Water Respiration - The Basis of the Living State

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Summary

"Real" liquid aqueous systems generally represent complex systems where the phase of polarized water, as recently propounded by Pollack in his description of "exclusion zone" water, contrasts with the coexisting, but much less well organized, bulk water. Polarized water is a potential electron donor (i.e., reducer). Under conditions where electrons may be donated to dissolved oxygen, the process is one of "slow water burning," equivalent to "water respiration." When carbon dioxide and nitrogen are present, free energy released in the course of this "respiration" can be used for performing (chemical) work, leading to the production of organic compounds, and further complicating the system as a whole. The same conclusions follow from the theory of coherent water based on the principles of quantum electrodynamics. Such dynamic systems meet the requirements of the "living state" based on the general theory of living matter formulated by Bauer.

Introduction

In everyday life there is little problem in distinguishing "animate" from "inanimate" things. However, the fundamental nature of the difference continues to escape strict definition in biological terms, although modern biology tries to make the differentiation from several different premises. From the structural approach, all living things contain specific molecular species that are not found in the inanimate world: bioorganic (macro)molecules, such as DNA, RNA, proteins, polysaccharides, and numerous smaller organic molecules. Even inorganic ions are present in living things in specific combinations and concentrations. Considerable progress has been made during the last century in studies of the chemical specificity of living things, and in our understanding of the roles of these arrays of molecules, whose assemblies perform particular functions that we constitute what we know as life ("vital" functions).

However, after fixation of living matter, all the substances persist, but life has vanished. Thus differentiating between animate and inanimate things demands a dynamic approach. A system can be considered "alive" only if it is indeed dynamic in nature, or to be more precise, a composition of particular dynamic processes - metabolism, multiplication, adaptability, excitability, specific reactivity to external stimuli, and the ability to grow and develop. However, any particular function characteristic of a living thing might also be found in inanimate systems. On the other hand, a system may exhibit "traces of life" when some of these functions are not performed at all. For example, life does not dis-

appear immediately from a drop of blood taken from the body. "Traces of life" will be found under appropriate conditions in individual cells isolated from this drop long after their isolation. Despite the fact that isolated cells are unable to accomplish the whole panoply of vital functions, there are nevertheless certain striking differences between such "simple" cells as living erythrocytes - devoid of both a "master-molecule" DNA and "master energy stations," mitochondria - and the same cells after they are fixed in a blood smear, the former retaining some metabolic activity whereas the latter is devoid of it.

It is evident that no process, animate or inanimate, can run without an energy supply and a means of transforming it into useful activity. The third approach taken in differentiating between animate and inanimate things is (bio)-energetic. Energy flow constitutes the foundation for both structural specificity and dynamic manifestations of living things. According to the current concept of bioenergetics, the source of energy supporting vital processes in the biosphere is ultimately sunlight. High-grade photonic energy absorbed by chloroplasts of green plants is the driving force for splitting water, followed by the transfer of the hydrogen atoms to CO2 and the release of oxygen - the "waste product of photosynthesis" - into the environment. Energy is accumulated in organic molecules in the form of loosely bound electrons. Living systems gain most of their energy from oxidation of these organic molecules. High energy electrons are abstracted from food substrates and transferred from one electron acceptor to another along the electron-transport chain of mitochondria to the final electron acceptor - oxygen, turning it into water. Energy gained in the course of these sequential reactions is stored in the "macroergic" phosphate bonds of ATP and somehow released as free energy on its hydrolysis to ADP, and can then be put to performing useful work. Thus, all life on the Earth exists ultimately through the controlled flow of energy from the Sun to the Earth. Although many details of the photosynthetic process and ATP synthesis in mitochondria are well known, the essence of the mechanisms of transformation of energy stored in ATP into free energy and from free energy into useful work remains enigmatic.

Based on these approaches, contemporary biology distinguishes living and non-living states primarily through a description of the complex chemical composition and specific dynamic manifestations found in the former compared with the latter. However, a strict definition of the "living state" still eludes us. Could it be that biologists cannot answer the question "What is life?" because they overlook some important features characteristic of living matter?

Water - The Forgotten Matrix of Life

Albert Szent-Gyorgyi (1957) stated that biologists might not be able to formally distinguish between "animate" and "inanimate" things because they concentrate on studying substances to the neglect of two matrices without which these substances cannot perform any functions - water and electromagnetic fields. He stressed that, although water is not only the mother, but also the matrix of life, "...biology has forgotten water or never even thought of it." Indeed, most studies in experimental biology are conducted on objects in which solid matter constitutes a significant part by weight. Water in cells has traditionally been considered merely a solvent in which biochemical reactions occur and an abundant reagent (on Earth) for hydrolytic reactions. But there are striking examples demonstrating that water in fact is in the widest sense the actual basis of biological organization.

Many plants and animals consist predominantly of water. For instance, some jellyfishes are >99% water by weight (Jankowski, 2000). Together, their "solids" - including bioorganic molecules, proteins, nucleic acids, carbohydrates, etc. - constitute no more than a fraction of a percent of their living mass. Among other things, they are "islands" of clear "living" water residing in a sea of "dead" water, containing enormous salt levels. Why does a jellyfish not lose all its water due to osmosis? Clearly water in a jellyfish exists in a form or phase which has dramatically different properties from this other inanimate phase represented by ambient water.

If the "alive" water of the jellyfish becomes separated from the traces of intermingled solids, it would turn to "dead" distilled water. Therefore, the "living state" of water of a jellyfish is some-

how invested with a small quantity of biomolecules with which it interacts; water in such a "living" state is probably no less responsible for the peculiar morphology of a jellyfish and its functional activity than bioorganic molecules. Without taking into consideration water-biomolecule interactions and the special properties thereby endowed upon them through this union, the nature of the "living state" will remain unfathomable.

By the middle of the last century, numerous papers were published in which it has been convincingly demonstrated that the thickness of zone of water hydrating hydrophilic surfaces and having the properties of "liquid ice" may reach tens and hundreds of water molecule layers and not just a few, as has usually been supposed (Henniker, 1949). With this being firmly established as the state of affairs, there will be far-reaching consequences regarding the true nature and characteristics of kinetics and thermodynamics of biochemical processes that define the living state of cells. It is evident that cytoplasm is crowded with macromolecules and their ensembles, constituting an altogether enormous surface area hydrated by water and, in turn, resulting in this the water assuming the properties of "liquid ice." (Wiggins, 2001) However, until recently few scientists have insisted that, in the presence of water residing in such a state, physical-chemical processes should be seen as different from those in dilute solutions (Pollack, 2001).

Szent-Gyorgyi (1956) discovered one of the most important consequences of water structuring - an exceptionally long living state of electronic excitation of different molecular species interacting with ordered water. He suggested that this property provides for energy transfer in biological systems, or more generally, that it explains how the bound energy of ATP and other fuel molecules can be transformed into free energy for performing useful work. He also considered life as an interposition between two energy levels of an electron, the excited state and the ground state. According to this notion, it is the electron (more precisely, electronic excitation) that goes round the circuit. Life is a little electric current going round and round.

Energy flux may serve not only as a source of free energy for multiple vital functions. According to the theory of dissipative structures developed by Prigogine and Nicolis (1977), energy flux through a non-organized system may drive the emergence of order out of chaos. Many authors believe that the theory of dissipative systems may provide new insights into an understanding of the behavior of living systems (Tiezzi, 2002; Rossi et al., 2008). This theory can be illustrated by self-organization in chemical reactions, e.g., the Beloussov-Zhabotinsky reaction (Beloussov,1959; Zaikin and Zhabotinsky,1970), in which spatial and temporal order emerges out of disorder. It is noteworthy that the overwhelming majority of these reactions proceed in aqueous systems. However, a special role of water is not usually considered in most studies of oscillatory and wave-like chemical processes. Only very recently has evidence appeared that water may play some other role in BZ-reactions besides that of an "indifferent" solvent (Magnani et al., 2004).

A definition of the living state that takes into account the special role of water in energy management by living systems as well as in their self-organization has to consider both the ideas of "aqua-bio-energetics" and the theory of dissipative systems. However, both concepts are based on the presumption that a living system emerges and stays alive due to energy (and matter) fluxes running through it. For an electrical current to run in any circuit, a potential difference between the inlet and outlet of circuit has to exist. Szent-Gyorgyi, in accord with the common opinion, considered that this potential difference is provided by the Sun, in particular by solar radiation that exerts initial electronic excitation in chloroplasts - the start of energy flow through living matter. The theory of self-organization in open systems also implies a continuous flux of energy running through them due to externally applied gradients of energy, e.g., heat as in the Benard cell.

