack *et al.*[31]), different pH (Chai *et al.*[32]) and spectroscopic properties (Chai *et al.*[33]), and separation of charge (Chai *et al.*[32]). More detailed information about ordered water properties may be found in Pollack *et al.*[31] Infrared radiation promotes formation of the exclusion zones (Chai *et al.*[32]). Ordering of water in living cells may depend on the phase of the cell cycle. NMR spectroscopy disclosed increased level of water ordering in the metaphase period of the M phase (Zimmerman *et al.*[34]).

Ordering of water is not limited to hydrophilic interfaces. The main agent in water ordering is the electric field. A strong electric field about 500–700 kV/m causes water ordering and forms a floating water bridge about 1–3 cm long between two glass beakers (Fuks *et al.*[35–37] and Giuliani *et al.*[38]).

Theoretical explanation of creation of the ordered water layer based on quantum electrodynamics was worked out by Preparata[39] and Del Giudice *et al.*[40] The "normal liquid" water contains two mixed phases: coherent domains whose linear dimension may be of about 100 nm and a gas-like phase. Coherent domains form the ordered water. Static electric field organizes coherent domains into exclusion zones. Organization structure of coherent domains is transferred by the action of

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the electric field into exclusion zone that is a macroscopic entity. Exclusion zone features may correspond–to some extent–to a transition structure between a liquid (that makes possible diffusion of protons) and a solid state material including quasi-free electrons. Del Giudice *et al.*[40] and Del Giudice and Tadeshi[41] suggested that the free electrons ("electron conductivity") of exclusion zones may have a strong impact on cell behavior.

III. MITOCHONDRIAL FUNCTION

Mitochondria are employed in energy supply system in the cell. Energy from pyruvate produced by fermentation and fatty acids is parceled out into small packets and then stored into ATP and GTP (adenosine and guanosine triphosphate) for biological utilization. In the process of ATP and GTP production chemical energy is converted into electrochemical proton gradient. Protons are transported outside the mitochondrial matrix space across the inner membrane and diffuse through the outer membrane into the mitochondrial surroundings creating a space-charge layer. The protons transported across the inner membrane serve not only for storage of energy and its splitting but also–together with the negative charge in the mitochondrial matrix space–for formation of the static electric field around mitochondria. Each mitochondrion is surrounded be a layer of a strong static electric field. Tyner *et al.*[42] measured intensity of the static electric field by fluorescent spherical particles 30 nm in diameter. Emission ratios at two different wavelengths of the fluorescent spectrum depended on the intensity of the electric field. When the results were analyzed complications caused by a short distance between mitochondria appeared. Very often the fluorescent particles measured the field generated by several mitochondria located in their vicinity, in particular in the plane above and below the observed one. Some measured values were assumed to represent the cytosolic region (not influenced by several mitochondria). Fig. 1 shows intensity of the static electric field up to a distance of 2 μm from a mitochondrial membrane.

The intensity values (after Tyner *et al.*[42]) are plotted as the black rectangles with a regression long dash line segment. The measured intensity was considered to yield the cytosolic values, i.e. the values from the regions that do not cross over other mitochondrial fields. The intensity of the static electric field displays nearly linear dependence on the distance from the mitochondrial membrane. Theoretical curve of the intensity of the static electric field in cytosol determined from the distribution of proton charge is plotted in the full line. The values drop significantly and rapidly near the mitochondrion and beyond a distance of the order of magnitude 10 nm they are much smaller than the measured ones. Therefore, it may be reasonable to assume that the cytosolic water around mitochondria is ordered as around the charged surfaces of biopolymer structures (interfacial ordering). For a planar parallel and a spherical organization of the model of ordered water the intensity of the static electric field is plotted in the dotted and the short dash curves, respectively. The measured intensity of the static electric field is in between these two limit curves. But the exclusion zone may be non-uniform and protons may diffuse into the ordered layer. Zheng *et al.*[30] assumed that the fact that the solute exclusion zones of 0.36 mm could be found in 150 mM salt solution argues against a purely electrostatic mechanism. But the ions may be expelled from the ordered region of cytosolic water and concentrated beyond the distant edge of the ordered region (diffusion may smear the boundary). Charge distribution depends on its concentration and on the intensity of the static electric field in the ordered region. Water ordering is a phenomenon changing water from a viscosity liquid to quasi-elastic gel affecting inner cellular processes, in particular providing low damping of the cytoskeleton vibration system.

