Mechanoelectrical and Photon-Generating Devices in Cells and Organisms: From Molecular Machines to Macroscopic Fields

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Abstract. The aim of this essay is to review what we know about the transformation of chemical energy into mechanical, electrical and photonic at the different scales of biological organization. We start from the “classical”, short-range mechanoelectrical protein machines emphasizing their capacity to slow down the rate of energy relaxation and to concentrate energy onto a restricted number of freedom degrees. Then we pass to the newly described “low entropy machines” and to the macroscopic electromechanical machines which create circuits of the organismal scales. At last, we come to photonic events, paying a special attention to their regular periodicity within several Hz range and to their relations with cytoskeletal structures and their developmental dynamics. We suggest, that this area of investigations should be related with the theory of self-organization and the notion of coherency.

Introduction
All the living beings are known to be far removed from thermodynamic equilibrium, using thus for their purposes and discharging into the outer space measurable amounts of mechanical, electrostatic and electromagnetic energy. Within several last decades a substantial progress was achieved in revealing molecular mechanisms, involved in the generation and transformations of these kinds of energy within a living matter. On the other hand, a simple question remains up to now unanswered – how these micromachines, having characteristic dimensions of about several nanometers and their own oscillations periods within $10^{11}$ Hz range integrate their activities for providing a coordinated behavior of macroscopic organisms whose linear and temporal dimensions are more than in dozen orders greater?

The aim of this essay is just to attract the interest of investigators to this fundamental problem, rather than to suggest its solution. We would like to start from bridging a gap between our knowledge of the molecular generators and transformers of energy and some biological and physical concepts dealing with macroscopic order in entire organisms. To these concepts belongs, on one hand, the idea of morphogenetic fields and, on the other, the self-organization theory (SOT). The concept of morphogenetic fields postulates that a developing organism is a system of position-dependent forces, regulated from the upper levels and molding successive embryonic shapes. Remarkably, a founder of this theory, Russian biologist Alexander Gurwitsch in his latest version regarded the molecules as the objects of field action, defining a field as a factor vectorizing a certain part of a molecular excitation energy [1]. This makes it reasonable to discuss the relations of this theory with a modern concept of so called protein-machines.

On the other hand, SOT is a well known and a perfectly elaborated theory using a qualitative analysis of non-linear differential equations for explaining how a new macroscopic scale can be generated on the basis of much more local interactions, possessing no linear scale at all [2]. Both morphogenetic field theory and a SOT, in spite of being originated quite independently from each other, became later on to a considerable extent converged.
Accordingly, we start from reviewing what is known about so called “protein machines”, that is, elementary transformers of the chemical potentials to mechanical, electrostatic and electromagnetic energy. We shall distinguish two types of such machines: individual protein molecules, creating the “classical”, or short range machines, and recently discovered low entropy machines, based upon a coherent behavior of large ensembles of water molecules. Then we shall describe electrical circuits in cells and entire embryos and show that they are extended up to the entire organisms scales and are tightly coupled with the patterns of mechanical stresses. Taking as example lower invertebrates, hydroid polyps, we demonstrate the role of electrical fields in orienting polarized growth.

Next, we come to the photonic events. Here we start from emphasizing the role of collective molecular interactions in photons generation. Passing then towards higher levels, we describe the existence of specific temporal patterns of photon emission with characteristic $10^0 - 10^2$ Hz range frequencies.

**Classical (short range) proteins-machines**

By text-book definitions [3] a protein machine consists of a molecule possessing ATPase activity, a fibril along which this molecule is translocated and a load which it transports. This definition fits such constructions as actomyosin and other microfilaments and microtubules associated motors, but it is too narrow and, most important, does not elucidate the basic physical principles of these devices. More broad definition embraces a wider class of the protein-machines, which transform non-vectorized chemical energy to a vectorized mechanical one, even if they do not bear any load and do not split ATP molecule at the given time moment. Several decades ago such devices got a remarkable name of “Brownian ratchets” [4] which meant that they transform chaotic (Brownian) molecular movement into a directed one. Actin microfilaments, pushing the leading edge of a crawling fibroblast, were often taken as an example. Subsequent investigations demonstrated however, that these “ratchets” are organized in much more complicated way as beforehand suggested. Most important role is played by a dimeric protein, formin, located at the +end of a double helical microfilament and oscillating with about 10 Hz rate between a screwed and relaxed state. As a result, the torsion energy of about 1 eV is periodically accumulated and discharged. This energy is equivalent to that released by splitting of about 10 ATP molecules. However, in this process no such splitting is taking place: by a model suggested [5] all what we have here is the exchange of elastic energy between formin and the adjacent microfilaments subunits, with some gain got due to establishment of hydrophobic bonds between the newly inserted actin subunits.

