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Chapter 10
Cellular electrodynamics in kHz–THz region

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Abstract: We review here theories and evidence of a cellular electrodynamic field in the kHz–THz region and its biological relevance. The endogenous cellular electrodynamic field has been predicted to contribute to the organization within the cell and to interactions among the cells. Any cellular pulsed or oscillatory process, which involves electrically charged or electrically polar molecular structure, generates an electrodynamic field. Energy supply to and low damping of an oscillatory process are necessary conditions for generation of a field, which is of higher intensity than the field of thermal origin. We describe cellular processes, which can give rise to an electrodynamic field in the kHz–THz spectral region and are likely to be fulfilling necessary conditions of energy supply and low damping. Our focus is on microtubule electromechanical vibrations, but also electronic conduction processes in DNA and proteins in general are briefly reviewed. We also review and assess experimental works aiming to detect cellular radiofrequency fields directly or indirectly. We conclude that evidence for the necessary physical conditions for cellular electrodynamic field is accumulating. However, there is still little direct experimental evidence for kHz–THz electrodynamic field of nonexcitable cells. We believe that near future can bring significant progress in this research field if appropriate cutting edge technologies in detection techniques are used.

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1. Introduction

Biological phenomena that cannot be reduced to direct chemical "contact" interaction between molecular partners have always either attracted attention of some scientists or scared off and discouraged others due to an apparent taste of mystery as was the case, *e.g.*, in the field of bioelectricity and electrophysiology (Geddes and Hoff, 1971; Cajavilca *et al.*, 2009). However, a rigorous scientific description of bioelectric phenomena became possible with the conceptual and technological progress enabling the clarification of physical processes underlying electrophysiology. Nowadays, the existence of electric activity of cells is well accepted; its biological importance in case of electro-excitable cells is indisputable, *e.g.,* for nerve and muscle cells of higher organisms. In addition, these electrophysiological phenomena are observed and studied for frequencies of a few kHz (Buzsaki *et al.*, 1992; Collins *et al.*, 2001) and are not expected to exist at higher frequencies (> 1–10 kHz).

Yet, let us imagine, on the one hand, a physicist who knows that the electromagnetic field on Earth (also due to cosmic radiation) displays much broader frequency spectra (see, *e.g.,* in Chapter 2 of this book). He may ask whether biological systems that evolved on Earth generate an electromagnetic field of a broader frequency range, say in kHz–THz region, than the one which is in intense focus of current electrophysiology? A biologist, on the other hand, might want to know whether such frequencies – assuming they exist – have a function, *i.e.* are of biological relevance. Could such cellular electromagnetic fields explain biological phenomena, which we either had overlooked or neglected because we considered them as artifacts since they did not fit into our concepts? The latter being, for example, interactions between bio-molecules that are faster and occur over larger distances than allowed by the classical model of diffusion-based distribution of molecules. Furthermore, if there was evidence - from at least a small number of experiments – for a high frequency biological electromagnetic field, we would like to know about the structures and processes that generate these cellular electromagnetic fields.

Electromagnetic fields are physical quantities directly measurable via their force effects. Therefore, using the proper technology, experimental evidence for cellular electrodynamic fields can be obtained[1]. This chapter

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[1] There is no strict difference between the terms electromagnetic and electrodynamic fields. With the prefix bio-, a term bioelectromagnetism is used to denote endogenous electromagnetic fields of biological systems. Yet, again, literature on bioelectromagnetism almost exclusively deals with low frequency fields (< kHz), while we stress the high frequency fields (> kHz). One can find in literature both terms bioelectrodynam-

summarizes the foundation for cellular kHz–THz electrodynamics. It thereby focuses also on the cellular origin of the field.

2. Why to research cellular electrodynamic fields

The working hypothesis of several authors is that the endogenous cellular electrodynamic field has an organizing function within cells and mediates interactions between cells.

2.1. Role of fields in intracellular processes

The role of the endogenous cellular electrodynamic field has been predicted as (i) transporting reaction components and (ii) driving the kinetics of chemical reactions (Pokorný *et al.*, 2005b,a; Pokorný, 2001). The theory on the cellular field, furthermore, predicts that certain cellular structures create spatially and dynamically complex patterns (local minima and maxima of field intensity) of the electrodynamic field (Cifra *et al.*, 2010; Havelka *et al.*, 2011; Cifra *et al.*, 2011b). This inhomogenous electric field pattern acts by force on molecules adding a deterministic component to their diffusion movement and thereby helping to organize the movement of the reaction components (Pokorný *et al.*, 2005b,a; Pokorný, 2001). In addition, the spatial and temporal organization of larger structures of the cell, *i.e.* the positioning of organelles and macromolecules) can be influenced by the electrodynamic field in ways similar to those described above (Cifra, 2012). Note that the recruiting of molecular reaction partners by long-range electrodynamic interactions has already been predicted by Fröhlich (Fröhlich, 1968b, 1972, 1970), later on again by van Zandt (Van Zandt, 1978) and recently re-assessed (Preto *et al.*, 2012). Furthermore, electrodynamic processes are assumed to play a significant role in cellular signaling (Priel *et al.*, 2005, 2006) as well as energy transfer (Cope, 1973). Finally, some researchers suggest that the disturbance of the endogenous cellular electrodynamic processes plays an important role in cancer (Pokorný, 2012).