But the assumption that the measured static field is generated only by one mitochondrion is very likely not fulfilled. Mitochondria occupy about 22 % of the cellular volume. There may be about 1000 (or more) mitochondria in a cell. For spherical mitochondria of about 0.6 μm in diameter the average distance between mitochondria is of about 0.4 μm. Exclusion zones around mitochondria may mutually cross over one another. Protons may be concentrated in the boundary regions where is the minimal value of the intensity of the electric field of the overlapping ordered layers of different mitochondria. The protons form diffuse layers between mitochondria. (The distribution of protons and dynamic equilibrium of their flow between the layer and the mitochondrial inner membrane deserve a detailed analysis.) Therefore, the cytosolic medium is under influence of a strong static

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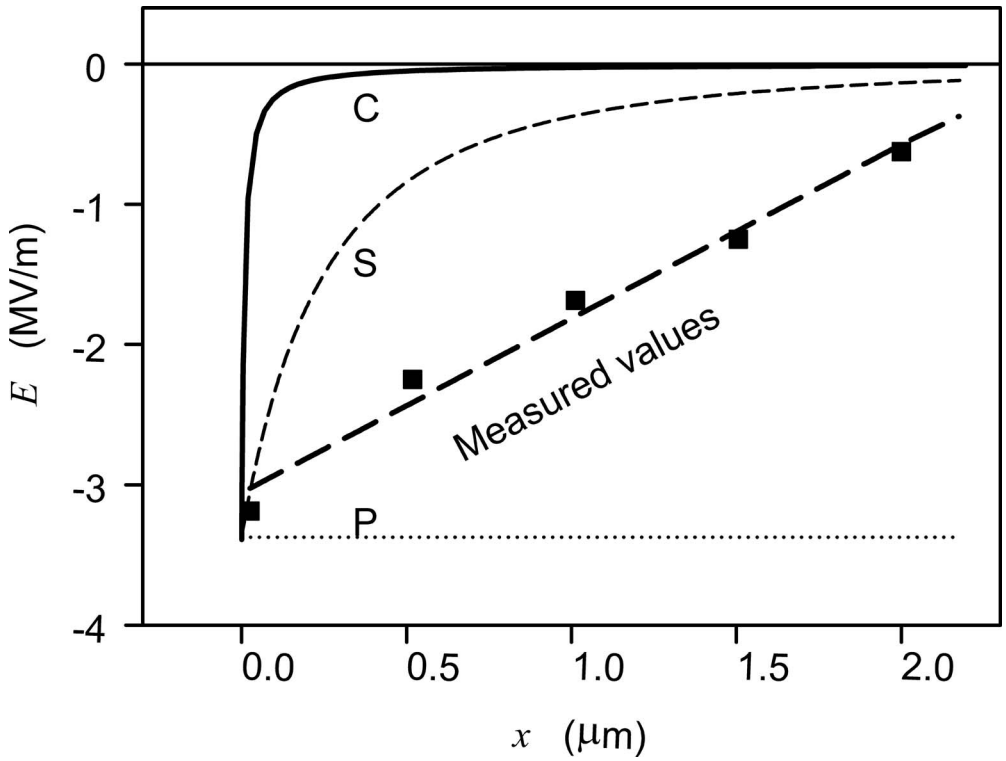


FIG. 1. Distribution of protons and electrostatic field in the vicinity of mitochondria. Black squares – experimental values of the intensity of the cytosolic electrostatic field measured by fluorescent particles (after Tyner *et al.*[42]) with the regression long dash line segment. The full line (C) – the classical theoretical curve of the intensity dependent on the proton distribution in the cytosol without considering ordered water layer. The dotted line (P) and the short dash curve (S) – intensity of the electric field in the ordered layer of water assuming distribution of opposite charges in the parallel plane layers and in the spherical symmetrical layers, respectively.

electric field that polarizes biological macromolecules and structures and shifts oscillation processes into highly non-linear regions.

Energy entering mitochondria is used for production of ATP and GTP with the efficiency of about 40 % or slightly greater. The non-utilized energy that may reach nearly 60 % (often denoted as the "wasted" energy) is liberated from mitochondria into cytosol in the form of photons in the UV (Tilbury and Quickenden,[43] Batyanov[44,45]), visible, and infrared region, chemical compounds, and heat.