However, it has recently become clear that organisms can flourish in the complete absence of sunlight and photosynthesis. Rich ecosystems have been discovered at the bottom of the ocean. There is no light and no oxygen from the atmosphere several kilometers below the ocean surface. The temperature does not normally ex-

ceed 2-4°C. Nevertheless, highly active aerobic animals, belonging to a variety of species, thrive in this cold darkness. This deep sea ecosystem is not apparently connected with other ecosystems living "in the sun." A possible source of energy for them could be provided by the heat coming out from the inner core of Earth. Their basic biochemistry and physiology is not essentially different from that of the animals living under the sun. The continuous flux of energy ("little electric current") in their body needed for growth, development and multiplication is sustained by their ability to extract energy and matter from their meager environment rather than by continual influxes of energy and matter from outside. This is not the specific property of deep-sea organisms - it is the common property of all living systems. Thus, both the ideas of Szent-Gyorgyi concerning the role of structured water in transformation bound energy of "food" into free energy of electronic and other forms of excitation, and the theory of Prigogine of dissipative structures able to self-organize, are necessary but are insufficient to provide a more comprehensive explanation of the living state. To take the next step in this direction, one needs to start from a formal definition of the state that can be considered "living" based on more general principles.

The Nature of the Living State According to Ervin Bauer

More than 70 years ago, the Russian biologist of Hungarian origin, Ervin Simonovich Bauer (1890-1938), formulated a set of fundamental principles to differentiate animate and inanimate systems (Bauer, 1935). Although the laws deduced from studies of inanimate nature also permit us to describe the mechanisms of particular processes going on in a living system, it becomes impossible to deduce their unity of holistic, active, and directed functions, based solely on these laws. However, unique properties of living things automatically follow from some of the postulates suggested by Bauer. These include metabolism, growth and development, multiplication, adaptability, excitability and reactivity, senescence, and even evolution as an innate law of development of living matter on Earth. Bauer stated that biology is an original science rather than a special component of contemporary physics and chemistry. Unfortunately Bauer's fate was tragic (a biographical sketch can be found in Web, ref. 1). His book "Theoretical biology" disappeared from the libraries for many decades. Up to now only few Russian biologists are aware of Bauer's theory that is practically unknown in the West (Voeikov, 1999). The following section briefly outlines the major points of Bauer's theory needed to substantiate the hypothesis of the crucial role of water in sustaining living state.

The Principle of Stable Non-Equilibrium

According to Bauer's first principle, the Principle of Stable Non-Equilibrium: "All and only living systems are never in equilibrium. At the expense of their free energy, they ceaselessly perform work against sliding toward equilibrium demanded by the physical and chemical laws appropriate to the actual external conditions."

Thus, Bauer asserts that a living system from the first moment of existence, its "birthright," appears in a non-equilibrium state, inherited from the parent system, which is living, and hence already in a non-equilibrium state. Furthermore, the non-equilibrium state is displayed at all levels of a living system organization, including the sustaining of chemical gradients, electrical gradients across membranes, and other phase boundaries, the non-equilibrium state of its macroscopic structures, and so on. Most important, it includes the non-equilibrium of the essential molecular components of living systems. Matter's non-equilibrium state is equivalent to its excited state, as opposed to its ground state. The structure of matter in an excited state differs from its structure in the equilibrium (ground) state. That is why Bauer defined the energy of an excited (non-equilibrium) state of matter, in a sense of "living" matter, as "structural energy." This stationary, although non-equilibrium state of matter, that is fundamental for the emergence of life, has been commented upon by many authors that have introduced peculiar concepts, such as the concept of negative entropy (negentropy) introduced by Schrödinger (1944).

Here one detects some similarity between the ideas of Bauer and Szent-Gyorgyi. According to the latter, it is the energy of electronic excitation that may be mostly efficiently transformed into work - a particular example being bioluminescence (Szent-Gyorgyi, 1957). According to Bauer, all the work performed by living systems is executed by its excited structures, which transit from the excited to the ground state in performing work.

However, the Principle of Stable Non-Equilibrium contains a stronger claim. It demands that a living system as a whole should persistently perform work for it to reside in an excited state as long as possible. Thus, those elements of the system that had transited into the ground state should be either re-excited or substituted by the new excited structures. According to the second principle of Bauer, this can be done only through the effort of a living system: "...all the work that may be performed by living systems is done only at the expense of structural energy (of its excited elements), that is, by forces generated by a living system itself." This thesis is in fact another form of expression of the Principle of Stable Non-Equilibrium. It stresses that a living system is intrinsically active. This activity cannot emerge by an assembly of basically passive elements, as extolled by conventional biology, but emerges from the transition of these components into a new state having properties different than those in isolation. This new state should be an active one which as we will see, occurs in liquid water. Living systems use their own structural energy to extract chemical energy of food or light energy in the case of photosynthesis (see below). This energy is converted into structural energy of the molecular constituents of living matter rather than being directly converted into work. To avoid the decay of such energy into heat, it is necessary to store the energy within extended regions able to keep it as the maintaining agent of long-lived excited states of the extended region. Besides, the more cooperatively the excited elements transit into the ground state, the more force they develop and the more efficiently the work is done. We will see that this is just the task performed by the coherence domains we will shortly introduce. Thus it follows from Bauer's principles that a living system has to be a coherent one.

Since work is performed against an equilibrium, free energy is consumed. Each excited element of a living system performing its job inevitably slides toward equilibrium, finally reverting to lifeless matter. In order to preserve the non-equilibrium state, a living system continuously repairs or substitutes its exhausted structural elements. Energy is needed to carry out this work, and according to the Principle of Stable Non-equilibrium, this energy comes from inherent non-equilibrium structures in a living system. Such work, aimed at keeping an individual living system from sliding toward equilibrium, was defined by Bauer as "internal work." Internal work is an intrinsic property of living systems. The work performed by machines and other inanimate systems is not aimed at preserving their structure or their ability to perform work. Their structure acts merely as a transformer of free energy that they receive from the external sources into work.

Internal work includes transformation of chemical energy of acquired food into structural energy of excited "living matter." A particular case is that of "self-digestion" (autophagy), the extraction and transformation of less valuable structural energy for more valuable structural energy.

The Principle of Augmentation of External Work Performance

No matter how efficiently internal work is performed, a living system gradually loses its free energy and the matter "charged" with it, and needs to replace them with new matter and energy (chemical energy of food, energy of light, and so on) consumed from its environment. Living systems normally have access to energy and matter from their environment that can be used for re-excitation or substitution of exhausted structural elements. Thus, the opportunity for preserving and even enhancing the non-equilibrium state nearly always exists within the biosphere. However, in order to retrieve supplies from its environment, the living system has to perform work; for example, work of contractile elements of a cell in finding food, which may be considered as external work in contrast to the internal work discussed above. It must then extract the useful structure-energy

substrates by digesting them in order to convert them into the form from which bound energy can be transformed into the structural energy to be used in metabolism.

Here we can see a cardinal difference between living things and inanimate systems; the latter are passive acceptors of energy that flows through them and is partially converted into work. Also outside sources may charge the inanimate system with energy, which is later transformed into work. Note that the current concept of bioenergetics outlined in our Introduction gave a similar picture of living systems. According to the generally accepted point of view all life on the Earth exists because of the energy flow from the Sun to the Earth. It follows logically from this reasoning that living things are conceived essentially as passive objects; they exhibit activity only due to an inflow of energy and matter, and because of the influence of external forces. True living matter, too, could be used occasionally as inanimate object; for instance, I can use a fisted hand as a hummer, however the core dynamics of a living object is basically at the expense of its structural energy. One can argue that green plants may get their energy from sunlight without any effort. However, chloroplasts serve as photochemical transformers only if their structure is already in a non-equilibrium state. Appearance of chloroplasts at a certain stage of a plant development and preservation of their non-equilibrium state is provided by the internal work. The latter includes extraction of chemical energy from organic substances of a plant cell and its transformation into structural energy of chloroplasts and other vital elements of plant cells. The dominating mode of energy extraction from organic compounds by living systems is respiration, and plants respire no less avidly than animals. Chloroplasts are dead if they do not respire; they are unable to transform light energy into chemical energy once isolated from the living cell. Plants may not need to do as much external work as animals, but they have to carry out many basic functions (e.g., intracellular transport of nutrients, changing in the position of leaves, of chloroplasts in response to changes of illumination, etc.). The point is that neither chemical nor solar energy can be retrieved from the environment and transformed into structural energy without external work being performed. In order to retrieve energy, the organism needs to be alive. Being alive requires the extraction of work from the internal stock of structural energy.