2.2. Role of fields in intercellular processes

Multiple authors have performed experiments that show effects at distances that were not predicted by a molecule-based diffusion model.

One class of experiments relates to the so-called dielectrophoretic effect of cells on surrounding particles. This was extensively investigated by Pohl *et al.* (Pohl, 1980b,a, 1981; Roy *et al.*, 1981; Pohl *et al.*, 1981;

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ics or cellular electrodynamics, the former being more general without scale limitations and the latter limited to the scale of the cells.

Pohl, 1982, 1983; Rivera *et al.*, 1985). In this effect, cells are attracting or repulsing micron sized dielectric particles. To test these assumptions, Pohl *et al.* were changing (i) the conductivity of the medium, (ii) the dielectric constant of the particles, or they were (iii) switching off the metabolism of the cells. They concluded that the observed changes in movement of the particles around individual tester cells were caused by an oscillating electric field that is, furthermore, generated in accordance to the metabolic activity of the cells.

Another class of theories and experiments was focused on electromagnetic force interaction between cells. Based on the assumption of Fröhlich's coherent electric oscillations generated by cells, Pokorný theoretically analyzed, the mutual attraction of cells (Pokorný, 1980; Pokorný *et al.*, 1983; Pokorný and Wu, 1998). His results suggested that cells should be able to interact electromagnetically (attract or repulse) up to the distance of 10 micrometers. There were also several experimental tests carried out on leukocyte sedimentation rate and adherence (Jandová *et al.*, 1987). Sedimentation rate of cells and measured force between the cells and glass slides substrate coincided with theoretical predictions of adherent force based on cellular electrodynamic activity. Most famous are the results of Rowlands *et al.* who observed that roleaux formation of erythrocytes does not simply follow Brownian laws of motion. It was suggested that the cellular electrodynamic fields generated as described by the theory of Fröhlich gives a plausible explanation for this complex group of cellular interactions (Rowlands, 1983; Rowlands *et al.*, 1981, 1982; Sewchand and Rowlands, 1983). Fröhlich predicted in his theory that coherent electric oscillations of biosystems mediate mutual long-range (on cellular/ molecular scale) resonance-like attraction. However, one has to be careful about experimental details and interpretation of the results.

Many experiments on electrodynamic cellular interactions were performed with a focus on the optical field of cells of many species (see Table 2. in (Cifra *et al.*, 2011a) or Ch. 8 in this book). There are, indeed, strong indications that the cells are able to interact through their endogenous photon emission under certain conditions. However, this refers to frequencies in the visible and UV region while here we focus on frequency ranges of microwaves and below.

To summarize this section, there are many interesting theoretical predictions and experimental observations that take into account the cellular electrodynamic field. Moreover, some of the observations can be hardly explained without assumption of non-chemical interaction that acts over distance. Nevertheless, it needs to be emphasized again that one has to be very careful about experimental details and interpretation of the results as various other non-field-like physicochemical phenomena can contribute to the observed results.

3. Which structures and processes generate the cellular electromagnetic field

3.1. Basis of electromagnetic field generation

All objects, whether living or nonliving, are continuously generating electromagnetic fields due to the thermal agitation of the particles that possess charge. The thereby generated electromagnetic spectrum is described by Planck's law for the ideal case of a blackbody in thermal equilibrium. Electromagnetic fields generated thermally have a random, non-coherent character. However, our question is whether the electromagnetic field of a biological entity is an electromagnetic field generated by an object due to its temperature or whether it is part of a biological property of a living system.

Physically, living biological systems are thermodynamic systems in a non-equilibrium state (*i.e.*, they have a different energy level than their surrounding) and they are open (*i.e.*, they can transfer energy and matter through the system). Such systems may locally decrease entropy (increase order). Since living systems are not in a thermal equilibrium, their electromagnetic (or generally, vibrational) spectrum may also deviate from thermal spectrum given by Planck's law. Furthermore, the important question is whether the generated biological electrodynamic fields can have a coherent component, since coherence enables very efficient energy and information transfer via the spatial and dynamic formation of interference patterns. The answer may be at least partially elucidated when we describe the structures and processes that are responsible for the generation of the cellular electrodynamic fields.