The main common feature of all the protein-machines is a considerable retardation of relaxation rate of the accumulated energy and enormous restriction (often up to one) in the numbers of freedom degrees onto which the relaxation is taking place [6-8]. At the same time, the amplitudes of the directed movements performed along the rested freedom degrees reach the characteristic dimensions of the machine itself (which is impossible in the case of man-made industrial machines). These properties are provided by a specific structure of protein macromolecules, which include:

- a relatively soft elastic spring accumulating energy in the form of elastic stresses. The spring consists of non-spiral parts and electrically charged groups;
- rigid “levers” which transmit stresses ($\alpha$-spirals);
- hinge joint-points, represented by small aminoacids, for example glycine;
- fixation points: hydrogen bonds, S-S- bonds.

The energy accumulated in elastic elements is estimated as $\approx 0.5$ eV per $5 \times 10^{-9}$ m (length of the element), while the lifetime of the metastable mechanically stressed states ranges between $10^6$ and $10^9$ s, which in about 15 orders exceeds the rates of self-frequencies of protein molecules ($10^{11} - 10^{12}$ s$^{-1}$)!

Thus, the main ones and tightly interconnected properties of the protein-machines are:

- very much retarded relaxations of accumulated elastic energy, producing quite large (in a macromolecular scale) and essentially vectorized shifts;
- coexistence and practical indivisibility of mechanical and electrostatic components, permitting
to define these machines as electro-mechanical.

Let us comment the latter point. The electrically charged groups (mostly negatively charged carbonyls
and positively charged aminoacids) contribute to the maintenance of mechanically stressed state of the
protein macromolecules. Same role should be played by the charged ligands, in particular ATP,
containing three negatively charged phosphate groups. Therefore, binding ATP to proteins should
increase electrostatic repulsion onto the latter’s surface and hence straighten the protein molecules,
supplying them by additional elastic energy. By Pollack [9] estimation the latter’s amount is twice as
great as that provided by ATP molecule splitting. Taking into consideration, that each next step of
practically all the signaling pathways is associated with phosphorylation of proteins, this kind of
molecular deformation should play a great, however up to now practically neglected role in cell
signaling.

Until now we were dealing with chemo-electro-mechanical transformers in the form of isolated
macromolecules (for example enzymes) acting in their immediate vicinity (non-exceeding the radii of
molecular interactions). Meanwhile, just discussed example of ATP-protein interactions led some
authors to postulate the existence of quite another class of machines, characterized by very much
extended ranges of action, including billions of uniformly oriented water molecules. These will be
described in the next section.

Low entropy machines.
In his “association-induction” theory Ling [10] points out that an ATP molecule adsorbed by a protein
is a powerful electron acceptor, reducing the electron density onto a protein surface within
considerable distances. As a consequence, “the liberated carboxyl groups start to absorb \( K^+ \) while \( NH^- \)
and \( CO^- \) groups liberated from participating in creating secondary structures become to interact with
water, forming a multilayer structure consisting of polarized and uniformly oriented water structures”
[10].

This is one among several scenarios of the low entropy water domains formation. As theoretically
predicted ([11, 12]; see also this volume), if the density of any ensemble of microscopic particles
exceeds a certain threshold, the particles start to oscillate in a coherent way. Such “coherent water
domains” (CWD) may extend up to 100 nm and consist of about \( 10^7 \) water molecules which oscillate
with \( 10^{11} \) Hz frequency. Due to a high degree of order, CWD are the areas of very low entropy and are
thus able to absorb non-coherent (heat) energy from the surrounding bulk water and transform it into a
“high grade” coherent one. Noteworthy, CWD absorb light in the infrared and UV spectral regions.
The absorbed energy may reach 12, 06 eV which is only \( \approx 0.5 \) eV lower than the energy of water
ionization. In other words, CWD possess a substantial amount of free or almost free electrons, which
results in the electrical potential difference between CWD and bulk water. In such a way, low entropy
areas are real machines, producing electrical energy. Also, they are similar to the above described
macromolecular machines (as well as to the photonic machines to be described below) by providing a
long life time for exciting electrons. Moreover, these machines are postulated to produce direct
mechanical effects by bringing together the molecules oscillating in unison with each other.

