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Chapter 1

The evolution of the biological field concept

Antonios Tzambazakis

Institute of Anatomy and Clinical Morphology, Department of Human Medicine, Faculty of Health, Witten/Herdecke University, Alfred-Herrhausen-Straße 50, 58448 Witten, Germany

Abstract: The dialogue with Nature about Time and Change has pointed to the functional synthesis of linearity with non-linearity since the times of Epicurus. The modern concepts of Quantum Coherence, Self-Organization, Deterministic Chaos and Reciprocal Causality in biology, also suggest an integration of linearity with non-linearity, of molecular with field aspects. In this review, we discuss the theories and experimental evidence on the existence, the role and the properties of a biological field, following the arrow of time in a scientific perspective that unites being with becoming, and particles with fields.

Correspondence/Reprint request: Dr. Antonios Tzambazakis, Institute of Anatomy and Clinical Morphology Department of Human Medicine, Faculty of Health, Universitat Witten/Herdecke, Alfred-Herrhausen-Straße 50 58448 Witten, Germany. E-mail: exangelus@hotmail.com

1. Introduction

Alexander Gurwitsch introduced for the first time the field concept into biology in 1912 (Gurwitsch, 1912). Gurwitsch tried to solve the biological problem of morphogenesis, and since chemical reactions do not contain spatial or temporal patterns a priori, he looked for a "morphogenetic field" as a supracellular dynamic law embracing all three levels of biological organization – molecular, cellular and morphological (Lipkind, 2006).

In 1923, Gurwitsch evidenced the existence of ultraviolet mitogenic rays able to stimulate cell division in onion roots (Gurwitsch, 1923). Numerous replications of experiments confirmed the existence of "mitogenetic" radiation, a term given by Gurwitsch. Such phenomena of weak bioluminescence were later on termed Ultra-weak Photon Emission (UPE) or Biophotons in modern bioelectromagnetic field theories.

The key influence to Gurwitsch can be traced to his friend and physicist Leonid Mandelstamm, who explained to Gurwitsch the advances in physics which led to the formulation of his morphogenetic field theory (Beloussov, 1997).

The experimentalists of that era were under the influence of two primal explanatory concepts in conflict, preformism and epigenesis. Epigenesis originates from Aristotle (384 BC-322 BC) and preformism can be retraced to Hippocrates (460 BC-370 BC). Preformism and epigenesis were involved in the logical structure of the two main doctrines of developmental biology the former represented in the developmental mechanics founded by Wilhelm Roux in 1886 and the latter in modern vitalism founded by Hans Driesch in 1908 (Lipkind, 1992). While in Roux's "mosaic theory of development" all parts of the organism develop along predetermined pathways and without influencing each other, in Driesch's view the state of each part of the organism was dynamically co-determined by the neighboring parts and function was dependent on the position within the whole. The mechanistic/reductionist view of Roux (Roux, 1895) became dominant with genetic determinism. In 1926, Thomas Hunt Morgan had formally separated genetics from embryology (Morgan, 1926), while Morgan's student Theodosius Dobzhansky redefined evolution as changes in gene frequency (Dobzhansky, 1937), giving rise to the modern evolutionary synthesis (Mayr, 2001) and to gene-centered views of evolution (Dawkins, 1976). However, recent discoveries in molecular biology revealed that the target of selection is the phenotype and not individual genes, since mutations and genetic recombinations occur in the context of all the constraints exerted on the organism, including those of the environment, where cooperativity may be as important as competition (Margulis and Sagan, 2002, Noble 2010). Vitalistic views faded out, but can still be found in such works as of Alistair Hardy (Hardy, 1965) that consider consciousness-related aspects of evolution.

The common functioning principle in the controversy between preformism and epigenesis or mechanism and vitalism is that they are both teleological linear concepts, since the pathways of development are predetermined towards an end, either by the action of vital or mechanical factors following the top-down or the bottom-up causal chain respectively. In the history of science, the controversy between mechanism and vitalism is also reflected in the argument between particle and field theories (Jammer 1980/81, Bischof 1995). The linear view of a changeless guiding principle underlies these controversies.

The pathway beyond linearity has its roots in the dilemma among being and becoming, expressed for the first time in the history of philosophy as the dilemma of Epicurus (342–270 BC). Hellenistic Philosophers believed that Philosophy, however technical and theoretical it may become, serves the interests of human happiness. If we understand the universe and its work-

ings, they urged, we may more easily find a way to live in accordance with nature (Shields, 2003). The dilemma among the changing world of Heraclitus (535–475 BC) and the changeless world of Parmenides (5th century BC), led Epicurus to extend the deterministic atom theory of Democritus (460–370 BC), and postulate that as atoms move through the void they clash and "swerve" from their otherwise determined paths and initiate new causal chains, providing indeterminism and novelty in the constantly changing material world, as also a basis for free will.

However, the first suggestion providing a physical mechanism for stochastic phenomena based on a vectorizing natural principle, appeared with Darwin's theory of biological evolution, which integrated necessity with chance, the determinism of adaptation with the indeterminism of varying conditions. Darwin's concept of evolution by means of Natural Selection (Darwin, 1859) provided a mechanism able to explain the evolution of structural changes observed in nature, and connected life through the arrow of time.