3.2. Basis for cellular electrodynamic field generation

Various cell functions are associated with moving charges in cellular compartments and, hence, generate electrodynamic fields. For example, membrane depolarization or neuron firing at several hundred Hz (Buzsaki *et al.*, 1992) generates oscillations of electric charges with higher harmonics creating an electric oscillations with a frequency up to 10 kHz (Collins *et al.*, 2001). However, this phenomenon is limited to a group of specialized cells in higher organisms and not all cells in an organism are involved in the process of membrane depolarization. The question arises whether non-specialized cells that are not involved in cell membrane depolarization are also capable of generating electrodynamic fields, and if so how. A graphical summary of our working model for the generation of the cellular electrodynamic field is depicted in Figure 1.

Generally we can distinguish three types of processes generating electrodynamic fields in cells:

- Mechanical vibrations of electrically polar structures (proteins) (kHz–THz)

- Free ionic oscillation (Hz–MHz)
- Electronic oscillations (Hz–THz)

Additionally, in combination these processes can form quasiparticles[2].

The above list of types of processes generating electrodynamic fields delivers the physically reasonable conceptual boundaries where to look for the realization of these processes in cells. As such, there may be multiple sources of cellular electrodynamic field finally combining into a spectrally and spatially complex total field. Yet, some general necessary conditions need to be fulfilled in order to generate nontrivial cellular electrodynamic fields:

- Energy supply
- Low damping of the oscillatory process: The term Quality factor (Q) is also often used in this context. Q is inversely proportional to the damping rate. If the damping is high, supplied energy quickly dissipates into all degrees of freedom, i.e. the system is heated up and the generated electrodynamic field is only thermal with very broadband frequency content.

3.2.1 Mechanical vibrations of electrically polar structures

The most straightforward (mechanistic) approach explaining the generation of the cellular electrodynamic field is based on vibrations of electrically polar biomolecular cellular structures. Such vibrations and modes of biomolecules are broadly studied by multiple types of spectroscopies (Barth, 2007; Chou, 1988; Painter *et al.*, 1982) and, hence are today widely acknowledged. It is not surprising that it was concluded that the frequency of vibrations depends on both the size and stiffness of the structure and the type of vibrational mode(s), since this is very well known from macroscopic physics.

Probable structures that lead to the appearance of a cellular field are the intrinsic electrically polar structures such as most proteins (Wada and Nakamura, 1981; Wada *et al.*, 1985; Nakamura and Wada, 1985)) or membranes. Membranes are electrically polarized due to different electric potentials generated by the presence of ions of opposite charge on both sides.

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[2] The real elementary particles, which are present in matter and relevant on biological scale are electrons, protons and neutrons. Yet, quasiparticles are emergent phenomena that occur in complex nanoscale systems and behave as if the systems contained (fictional) particles. Contrary to modeling with coupled elementary particle types, the theoretical work with quasiparticles is very useful since both, the mathematical formalism and the physical understanding significantly simplify the description of field-related phenomena (but limited only to those).

To summarize, the basic idea is that the metabolic energy induces vibrations in electrically polar molecules, which, in turn, then generate a cellular electrodynamic field. The following section reviews the most important works that can be categorized under this idea.

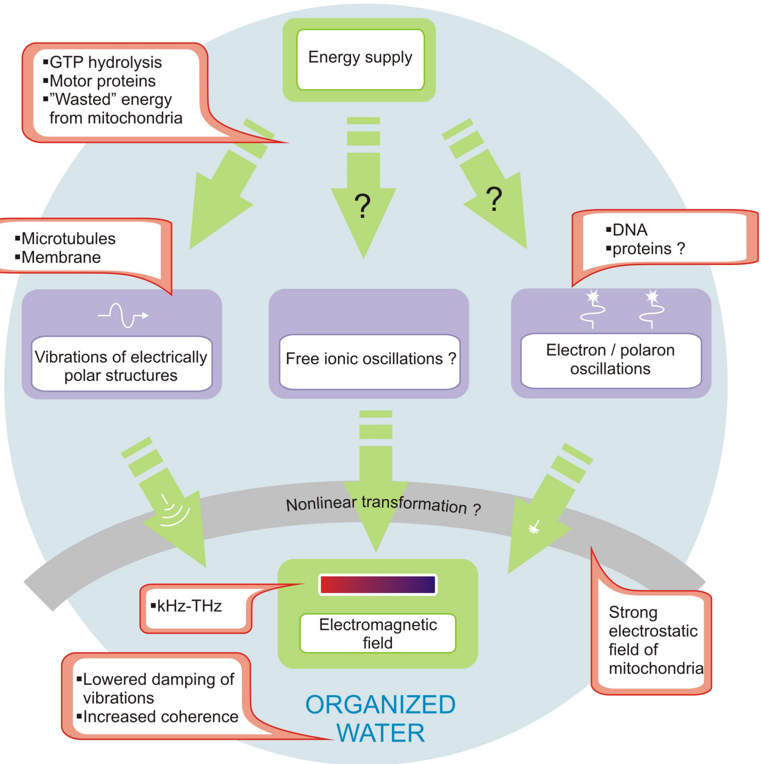

Figure 1. Working model of the generation of a cellular electrodynamic field. Vibrational (phonons – heat) energy from several metabolic sources is supplied to microtubules and membranes to excite their electrically polar vibrations. These vibrations are expected to work in nonlinear regime (*e.g.* due to strong static electric field from mitochondria) which allows for energy exchange among frequencies (vibration modes) and other properties – see text. Organized water surrounding biological structures is expected to cause lowered damping, thus increased coherence, of the vibration modes compared to bulk water. Frequencies of the biological electrically polar vibrations and of thereby generated electromagnetic field are most likely lying in the range kHz–THz.