IV. CELLULAR ELECTROMAGNETIC FIELD

The eukaryotic cell cytoskeleton is a highly dynamic structure that reorganizes continuously in response to cell changing shape, division, and environmental conditions. The cytoskeleton has a wide spectrum of functions. It organizes the cell, keeps its geometric stability, participates in cell motility, makes possible ribosomal and vesicle transport, has a special role in mitosis, and transduces pressure and tension. The cytoskeleton is composed of microfilaments, intermediate filaments, microtubules, and accessory proteins. All the cytoskeleton parts are mutually connected and form a three-dimensional network in the cell. The center of the cytoskeleton is the centrosome. Microtubules start to polymerize at the centrosome in radial direction. In the interphase some of them are connected to proteins at the membrane. In the M phase microtubules form a mitotic spindle with two poles (centrosomes). In the interphase mitochondria may be aligned along microtubules. In the M phase mitochondrial distribution is not known. Organization of mitochondria might be a special

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issue of the cellular static electric and electromagnetic field. The cell may form an electromagnetic cavity resonator with dielectric walls. The position of the microtubules and the centrosome may be controlled by the cavity electromagnetic field. The space distribution of the field and the acting forces are different in the interphase and in the M phase (in the one pole and the two poles structure, respectively). Mitochondria may move together with the ordered water and the proton space charge layer. The final effect may be assessed using real parameters of the system. Therefore, effect of the cellular electromagnetic field on mitochondrial organization remains an open question. On the other hand the static electric field might participate in mitochondrial space distribution too. Very often mitochondria remain in position where they cover unusually high ATP consumption. Due to the proton transfer and the strong static electric field mitochondria might provide a long range interactions with the "energy consumption site". The sites of increased energy consumption in the M phase have different locations in comparison with the interphase period.

Microtubule is a cylindrical structure formed by protofilaments composed of tubulin heterodimers. A tubulin heterodimer consists of two globular proteins. Both have a relative molecular mass of about 55000, but their masses are not equal. Each heterodimer is an electric dipole whose dipole moment is of about 1000 Debye (10^{-26} Cm)–Satarić *et al.*[46] and Tuszyński *et al.*[47] The induced dipole moment per dimer arising only from the motion of mobile electrons or protons was estimated to be 200–400 Debye (Stracke *et al.*[48]). Mechanical oscillations are connected with polarization changes.

Energy is supplied into microtubules. The microtubules are dynamic polymers that display dynamic instability. In the interphase the microtubules connected to the structures at the cellular membrane have a turnover of about 18 hours (Pelling *et al.*[49]). After this period they are replaced by other microtubules. The microtubules with the free end have a turnover of about 10 min. They are growing and shrinking. After polymerization GTP in the β tubulin is hydrolyzed to GDP (guanosine diphosphate) and a part of the released energy is stored in the microtubule structure. In the M phase microtubules polymerize in the central part and depolymerize at the poles of the mitotic spindle (this process is called treadmilling). Both mechanisms of dynamic instability supply energy to microtubules.

Motor proteins transporting "cargo" move along microtubules. A part of the energy of motion is transferred to the microtubules. But the motor proteins might also cause disturbances and damping of microtubule oscillations. In the interphase the greatest energy supply to microtubules is very likely provided by non-utilized energy liberated from mitochondria (Pokorný *et al.*[18]).

Frequency spectrum of biological electrodynamic activity is very wide. Spectral lines were measured from acoustic to visible range. Pelling *et al.*[50,51] measured mechanical membrane oscillations by AFM (atomic force microscope) at 1.63 and 0.87 kHz at the temperature of 30 and 22°C, respectively. Mechanical and electrical oscillations in the acoustic band were confirmed by Jelínek *et al.*[52] Pohl[8] assessed the frequency of oscillations from the dielectrophoretic atraction of dielectric particles in the range 5 kHz–1 MHz. Kirson *et al.*[15,16] described disturbances of internal cellular electrodynamic field and consequently also polymerization of the microtubules in the M phase by external electromagnetic field in the frequency range 100–300 kHz. Hölzel and Lamprecht[9] and Hölzel[10] measured electrodynamic activity of yeast cells and alga cells in the frequency range 1.5–52 MHz. Pokorný *et al.*[13] observed and evaluated electrodynamic field generated by yeast cells in the frequency band 8–9 MHz. The measured activity was associated with mitosis. The high activity coincides with the rearrangement of the microtubules into a mitotic spindle, with binding of chromatids to kinetochore microtubules, and with the elongation of the mitotic spindle during anaphase A and B. Vedruccio and Meessen[17] disclosed interaction of the electromagnetic field with cancer tissue at 465 MHz and the first and the second harmonic component corresponding to resonant interaction. Albrecht-Buehler[53–55] proved the ability of cells to detect electromagnetic signals of other cells in the red and near-infrared range. The cells are able to sense the radiation and to determine the direction to the source.