This applies to all living systems, animals, plants and microorganisms. Indeed, microorganisms residing under fairly constant external conditions may exist for a very long time in a stable non-equilibrium state due to the performance of internal work while doing negligible external work. Such situations in biology are not at all rare. For example, estimates of the generation time of soil prokaryotes in the region of 3 years and of deep subsurface (terrestrial or marine) prokaryotes of up to 2000 years have been estimated (Whitman et al., 1998). But changes in external conditions result in loss of structural energy where their non-equilibrium is jeopardized. Once this energy is dissipated, an organism inevitably slides into an equilibrium state and would be considered dead. But if this energy can be transformed into free energy to perform external work aimed at recovering resources from environment, a living system may then compensate for the losses of its initial stock of structural energy and survive.

We need to emphasize here an important and specific property of living systems. According to the Principle of Stable-Non-Equilibrium, living systems automatically perform only internal work. But they cannot sustain a non-equilibrium state forever without gaining energy and matter from their environment. For this they have to perform external work. During the performance of external work, a living system loses its structural energy, thus sliding toward equilibrium. Reduction of non-equilibrium state of a living system resulting from its own efforts, contradicts the Principle of Stable Non-equilibrium. Insofar as a living system cannot violate the principle of its existence, it may perform external work only by infringing on the non-equilibrium of its structures, under the influence of external impulses. Thus external influences, irritations, infringing to a certain extent on the non-equilibrium of a living system, have the effect that the energy freed is spent to perform external work rather than internal work.

Even the most primitive organisms have more or less specialized organs to react to stimuli that

can affect its non-equilibrium status. Stimuli are necessary for living organisms since they help them to transit from one state to another, thus implementing the principle of stable non-equilibrium. A living organism uses the energy and matter coming from outside to "irritate" itself and induce the transition to a different internal configuration, maintaining at the same time its own non-equilibrium. Hence, the notion that living things are "open systems" should refer specifically to their openness to external stimuli. However, this idea is similar, but not identical, to the notion of "open systems" applied to inanimate systems. A living system becomes open to deal with energy and matter in its environment only in response to adequate stimuli (physiological irritants).

Although doing external work contradicts the Principle of Stable Non-Equilibrium, a living system will lose its non-equilibrium faster without doing at least some external work. Each individual living system independent of its longevity sooner or later passes away - turns into non-living matter. Nevertheless, life as we know it can be sustained for billions of years on Earth because the species to which individuals belong may exist for indefinitely long periods of time as a chain of descendants. In fact, any individual - animal, a plant, or microorganism - has to be envisaged as an element in a series of self-reproducing individuals. But the stock of structural energy that each individual living system inherits from its parent at the moment of its birth is not enough to maintain this chain, i.e., leave viable descendants - it is only enough to sustain a non-equilibrium state for a short period of time. To leave viable descendants, a living system has to grow, which means the overall increase in mass of excited matter and hence in the amount of structural energy available to perform both external and internal work performance.

Growth of any living organism is not just a mechanical augmentation of its living mass of the kind seen in the growth of a crystal. Starting from a seed, a fertilized egg, or a "newborn" bacterial cell, new structural elements arise during growth including structures specialized to perform external work. Sensitivity of a living system to external stimuli also is perfected. As a result, the ability of a living system to perform external work increases, and this sequence of events can be seen as its development. In fact, some biologists consider organic growth, or the increase of living mass of an organism, as the expression of development (Sabinin, 1963).

Growth and development are intrinsic and basic properties of living matter; without them, living matter cannot be sustained. Thus, Bauer introduced the third principle characterizing the basic properties of living processes: the "Principle of Trend Augmentation of External Work Performance." This principle characterizes the necessary vector of development at all the levels of biological organization starting from individual cells, organisms, etc., to the evolution of all life on this Earth. Augmentation of external work performance is realized as a trend, rather than a straightforward process, because simplification, dedifferentiation, degradation constitute the integral features of any normal vital process. For example, protein turnover in cells and tissues represents protein synthesis and protein degradation. Multiple apoptosis of healthy cells naturally occurs during embryogenesis in all multicellular organisms. Without regular apoptosis normal development is impossible (Potten and Wilson, 2004).

Any newborn living system possesses an initial stock of structural energy inherited from its parent(s). It can be converted into free energy (F) for internal and external work performance. According to Bauer, this stock may be formally considered as the product of the "living substance potential" (μ), defined as "structural energy of the unit of living matter," and of mass of "living matter" (m) - matter residing in an excited state. Thus initial stock of free energy (Fo) can be defined as:

$$[1]\quad F_o = \mu_o * m_o$$

In the course of growth and development, "m" increases, due to consumption of food and transformation of the consumed matter, into an elevated non-equilibrium state. Augmentation of "m" (increase of structural energy reserves) is defined as "assimilation". The work for "m"

augmentation is performed at the expense of decline of the initial potential μo - dissimilation. Assimilation dominates over dissimilation until a maximum value of living mass (M) and related Fmax characteristic of the given living system (organism) is reached. The limit of growth is determined by μo and mo, but depends also on the conditions of growth and quality of food and other external sources of energy. Thus growth and development correspond to an increase of overall stock of structural (free) energy F, from the initial value Fo = μo*mo to a value of Fmax= μ(M) *M, where μ(M)<μo and M>mo. According to the formal analysis of growth and development performed by Bauer, Fmax and μo are related as given in equation 2:

[2] $F_{max} = \mu_o * M * e^{(mo - M)/M}$

where e is the natural logarithm base = 2.718.

In the case of living systems in which $m_o << M$ (e.g., most multicellular organisms whose eggs or seeds are tiny in comparison to the mature animals and plants), the equation reduces to $F_{max} = \mu_o * M/e$. In other words, and in this particular case, the limit of growth is reached when μ declines to the value of μ_o divided by e.

Growth is essentially an anti-dissipative process. Although energy dissipation due to "dissimilation" when external work is performed takes place, augmenting of structural energy stock and capacity to perform work prevails. This process may be figuratively illustrated as an avalanche. Imagine that somebody standing on a mountaintop drops a snowball onto the snow, and an avalanche is initiated. In the course of the avalanche development, its potential ("μ"), defined as the height difference between the top and foot of the mountain, decreases. At the same time the free energy of the avalanche increases to some limiting value ("F_{max}"). Although it is but a distant analogy, it shows that in branching chain processes, free energy may grow substantially from a very small initial stock.

What happens when the limit of growth (M, F_{max}) is reached? Assimilation and dissimilation continue, but when μ declines to a limit value, more structural energy is used for external work that can be gained due to its performance. Thus dissimilation dominates over assimilation; the whole stock of structural energy and ability to perform work now decreases. The first stage of the life cycle of the living system - the stage of growth and development - inevitably gives place to the second stage, which is senescence. Duration of the second stage of any individual living system life cycle is determined by the structural energy gain (F_{max}) at the stage of its growth and development and the efficiency of Fmax utilization. The latter depends upon many internal and external factors discussed elsewhere (Voeikov, 2002). Thus, the life cycle of any living system includes two stages showing opposite vectors in terms of the changes in structural energy. The same happens in a more violent and less controlled way to an avalanche after it reaches its maximum free energy. It continues to slide down, but inevitably its force declines until it stops.

The "Basic Process" - The Guarantee of the Firmness of the Living State

Although senescence is an inevitable outcome of Bauer's principles, they also offer a basis on which the vitality of living matter can continue after the limit of growth has been reached. Fasting is one of the universal means of prolonging lifespan for animals from worms to highest vertebrates (Weindruch and Walford, 1988). Experiments with intermittent fasting performed at the beginning of the 20th century had shown that medusas and worms starved for several weeks can reach a size smaller than that at which they hatched from the egg. But after feeding, both grow and show many features of physiological rejuvenation. Life span of invertebrates exposed to intermittent starving may be prolonged by up to 20 fold in comparison to well fed controls. Fasting can prolong the lifespan of animals such as mice and rats by 50% or more.

In the context of Bauer's theory, diminution of the size of a living system is the loss of "m" (mass of living matter), and rejuvenation is equivalent to increase in the value of μ (the potential of the residual mass). The process occurring during fasting follows a dynamical path different from the one followed in assimilation-dissimilation dynamics, since this new process is equivalent to restoring the initial energy stock of the living

organism. Bauer defined this alternative physiological process as the "Basic Process" because it underlies all forms of reproduction of living systems - the basis of the maintenance of life under a variety of external conditions. Thus, it corresponds to the increase in the potential of one part of a living system at the expense of energy taken from another part. The entity losing the non-equilibrium state "dies," while the excitation to a higher level of the entity conserving the non-equilibrium state increases.

During fasting a particular form of the Basic Process takes place - "self-digestion" or autophagy. Increasing the μ of a living system allows the process of normal metabolism to be restored, in the course of which "m" can once again increase due to metabolism at the expense of diminution of μ when F of a living system also increases. Multiple events of switching on the Basic Process after Fmax is reached followed with the recommencement of metabolism allows the continuous existence of a living system in a quasi-steady state exhibiting oscillatory patterns, slowing in such way the tendency of the whole system toward equilibrium.