The biological field theory of Gurwitsch reflects a further conceptual shift from the linear view of particle-field dichotomy to a non-linear view of particle-field interactions, evident in the last version of his theory and the conception of Non Equilibrium Molecular Constellations, that can be considered as a the earliest formulation of the "dissipative structures" as described in modern self-organization theory (Nicolis and Prigogine, 1977). The concept of living organisms as non-equilibrium (open) systems proposed by Gurwitsch, suggested that living order exists in a state of non-equilibricity due to the action of biological fields (Gurwitsch 1923).

Cooperative non-linear interactions are fundamental elements in modern biological field theories. Linearity is based on the absence of interactions among the parts of a system which latter is therefore determined by its initial conditions only and thus the whole can be reduced to its parts. Nonlinearity implies evolution and novelty as inherent properties of a system which parts are in constant dynamical interaction, thus not determined by initial conditions, and whose description cannot be deduced from the properties of its elements alone. The importance of interactions has gained considerable attention in self-organization and system biology approaches of the organism that consider reciprocal causality - simultaneous top-down and bottomup causal chains - through feedback control mechanisms among the whole and the parts of the organism (Gilbert and Sarkar 2000, Noble, 2006, Longo, 2012), taking into account the need for integration of epigenetic processes involved in gene regulation, and even non-genetic informational pathways as higher levels of cellular control (Strohman, 1997, Steele, 1998, Jablonka and Lamb, 2005). In addition to upward causation, cellular and tissue events i.e. physical/mechanical stresses occurring, may act reciprocally but also downwardly modifying the expression of these genes at a later time

(Farge, 2003). Cancer can also result from altered chemical and physical interactions as a tissue-level phenomenon (Maffini et al., 2004), and this view of cancer, contrary to its mutation-centered counterpart, explains the fact that cancerous cells reverse their "malignant" properties when placed within normal tissues (Bussard et.al, 2010).

Reciprocal causality is also evident in the approach of Gurwitsch focusing on the *cooperative nonlinear interactions* among molecules and field as elementary for the establishment of biological order. Gurwitsch suggested that the biological field is produced by the developing body itself and regarded the molecules as the objects of field action, he defined the field as a factor vectorizing a certain part of molecular excitation energy and stated that "the field is somehow associated with the molecules of chromatin, but only when they are chemically active" (Gurwitsch, 1944).

2. Historical development of theoretical concepts and experimental investigations

2.1 Biological field concepts

The debate among Roux and Driesch stimulated the development of organismic biology and the concept of the biological field. The morphogenetic field of Gurwitsch gained support by Ross Harrison in 1918 (Harrison, 1918), and by Hans Spemann's "field of organization" in 1921 (Spemann, 1921). The organismic school tried to bridge biochemistry and morphology (Bischof, 2003), inspired the research for "organizer substances", "gradient fields", as also for "organizing principles", with corresponding research carried out by Ross Harrison, Charles Child, Paul Weiss (Weiss 1939), Joseph Needham (Needham, 1950), and Conrad Waddington (Waddington, 1957). The organismic view has led to systems biology that takes account complexity, emerging properties, multi-level functionality and reciprocal (top-down and bottom-up) causality, identified in the works of Claude Bernard, Ludwig Bertalanffy, Robert Rosen, Brian Goodwin, Scott Gilbert (Gilbert and Sarkar, 2000), and Denis Noble (Noble, 2006). In accordance to such views, Goodwin (Goodwin and Webster, 1982) as also Gilbert (Gilbert et al., 1996), have proposed a feedback loop between morphogenetic fields and gene activity.

2.2 Biophysical field concepts

Although the first to introduce the field concept into biology, Gurwitsch did not share the same views with the organicists, and introduced the idea of a field of force "Kraftfeld", as a supracellular ordering principle corresponding to "spatial but immaterial factors of morphogenesis" (Beloussov, 1997). Scheminzky was the first to describe a cellular electromagnetic field (EMF) for the visible spectrum (Scheminzky, 1916) fol-

lowed by the consecutive discovery of an EMF in the UV region (Ludwig. 1918, De Fazi, 1924). Independently, Gurwitsch did experiments with onion roots (Gurwitsch, 1923) and observed the involvement of UV emission triggering cell divisions suggesting the existence of a form of cellular radiation of an electromagnetic nature, which he termed "mitogenetic radiation". This study of Gurwitsch was the first to suggest that the emanation of light is not an incidental property of cells but might have relevance to signaling, and for this he was repeatedly nominated for Nobel Prize among 1923-1938. Gurwitsch and his colleagues used prisms for spectrum analysis and biological detectors (yeast cell cultures) for measurement of mitogenetic radiation (Gurwitsch and Gurwitsch, 1959). They found "finger-print" spectra for several enzymatic reactions and noticed spectral changes in light emission from cells following physiological changes. The apparent involvement of molecular events in these processes of mitogenetic radiation convinced Gurwitsch for the existence of collective states of molecules that he termed Non Equilibrium Molecular Constellations (NEMC), the first postulation of "cooperative phenomena" as the basis of life processes (Bischof, 2003). The NEMC's indicated the presence of vectorial factors within cells, and thus Gurwitsch saw the mitogenetic rays as indirectly related to morphogenetic fields (Beloussov, 2012).

Inspired by Gurwitsch's work, mitogenetic research from several independent laboratories in Europe and USA gave rise to hundreds of papers, several books and dozens of reviews in the 1920s and 1930s (Beloussov 1997, Cifra 2009). Gurwitsch's work was supported by many Russian and Western workers but in view of the contradictory results obtained with biological detectors, some researchers introduced physical detectors such as the photographic plate and the UV-sensitive Geiger tube (Rajewsky, 1931, Siebert and Seffert, 1933, Audubert, 1938). Unfortunately, despite confirmation of his results by the later Nobel laureate D. Gabor, the scientific community forgot Gurwitsch's work since the results using physical detectors were as variable as those obtained with biological detectors.