What might be a biological role of such machines and, in particular, of a coherent state of water
domains? This is as yet non-answered question of a basic importance. Del Giudice et al speculate [11],
that such a state is important for providing an extreme temperature stability within the living systems,
an avoidance of Joule effects during ions traffic and, most important, a precise meeting of the partner
molecules during enzymatic reactions. It is worth mentioning in this respect, that already several
decades ago the Russian genetic Josef Rapoport, a discoverer of the chemical mutagens, as discussing
why genetic reproduction is so precise, came to the idea that “genetic material” should have a capacity
to be in a low entropy state under room temperatures. He emphasized also a high correlation of
mutagenic effects of chemical substances with their dipole moments [13]. (Strange as it may look today, by the urgent requests of a couple of outstanding Russia scientists, including a Nobel prizer Igor Tamm, the entire first edition of Rapoport’s book was destroyed, because the author’s suggestions “contradicted firmly established physical laws”! Significantly, several years before same arguments were used for rejecting the first B.P. Belousov paper about periodic chemical reaction, so famous in the near future).

A sensitivity of the living matter to microwaves can be also associated with the presence of CWD [12]. Here we are confronted with a rare for biology situation where theoretical predictions are ahead of experimenting; this is a challenge to the lab biologists to make everything possible for exploring the role of low entropy machines, because this can revolutionize the entire image of cell biology.

**Macroscopic electrical circuits and their coupling with morphomechanics**

With the use of vibrating electrodes techniques it became possible to detect measurable electric fields in the immediate vicinity of the living samples, including single cells [14]. So far as the force lines of electric fields must be closed, they should also pass, in a reverse polarity, through the cells themselves. The first measurements performed on the egg cells of brown algae indicated 2-20 mV potentials between the opposite cell poles and 5 μA/cm² current density throughout the cell. The negative pole corresponded to the site of a rhizoid growth (Fig. 1A). Similar indices and, what is mostly remarkable, similar polarity (the growing/extending part corresponding to the negative pole, while a shrinking/contracting one to the positive one) took place in other samples as well.

Mostly interesting for morphogenesis are electrical circuits established in developing Vertebrate embryos [15]. In these, force lines of electrical fields enter the apical domains of morphogenetically inactive epithelial cells and leave the same cells through their opposite, baso-lateral domains. As a result, the apico-basal flow of the positive sodium and potassium ions (accompanied by chloride ions) is established, increasing osmotic pressure in subepithelial cavities and promoting thus their swelling and a stretching of the overlain epithelium. On the other hand, same embryos apically contracted cells acquire a reverse electrical polarity and become the sites where the force lines are leaving embryonic tissues (Fig. 1B). These cells occupy morphogenetically most active contracted regions (blastopore, primitive groove). As a result, we get essentially *macroscopic* electrical circuits, which at the same time precisely coincide with what we call the morphomechanical feedbacks (Fig. 1C). The latter are the positive feedback loops between the extended and contracted areas of an epithelial layer: extension enhances contraction and vice versa [16]. As development proceeds, the corresponding patterns become even more complicated (Fig. 1 D-G).
Fig. 1. Electromechanical coupling in eggs and embryos. In this and the next figure electrical vectors correspond to the movements of positive charges. A: outgrowing egg of brown algae, Pelvetia. Negative pole fits the growing rhysoid (below). B: Amphibian embryo at neurula stage. Positively charged are the grooves, negatively charged is the skin ectoderm. C: a mechanoelectric map of a blastula stage of amphibians embryo. Animal ectoderm (above) is negatively charged and stretched due to transport of ions and corresponding osmotic water inflow. To the opposite is the contracted positively charged blastoporal zone. D-G: patterns of tension lines (dense) at the successive developmental stages of a frog embryo (from blastula to neurula). Red areas correspond to the points of tension lines convergence (contracted regions) and presumably to the positive poles of electric fields.

Mechanoelectric machines for pulsatorial growth.

Hydroid polyps, the representatives of lower Invertebrates, form the colonies with quite precise and species-specific branching patterns (Fig. 2A). The branched stems are closed tubes consisting of two cell layers which behave in a roughly similar way, permitting, at the first approximation, to regard the stems as one layered formations. During growth several dozens cells arranged at the stem tip (distal part) for each next minutes are swelled and rotate towards perpendicular orientations, to be later on shrunken and taking oblique positions. The first phase coincides with stem’s elongation (extension phase) while the second one with its partial shortening (retraction phase) (Fig. 2B, A-D). These periods are called growth pulsations (GP). GPs are characterized by finely regulated temporal-amplitude patterns (Fig. 2C, A-E). Extension GP phases are associated with the osmotic water inflow within cell vacuoles while retraction phases with water outflow.