A phenomenon that fits exactly with Bauer's definition of the Basic Process routinely takes place during the natural life cycle of multicellular organisms, namely apoptosis. It is noteworthy that intense apoptosis takes place during embryogenesis, in particular affecting nervous and germ cells (Jacobson et al., 1997). Equally interesting is the observation that the intensity of apoptosis can increase 5-fold during caloric restriction of adult animals (Wachsman, 1996). To our knowledge, the bioenergetics of apoptosis have yet to be properly considered, especially if it is indeed a major manifestation of Bauer's Basic Process. Although different, autophagy and apoptosis seem to play a comparable role in the living process. Both processes appear to be manifestation of a process of concentration of internal energy, that we will see later to be at the root of the onset of coherence. Energy is extracted from some degrees of freedom that, from this very moment, are excluded from further involvement in the process, and concentrated on fewer of them. We will see in the last section that this process may not violate the Second Law of Thermodynamics.

The major biological function of the Basic Process is to ensure that living systems can reproduce and multiply. During its growth, a cell needs to double the stock of its structural energy over Fo that was inherited from its mother (Fmax ≈ 2 Fo) if it is to divide and leave a viable progeny. Only then can it in turn supply both its daughter cells with the same Fo and ensure multiplication. But growth occurs at the expense of the decline of potential μ. Since the value of Fmax , attained when the limit of growth is reached, is equal to μ*M, the limit of mass (M) should exceed 2mo where μ < μo. Then the Basic Process should occur in a mother cell before its division. Due to the Basic Process, the potential of the mother cell increases to the value of μo at the expense of structural energy drawn out of the excess of its mass, and both daughter cells are endowed with the potential for their growth and development.

At first sight the Basic Process would seem to violate the second law of thermodynamics, because instead of energy dissipation it is actually referring to energy concentration. However, analogies of the Basic Process can be seen in the inanimate world. They are known as "fluctuations" - spontaneous elevation of energy density in one part of a certain system at the expense of the energy density decline in other parts. Lightning from a thunder cloud is an example of an accumulation of electrical potential in a localized part of space (and the origin of lightning continues indeed to be a matter of debate, see MacGorman and Rust, 1998). Although the mechanism behind the Basic Process may have something in common with "fluctuations" in the inanimate world, it differs in that these fluctuations occur in living systems most of the time, in accord with the major postulate of their existence, Bauer's Principle of Stable Non-Equilibrium. Dynamics of living matter is indeed in a permanently fluctuating state!

Thus, the dynamics of the living state follows automatically from the principles formulated by Bauer: the principle of Stable Non-Equilibrium, including the thesis that a living system generates forces for any work that is done due to the active state of its material constituents, and the principle of the Trend Augmentation of External Work Performance. This encompasses

all levels of life - from the single cell with its metabolism and self-reproduction to the development of multicellular organisms, right through to the evolution of the biosphere itself. Thus, a system may be defined as "living," or as residing in the "living state," if and only if it obeys all the principles considered above.

However, the parameters "μ" and "m" on which stable non-equilibrium is based were introduced into Bauer's theory without an explanation of their origin. Thus, this theory implies the existence of a "primordial egg", already equipped with a stock of structural energy and a potential high enough to give rise to further growth, development, and multiplication. Furthermore, matter that resides in a stable non-equilibrium state, possessing structural energy and performing useful work, has only very loosely been defined. Bauer calls this matter "living protein," although he himself made the reservation that he did not mean by "living protein" chemically defined protein molecules per se, but rather some special non-equilibrium state of biological colloids enriched with such macromolecules (predominantly proteins). Probably because of this vagueness, even the few biologists acquainted with Bauer's theory - including those showing some empathy with it - did not accept the idea, being seemingly too non-specific.

Below we show that recent discoveries of the unique properties of water can provide a rational means of filling some of these shortcomings of Bauer's theory. We will also try to define the "primordial egg" of the material system.

Water in Living Systems as the Primary Source of Structural Energy

Aerobic Respiration and Combustion

All living systems gain energy from oxidation-reduction reactions - electron transfers from substances that can hold them more weakly to ones that can hold them more strongly. It is known that the largest energy supply is provided by electron transfers to oxygen, either directly or through a chain of mediators. That is why the vast majority of living organisms now draw energy from aerobic respiration.

Lavoisier (in a republished version of his 1864 book) defined respiration as "a slow combustion of carbon and hydrogen, similar in every way to that which takes place in a lighted candle, and in that respect, breathing animals are active combustible bodies that are burning and wasting away." Currently respiration is seen primarily as the process occurring in mitochondria, where high energy electrons abstracted from carbohydrates and fats pass along a series of molecules, losing their energy in a step-wise manner. This energy is used to synthesize ATP. Oxygen serves as the final electron acceptor for eliminating low energy (spent) electrons and allowing additional electrons to pass along the chain (Babcock, 1999). Because energy units released in mitochondrial oxidation are equivalent to quanta of middle-far IR-photons (≤0.5 eV), this process is analogous to smoldering.

Genuine combustion "which takes place in a lighted candle" is a consecutive reduction of oxygen to water with four electrons ("one electron reduction"). By this means, quanta of energy equivalent to energy of visible and even UV photons (>1 eV, high density energy) are generated. Genuine combustion has not so far been considered as relevant in bioenergetics. One of the reasons is that, historically, bioenergetics had been restricted to the processes of ATP synthesis and utilization (despite the fact that the mechanism of conversion of low density energy of ATP into useful work remains unclear). Incidental to one electron oxygen reduction, reactive oxygen species (free radicals, peroxides) arise that can damage bioorganic molecules. The idea that "harmful" reactive oxygen species (ROS) arise only due to "mistakes of metabolism" has dominated biochemistry for several decades. It has only recently become clear that ROS play a fundamental role in normal physiological processes; indeed, they are indispensable in the operation of all bio-regulatory processes (Droge, 2002; Voeikov, 2001; 2006). The common belief that under normal physiological conditions only a few percent of oxygen leads to ROS production is incorrect. Due to the ubiquitous presence of enzymes belonging to NADPH-oxidase family, as also to other means of direct oxygen reduction even under resting conditions, up to 20% of all consumed oxygen is directly reduced and goes to ROS production (Souza et al., 2002), a proportion that can in-

crease up to 70% when metabolism is enhanced (Tramarchi et al., 2000).

The process of one electron oxygen reduction consists of several steps and is usually presented in the form given by Green and Hill (1984):

[3] $O_2 + e^- + H^+ \rightarrow HO_2\bullet$ (superoxide radical)

[4] $HO_2\bullet + e^- + H^+ \rightarrow H_2O_2$ (hydrogen peroxide)

[5] $H_2O_2 + e^- + H^+ \rightarrow H_2O + HO\bullet$ (hydroxyl radical)

[6] $HO\bullet + e^- + H^+ \rightarrow H_2O$

However, the one electron reduction of oxygen is enzymatically catalyzed in an organism. NADPH-oxidase is the major enzyme catalyzing the direct oxygen reduction:

[7] $NADPH + 2O_2 \rightarrow NADP^+ + 2O_2^- + H^+$

Superoxide radicals produced by NADPH-oxidases are immediately eliminated by superoxide dismutases:

[8] $HO_2\bullet + HO_2\bullet^- \rightarrow H_2O_2 + O_2$,

and hydrogen peroxide is eliminated by catalase:

[9] $H_2O_2 + H_2O_2 \rightarrow 2H_2O + O_2$

Thus the whole chain of reactions of one-electron oxygen reduction should be rewritten as follows:

[10] $4(O_2 + e^- + H^+) \rightarrow 4HO_2\bullet + E$

[11] $2(HO_2\bullet + HO_2\bullet) \rightarrow 2H_2O_2 + 2O_2 + E$

[12] $H_2O_2 + H_2O_2 \rightarrow 2H_2O + O_2 + E$

[13] $4O_2 + 4e^- + 4H^+ \rightarrow 2H_2O + 3O_2 + (\sim 8\ eV)$

From this notation, several important conclusions follow. First, if there is less than a 4-fold excess of oxygen over the electrons, combustion does not go to completion, allowing intermediate ROSs to accumulate, which can initiate chain reactions with bio-organic molecules, thereby corrupting them. Thus, an adequate supply of oxygen is necessary to maintain a low stationary level of ROS and other free radicals. Second, all these reactions assume recombination of unpaired electrons, and such reactions are sources of energy quanta equivalent to electronic excitation energy (> 1 eV). For example, the energy yield in the dismutation of two superoxide radicals is equivalent to a near IR-photon ($\lambda \sim 1269$ nm), sufficient to convert oxygen from its (triplet) ground-state to a singlet (excited) state. When two singlet oxygen particles simultaneously move to the triplet state, the energy of electronic excitation can be "pooled" and a double quantum of energy (equivalent to $\lambda \sim 635$ nm, red light) is released (Cadenas and Sies, 1984). Decomposition of two molecules of H_2O_2 donates the energy equivalent of 2 eV or $\lambda < 610$ nm. When SOD dismutates $HO_2\cdot$ (Eq. 11) or catalase decomposes H_2O_2 (Eq. 12), quanta of high-density energy should be generated with some megahertz frequencies due to the very high turnover numbers of these enzymes. This prevents energy from being spontaneously dissipated as heat and is favorable for energy pooling to even higher quanta.