Measurement of microtubules in vitro was performed by Sahu *et al.*[14] but the results have not been published as yet. The individual microtubules were polymerized in the oscillating electric field. Sahu *et al.*[14] describes ballistic conductance of electrons moving along spiral orbits with different steepness and several resonant frequencies in the microtubules around 10 MHz.

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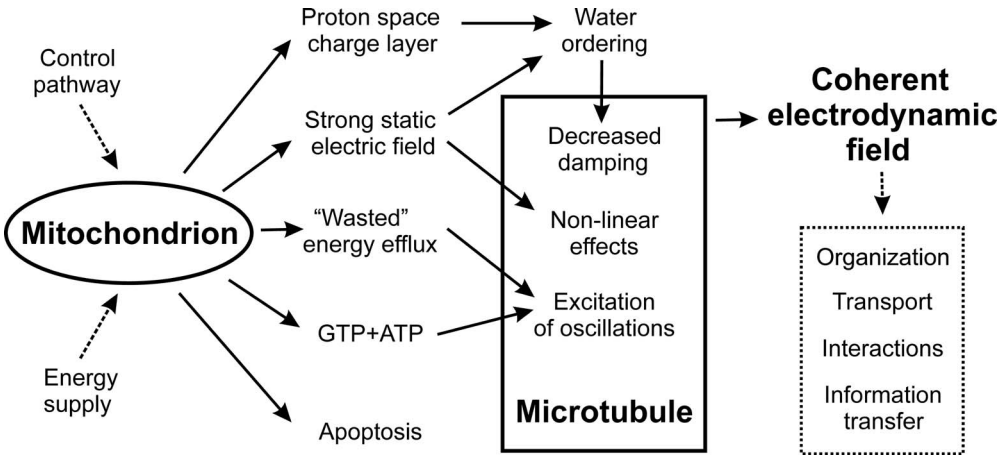


FIG. 2. Physical aspects of biological activity – physical mechanisms depend on mitochondrial function. Mitochondrial transport of protons into cytosol leads to generation of a strong static electric field and a high level of water ordering. As a consequence damping of oscillations in microtubules is low. Microtubule oscillations may be highly excited by energy supply, in particular by liberation of the non-utilized energy ("wasted" energy) from mitochondria.

The electrodynamic field measured at living cells is assumed to be generated by fundamentally non-linear elasto-electrical oscillations of microtubules. The oscillations may display several resonant frequencies as follows from AFM measurements in the acoustic region and interaction of external electromagnetic fields with living cells, in particular in the 0.1–0.3 MHz and 465 MHz regions. A direct measurement of coherent resonant signals using special nanotechnological systems at physiological temperature may disclose essential spectral properties of microtubules, their structures and cells.

V. PHYSICAL PROCESSES IN CELLS

The interplay of mitochondria with microtubules may form an essential basis for physical processes in cells. A decisive factor for adjusting non-linear properties of microtubules and formation of ordered cytosol water might be the static electric field created around mitochondria. Non-linear properties make possible transformation of random excitation into coherent oscillations in microtubules. Ordered water is a quasi-elastic medium providing low damping of microtubule oscillations. Non-utilized energy efflux from mitochondria supplies energy exciting oscillations, shifts the system far from thermodynamic equilibrium, and establishes the coherent state. Electrodynamic field generated by microtubules may play a significant role in biological activity. The electric oscillating field might produce a traction force (predicted by Frauenfelder *et al.*[56]) for directed transport of material, morphological force for organization of cellular structures, interaction force for intra and inter-cellular purposes (Pokorný,[20,21] Pokorný *et al.*[22]), and may serve as a medium for information transfer. A schematic picture of physical links in cellular activity is given in Fig. 2 (Pokorný *et al.*[18]).