Free ions within the cell and electrons/polarons in biomolecules are able to oscillate in kHz–THz region (up to only MHz for ions). However, the mechanism of how the metabolic energy can excite oscillations of biomolecular electrons/polarons and free ions in these frequency regions haven't been analyzed yet.

Fröhlich's theory

In 1968, Herbert Fröhlich postulated that biological systems exhibit coherent longitudinal[3] vibrations of electrically polar structures (Fröhlich, 1968a,b, 1969). In order to fit into the Fröhlich's model, a system has to fulfill the following necessary conditions:

- electric polarity
- vibration modes in radiofrequency / THz region
- sufficient energy supply
- nonlinearity

Electrically polar structures contain electric charges. When they vibrate, they become able to generate electrodynamic fields. The original Fröhlich model was general and as such did not limit this process to any particular cellular structure. From his model it follows that when the energy supply exceeds a critical level, then the polar structure will enter a condition in which a steady state of nonlinear vibration is reached. This would, furthermore, result in energy storage of highly (coherent) ordered fashion in single or few degrees of freedom. This order expresses itself in a long-range phase correlation, which is physically similar to superconductivity and superfluidity, where the behavior of particles is communal and inseparable. The energy source in this model is metabolic energy, and the nonlinearity[4] of the vibrating system is caused by a strong static electric field. The existence of very strong static electric fields in the cell membrane led Fröhlich to consider cellular membranes as the source of the postulated vibrations.

Fröhlich's model created much enthusiasm in the scientific community. Based on his theory, it was predicted that the biomolecular elctrodynamic field would appear in the range of 100 to 1000 GHz. While some researchers

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[3] Longitudinal vibration modes in matter have been considered by Fröhlich (1969), because they don't lose energy by radiation (at least in bulk matter) in contrast to transversal vibrational modes as is well known in solid state physics.

[4] A nonlinear system is one that does not satisfy the superposition principle, or one whose output is not directly proportional to its input. In the context of Fröhlich's model it is important note that nonlinearity enables transfer of energy between various frequencies, which is not possible in linear systems. In Fröhlich model, nonlinearity enables channeling (condensation) of energy into one or few modes (frequencies).

used Raman spectroscopy to probe for vibrations in the predicted frequency region and reported results apparently confirming the nonthermal vibrations predicted by Fröhlich (Webb *et al.*, 1977; Webb, 1980; Drissler and Santo, 1983; Drissler and MacFarlane, 1978; Del Giudice *et al.*, 1985), others criticized these results as being an artifact (Layne *et al.*, 1985; Layne and Bigio, 1986; Furia and Gandhi, 1984, 1985; Cooper and Amer, 1983). Ever since its appearance, Fröhlich's model continued to inspire studies and models that were addressing his original theory (for review see (Fröhlich and Kremer, 1983; Fröhlich, 1988; Pokorný and Wu, 1998; Cifra *et al.*, 2011a; Reimers *et al.*, 2009)). Even though highly skeptical authors (Reimers *et al.*, 2009) admit to a certain extent the feasibility of his theory, it is not widely accepted that processes as described in Fröhlich's model are really happening in living cells. This is so because the available experimental evidence from studies with biological systems is controversial.

Anyone interested in a good and brief description of Fröhlich's theory may read the article (Šrobár, 2012a) where the model is explained in a clear and exact language.

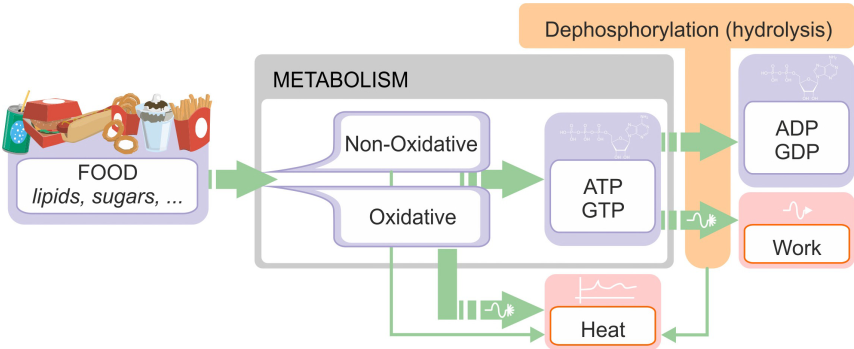

Figure 2. Transformation of food to energy which can (i) perform work (via ATP), *e.g.*, in terms of protein motion, (ii) induce vibrations and (iii) heat. Note that heat can be also understood as a broad frequency spectrum of vibrations and, further, that oxidative metabolism includes mitochondria-dependent heat generation.