If it is assumed that the share of oxygen being one-electronically reduced can reach much of all the oxygen consumed during respiration, Lavoisier's statement that "breathing animals are active combustible bodies that are burning" does not seem just a metaphor, but suggests something very deep. Some real burning should occur in living organisms. But how can burning occur in water representing the major component of any living matter? We will address this

point in the next section.

Burning in Water and Burning of Water

In 1794, it was discovered that no burning could take place without water. The British chemist, Elizabeth Fulhame, stated that water is the necessary catalyst (or intermediate) of combustion of coal, as "water is the only source of the oxygen, which oxygenates combustible bodies while hydrogen of water binds to oxygen of air and forms a new quantity of water equal to that decomposed" (cited after Laidler and Cornish-Bowden, 1997). The equation $C + O_2 \rightarrow CO_2$ describing burning of coal (carbon) needs to be rewritten according to Fulhame as a sequence of events:

[14] $C + 2H_2O \rightarrow CO_2 + 4H$; $4H + O_2 \rightarrow 2H_2O$

The true mechanism of coal burning may not be described by this sequence of equations, but it still shows that water is indeed a "combustible body" because it reduces oxygen, being an electron donor for it.

Fuhame's discovery was soon forgotten, but in 1877, G B Dixon also came to the conclusion that water is indispensable for burning. He revealed the necessary role of water in the combustion of carbon monoxide ($2CO + O2 \rightarrow 2CO2$). It turned out that a very dry mixture of CO and O2 could not be ignited with a spark unless a drop of water was added to a vessel with these gases. Even traces of water absorbed on a vessel wall were enough to provide ignition of these gases. Experimental studies continued for more than half a century into the catalytic role of water in combustion (Bon, 1931). Water was shown to serve as an electron donor to oxygen molecules, while oxygen thus generated combined with the combustible body, turning CO into CO2. In spite of the significant efforts of some of the era's most outstanding chemists (M Traube, D Mendeleev, and others), the detailed mechanism of the reaction was not established and the phenomenon was once again forgotten.

Although no theoretical foundation for the explanation of catalytic role of water in combustion currently exists, more and more practitioners exploit this property of water. For example, dozens of patents worldwide were issued for devices and methods for burning coal slurry-water suspensions, in which water was present at up to 50% by weight. The inventors and practitioners note that the temperature for the ignition of these suspensions may be hundreds of degrees lower than that needed to set alight "dry" coal and that combustion goes on much deeper (Web ref. 2).

One may argue that combustion in "simple" inorganic system and oxygen utilization in complex living systems are unlikely to have anything in common. However, an unexpected discovery was made in 2000. It transpired that all antibodies (immunoglobulins), irrespective of their species and antigenic specificity, and some other proteins (including beta-galactosidase, beta-lactalbumin, and ovalbumin) could catalyze oxidation of water with singlet (excited) oxygen to form hydrogen peroxide (Wentworth et al., 2000). Since water here is the electron donor for oxygen reduction, this process is indeed equivalent to water burning. With regard to immunoglobulins, it was shown that in their "active centers," two or more water molecules may be arranged within specific structures so that they provide their reducing properties through their collective interactions (Datta et al., 2002). In principle, water burning may occur in the absence of specific enzymes, provided that the conditions favor the arrangement of water molecules in collectives where they can exercise their reducing properties.

Before proceeding further, let us summarize the facts just discussed. First, respiration is the major source of energy in living systems. Second, a significant part of oxygen consumed in the course of respiration is due to one-electron reduction - combustion. Third, water is a necessary catalyst in the process of combustion. Finally, we must keep in mind that water is the predominating molecular species in all living systems (at a concentration of up to 50 M). Will it not, therefore, participate in the process of combustion - a significant part of respiration - in living systems in a manner similar to the role it plays in combustion in inorganic systems?

Water as the Source of Free Energy

A water molecule is considered a very poor electron donor - the energy of water ionization is 12.6 eV, which corresponds to an excitation temperature of 145,0000C. However, this may not be true, as we might find from some experimental evidence. In a series of recent papers, Pollack and his associates pointed out that water hydrating hydrophilic surfaces is very different from bulk water in viscosity, density, freezing temperature, relative permittivity - so different that it may be considered a fourth aggregate state (e.g., Zheng et al., 2006, and references therein). Pollack discovered that thickness of this layer may reach hundreds of microns, much larger than previously supposed. His experimental models allowed for the detection of properties that could not previously be seen. Because many substances readily soluble in bulk water have low solubility in this water, Pollack defined water adjacent to hydrophilic surfaces as the "Exclusion Zone Water (EZ-water)." These results have produced a consistent framework, some elements of which have been anticipated by a number of pioneers. For the sake of simplicity, we use for our discussion the results of Pollack that outline a consistent picture.

For further discussion, we will consider the following unexpected features of EZ-water as most important.

1. EZ-water has negative electrical potential with respect to the bulk water adjacent to it (down to -150 mv);

2. protons concentrate at the boundary between EZ-water and bulk water;

3. EZ-water has a prominent peak of light adsorption at 270 nm, and it emits fluorescence when excited with this wavelength. The thickness of the EZ-water layer increases when illuminated with visible and especially with IR radiation.

All these features strongly suggest that electrons in this water are much less bound (in other words, they reside at a much higher state of excitation) than electrons in bulk water. Hence, a much lower energy of excitation is needed to make them free. As radiation, especially light in the IR part of the spectrum, increases the thickness of the layer of EZ-water, thereby increasing its electron-donating capacity, EZ-water becomes a practically inexhaustible source of electrons. Thus EZ-water may be considered as residing in a stable non-equilibrium state with respect to bulk water, which represents ground-state water.

To convert the potential energy of quasi-free electrons in EZ-water into free energy capable of performing work, an acceptor of these electrons is needed. Normally, this acceptor is always available, i.e., oxygen. Water is the ultimate source of oxygen on Earth. Biological photosynthesis is not the only way to produce oxygen, but it is nevertheless a highly efficient way. There is strong evidence that under relatively mild conditions - freezing-thawing, evaporation-condensation, sonication within audible frequencies, filtration through narrow capillaries (Domrachev et al., 1992), stirring of water with fine powders of NiO, Cu2O, Fe3O4 (Ikeda et al., 1999) - water can split and produce oxygen. Thus if EZ-water is in contact with bulk water in which oxygen is dissolved, EZ-water will donate electrons to oxygen. The overall reaction of complete oxygen reduction may be:

[15] $2H_2O$ (EZ-water) + O_2 --> O_2 + $2H_2O$ (Bulk water) + n*hν (Energy)

Although the molecular species on the left and right sides of this equation are the same (water and oxygen) up to 8 eV of high grade, high potential energy may be donated by this reaction for every fully reduced O2 molecule. Water on the left (in bold) belongs to a stable non-equilibrium (excited) structure, i.e., EZ-water. Water on the right side of the equation in italics is ground-state (bulk) water. It is the "structural energy" (Bauer's analogy) of EZ-water that is released when two water molecules belonging to this stable non-equilibrium structure revert to ground-state water molecules.

It is important to note that the process of EZ-water "burning" (oxygen reduction by electrons abstracted from the "fuel") should proceed like any other burning as a branching (avalanche-like) chain reaction and it should obey particu-

lar laws pertaining to such processes (Voeikov and Naletov, 1998). Combustion may start only when the oxygen concentration exceeds a certain threshold, and should be initiated with some triggering stimulus whose energy may be incommensurably smaller than energy released in the course of the reaction development. Any energy released should further promote excitation of EZ-water and oxygen, resulting in a reinforcement or invigoration of the burning process. When the availability of either oxygen or electrons falls below threshold levels, burning is dampened. However, so long as hydrophilic surface-organizing EZ-water exists, water molecules from the bulk may be recruited to the EZ-water. In addition, part of energy released in the course of burning inevitably degrades as heat - the IR-part of spectrum - which may induce further increase of EZ-water and its potential, i.e., its stock and level of excitation of quasi-free electrons. During this period, oxygen - a product of the reaction [15] - again accumulates, and a new wave of water "burning" may arise. Thus the process could become oscillatory (Voeikov et al., 2001). In turn, energy will be released in an oscillatory manner and may serve as a pacemaker for coupled reactions (see below).