2.3 Early bioelectromagnetic field concepts

However, mainly based on electrophysiological experimental work, some early proposals of bioelectromagnetic field concepts were made by Keller (1918), Laville (1925), Lakhovsky (1929), Burr (1935), Crile (1936), Lund (1947), Becker (1961), and Reich (Reich, 1948). Lakhovsky was the first to use high-frequency EM fields to treat cancer, with his multiple wave oscillator generating the whole spectrum frequencies from 750 KHz and up to the visible spectrum of 300 THz (Lakhovsky, 1929). The conclusions of Lund, based on decades of work in bioelectric potentials of plants and animals, are in line with Harold Saxton Burr who postulated that "the pattern of organization of any biological system is es-

tablished by a complex electrodynamic field, which is in part determined by its atomic physicochemical components, and which in part determines the behavior and orientation of those components" (Burr et al., 1935, Burr, 1972).

Only after World War II, when the invention of the photomultiplier tube (PMT) became available to biomedical researchers, the very sensitive and reliable PMT measurements proved the existence of cell radiation beyond any doubt (Bischof, 1998). The PMT allowed direct measurement of very small quantities of emitted light in the visible spectrum. The first PMT studies involved photon emission from green plants, including three species of algae, following irradiation with visible light (Strehler and Arnold, 1951). In 1954 Colli and Facchini (Colli and Facchini, 1954, Colli et al., 1955) detected weak visible region (400-700 nm) luminescence from seeds germinating in the dark. Only few of the mitogenetic researchers maintained that the organism acts as an emitter and receiver of electromagnetic frequencies for its regulation and structuring. In this tradition are the biologists Kaznacheev, Dombrovskii and Inyushin. In the 1960s several Russian groups headed by Tarusov, Konev, Vladimirov, Zhuravlev, and also other groups, studied the visible region luminescence from many plant and animal species. Zhuravlev and Seliger published the first working hypothesis for the Ultraweak Photon Emission from biological systems, the "Imperfection Theory", theorizing that UPE is produced as a result of metabolic "imperfections" based on the recombination of free radicals which are mostly oxidative chemical by-products. Koney was the first to employ the UV-sensitive PM tube to detect UV photon emission from living organisms. Konev's group by 1969 had already studied over 100 different species of organisms covering eight systematic types, including 13 algae, 9 yeast and 8 bacterial species (Koney, 1966, Ruth, 1979).

2.4 Modern bioelectromagnetic field concepts

The accumulation of experimental evidence led to the breakthrough of modern bioelectromagnetic field theories in 1970, stimulated by Alexander Presman's review on the work of Soviet bioelectromagnetics researchers (Presman, 1970). A number of developments that contributed to the modern bioelectromagnetic field theories include the concepts of non-equilibrium thermodynamics, negative entropy, self-organization, dissipative structures, biological coherence, and advanced quantum optics such as non-classical light and cavity quantum electrodynamics.

2.4.1 Non-equilibrium thermodynamics

The introduction of the concept of living organisms as thermodynamically open non-equilibrium systems can be traced to Gurwitsch, Bauer, Vernadsky, and Bertalanffy. It was extended with the concept of negative entropy introduced by Schrödinger, further developed by Gyorgyi, and mathemati-

cally formalized by Prigogine (Prigogine, 1947). Schrödinger maintained that living organisms preserve their high order by transferring entropy (low-organized energy) to the external world, while they feed on negative entropy (highly-organized energy) from the environment (Schrödinger, 1944), and Gyorgyi incorporated the negentropy concept in his theories on the excitation/de-excitation dynamics and the role of charge transfer in the organism (Szent-Gyorgyi, 1957).

2.4.2 Self-organization and coherence

The concepts of Coherence and Self-organization established a sufficient theoretical basis able to integrate molecular and field aspects. At the International Conference "From Theoretical physics to Biology" at Versailles (Marois, 1969), Ilya Prigogine introduced his theory of dissipative coherent structures (1977 Nobel Prize in Chemistry), while Herbert Fröhlich introduced his theory of biological coherence. The proposal that living organisms are open systems able to "self-organize" under energy flow explained how biological systems use nutrition as an external pump to establish a stable state far from equilibrium, similarly to the Bénard convection cells or the (optically pumped) laser. In both cases, critical energy supply to one or a few collective modes of vibration results in a phase transition to a large-scale dynamic order in which all the molecules or atoms in the system move coherently, dominated by just a few degrees of freedom, while the non-thermal storage and stabilization of the modes lift the system to a stable state far from equilibrium.