Microtubules

After the discovery of the cytoskeleton in 1970s, microtubules (MTs) became a serious candidate for being sources of cellular electrodynamic fields. This was due to the fact that MTs fulfill the requirements needed for a Fröhlich system and to generate of electrodynamic fields. Nowadays, microtubules are considered not the only possible candidates but most probable and most widely studied ones.

Microtubule structure and electric polarity

MTs have a well-known and accepted structure, composed of tubulin heterodimer subunits that are electrically highly polar (Mershin *et al*., 2004; Tuszynski *et al*., 2002). MTs resemble hollow tubes (Dustin, 1984) whose growth (driven by tubulin polymerization) is nucleated by centrosomes or other microtubule organizing centers. The electric polarity of tubulin heterodimer was predicted from its atomic structure (Mershin *et al*., 2004; Tuszynski *et al*., 2002) and was also probed in several experiments (Mershin *et al*., 2004; Schuessler *et al*., 2003; Böhm *et al*., 2005).

Energy supply to microtubules

MTs in vivo are characterized by their perpetual alternation between growth (tubulin polymerization) and shrinking (MT depolymerization). This dynamic instability results from a constant influx of energy via the assembly and then followed by the disassembly of GTP rich tubulin heterodimer subunits (Caplow *et al*., 1994; Caplow, 1995; Caplow and Shanks, 1996). A further energy supply to MT vibration is assumed to come as a fraction of energy used for the movement of motor proteins aligned with MTs. Finally, the energy that is dissipated from mitochondria may also translate into vibrational MT-movement resulting in the generation of an electrodynamic field (Pokorný *et al*., 2008; Cifra *et al*., 2010). Mitochondrial ATP production by the citric acid cycle has an efficiency of ca. 40%. The remainder of the energy usually dissipates as infrared vibrations as well as infrared and optical (Hideg *et al*., 1991) radiation. In short, the efflux of energy from the mitochondria represents the most significant source of energy which may lead to the excitation of MT vibrations. The amounts of energy generated by the above-mentioned processes are well described in the literature. The open question is if this energy can actually excite vibrations of microtubules or other structures without immediate dissipation into heat.

Nonlinearity of microtubule vibrational dynamics

Mitochondria were also found to be sources of strong static electric fields, namely in the range of 10^6 V/m, presumably due to the creation of a proton gradient. This static electric field of mitochondria penetrates up to a few micrometers into the cytosol (Tyner *et al*., 2007). At first sight, this is a controversial finding because in ionic solutions the static electric field should be effectively screened by counterions within few Debye lengths, *i.e.* a few nanometers. Yet, some authors argue (Tyner *et al*., 2007) that the simple ionic solution is not a proper model for intracellular water and, instead that a complex fluid and gel-like model where the ion-mobility is hampered reflects experimental reports much better (Zheng and Pollack, 2003; Zheng *et al*., 2006; Pollack *et al*., 2006).

Most interesting here is the regularly found alignment of mitochondria along MTs. It is expected that the vicinity of the two structures combined with their electric properties lead to nonlinear electrodynamics of MT (Šrobár, 2009; Šrobár, 2012b) as the strong electrostatic fields of mitochondria shifts the vibrations of the microtubules to a nonlinear regime. It is the nonlinear regime in Fröhlich's theory that enables the excitation of polar vibrations of molecules above their thermal level so that an electrodynamic field around them can be generated.

Vibrations of microtubule and their damping

Microtubules are theoretically predicted to display collective vibrations in the regions between kHz and GHz (10^3–10^9 Hz) region (Sirenko *et al*., 1996; Gu *et al*., 2009; Wang *et al*., 2009; Deriu *et al*., 2010). The excitation of MT vibrations were the mainstay of the model that was proposed by Pokorný (Pokorný *et al*., 1997; Pokorný 1999; Pokorný *et al*., 1998) who analyzed the longitudinal vibrations with slip boundary conditions: he concluded from his calculations that vibrations of microtubule should not be not overdamped.

Some scientists raised doubts about the possibility of his theory because they assumed that a viscous cytosol should dampen any vibrating cytosolic organelles (Foster and Baish, 2000; Adair, 2002). The cytosol could have a dampening effect on organelle vibrations if there was a ”no-slip” boundary condition between cellular structure and the surrounding cytosol. However, it was argued (Pokorný , 2003, 2005) that lowered mobility of ions in the cytosol results in a ”slip” between microtubules, their adjacent ionic layers and the cytosol, making microtubule vibrations in the cytosol physically plausible. Even though there are further arguments for the plausibility of underdamped microtubule vibrations in vivo (Pokorný *et al*., 2011) the actual quality factor of microtubule vibration modes remains still an open question demanding careful spectroscopic studies. Only two pioneering published experimental studies on microtubule vibration are currently available, but none of them deliver an estimation of the quality factor of MT oscillations from measured data (Hameroff *et al*., 1986; Pizzi *et al*., 2011).