VI. CANCER DISTURBANCES

Suppression of oxidative metabolism is a general feature of cancer cells. One type of the Warburg effect is shown in Fig. 3. Cancer process inhibits oxidative energy production of ATP and GTP that may be caused by diminished proton transfer across the inner mitochondrial membrane. Warburg assessed ratio of the amount of energy produced by the fermentation and the oxidation (respiration) process in healthy and cancer cells. In healthy cells the oxidation energy production may be even 100 times greater than the fermentation one (for instance in kidney and liver cells). With the exception of the cancer cells with reversed Warburg effect (Pavlides *et al.*[57]) fermentative production in cancer cells is bigger than in healthy cells. In the cancer cell fermentation may participate in energy production approximately by 1/3–2/3 part of the total output and the average value may be of about

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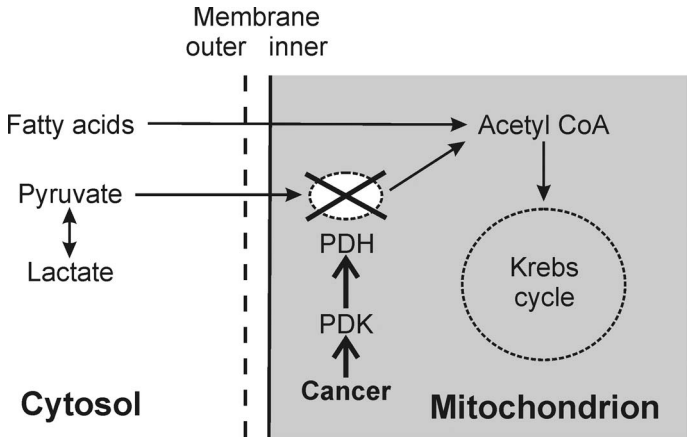


FIG. 3. A schematic picture of glycolytic phenotype of cancer cells (Bonnet *et al.*[68]). The pyruvate pathway is blocked by cancer PDK (pyruvate dehydrogenase kinase). PDH (pyruvate dehydrogenase) enzymes in the mitochondrial matrix phosphorylated by PDK are dysfunctional and pyruvate is not broken down into the two-carbon acetyl group on acetyl CoA (Coenzyme). Only about one half of protons is transferred into the intermembrane space than in fully functional mitochondrion. But similar effect of the proton transfer inhibition may be caused by other defects in the Krebs cycle.

one half (Warburg[1,2]). If the cancer and the healthy cells have the same amount of the total energy and the same mitochondrial efficiency of utilization of the electrochemical proton gradient (by ATP synthase protein complexes) then only about one half of protons are transported across the inner membrane in comparison with a "healthy" mitochondrion. The non-utilized energy liberated from mitochondria is correspondingly lowered too. The static electric field is weaker and ordering level of water diminished. Damping of oscillations in microtubules is increased, excitation lowered, and non-linear properties shifted towards linear region. Power and coherence of the electrodynamic field are diminished. Coherent processes in the cell are disturbed, and the random ones play a more important role (Pokorný *et al.*,[18,19] Pokorný[23]). Mitochondria are the boundary entities between chemical-genetic and physical processes.

Mitochondrial dysfunction may develop in the period before appearance of malignant properties. In the cervical cancer mitochondrial dysfunction turn was assessed in the period from precancerous to cancer cells (Jandová *et al.*[58]). Therefore, the disturbances of the electromagnetic activity in cancer cells might be responsible for malignant properties. Interaction forces between healthy cells may be greater than those between cancer cells. The healthy cell may pull the cancer cell into healthy tissue. This mechanism may be responsible for local invasion (Pokorný[59]). The metastatic phase starts with disorganization of the cytoskeleton (Beil *et al.*,[60] Suresh *et al.*,[61] Suresh[62]). After disturbances of the cytoskeleton the frequency spectrum and the spatial pattern of the generated electrodynamic field may be altered to such extent that the cancer cell loses connection with the surrounding cells in the tissue, can leave the tissue, move freely in the body, and form a metastatic nodule even in distant organs.

VII. DISCUSSION

Warburg effect (Warburg *et al.*[1]) disclosed nearly ninety years ago had been accepted as a secondary side effect for a long time. This point of view was revisited in the last decade and analysis of the mitochondrial dysfunction and its treatment is an urgent issue now. Warburg effect is one of the most important links along the cancer transformation pathway. But consequences of the mitochondrial dysfunction were not elucidated. The Fröhlich's hypothesis makes possible to analyze consequent disturbance. Nevertheless, Fröhlich's hypothetical prediction of coherent electrodynamic activity of living systems was classified as impossible due to strong viscosity damping by water (Foster and Baisch[63]) or generally low quality factor of biological oscillators (Reimers *et al.*[64] and Mc Kemmish *et al.*[65]). Above it, their analysis is based on replacement of the essentially

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non-linear Fröhlich's system by a linear one (they neglected non-linear interactions between elastic and polarization fields). Experimental data on water ordering and measurement on microtubules prove and strongly support the Fröhlich's idea of electrodynamic activity of biological systems.