2.4.3 Dissipative structures

Prigogine explained self-organization processes on the basis of non-linear thermodynamics (Prigogine, 1945, Nicolis and Prigogine, 1977), where the flows of irreversible processes are non-linear functions of the thermodynamic forces (temperature, chemical concentration gradients). Non-linear thermodynamics, explained life phenomena such as the emergence of novelties, and the increase of complexity, on the basis of evolutionary "branching points", where the dynamical instability of the system rising at a threshold distance far from equilibrium, gives rise to an unpredictable and thus irreversible process of selection among a variety of stable modes of system function through the amplification of appropriate fluctuations, leading to the formation of dissipative structures. A dissipative system or structure is characterized by the spontaneous breaking of spatial and temporal symmetry, and the formation of complex structures in which, above a critical value, certain fluctuations are amplified and give rise to mesoscopic and macroscopic long-range supramolecular correlations among the interacting particles. The amplification of fluctuations results from feedback processes giving rise to coherent phenomena, such as the coupling between non-linear oscillators that could be biochemical oscilla-

tors, electromagnetic field and resonating biomolecular structures etc. gene regulation for example, in the bacterium E.coli the lac genes are organized into an operon, a part of the bacterial genome. The lac operon synthesizes certain enzymes for metabolizing lactose to glucose, and which enzymes are affecting the transcription rate of lac operon exerting positive and negative feedback on their own synthesis. Thus, since products feedback on reactants, spatial symmetry breaks among them, and provides the capacity for selection towards various stable states of lactose and glucose distribution. The transition from the non-induced state to the induced state of oscillatory (periodic) enzyme synthesis and vice versa, breaks the temporal symmetry and is an allor-none phenomenon that depends on threshold values of various constraints such as the lactose and glucose average concentration levels in the cell. Above threshold values, feedback among the lac genes and their corresponding enzymes amplify positively or negatively the concentrations of lactose and glucose (amplification of fluctuations) providing self-regulation of the lactoseglucose metabolic pathway. Since the more complex a system is, the more are the types of fluctuations that put in danger its stability, and the expansion of communication (feedbacks, resonances) among system parts brings stability, it seems that evolution towards higher complexity is based on an antithesis among stability through communication and instability through fluctuations, which antithesis also determines the threshold of stability/sensitivity of the system. Prigogine pointed that the origin of life may be related to successive instabilities giving rise to successive amplifications that have led to a state of matter of increasing coherence (Prigogine, 1980), a concept later formalized as expansion of coherent states (Popp. 1992).

2.4.4 Coherent excitations

The concepts of non-equilibricity and cooperativity were extended from the molecular level into the domain of bioelectromagnetics with Fröhlich's concept of coherent excitations. According to Fröhlich, biological coherence results from long-range quantum mechanical phase correlations of the electromagnetic fields coupled to coherently excited particles in living systems (Fröhlich, 1968). Biological macromolecules act as collectively vibrating electric dipoles, forming an oscillating system in nonlinear interaction with a heat bath (essentially cell water and ions suspended in it). Spontaneous coherence arises through: (i) a critical supply of metabolic energy that allows the strong excitation of coherent longitudinal electric modes (of these macromolecules) which are stabilized by elastic deformations based on electron-phonon autocatalytic non-linear couplings, combined with (ii) non-linear supply of spectral energy where the energy fed into the branch of longitudinal electric modes gets channeled into one or a few vibration modes, finally leading to the establishment of coherent excitations, i.e. coherent oscillation states. Fröhlich suggested that biomolecular EMFs between 100-1000 GHz can originate from the strong fluctuations of the 10^5 V/cm electric field produced by the cellular membrane. Fröhlich's model was supported i.e. by the detection of non-thermal cellular radiation concerning the 0.3–10 µm IR (Fraser and Frey, 1968) and the 0.2–2 mm radiowave range (Gebbie and Miller, 1997), and by the so-called *rouleaux formation* of erythrocytes (Rowlands et al., 1981, Rowlands, 1982, Sewchand and Rowlands, 1983) where the adherence of equally charged cells can be satisfactorily explained only by a coupling of coherently oscillating cells.

2.4.5 Cancer and loss of coherence

Fröhlich formulated later a related hypothesis (Fröhlich, 1988) wherein he deduced that the state of cancer is due to the loss of coherence and can possibly be restored by external irradiation with the correct resonant frequency, which was in fact supported from research on non-thermal biological effects of electromagnetic radiation by Webb (Webb et al., 1968, Webb et al., 1969) and Devyatkov (Devyatkov, 1973). Additional evidence came, on the one hand, from biophoton research claiming loss of coherence in cancer (as compared to healthy) cells (Schamhart et al., 1987, Scholz et al., 1988, Popp, 2009) and, on the other hand, from the application of Microwave Resonance Therapy (MRT)/ Extremely High Frequency Therapy (EHF) (Kositsky et al., 2001, Hyland, 2008) aiming to restore coherence (Sitko et al., 1994, Grubnik et al., 1998, Giuliani and Soffritti, 2010). Recent evidence revealed amplitude-modulated radiofrequencies to exhibit a tumor-specific resonant action that blocks the tumor growth by affecting gene expression and disrupting the mitotic spindle of cancer cells (Barbault et al., 2009, Costa et al., 2011, Zimmerman et al. 2012). These forms of non-invasive cancer therapy obviously can be linked with cancer diagnostics based on biophotons being an interesting cell characteristic for assessing the health state.

2.4.6 The cell membrane as source of cellular EMF generation

Many research groups were inspired by Fröhlich's suggestions (Cifra et al., 2011) trying to address the topic of coherently oscillating cell membranes, e.g. the model of EMF generation postulated by Devyatkov and coworkers (Devyatkov, 1973, Betskii et.al., 1988) is based on acoustic-electrical waves that exhibit a millimeter EM radiative component. Further, spectroscopic detection of cell membrane vibrational states report mechanical oscillations in the region of a few hundreds of Hz (Piga et al., 2007, Hargas et al., 2008, Koniar et al., 2009) as well as in the region of GHz (using Brillouin spectroscopy) and THz (using Raman spectroscopy) (Webb, 1980, Drissler and Santo, 1983, Del Giudice et al., 1985).