By the model suggested [16], GPs belong to the category of autooscillations with a considerable mechanical component. The main feedback loop is created by the activation of mechanodependent Ca$^{2+}$ channels due to stretching of cell membranes at the extension phase. As a result, the isolated
Vacuoles (Fig. 2D) are fused into the outside opened channels, leading thus to water outflow and hence to the shift towards retraction phase (Fig. 2E).

Meanwhile, it turned out that GP can be also regulated by external electrical fields, properly oriented in respect to the disto-proximal stem polarity [17]. Namely, if applying to a growing stem a descending (positive pole to the distal and negative to the proximal stem pole) 1-3 V/cm electric field (current density 20-150 μA/mm²) GPs were arrested at the retraction phase (Fig. 2F), while in the case of an ascending field (negative pole to the distal) the arrest took place at the extension phase (Fig. 2G). If the electrical field was applied perpendicularly to the stem axis, in the case of the negative pole apical location the reactions were the same as in the case of its distal location. All the reactions were completely reversible. The electrically induced arrests were characterized by specific vacuolar patterns: at the extension phase cells were full of small spherical vacuoles, while at the retraction phase large intercellular spaces could be observed.

In both frames red contours display external electric fields which arrest GP at the given phase, pink solid contours outline disto-apical domains of cell membranes assumed to contain electrically non-excited Ca²⁺ channels while pink dotted contours outline proximo-basal membrane domains containing electrically excited channels. Blue contours in E display endogenous currents which according to our model act periodically, triggering the passage from F to G. F: growth arrest at the
retraction phase, positive pole of external field to the distal. G: growth arrest at the extension phase, positive pole to the proximal. Scaling angle under F, G: horizontal line is 10 min, vertical line 10 μm.

In order to explain the polar effects of external electrical fields one can assume that the electrically non-excitable Ca\(^{2+}\) channels are predominantly located at the distal and apical areas of cell membranes (Fig. 2 D, E, solid pink contours) while those excited by electrical depolarization in the proximal and basal areas (dotted pink contours). Obviously, under these conditions a descending electrical currents should stimulate, while the ascending one hamper Ca\(^{2+}\) ionophoretic inflow. These flows are depicted in Fig. 2 D, E by red contours. As a result, in the first case the cells will be arrested at the retraction, while in the second one at the extension phase, which is just the case. Such an arrangement of Ca\(^{2+}\) channels should be regarded as a manifestation of a universal property of so called planar cell polarity playing an important role in cell differentiation [18].

Most interesting would be to apply these suggestions to the normal growth patterns of hydroid polyps, taking into consideration the mechanosensitivity of Ca\(^{2+}\) channels, induced by cells periodic swelling. Within such a context, we can regard their growing tips as a kind of biological dynamo-machines, transforming periodic stretching of cell membranes into electric currents mediated by Ca\(^{2+}\) flows. These latter are depicted in Fig. 2E by two conjoined blue contours, indicating the currents via non-excitable Ca\(^{2+}\) channels of the distal and apical cell membranes. These currents should reach their maximal values just before the retraction GP phase (shown in E) and induce the transition to this phase.

**Generation and temporal patterns of photon emission in cells and embryos**

Ultraweak photon emission (UPE) of the living objects has been discovered almost 90 years ago and since then its existence has been confirmed in a great number of studies (recent reviews: [19, 20]), although the views upon its biological role and physico-chemical mechanisms of photons generation remain to be quite diverse. Two main different (but not necessarily mutually exclusive) theories upon UPE origin are forwarded. According to the first one, photonic level energy is produced as a result of recombination of free radicals which are the by-products of many chemical reactions, mostly oxidative. By the second view, the photonic level may be reached by summation of smaller portions of energy released during fast enough collective molecular interactions in the dense and/or ordered medium. Slawinsky in his very instructive paper [21] gives several examples of such processes. For example, relaxation of 9 supertwists in DNA molecule liberates 2 eV per 0,01 s only; enzymatic splitting of acetylcholine at the postsynaptic membrane releases up to 1,2 eV even within a smaller time period (4x10\(^{-7}\) s). On the other hand, a slow relaxation of excited states, mentioned beforehand as a main feature of the proteins-machines, should also increase the probability of a summation of small portions of energy up to photonic level. Therefore, chemo-mechanical and photon-generating devices should share the same fundamental properties.