To conclude this review about the feasibility of microtubule oscillations, the very interesting findings of A. Bandyopadhyay on microtubules should be mentioned. His team performed recent experiments, which go beyond the study of vibrational properties of microtubules and include also electronic properties, which are more generally described in subsection 3.2.3. His results suggests that microtubules manifest (i) resonant-like response of DC conduction to specific applied radiofrequencies (ii) Fröhlich-like condensation (iii) coherent radiofrequency emission after pumping with radiofrequency signal and other intriguing features (see Bandyopadhyay, 2011, 2012; Sahu *et al.*, 2013a,b).,

Vibrations of other cellular structures

Technically, any cellular structure or substructure can oscillate at its resonance frequency – eigenfrequency when excited by energy unless strongly damped. For example, Smith calculated that a spherical cellular membrane has a mechanic resonance frequency of 10^{10} Hz (10 GHz) (perpendicular to the membrane surface) and a mechanical circumferential resonant frequency of 10^{8} Hz (100 MHz) (parallel to the membrane surface); the electromagnetic resonance of the cell membrane (again parallel to the membrane surface) occurs at a frequency of 10^{13} Hz (10 THz) (Jafary-Asl and Smith, 1983).

Weak resonances in the region around 36-38 GHz have also been detected on erythrocyte ghosts in suspension (Blinowska *et al.*, 1985). This result has been attributed to the vibration modes of the cell membrane which roughly fit the prediction of Smith (Jafary-Asl and Smith, 1983).

3.2.2. Ionic oscillations

An electrochemical model was proposed by Pohl where he suggested that electrodynamic fields can be generated within the cells by the coupling of oscillating chemical reactions with physically mobile ions, finally leading to charge waves (Pohl *et al.*, 1981; Pohl, 1982). In his model, the oscillations of ions can be induced by chemical reactions, where the direction of oscillations will be steered by filamentous cellular structures. Pohl's model for the generation of cellular electrodynamic oscillations has not been developed further. Since many types of chemical reactions generate also sound emission with spectra up to 1 MHz (Betteridge *et al.*, 1981; Wentzell and Wade, 1989), oscillatory chemical processes up to this frequency cannot be excluded. However, the current author does not know about the existence of periodic high frequency chemical oscillations that come from biologically relevant models.

3.2.3. Electronic oscillations

One of the necessary conditions for kHz - THz electronic oscillations in biomolecules is their electronic conductivity. One biomolecule that is known to conduct electrons is DNA (Fink and Schönenberger, 1999; Abdalla, 2011). One speaks (for DNA) of a so-called phonon assisted conductivity attributed to polarons (Conwell and Rakhmanova, 2000; Endres *et al.*, 2004; Henderson *et al.*, 1999), which are quasiparticles that involve charge (here electron) and associated deformation of the lattice (cloud of phonons). The DNA polaron-based conductivity is now a widely and intensively studied scientific field. Due to these conductive properties, a collective of authors labels DNA as an antenna for electromagnetic fields (Blank and Goodman, 2011).

While proteins were for a long time generally accepted to be non-conducting (Kertesz *et al.*, 1977), some theoretical predictions propose conduction or semiconduction to occur in them (Szent-Gyorgyi, 1941; Cope, 1973). Indeed, there is strong current evidence that metaloproteins enable enhanced electron transfer (Gray and Winkler, 2005). It has also been shown that aromatic amino acids, such as tryptophan, promote electron conduction (Shih *et al.*, 2008). There is, furthermore, a very recent example of semiconduction of a metal-reducing bacterial polypeptide named geopilin (Reguera *et al.*, 2005; Veazey *et al.*, 2011; Feliciano *et al.*, 2012) found in several types of bacteria (Gorby *et al.*, 2006), which led the authors to propose that conductive bacterial polypeptide nanowires represent a common bacterial strategy for efficient electron transfer and energy distribution.

The other theory of biological charge conduction and electrodynamic generation relates to electrosoliton[5]. Electrosolitons can be viewed as a quasiparticles involving electrons that could provide transport of charge in biological systems and were considered as an important contender of electrodynamic field generation in the microwave frequency region (Brizhik and Eremko, 2003; Brizhik, 2003; Brizhik and Eremko, 2001; Musumeci *et al.*, 2003). These works have been inspired by a seminal work of Davydov who theoretically predicted the existence of solitons in proteins, α-helixes (Davydov, 1979), although his idea was originally dealing with soliton of zero total charge (exciton). Physically, there is a tight relation between electrosoliton and polaron (Brizhik and Eremko, 2003), because they both involve charge and interact with lattice vibrations (phonons). However, for a soliton to appear, non-linear interactions within the lattice have to occur (Cantu Ros *et al.*, 2011). Although other types of solitons (optical, water waves) are perfectly accepted to exist and their properties are being technically exploited in physics, there is still no clear direct and broadly accepted experimental evidence for Davydovs solitons or electrosolitons to exist in biological systems (Austin *et al.*, 2009) and there are ongoing theoretical debates whether it can exist at all (Lomdahl and Kerr, 1985; Xiao, 1998).