2.4.7 The microtubule theory of cellular EMF generation

The microtubule model postulated by Jiri Pokorny is based on the capability of cellular microtubules for generation of coherent oscillations in the region from 1 kHz to 100 GHz (Pokorný et al., 1997, Gu et al., 2009, Havelka et al., 2011). The electromagnetic field measured at living cells is assumed to be generated by non-linear elastic-electrical oscillations in microtubules, and mitochondria provide the main conditions for generation of coherent electrodynamic field by microtubules: (i) energy supply (ATP, GTP, liberation of non-utilized energy), (ii) strong static electric field able to shift microtubule oscillations into highly non-linear region, (iii) low damping of these oscillations through the formation of an ordered water layer around mitochondria. According to this model, cancer develops as a result of mitochondrial dysfunction (Warburg-effect), associated to suppression of the oxidative production of ATP and GTP (which plays an important role in the regulation of cell division) and its replacement by fermentative one, preceding the biochemical and genetic alterations taking place in the cancer transformation pathway. As a consequence, there is a decreased level of water ordering linked to damping of microtubule oscillations, and the power and coherence of the generated electrodynamic field are diminished (Pokorny et al., 2012). Supporting evidence concern detection of cellular electromagnetic field in the KHz-MHz region (Hölzel, 2001, Jelínek et al., 2009, Cifra, 2009), in the GHz region (Jelínek et al. 2005, 2007, Kucera, 2006), during cell mitosis (Jelínek et al., 1996, 1999), during cell replication phases (Pokorny et.al, 2001), mitochondrial ROS production as source of UPE (Hideg et al., 1991, Cadenas et al., 1980, Creath, 2008), mitochondria as source of near-IR EMFs (Albrecht-Buehler, 2000, Tuszynski and Dixon, 2001), and cancer diagnosis based on damping of microtubule oscillations (Pokorny, 2011).

2.4.8 The emanation from equilibrium

Both, the amplification of fluctuations (as proposed by Prigogine) and coherent excitations (as proposed by Fröhlich) suggest that living organisms are able to amplify very weak signals. Further, both concepts point to non-linear processes of autocatalysis able to account for signal amplification, decrease of entropy, and the creation and establishment of a stable state far from equilibrium. However, at the Versailles conference (Marois, 1969), Fröhlich had discussed with Prigogine that the thermodynamical approach, since it cannot distinguish between a living organism and a non-living system of equal entropy state, provides the necessary but not the sufficient condition to explain self-organization phenomena. Fröhlich pointed out that a sufficient concept should include a quantum mechanical approach to explain the emergence of self-organization which is the essential characteristic of life, by providing a selective organization principle that refers to a few degrees of freedom only

and, hence, is irrelevant to entropy. Recently, strong evidence has emerged that quantum coherence is playing an important role in photosynthesis (Engel et al., 2007, Collini et al., 2010, Panitchayangkoon et al., 2011), in bird navigation (Rodgers and Hore, 2009) and in the sense of smell (Franco et.al., 2011).

2.4.9 Biophoton Theory and DNA as source of cellular EMF generation

The investigation of the nature of non-linear processes able to account for the emanation from equilibrium came from concepts such as the "Biophoton Theory" developed by Fritz-Albert Popp. In the period after 1970, research on UPE continued from groups associated with Slawinski (Poland), Boveris (USA), Quickenden (Australia), Inaba (Japan), and Popp (Germany). But, while most researchers assigned to the Imperfection Theory, Popp based the phenomenon on the principle of coherence and introduced the term "biophoton" (Popp, 1976) to distinguish these ultra-weak signals from classical bioluminescence and to, further, indicate a biological quantum phenomenon with bio-informational character. Popp developed applications on medical diagnostics (Popp. 2007) and on food quality (Vogel et al., 1998), as well as models on biological evolution (Popp et.al., 1992). According to the Biophoton Theory (Popp et al., 2003), UPE originates from a delocalized coherent electromagnetic field of optically coupled emitters and absorbers, stabilized and operating at the laser threshold far from equilibrium in the sense of Prigogine's dissipative structures. The concept includes a "photon sucking" communication mechanism based on destructive interference by phase conjugation (Popp and Chang, 2000, Popp et al., 2007). Popp postulated a DNA laser-model being the main source of coherent ultraweak photon emission (Popp et al., 1979, Popp and Nagl, 1983). Electromagnetic and mechanical joint vibrations of photons and phonons in the DNA-lattice (DNA-polaritons) make it a perfect candidate for absorption, storage, and emission of coherent photons (Popp and Nagl 1986, Li et al., 1990, Li, 1992). This hypothesis is not proved besides a few supporting indirect evidence (Rattemeyer et al., 1981, Popp et al., 1984). There is no direct evidence for coherent lightemission from DNA and there exist arguments concerning the mathematical deduction of coherence from Popp's experimental data (Salari and Brouder, 2011). Biophoton emission was detected in fractions of cells containing nuclei and DNA, but there was no emission in purified DNA, and neither in cell fractions containing cytosol, mitochondria, or ribosomes (Van Wijk et al., 1995, Van Wijk et al., 1997). However, studies on isolated nuclei revealed a light-induced UPE (Delayed Luminescence) of higher intensity than from whole cells, and point to the nucleus as a possible source of ultraweak photon emission (Niggli, 1996). Nevertheless, many experimental data are coming from the work of Popp and coworkers concerning UPE, from unicellular organisms to plants, animals and humans, in the IR, optical and