Similar estimations make it probable that the photonic level energy is accumulated in cytoskeletal structures and can be released during their physiological or artificial destruction. Thus, by Pokorny [22] estimations, a single microtubule stores a power of about 10\(^{-14}\) W/cm, obtained due to a rapid post-polymerization GTP hydrolysis. Taking an average microtubule length of about 10µm, and assuming that no less than 100 microtubules per second are polymerized in a close vicinity, we get a power of about 10\(^{-15}\) W, produced in a proper proximity and thus be potentially able to sum up to a photonic level. This amount of energy exceeds in two orders the power of a photon emission, sensed by a standard photomultiplier. Last but not least, the photonic level energy can be accumulated in the above described coherent water domains.

Here we give a brief account of our UPE measurements from cell cultures and embryos, obtained within two last decades in the International Institute of Biophysics (Neuss, Germany). The main aims of the measurements were:

- to check a UPE role in cell signaling;
- to look whether and to what extent UPE is affected by destruction of cytoskeletal elements and cells-substrate contacts;
- to follow UPE dynamics in the developing embryos of a fish, *Misgurnus fossilis*.

In all these studies our interest was focused on the temporal (periodic) patterns of UPE in several Hz range. Correspondingly, we have measured UPE Fourier spectra in terms of either periodograms or spectral densities for $10^0 - 10^2$ s successive time periods. Some of results were also presented as autocorrelation diagrams of Fourier spectra because they give more obvious and detailed image of the signals structure. For more details see [23-25].

1. Photonic component of cell signaling.

FGF (fibroblast growth factor) is a universal ligand for a number of signaling pathways playing quite different roles [3]. In particular, FGF stimulates the entrance of fibroblast cells into a cell cycle, promoting thus their proliferation. We were interested to know, whether FGF-1 addition ($10^{-9}$ g/ml) to a monolayer culture (about $10^5$ cells) of mouse fibroblasts (line C3H10T1/2) affects in some way the UPE temporal patterns.

First of all, it turned out that the addition of FGF did not increase the average UPE intensity (Fig. 3A). Moreover, the presence of cell cultures also did not exceed UPE as compared with that of a cell-free medium (Fig. 3, cf B and C), while the latter one was significantly greater than the background photomultiplier level. From this we conclude that the measured signals are related to UPE produced by oxidative reactions within a cell-free medium. Meanwhile, addition of the FGF-induced cell cultures led in few minutes to the appearance of pronounced and gradually evolved regular enough UPE oscillations within $10^1 - 10^2$ s range (Fig. 3C, D).

Interestingly, UPE measurements performed on the monolayer cultures of hyppocamp (mid-brain) cells revealed a similar evolution of periodic patterns, now going on spontaneously, without any intervention from outside (Fig. 4). Such an activity may be attributed to inherent properties of nerve cells.

2. Effects of cytoskeletal drugs and trypsin upon UPE Fourier spectra.

As seen from Fig. 5C, the addition of cytochalasine D (10μg/ml), the drug preventing self-assembly of microfilaments, produced in few minutes a group of spectral density peaks (2s, 13s and 130s periods), two of which were preserved up to 20 min and accompanied by 28s peak. Worth mentioning, most of the periods relate to each other as integer numbers. Much more pronounced periodicity, taking place immediately after the drug addition, can be seen in autocorellogram (Fig. 5B).
Fig. 3. UPE of a monolayer fibroblast culture under the action of fibroblast growth factor (FGF-1). A: a record. B: a 100-fold aggregated record of a cell-free medium. B: same with fibroblast culture. Note several outstanding peaks, no increase in the overall intensity. In A-C horizontal axis is minutes, vertical axes UPE intensities count/sec. D: autocorellograms of 5 min long successive UPE Fourier spectra, displaying evolution of spectral patterns.

Fig. 4. Successive 5 min long (separated by 10 min intervals) Fourier spectra (in terms of autocorellograms) of spontaneous UPE from monolayer culture of hyppcamp cells.
Fig. 5. Fourier patterns of UPE under the action of Cytochalasine D (CD) upon monolayer fibroblast culture. A: UPE record (vertical arrow indicates the moment of CD application) and 5 min long records of Fourier patterns before and after CD application in terms of autocorrelograms. Note increase of spectral coherency soon after CD application. B: evolution of Fourier spectra (periodograms) within 20 min after CD addition, as compared with the same intact sample. Periods (in seconds) of the most outstanding peaks are shown.