If not all electrons released are used for oxygen reduction and some of them combine with protons accumulated in the vicinity of EZ-water (Klimov and Pollack, 2007), hydrogen molecules will be generated. If these leave the aqueous system, its oxygen concentration effectively increases, providing for more active combustion. This possibility may explain why many aerobic animals may flourish in an environment practically devoid of molecular oxygen (the deep-sea fauna discussed earlier) - they may themselves produce it from their internal water. This may also explain how endogenous oxygen is produced in the body of land animals, including human beings under some extreme conditions (Timochko et al., 1996).

Properties of a biphasic aqueous system where one of the phases is represented by non-equilibrium EZ-water and the other operates much closer to equilibrium ("bulk" water) are consistent with Bauer's Principle of Stable Non-equilibrium because at least part of energy released may be used to restore the EZ-water component. The second principle of Bauer according to which "...all the work that may be performed by living systems is done only at the expense of structural energy (of its excited elements), that is, by forces generated by a living system itself," also holds true because it is the "structural energy" of EZ-water that is being converted into free energy. On this basis, we consider that EZ-water represents the "primordial egg" possessing the initial stock of structural energy (Fo = μo*mo) that may be used for work against equilibrium.

What kind of external work may be performed by EZ-water for self-sustaining and increasing the total stock of the system's structural energy? If CO2 and N2 are present in such an aqueous system, then energy of electronic excitation released in the course of oxygen reduction can be used in their activation. Due to the reductive potential of EZ-water, carbonyls and amines may be produced. This allows for initiation of chains of chemical reactions known as amino-carbonyl reactions in which complex organic molecules arise and polymerize (Koldunov et al., 2000). Hydrophilic polymers and their assemblies arising in water present new surfaces that will create EZ (vicinal) water. How efficiently a small quantity of biopolymers will turn bulk water into EZ-water can be demonstrated by our earlier example of the jellyfish. This conversion results in the overall/buildup of a stock of structural energy. Consequently, water in such a system may perform more and more external work. Thus the third Principle, the Principle of Increasing of the External Work Performance, is also at work here.

Branching chain reactions play a key role in the process discussed. Regarding such reactions, it is interesting to recollect the proposition of Sir Cyril Hinshelwood (1966) who, together with Nikolai Semenov, was awarded the Nobel prize for the discovery of branching chain reactions: "... It is very possible and even is rather probable, that from the very instant of life's emergence on the Earth, a giant branching reaction has taken place."

Thus, the properties of aqueous systems representing EZ-water contacting ground-state (bulk) water containing carbonates, nitrogen

and other inorganic "impurities" meet all the requirements of Bauer's principles defining the living state. However, we have to ask the question of whether the non-equilibrium (energy-rich) state of water is induced only by preexisting surfaces that it hydrates, or whether it is an intrinsic feature of water that may exist in an able-to-perform-work stable non-equilibrium state even in the absence of such surfaces.

A Physical Understanding of the Dynamics of Biological Water

In this section we will try to explain the biological properties discussed above and in particular the dynamics of water within the framework of quantum physics. Why it is necessary to involve quantum physics? So far, many attempts to understand the behavior of liquid water have been pursued along classical descriptions of a static two-body interaction between water molecules, assuming that the collective N-body interaction among molecules could always be reduced to a sum of two-body interactions. The most widespread model has been the one based on so-called H bonding (Amgell, 1983; Chen and Teixeira, 1986). Each water molecule is assumed to develop two protuberances of its own electron cloud, and also to have two invaginations of the same electron cloud induced by the electrostatic attraction between electrons and positively charged H-nuclei. Assuming that each protuberance of one molecule fits into a corresponding invagination of a neighboring molecule, the well known property of the tetrahedral coordination of water molecules emerges; each molecule is bound to four other molecules put on the vertices of a tetrahedron having the given molecule at its centre. An H-bonded network should therefore be the basic structure of water. However, in order to fit the experimental results of neutron and X-ray scatterings, together with the observed thermodynamical properties of water, it is necessary to assume that each H-bonded network is indeed flickering. A fraction of molecules at each temperature T will not be bonded so that there is a dynamic equilibrium between bonded and non-bonded molecules. In order to fit the observations, it is necessary to assume a lifetime τ for the H-bonding, dependent on temperature. At T=240 K, τ=20 picoseconds, whereas at T=300 K, τ=2 picoseconds. The very small value of the H-bond lifetimes presents a major problem to the physical theory. How is it possible to apply static field approximation to describe an electric structure, as the H-bond actually is, lasting only a few picoseconds? The fast fluctuation of this electrically charged structure is actually making it an antenna having an oscillation frequency in the infrared region. Moreover the wavelength of this oscillation is large enough to cover a huge number (many millions) of molecules producing a collective motion that cannot be reduced to a sum of two body scatterings. The above consideration suggests that ordinary quantum mechanics, namely the theory describing the motion of a small number of bodies subjected to their mutual attraction only, is not the correct conceptual framework for the investigation of liquid water. An intrinsic many-body theory such as quantum field theory (QFT) should be brought in.

In this new framework the physical situation could be conceptualized as follows. As for all quantum objects, a water molecule cannot do other than fluctuate. Fluctuations will occur between the ground state and a particular excited state. They give rise to a corresponding fluctuation of an electromagnetic field of wavelength:

[16] $\lambda = hc/Eex$

where h is the Planck constant, c is the speed of light and Eex is the energy of the excited state. Within a region the size of λ, all the molecules are acted upon by a field having the same well defined phase (this is indeed the property of the coherence). So during the lifetime of the fluctuation, they will move in unison, and this region we will call the Coherence Domain (CD). When the density N/V of the water molecules is low, as in a gas or vapor, the lifetime of the fluctuation is very short and the structure of the coherence domain disappears quickly, producing only a very modest correction (real gas) with respect to the structure of the ideal gas. However, it has been proved (Preparata, 1995) within the theoretical framework of Quantum Electro-Dynamics (QED) that when the density exceeds

a critical threshold and temperature T is below a critical value, the CD can exist much longer since the energy per particle of each component becomes lower than its energy when free. In the case of liquid water, the average energy of an oscillating molecule at room temperature is estimated at 1.53 eV, with the average energy of the induced e.m. field being 3.55 eV per molecule, whereas the attractive interaction energy between the field and molecule being -5.34 eV, giving a net balance of -0.26 eV in the coherent situation with respect to the free non-oscillating particle case. The actual critical value of threshold density of water is simply given by the value when the interaction energy between field and particles overcomes the positive energy necessary to excite water molecules and produce the field. In other words, when the assembly of molecules becomes dense enough, the e.m. field produced by the molecule fluctuation becomes large enough to keep the molecules oscillating and transform the phenomenon from a transient to a stationary state. A rigorous mathematical treatment can be found in the literature (Preparata, 1995; Arani et al., 1995; Del Giudice and Vitiello, 2006).

The selection of the particular excited state involved in coherent oscillations results from competition between all the excited levels. The winner is the state that reaches the critical threshold most quickly. In the case of liquid water, the selected excited state is the 5d level of the molecule electron cloud at 12.06 eV, only 0.54 eV below its ionization threshold, so that $\lambda = 0.1$ μm. The coherent state is the superimposition of these two configurations whose weights are 0.87 and 0.13 respectively, so that in every moment in the CD there are 13% almost free electrons per domain. Del Giudice et al. (1995) have shown the almost free electron oscillates up to ~0.35 Å away from the electron core. Coherent water is thus a potential electron donor, i.e., the same as EZ-water.

For a complete description of a dynamic liquid, one also needs to consider the thermal collisions among molecules that would spoil the coherence acquired by electrodynamic attraction. Thus a situation can be reached where molecules are attracted and kept in tune by a coherent e.m. field within the CDs, and are simultaneously being pushed out of tune by thermal collisions. The mathematical theory worked out by Arani et al. (1995) provides an estimate at each temperature and the fraction of molecules in the coherent state. As in the Landau model of liquid superfluid helium, each molecule in time goes across the two fractions such that CDs in a pure liquid go through a continuous process of birth and death.

It needs to be appreciated that the electrodynamic attraction responsible for CD formation is a truly collective process, which cannot be found when only a few particles interact. It is simply the molecular oscillation induced by the collective electrodynamic process that explains the formation of the protuberances at the origin of each binding, whose time-dependence arises from the oscillatory character of the coherent dynamics. To calculate the total binding energy of the molecules in a CD, one has to add to the energy gap (electromagnetic binding energy) the electrostatic contribution of the static dipole interaction that brings the total binding energy to 0.42 eV per molecule.