Mitochondrial function conditions physical processes in living cells. Mitochondria are unique organelles in the cell. Mitochondrial function is regulated by chemical messengers. But besides triggering the apoptosis by chemical means mitochondrial main role is not in chemical region. Mitochondria are the boundary organelles accepting chemical signals and building conditions for physical processes. Mitochondrial malfunction degrades physical processes in cells. Physical links along the cancer transformation pathway should be studied and specified.

There are several important directions for the future research. Experimental research of in vivo and in vitro electrodynamic fields of living cells or cellular structures (for instance microtubules) is possible due to development of nanotechnology. The total turnover of power of a cell may be of the order of magnitude about 10^{-13} W. This value of the turnover of power was measured on yeast cells (Lamprecht[66]). A similar amount of power may be supplied for excitation of electrodynamic oscillations (for instance, non utilized energy liberated from mitochondria). Taking into account efficiency of conversion of random supply to coherent oscillations, number of microtubules in the cell and power distribution in particular frequency spectral lines, the power exciting individual microtubule spectral line may be of about 10^{-17} W. For a high quality factor the maximum power stored in the oscillating microtubule may be of about 10^{-15} W. But the measurement system may significantly damp the oscillation system and change its frequency spectrum. The electrodynamic oscillations may be measured at a patch of linear dimension smaller than about 1 μm corresponding to the microtubule binding spot at the inner side of the membrane (Kučera *et al.*[67]). Measurement should be performed at the physiological temperature of living cells. In vitro measurements of microtubules should disclose parameters for assessment of their electrodynamic characteristics.

Theoretical research should explain the main conditions for water ordering around mitochondria and its characteristic properties, generation of coherent electrodynamic field by microtubules, interaction in the biological system through the electrodynamic field, creation of a general quantum theory of coherence in biological systems, and–very likely–development of a novel non-linear quantum (electrodynamic dynamic field) theory for biological systems.

Important point concerns convergence of classical biology and biochemistry with a novel biological physics. Further research should bridge a gap between the chemical and genetic processes on the one hand and physical ones on the other hand. Understanding of biological activity and cancer transformation pathway requires conversion of both parts. Biochemical, genetic, and physical mechanisms are mutually dependent and equally important. A more sophisticated model of biological activity should be built.

Important part of cancer transformation is a special case of physical processes in living cells and their theoretical and experimental investigation. Mitochondrial dysfunction featured by decreased proton pumping from the matrix space results in fundamentally disturbed electrodynamic field in cancer cells (Pokorný *et al.*[18]). Diminished power and coherence of the electrodynamic field may be the most pronounced difference between the healthy and the cancer cells in the clinical phase. Therefore, mitochondria and physical processes should be targeted for cancer treatment. The standard therapeutic strategy is based on cancer cell killing. But such treatment may also damage healthy cells and limits its further application to treatment of recurrent tumors. The therapeutic strategy may be first of all based on restoration of normal cell function. For instance, opening the pyruvate pathway in mitochondria by inhibition the PDK restores mitochondrial normal function and unlocks the apoptotic pathway. The physical processes in the cell and the cell itself are reversed to normal operation. Consequently, if the cell system is damaged too much then apoptosis is triggered. Targeting mitochondria acts in the region of the main differences between healthy and cancer cells.

VIII. CONCLUSIONS

Cooperation of mitochondria and microtubules is a unique phenomenon in living cells. Mitochondria are multifunctional organelles controlled by chemical and genetic signals and providing conditions for physical mechanisms. Mitochondria pump protons across the inner membrane,

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produce ATP and GTP, and liberate the non-utilized energy. Protons pumped from the matrix space cause water ordering, formation of the zone of a strong static electric field in the cytosol, and the proton space charge layer.

Microtubules may generate electrodynamic field providing fundamental biological functions. The strong electric field conditions non-linear interactions. Damping of microtubule oscillations by organized water is very low. Liberation of non-utilized energy from mitochondria supplies energy for oscillation.

Mitochondria dysfunction in cancer cells may cause increased damping of microtubule oscillations, diminished energy supply, and shift the non-linear properties towards linear region. Power and coherence of the generated electrodynamic field is diminished.

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