UV spectrum, on spontaneous and light-induced UPE (Multi-author review, 1988, Popp and Beloussov, 2003, Kobayashi 2009), detection of light-induced UPE as a tool for investigating coherence properties (Popp et al., 1993, Yan et al., 2005, Musumeci et al., 2005a), and for cancer diagnosis (Takeda et al., 2004, Musumeci et al., 2005b, Popp, 2009). Furthermore, in line with Popp's experimental evidence, there is a great abundance of data on non-chemical cellular electromagnetic interactions (Fels, 2009, reviews by Trushin, 2004 and Cifra, 2011).

2.4.10 The Electrosoliton theory of cellular EMF generation

Solitons sensu Davydov (Davydov, 1985) are nonlinear states of electrons or AMID-1 excitations of peptide groups, bound with local lattice deformation of macromolecules (electron-phonon coupling), which can propagate along macromolecules, such as DNA and polypeptides, in the form of electrosolitons and provide energy and charge transport in metabolic processes without energy dissipation over macroscopic distances. The propagation of electrosolitons is accompanied by coherent radiation of electromagnetic waves in the form of superposition of harmonics with multiple frequencies (Brizhik and Eremko, 2003, Brizhik, 2008, Scordino et al., 2010). An alternating electromagnetic field of characteristic frequency is created due to this radiation. The field frequency is determined by soliton velocity and the main harmonic is estimated at 1 THz, in agreement with Fröhlich's model (Fröhlich, 1988). The high-frequency alternating EMF of an electrosoliton affects electrosolitons in other chains. Due to the mutual influence via the emitted electromagnetic fields, electrosolitons tend to gain equal velocities. The longrange interaction among electrosolitons results in the dynamical synchronization of their motion and in the tuning of their radiation frequencies. Due to this fact, the radiation fields of electrosolitons become coherent, and the intensity of the total endogenous field is proportional to the number of electrosolitons. The bigger is the number of electrosolitons, the more intensive metabolic processes occur in a system. This synchronization has a selfregulating impact on the metabolic processes in a biosystem, and can also be stimulated by weak external EMF provided it has the frequency equal to the frequency of the endogenous EMF, constituting a plausible mechanism of microwave resonance therapy.

2.4.11 The Water Coherence Domains theory of cellular EMF generation

A major role of cellular water in generation of electronically excited EMF is proposed by the concept of Water Coherence Domains (Voeikov and Del Giudice, 2009, Del Giudice et al., 2010, Brizhik et al., 2011). Each photon coming out from the EMF background (thermal bath and quantum vacuum) can resonate with water molecules present in its volume, so that a pile up of photons occurs within the volume (Coherence Domain) giving rise to a size-

able EMF. At a given time Coherent Domains of Water oscillate at a given frequency attracting excited oscillating biomolecules able to resonate with the same frequency, and all molecules oscillate in phase with the self-trapped electromagnetic field. The attracted molecules react chemically among them and release energy in a non-thermal way through solitons, providing localized nonlinear charge transport and directionality to the supplied energy by "ratchet effect".

Evidence supporting the existence of water CDs (Zheng et al., 2006, Chai et al., 2009, Pollack et al., 2009) reveals that water near interfaces exhibits quite different properties than bulk water. Evidence on the key role of cellular water in generation of electronically excited EMF has been reported for various processes related to ROS production (Vaks et al., 1994) and studies on "water respiration" in bicarbonate solutions (Voeikov et al., 2010). Supporting studies from human body investigations claim an infrared detection (3.5-5 µm) of the soliton states of longitudinal water CDs that are formed in water layers bound along aligned collagen fibers in connective tissues (Brizhik et al., 2009). In addition, polarized light microscope studies revealed that living organisms can display colours as a function of the coherent motions and coherent alignment of interfacial water and the accompanying molecular dipoles existing in liquid crystal mesophases within the tissues (Ho, 1993). There are also reports assigning a main informational capacity to water and concern detection of low frequency electromagnetic signals produced by aqueous structures surrounding bacterial DNA sequences (Montagnier et al., 2009a, 2009b), also proposing the use of spectra from aqueous DNA solutions for diagnostic purposes (Giuliani et al., 2011).

2.4.12 Contributing concepts

Concepts that have contributed to modern biological field theories include the "bioplasma theory" postulated by Inyushin (Wolkowski, 1983), the physicochemical luminescence model of Slawinski (Multi-author review, 1988), and the electrochemical model of Pohl (Pohl, 1981, 1982). Supporting evidence of the Pohl model concern oscillating chemical reactions such as the Beloussov-Zhabotinski reaction (Voeikov et al., 2001a, 2001b, Epstein et al. 1996) and the indirect detection of cellular EMF radiation by dielectrophoresis (DEP) among 5 kHz–9 MHz (Pohl et al., 1985, Jandová et al., 1987, Holzel, 2001).