An interesting phenomenon occurs at the interfaces between the liquid and the hydrophilic surface. The attraction between the liquid and the surface could be strong enough to compensate for the disruptive effect of thermal collisions, thereby stabilizing the CDs, whose lifetime could thus be days, weeks, or even months. Interfacial water permanently exhibits a coherent structure, whose long range dynamics become observable (Del Giudice and Tedeschi, 2009; Del Giudice et al., 2009). We predict that the properties of such coherent interfacial water are those of EZ-water.

The presence of a trapped e.m. field within the CD produces a strong field gradient on the boundary. According to the well known formula (see any standard textbook of electrodynamics):

[17] $F = -Q^2/M \text{ grad } A^2$

where A is the magnetic vector potential of the field, Q is the particle charge and M the particle mass, molecules get stretched since elec-

trons are repelled tens of thousands times more strongly than nuclei due to the high value of nucleus/mass ratio. In this way, in the boundary region of the CD, whose depth has been estimated at ~40 Å (Del Giudice et al., 1995), a multilayered polarized structure appears where all almost free electrons are oriented outwards with respect to their parent molecules, with distances from the electron core ranging from 0.35 to 0.70 Å. As a consequence, it is possible to show the existence at the interface CD-non coherent water of a capacity per unit area of 20 μFarad/cm2, and an electric potential difference ranging from 50 to 120 mV.

The appearance of this electric potential jump on the outer surface of water CDs, whose value is in striking agreement with the generally accepted cell membrane potential, is naturally present and is not the consequence of any external supply of energy. It is the consequence of the inner dynamics of water that produces this potential, by releasing energy to the environment. This result agrees completely with Bauer's Principle of Stable Non-Equilibrium, since free energy necessary to produce internal work is extracted from the inner energy of the system during the transition from non-coherence to coherence.

Let us now address some thermodynamical implications. According to the first principle of thermodynamics, we can write for a general system at constant temperature:

[18] $W=F2-F1=(U-TS)2-(U-TS)1=U2-U1-T(S2-S1)$

where W is the work done, F is the free energy, U is the energy, S the entropy, and T the temperature; index (1) refers to the non-coherent state, and index (2) to the coherent state.

Eq. (18) summarizes the demands of Thermodynamics. Let us discuss how the system could do positive work: W>0. Two possibilities can be recognized:

1. Inert matter. In this case the entropy of the system increases S2>S1 so that positive work can be produced only if U2>U1 (inflow from outside), whereas the positive quantity T(S2-S1) is the amount of external energy that heats the system and is the cost of the process.

2. Living matter. In this case the onset of coherence described above implies S2<S1, that compels also to have U2<U1, in order to abide to the Second Law of Thermodynamics. In this case the cost becomes U1-U2 whereas the work is performed by virtue of the positive quantity T(S1-S2)!

This conclusion agrees fully with the Bauer's principles. The system extracts energy from its internal reservoir and uses part of this energy to perform work. Thus we get the possibility of the following cycle:

1. production of work through the transition from non-coherence to coherence

2. restoration of internal stock through the transition from coherence to non-coherence

Let us now return to interfacial water.

The presence of a reservoir of almost free electrons produces two major consequences. First, creation within liquid water of a reducer (CD) that can supply redox reactions. The release of electrons can occur through the quantum tunnel effect; the almost free electrons should cross an energy barrier whose height is (0.54-X) eV, where X is ~0.1 eV due to the electric potential difference existing on the boundary of the CD. We get a height of ~0.44 eV coinciding with the electronegativity of the molecule O2 that becomes the privileged receptor of the electrons tunnelling out of the CD. The result of this tunnelling is that a coherent molecule H2O gives rise to the ion pair $H2O+\bullet$ and $O2-\bullet$, and these are the starting points of a chain of reactions (Hinshelwood, 1966; Voeikov and Naletov, 1998). Second, this reservoir of almost free electrons can be excited by small amounts of external energy producing coherent excited states (vortices), whose lifetime could be very long due to lack of attrition within the CDs. The long life of single excitations enables a huge number of excitations to accumulate, producing higher and higher excited coherent states. As a consequence, CDs become devices that dynamically store large amounts of energy. Energy is

collected in the environment as low grade (high entropy) energy and transformed into high grade (low entropy) energy able to do external work, as has long been argued by both Szent-Gyorgyi and Bauer. Notably Bauer's Principle of Increasing of the External Work Performance is operative here.

The energy stored in the CDs cannot be released thermally due to coherence. The only possible decay is through a chemical channel, as follows. Non-aqueous molecules, provided they resonate with water CDs, can be attracted into them as "guest molecules." Doing so, they lose their independence but share the ownership of the energy stored in the CD. The coherent system "water plus guest molecules" becomes a multimode laser (Del Giudice and Tedeschi, 2009). When the energy stored in the CDs matches the activation energy of the whole array of guest molecules, the system discharges and completes its oscillation, which is then the result of the interplay between electromagnetism and chemistry. Hence biochemical reactions do not occur in a diffusive manner, but are driven by a coherent e.m. field according to a code of mutual molecule recognition and recall based on the resonance. A side effect of this dynamics is that water CDs are free to oscillate, thereby creating the possibility of the onset of a coherence among them (supercoherence), according to the same dynamics that produced their appearance out of single molecules (Del Giudice and Tedeschi, 2009; Del Giudice et al., 2009). A hierarchical structure of nested coherence domains is generated, followed by improvement in the coherence of the components. This is the consequence of an uncertainty principle between the number of components N and the phase Φ,

[19] $$\Delta N \, \Delta \Phi \geq h$$

where h is the Planck's constant. Since $\Delta N < N$, the uncertainty $\Delta \Phi$ of the phase reduces as N increases, making the system more coherent when the number of the participants to the coherent oscillation increases. The appearance of supercoherence, namely coherence among the coherent domains then produces additional negentropy and, according to Bauer, increases the work done on the environment. The dynamics of life implies the emergence of a law of evolution in the biosphere that increases the coherent correlations among its components, and by so doing, maximizes the work performed by them.

Conclusion

Water is the unique substance that within a certain range of boundary conditions (pressure and temperature) creates a system residing in a stable non-equilibrium state due to coexistence of its two phases that have different thermodynamic parameters. One of the phases is represented with low entropy coherent domains (Exclusion Zone water) and the other is high entropy "bulk" water. This dual system can perform internal work to sustain its non-equilibrium state due to negentropy arousal from spontaneous non-coherent to coherent state conversion. It can also execute external work for its growth and development due to free energy generated by water respiration. Thus water properties under conditions of adequate (not excessive) heat supply agree with all the principles on which Bauer's theory of living matter is based, and may be considered as a primary substance residing in a living state. It follows that the conditions required for the emergence of living systems was the availability of liquid water and that their further development depended upon the availability of a few chemical elements from which more and more complex hydrophilic surfaces would continuously be generated.

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Discussion with Reviewers

Denys Wheatley[1]: Is water its own catalyst, or is it necessary to have some other catalyst in this process of water respiration? The coal analogy is interesting but indirect. It is perhaps the question of whether a surface (or some particular surface) is an absolute requirement; if so, what surfaces are important – those of protein, or perhaps lipid membranes? Frey-Wyssling maintained that all life is surfaces, reiterated to some extent in one of Szent Gyorgy's dictums.

Vladimir Voeikov and Emilio Del Giudice: The process that we define here as "water respiration" is essentially water oxidation coupled with oxygen reduction in aqueous systems where the two phases — "organized" water (interfacial water, EZ-water, coherent water domains) and "bulk" water — coexist. The coexistence of two aqueous phases is the necessary, though apparently not sufficient, condition for "water respiration." According to Pollack's data, the interface is more negatively charged than the bulk water and the larger its area, the thicker is the layer of EZ-water and consequently the larger is its electron-donating capacity. From this point of view EZ-water present in the nucleus should exhibit the highest potential with respect to intracellular water. The EZ-water present in the nucleus should also exhibit the highest electron-donating capacity since DNA has the highest specific charge density among all the biopolymers and supramolecular structures.