Studies in this subsection indicate feasibility of electron conduction in biomolecules. Polaron conductivity is well accepted in DNA and is an ongoing research question in the case of proteins. However, the further two fundamental questions remain for the feasibility of electronic oscillations in biomolecules:

- How can the metabolic energy input result in collective excitation of electron/polaron oscillations? Could such oscillations, give rise to an electrodynamic field

[5] An electrosoliton is an electrical counterpart of a soliton. Soliton is a self-reinforcing solitary wave (a wave packet or pulse) that maintains its shape while it propagates.

- Do electron/polaron oscillations exhibit lower damping than electrically polar vibration states (as mentioned in section 3.2.1)?

4. Experimental evidence for cellular electrodynamic fields

There is an accumulating evidence for the necessary conditions for generation of cellular electrodynamic field as described in section 3.2. However, apart from various indirect evidence there exist just several pioneering works on direct experimental detection of cellular electrodynamic activity.

4.1. Indirect cellular EMF detection by dielectrophoresis

An electric oscillation can be detected indirectly using a technique called dielectrophoresis (DEP) (Pohl, 1978). In this technique, electric oscillations are detected as effects of a non-uniform electric field on a neutral particle via a polarization force. One of the pioneers in measuring cellular electrodynamic fields using the DEP method was Herbert A. Pohl (Pohl, 1980b,a, 1981; Roy *et al.*, 1981; Pohl *et al.*, 1981; Pohl, 1982, 1983; Rivera *et al.*, 1985). In the DEP method, the electric field induces a dipole moment in sample particles and the resulting force acting on them is the force of an electric field on a dipole. Since Pohl used small particles of a few micrometers in size to probe cellular electric oscillations, he often used the term "micro-DEP" (μ-DEP). In this method, particles were either repelled from or attracted to the surface of cells depending on whether particles had a lower dielectric constant ($BaSO_4$, SiO_2, Al_2O_3) or higher dielectric constant ($BaTiO_3$, $SrTiO_3$, $NaNbO_3$) than the suspending medium, which was usually water-based. Pohl estimated that the frequencies of cellular electrical oscillations were in the radiofrequency range (5 kHz to 9 MHz) (Pohl, 1980b; Pollock and Pohl, 1988). In his experiments, he tested several types of cells such as bacteria, fungi, algae, nematodes and mammalian cells, all of which showed, under suitable conditions, a dielectrophoretic effect interpreted to be caused by a cellular electrodynamic field (Pollock and Pohl, 1988). Other investigators reported similar findings for diverse cell types including human leukocytes (Pohl and Lamprecht, 1985; Hölzel, 1990, 2001; Pokorný, 1990; Jandová *et al.*, 1987).

4.2. Indirect experimental evidence for cellular kHz–GHz oscillations through effects of external fields

There is large body of experimental work (a few hundreds) on the external electromagnetic field resonance effects on (at specific frequencies) biological systems, (for a review see Cifra *et al.*, 2011a; Belyaev, 2005a,b). Especially Russian authors (Betskii *et al.*, 2000; Devyatkov, 1973) interpreted these results as a proof of internal cellular electrically polar vibrations being affected by external fields. The idea was that such resonant effects are possible only if there are structures in the cell which are able to vibrate with high quality factor at the same frequencies as those applied externally, *i.e.* resonate. Their following argumentation was that if there is a cellular structure able to resonate (oscillate) with an external electromagnetic field, then it is able to generate electromagnetic oscillations under the condition that (metabolic) energy is supplied, see Golant, 1989a,b and Devyatkov *et al.*, 1991, p.66 for original Russian texts and Golant (1994); Betskii *et al.* (2000) for English texts. However, the resonant biological effects of electromagnetic fields can also be explained by other, though more complex, mechanisms such as (i) influence of field on triplet free radical chemistry (Keilmann, 1986), (ii) hydrodynamic flow due to inhomogeneous surface heating of the water-like biological samples (Khizhnyak and Ziskin, 1996) and due to hypothesised oscillations of water molecule polymers (Sinitsyn *et al.* (2000)).