A morphogenetic field concept has been synthesized by Lev Beloussov, where the coherence of the field is based on the cooperativity of mechanoe-lectrical and photon-producing molecular/supramolecular machines that transform low-grade energy stored in chemical bonds, into high grade mechanical, electrical and photonic energy, reducing the number of freedom degrees of the liberated energy through autocatalytic feedback couplings between them, regulated by macroscopic order parameters such as mechani-

cal stresses, electrical fields and factors regulating UPE temporal regimes (Beloussov, 2011). Importantly also there are evidence which show that the order in biosystems influences the statistical and coherence properties of light-induced UPE (Yan et al., 2005, Budagovsky et al., 2002).

There are also some informational field models developed by Wolkowski, Laszlo, Rein, Pribram, Miller, Taylor, Bearden, Smith, Bohm, Tiller, and Ho (Bischof 1998, 2003), postulating biological effects of vector and scalar potentials mediating among the quantum vacuum and the quantum states of solid matter by controlling the phase of electromagnetic fields. Popp has also postulated that the property of "photon sucking" through destructive interference, is based on strong Casimir forces resulting from the interaction of vacuum fluctuations with rather narrow (local) vacuum states formed among double polarizable layers such as the DNA-helix or the cellmembrane (Popp et al., 1995).

Also significant for the integration of the models on cellular EMF generation in the kHz–GHz range with the models on UPE (visible and UV range), was the proposal by Swain and Popp for a mechanism of upconversion of photons in the range of GHz frequencies that, under certain nonlinear conditions, could give rise to visible photons (Swain, 2006, Popp, 2006, Swain, 2008).

3. Towards quantum biology

Judging from the overall picture, there is obviously no privileged causal level in biology, but cooperative interactions among the top-down and bottomup causal chains, field forces and physical/mechanical stresses that are working hand in hand with molecular events, a reciprocal causation among macroscopic, mesoscopic and microscopic levels, fields and molecules. One could suggest that an important step further in the development of the biological field concept, will need the integration and clarification of the main self-organization mechanisms that provide the network of nonlinear autocatalytic feedback couplings able to account for the system coherence-noncoherence transitions and the localized directional non-thermal charge transport processes. Necessary integration steps should involve a quantum field clarification of interactions among the main cell structures involved in generation of UPE and coherence e.g. mitochondria/microtubules, water, DNA, cytoplasmic membrane, and their participation in localized nonlinear charge transport processes (e.g. solitons) and in delocalized nonlinear information vector processes. It will be also necessary to experimentally clarify the phase coupling mechanism with the EMF background (heat bath and quantum vacuum).

A crucial step forwards will be the coupling of the field informational vectors to the molecular informational networks of the cell. The non-local

biophoton field seems to be coupled to various coherent and non-coherent states e.g. solitons, excitons, polaritons etc. but most of these interactions cannot be measured directly, since the only way of registering is the rough count outside of living material (Popp, 2002). Thus, an essential point of future studies should be the stimulus application of specific resonant frequencies and correlations with subsequent effects in molecular processes of cell regulation such as gene expression and metabolic interactions in multienzyme metabolic domains, that will need the combination of EMF application techniques like EHF/MRT technologies, with molecular techniques like genomics/ metabolomics/bioinformatics, as also far-field and near-field EMF detection techniques able to provide information on affected coherence properties of the system e.g. through assess of spectral distribution parameters. Future experiments should also focus in the up-conversion (or downconversion) mechanisms among RF/MW, IR and visible/UV photons. The combination of various detection/stimulus technologies in different spectra will be essential.

As evidenced from the exponentially growing number of publications, research groups and conferences dedicated to the subject (Table 1), the biological field concept has evolved from the times of Gurwitsch following several routes and modulations as a result of the conceptual and technological scientific advances in the course of history until the modern era (Table 2), and has enriched Self-Organization Theory with the notion of Coherence, declaring that cooperativity, irreversibility and probability are intrinsic properties of Nature. These investigations represent a continuation of the dialogue about Time and Change, and provide an evolutionary view of Nature which goes beyond a mechanical timeless automaton as also beyond a meaningless random game, where biological processes no longer need to be based on the dichotomy between a transcendental controlling principle and a mechanically controlled inert organism.

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Detection method	Organism/ structure	EMF fre- quency/ wavelength	Phenomena/ effects	References
Biological detectors	onion roots, yeast cells, sea-urchin gastrula, (list not complete)	UV	cell cycle phases, enzymatic reactions, degradation radiation	reviews: Rahn (1936), Gurwitsch and Gurwitsch (1959), Ruth (1979)
Physical detectors: Photographic plate, UV-sensitive Geiger tube	yeast cells, onion roots, frog nerve excited nerve, (list not complete)	UV	various biochemical processes: yeast fermentation (list not complete)	Scheminzký (1916) Ludwig (1918) Siebert (1933) Audubert (1938) Rajewsky (1931)
Photomultipliers, Electron Multiplying CCD cameras	alga, yeast cells (list not complete)	RW/MW (kHz, MHz, GHz)	cellular EMF oscilla- tions, mechanical vibrations, EM reso- nance of cell mem- brane (list not complete)	Pohl and Pollock (1986), Jelínek et al. (2009), Cifra (2009) (list not complete)
	frog muscle	0.2–2 mm (IR/THz)	non-thermal radiation	Gebbie and Miller (1997)
	crab nerve	3–10 μm (IR)	non-thermal radiation	Fraser and Frey (1968)
	bacteria, seeds, organs, eggs, plants, fungi, mitochondria, erythrocytes, leucocytes, insects, vertebrates (list not complete)	IR, visible, UV	various phenomena concerning spontane- ous and photo-indu- ced UPE: UPE syn- chronization, UPE patterns during cell cycle phases (list not complete)	Multi-author review (1988, 1992, 2003, 2008) (list not complete)
Dielectrophore- sis	bacteria, mammalian cells, human leucocytes	5 kHz– 9 MHz	cellular EMF oscilla- tions, variations during mitosis (list not complete)	Pohl (1985), Pokorný (1990) (list not complete)
Spectroscopic techniques	mammalian cells, human liver, Escherichia coli (list not complete)	hundreds of Hz, THz	non-thermal mechanical vibra- tions, Raman shifts based on mechanical vibrations	Koniar et al.(2009), Del Giudice et al. (1985) (list not complete)
Electromagnet- ic distant inter- actions using: Photomultipli- ers, Barrier- method	mitochondria, ciliates, insects, vertebrates (list not complete)	IR, visible, UV	growth polarization, lipid peroxidation, proliferation (list not complete)	Galle et al. (1991), Fels (2009), Trushin (2004), Cifra (2011) (list not complete)
Effect of EMFs on biological systems using: EMF signal generators	yeast cells, plants, animals, humans (list not complete)	UV, RF, MW, spectral power density $10^{-6}-10^{-21}$ W/Hz	tumor growth inhibi- tion, analgesia, (list not complete)	Grubnik et.al. (1998), Costa et al. (2011), Zim- merman et.al. (2012) (list not complete)