Similarly, less than 1 min after adding 10^{-4} M colchycine (agent preventing microtubules assembly) monolayer fibroblast culture responded by appearance of new spectral density peaks which also relate to each other as integer numbers (2s, 10s, 40s and 200s periods). Later on these peaks gradually smoothed (Fig. 6A).

UPE reaction to trypsin/EDTA (0.025%) addition (which led to the loss of cell-substrate contacts) was very dramatic, leading to the formation of several outstanding peaks (some of which also related to each other as integer numbers) already in few minutes after drug administration (Fig. 6B). Later on the peaks gradually smoothed out.

Therefore, the results (6-1) and (6-2) indicate the existence of rather specific and gradually evolving UPE regimes which point, most probably, to the periodical exchange of low intensity photonic pulses between the external medium and living samples. In the cases (6-2) such pulses can be characterized as “alarm signals”, since they are associated with destructive processes.
Fig. 6. Evolution of UPE Fourier spectra (in terms of periodograms) after the action of colchicine (A) and trypsine (B) to the monolayer culture of fibroblast cells. Designations as in Fig. 5.

3. Dynamics of UPE Fourier patterns during the development of a fish, *Misgurnus fossilis*.

Fig. 7 displays typical Fourier patterns in terms of spectral densities (middle row) and autocorrelation diagrams (right row) for the batches of eggs and embryos of several successive developmental periods (shown at left). While non-fertilized eggs are characterized by rather chaotic and uncorrelated Fourier spectra, those entering the cleavage period exhibit highly ordered periodic patterns, which later on become again less ordered. However, some other, hardly formalized but nevertheless significant signs of temporal organization can be traced at the advanced developmental stages as well (three lower lines).
Fig. 7. Evolution of UPE Fourier spectra at the successive stages of Misgurnus fossilis development (left column) in terms of spectral densities (middle column, horizontal axes cover 5 Hz) and the corresponding autocorelograms (right column). Each spectrum was recorded within 2 min.

Discussion

As it was briefly mentioned beforehand, a founder of a morphogenetic field theory, Alexander Gurwitsch, proposed that the dynamic order in the living organisms is supported by a single vectorizing factor, acting in the same way in all the structural levels, from molecular to organismal. Today we can see that the reality is much more complicated and fragmented. What we observe at the molecular level, is a set of devices (machines) accurately collected from specific molecules (mostly proteins) which prevent a chemical energy stored in molecular bonds from chaotic dissipation by transforming it into a high grade (low entropy) mechanical, electrical and photonic energy. In doing this, all the molecular machines (not only electromechanical, but also photon-producing), in spite of all their intrinsic differences, share the common property of retarding the relaxation times and extensively reducing the number of freedom degrees for the liberated energy.

This is however only the first step which is required for extending the dynamic order up to the macroscopic space-temporal dimensions. For fulfilling such a task, that is, for passing from, by rough estimations, $10^8 \text{cm}/10^0 \text{s}$ range (typical for supramolecular events) to a macro-morphological realm ($10^1 \text{cm}/10^3 \text{s}$ range) another set of powerful “+” and “-” feedbacks between the molecular/supramolecular machines should come into action, which is to be regulated by macroscopic parameters. Only under these conditions, a set of machines should be transformed into what we call the morphogenetic fields.

At the present time just the first evidences on the existence and nature of such feedbacks are accumulated (e.g. [26, 27]). It becomes widely accepted, that a great repertoire of molecules, supramolecular structures and signaling pathways becomes involved in these feedbacks. Under these conditions, it looks rather ineffective to construct a deterministic picture of such feedbacks, enumerating their details one after other. Instead, following the SOT principles, we should concentrate ourselves in outlining a restricted number of so called order parameters, controlling the behavior of an
entire system. It is highly plausible, that mechanical stresses, electrical fields and the factors regulating UPE temporal regimes belong to such parameters.

In addition, the traditional SOT approaches should be enriched by a notion of coherency. Such events as a maintaining of a dynamic order over enormous range of the dimensional and temporal scales and, more specifically, a wide presence of integer frequencies in UPE Fourier spectra unequivocally point to such a coherency. On the other hand, as already mentioned, a high degree of coherency has been described to intracellular water domains. By bringing together these as yet scattered evidences, one may hope to reach much higher level of understanding of the energy transformation in living systems.

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