4.3. Direct electronic detection

Already some work aimed at the direct electronic detection of electrodynamic cellular signals has been done (Table 4.3). The first direct evidence for electrodynamic field generation in the spectral region of kHz–GHz by cells was attempted to be obtained in a series of experiments that used direct electronic detection from a single cell or a suspension of cells. Using a spectrum analyzer, Jafary-Asl and Smith claimed to find electrodynamic signals emitted from *Saccharomyces cervisiae* in the range of 7–80 MHz (Jafary-Asl and Smith, 1983; Del Giudice *et al.*, 1989). Later on Rivera and Pohl (Pohl and Pollock, 1986) detected a spectrum of signals from the alga *Netrium digitus* with peaks around 7 and 33 kHz. But Hölzel who extensively analyzed the frequencies of different groups of cells in the MHz region (Hölzel, 1990; Hölzel and Lamprecht, 1995, 1994; Hölzel, 2001) disagreed with Jafary-Asl and Smith claiming that the frequencies they had reported were mainly artifacts probably due to a positive feedback coupling in the amplifier. However, with improvement in detection techniques other researchers claimed to successfully detect cellular electrodynamic fields, *e.g.*, during the process of mitosis of yeast cells, in MHz region (Jelínek *et al.*, 1999, 1996; Pokorný *et al.*, 2001).

Organism	**Frequency or wavelength**	**References**
Netrium Digitus (Algae)	7 kHz, 33 kHz	(Pohl and Pollock, 1986)
Saccharomyces cerevisiae (yeast)	0.4–1.6 kHz	(Jelínek *et al.*, 2009; Cifra, 2009)
	1, 7, 50 (60)–80 MHz	(Jafary-Asl and Smith, 1983; Del Giudice al., 1989)
	8-9, 8.2 MHz	(Jelínek *et al.*, 1999, 1996; Pokorný *et al.*, 2001)
	1.5, 2.6, 5.7, 18, 52 MHz	(Hölzel, 1990; Hölzel and Lamprecht, 1995, 1994; Hölzel, 2001)
	42 GHz (attempts only, not considered significant)	(Jelínek *et al.*, 2002, 2005, 2007; Kučera, 2006)
Schizosaccharomyces Pombe (yeast)	3.1, 4.8 MHz	(Hölzel, 1990; Hölzel and Lamprecht, 1995, 1994; Hölzel, 2001)
frog gastrocnemius muscle (electrically stimulated)	0.2–2 mm	(Gebbie and Miller, 1997)
electrically stimulated nerve from blue crab *Callinectes sapidus*	3–10 μm	(Fraser and Frey, 1968)

Table 1. Direct electronic detection of electrodynamic cellular signals up to the THz region. Indirect detection of cellular electrodynamic fields, for instance by its dieletrophoretic effect, is not included.

Statistical analysis revealed four peaks in detected power during the mitosis. It was suggested that these peaks of the cellular electrodynamic activity can be related to the microtubules reassembling into the mitotic spindle, with binding of chromatids to kinetochore microtubules, and with elongation of mitotic spindles during anaphase A and B (Pokorný *et al.*, 2001). Experiments aimed at the detection of cellular electrodynamic activity in the region around 42 GHz (Jelínek *et al.*, 2002, 2005, 2007; Kučera, 2006) has been carried out with very limited success.

A recent review (Kučera *et al.*, 2010) elucidates reasons for the limited success of experiments on the direct electronic detection of cellular electrodynamic field. Practically all hitherto used measurement systems haven't fulfilled at least some necessary technical requirements which stem from identified and predicted biophysical properties of cellular electrodynamic sources. Such technical requirements include mainly nanoscopic resolution of sensor and suitable input electrical characteristics of preamplifiers. This was caused by the ignorance of the early authors on the one hand and also by technological limits of that time on the other hand.

5. Conclusion

The research of high frequency (kHz–THz) cellular electrodynamics has a 40 years long history. As the initial enthusiasm to seriously test early theories has been hindered by technological limitations, this research field had a rather slow scientific evolution. Yet, current technology together with basic physical concepts allowed identification of cellular structures and processes that could give rise to a cellular electrodynamic field. What is needed now is to establish if there is really any nontrivial specific role, *i.e.* the biological relevance of cellular and biomolecular electrodynamics. As electrodynamic fields do have the property to act on charged structures and as exactly such charged structures cause these fields, we can assume that there exists a feedback system between the charged structures and the field. This, however, is of great significance because it induces the possibility of an electrodynamic contribution to the organisation of molecular cell processes. We see several experimental indications that biological electrodynamic fields may mediate the interaction among biomolecules and biosystems. However, the development of bioelectro-dynamics bears also a new understanding of physical interactions in biology presumably not only for the smallest scale of biomolecules but up to the scale of multicellular organisms.

Finally, if the hypotheses of a) underdamped electronic/electrically polar mechanical oscillations in microtubules and other biomolecules, which would be measureable with new generation of sensors and b) the biological significance of these oscillations in biomolecular reaction rate and *e.g.* further in mitosis or cell adherence will be confirmed, the future applications of bioelectrodynamics could lead to the controlled development of new non-invasive diagnostic methods and therapies based on electromagnetic fields and modification of biomolecules, the substrate of endogenous biological electrodynamic fields.

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