 Table 1. Investigations of electromagnetic field properties of living systems.

Approach	Concept	Major concept authors - References to books and/or articles
Reciprocal causality	Biophysical field	Del Giudice E. et.al. (2010). Water dynamics at the root of metamorphosis in living organisms. Water 2, $566-586$.
		Brizhik L./Eremko A. (2003). Nonlinear model [] self-regulation of metabolic processes in biosystems, Electromagnetic Biology and Medicine 22:31-39
		Pokorny J. et.al. (1997). Vibrations in microtubules. Journal of Biological Physics 23, 171-179.
		Ho M.W. (1993). The Rainbow and the Worm. World Scientific
		Popp F.A. (1976). Biophotonen, Verlag für Medizin Dr. Ewald Fischer, Heidelberg
		Fröhlich H. (1968). Long-range coherence and energy storage in biological systems, International Journal of Quantum Chemistry Vol.2, pp.641-649.
		Gyorgyi A.S. (1957). Bioenergetics. Academic Press.
		Burr H.S./Northrop F. (1935). The electro-dynamic theory of life, Quarterly Review of Biology, Vol.10 pp.322-333.
		Gurwitsch A.G. (1912). Die Vererbung als Verwirklichungsvorgang, Biologisches Zentralblatt, vol. 32, no. 8, pp. 458-486.
	Self-organi- zation	Longo G. et.al. (2012). Is information a proper observable for biological organization? Progress in Biophysics and Molecular Biology 109, pp.108-114
		Karsenti E. (2008). Self-organization in cell biology: a brief history. Nature Review Molecular Cell Biology. Mar.9(3): 255-62
		Camazine S. et al. (2001). Self-Organization in Biological Systems. Princeton University Press.
		Ball P. (1999). The Self-Made Tapestry: Pattern Formation in Nature. Oxford University Press.
		Kauffman S. (1995). At Home in the Universe: The Search for Laws of Self- Organization and Complexity. Oxford University Press.
		Haken H./Graham R. (1971). Synergetik, Umschau in Wissenschaft und Technik Heft 6, p. 191
		Prigogine I./Nicolis G. (1967). On symmetry-breaking instabilities in dissipative systems. J. Chem. Phys. $46,3542-3550$.
	System theory	Soto A.M./Sonnenschein C. (2011). The tissue organization field theory of cancer. BioEssays $33,332\text{-}340.$
		Noble D. (2006). The music of life. Oxford University Press.
		Kirschner M./Gerhart J. (2005). The Plausibility of Life: Resolving Darwin's Dilem ma. Yale University Press.
		Gilbert S. et.al. (1996). Resynthesizing evolutionary and developmental biology. Dev. Biol. 173(2), 357–372
		Goodwin B./Webster G. (1982). The origin of species: a structuralist approach, Journal Social Biol. Struct. $5\ 15\!-\!47$
		Bertalanffy L.V. (1968). General System Theory. Braziller.
		Rosen R. (1968). A Means Toward a New Holism. Science 161(3836): 34–35
	Organicism, Holism, Morpho- genetic field	Waddington C. (1957). The Strategy of the Genes. Allen and Unwin.
		Needham J. (1950). Biochemistry and Morphogenesis. Cambridge University Press
		Weiss P. (1923). Naturwissen. 11, 669
		Spemann H. (1921). Die Erzeugung [] taeniatus. Roux Arch. Entwicklungsmech. Org. 48: 533–570
Top down causality	Vitalism	Hardy A. (1965). The Living Stream. Harper and Row. Driesch H. (1908). The Science and Philosophy of the Organism. The Gifford Lectures. Adam & Charles Black.
Bottom up causality	Reduction- ism	Dawkins R. (1976). The Selfish Gene. Oxford University Press.
		Dobzhansky T. (1937). Genetics and the Origin of Species, Columbia Univ. Press.
		Morgan T. H. (1926). The Theory of the Gene, Yale Univ. Press.
		Roux W. (1895). Einleitung. Roux's Arch. Entwicklungsmech.Org. 1, 1-42.

Table 2. Evolution of concepts on biological order and causality approach.

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