"Water respiration" — as well as other branching chain reactions of combustion — needs several conditions to be satisfied in order to start and to proceed. First, concentrations of reagents should exceed certain threshold levels; second, an initiation stimulus is needed to "spark" the process; third, in most cases certain catalysts are needed for the process to go on effectively. We believe that water respiration also needs the presence of catalysts, though this peculiarity was not discussed in the paper. One of the most interesting "impurities" that could play the role of a catalyst in the processes related to water splitting and burning might be the family of carbonates and, in particular, the bicarbonate:

$CO_2 \ll H_2CO_3 \ll HCO_3^-$

Carbonates are commonly present in water because of the high solubility of CO_2 in water (CO_2 is 30-35 times more soluble in water than O_2) and because of the wide natural occurrence of carbonates in nature. Thus, HCO_3^- easily reduces one of the products of water splitting, hydroxyl radical ($HO\bullet$), turning it into carbonate $CO_3^{-\bullet}$. The latter may support water oxidation, oxidize hydrogen peroxide, and give rise to the emergence of organic compounds such as oxocarbons; the latter are able to originate cyclic red/ox reactions. A network of coupled and mutually supporting red/ox reactions emerges, yielding energy of electronic excitation. Thus (bi)carbonates may be regarded as peculiar catalysts of water "burning." Experimental data on the role of bicarbonates in sustained process of combustion occurring in aqueous bicarbonate solutions will be published soon (manuscript in preparation).

We discuss now as a final point a feature entirely new that the dynamics of catalysis acquires in a coherent environment. As described in the last section of our paper, a coherence domain encloses a self-trapped electromagnetic (e.m.) field; in the case of water the frequency of this field (in energy units) is 0.26 eV, an IR frequency. Molecules able to oscillate on the same frequency, modulo kT, are attracted mutually within the domain. This is a well-known Electrodynamics theorem widely used in the Laser applications to Chemistry. When this electrodynamical mechanism works, the biochemical dynamics acquires the following properties:

a) a selective attraction among molecules gets developed; only molecules able to resonate among them and with the CD are able to interact through this mechanism, whereas non-resonating molecules ignore each other and can interact through random collisions only.

b) this selective attraction has a much higher rate than the diffusive molecule interaction, since the latter occurs through quite slow random movements whereas the former is a long-range one (the range is the size of the CD, namely several hundreds of Angstroms) and is mediated by an attracting force, so that the rate of the electromagnetically assisted chemical interaction is much higher than the rate of the diffusive interaction

c) the output energy of each chemical reaction is received by the CD and modifies its frequency of oscillation, that in turn modifies the molecule species able to interact. In this way the surface of CDs becomes the site of an electromagnetically assisted catalysis able to evolve with time as a product of its past history.

Wheatley: This raises a second question of whether clathrates might (on bulk alone) provide a free energy source in a similar way, should a surface not be mandatory. What percentage of the basic energy supply would come from this source rather than EZ water?

Voeikov and Del Giudice: Clathrates (dependent on the nature of the "kernel" forming them) are likely "seeds" to organize more or less thick aqueous shells around them, and such a shell may have reducing properties characteristic of coherent domains or EZ-water. Such domains may contribute to the process of water respiration in an aqueous system containing them. One may suggest that some peculiar properties of highly diluted aqueous solutions of hydrophilic nanoparticles (for example, Neowater®, hydrated fullerenes solutions prepared according the method of G.V. Andrievsky, silver colloid solutions, etc.) may be related to water combustion processes proceeding in them. Circumstantial evidence supports such a suggestion, though its direct proof is certainly needed. It is difficult to evaluate what percent of the basic energy supply for vital functions would come from this source in comparison with EZ-water.

Wheatley: Would not a "quasi-steady state" cell (in fact it must be involuting, even if very slowly as Bauer appreciated) be burning (degrading) proteins while it is structurally rearranging itself in the survival process (i.e., delaying the inevitable)? Perhaps this provides much of the energy required? Or is this insignificant compared with water combustion?

Voeikov and Del Giudice: The concept of water combustion as a source of high density energy for supporting living cells in a stable non-equilibrium state does not rule out but rather supplements other well-known processes providing energy supply for the performance of vital functions such as aerobic and anaerobic glycolysis (fermentation). The difference between the two ways of energy production is not in the quantity of energy generated through each of them, but in energy quality. This idea is not original. Half a century ago Albert Szent-Gyorgyi suggested that there exists the mode of respiration alternative and complementary to the mitochondrial one: "Is it not that there are two independent systems of energy production, both using O2 as their final electron acceptor, the one located in mitochondria and responsible for the production of ATP, while the other is located in basic cellular structures themselves which have to be maintained in their peculiar (metastable) state? ... Why could the high energy electrons of DPNH or TPNH not be placed more directly on the living structure which could couple them to O2 using their energy more directly?" (Szent-Gyorgyi A, 1960. Introduction to a supramolecular biology. NY & London: Academic Press, 128-129).

One system of energy production or another would dominate, depending on the physiological state of a cell or an organism. We tried to illustrate this point in the paper. Indeed, at the stage of "quasi-steady state," the one-electron oxygen reduction — at which energy of electronic excitation is generated — tends to be less pronounced than at the stage of growth and development. The classical system of energy production (aerobic glycolysis) tends to dominate. Regarding proteins: their caloric value is low in comparison to that of carbohydrates and fats, though they may be cleaved to amino acids, and some of them may be converted to glucose through the process of gluconeogenesis.

Wheatley: If the cell represents primarily a body of water that has become uniquely organized (JZ Young referred to a whirlpool as a body of water that, because of its particular organization, can be consider a definite entity or phenomenon of nature), and we know it is always in a state of flux within itself and in relation to the rest of the universe (i.e., its environment), then can we really distinguish as Bauer believed between "internal" and "external" energy when active cells are always in its mother liquor or medium (water) on the "outside" as well as on the "inside"? Is this not a continuum rather than distinctly separate phases?

There is one fundamental challenge to this hypothesis. If much of the basic "free" energy of cells comes from the low activation energy of the more weakly bound electrons in I-water (the more organized water of an EZ) as hypothesized, what are the most important experiments required to provide tangible evidence for it? I refer here specifically to experiments on living systems and not physical models per se.

Voeikov and Del Giudice: This is a very deep question. Peculiarity of water in Biosphere is that this substance provides for the continuum (interlacement) of living things with their environments on all the levels of living matter organization. On the other hand, water in different domains coexisting with each other reside in many different energy states. The potential difference between adjacent aqueous phases provides for the work performance. The example of a whirlpool is a good illustration of the indissoluble coexistence of continuity and heterogeneity: a whirlpool can exist only when on the one hand a constant influx of "low grade energy" water is available and on the other hand an outflow exists. Under theses conditions a whirlpool represents a body of water with sometimes extremely high energy potential (charged with high grade energy) that can perform such forms of work that can never be performed by even great mass of "low grade energy" water.

Regarding the fundamental challenge to this hypothesis and experiments on living systems we may suggest to take for the research such living systems that are essentially WATER, for example a jelly fish. Using this living system as a model object, many experiments may be performed on it to evaluate what is the role of jelly fish's water in energy supply for the performance of its vital functions.

Mae-wan Ho[2]: I have proposed and refined a 'thermodynamics of organized complexity' in successive versions of The Rainbow and the Worm, The Physics of Organisms (1993, 1998, 2008, World Scientific, http://www.i-sis.org.uk/rnbwwrm.php) that presents organisms as circular, or dynamically closed zero-entropy systems that store energy over all space-times. (see also Ho MW and Ulanowicz R. Sustainable systems as organisms? BioSystems 2005, 82, 39-51, http://www.i-sis.org.uk/onlinestore/papers1.php#section3). Stored energy is by definition coherent energy, which is why certain organisms can remain dormant and alive without metabolism, as James Clegg has shown. How would that affect your description of EZ water for the living system?

Voeikov and Del Giudice: First, we would like to make a general statement. The concept of coherence does not coincide with the concept of order. Every coherent system is ordered, but not every ordered system is coherent. A battalion deployed in the court of the barracks is ordered, but not coherent; a ballet is a good example of coherence. In order to have coherence you need an oscillation having a definite phase, so that an ensemble of objects kept together by static interactions, such as H-bonds or whatever other static bonds, cannot be coherent since they cannot have a definite phase. In order to have coherence you need the coupling of matter with a long range gauge field that at the scale of atoms and molecules cannot be other than the e.m. field.

In the case of life, the role of fluctuations becomes crucial since we are not faced by a single coherence but by a complex array of coherences continuously transiting one into another through intermediate steps of non coherence. This further complexity of coherence corresponds to the emergence of negentropy into the system. That is also why life is an out-of-equilibrium phenomenon. In such a fluctuating system you cannot define state functions, but goal functions only. Entropy has not a defined value but oscillates during the process. At beginning energy coming from outside accumulates on a large number of degrees of freedoms. Subsequently the system undergoes a coherent transition that decreases sharply the entropy of the system and just this curtail of degrees of freedom coincides with negentropy (introduced by Boltzmann, Schroedinger, Szent-Gyorgyi, and Prigogine), transforming this unordered energy into "meaningful" free energy, concentrated on a small number of collective degrees of freedom. This is just the pulsation of the living organism characterizing life.

Energy can exist in two qualities: an active form that is performing work and the passive one that is the reservoir from which the organism

sucks energy. The major point of Bauer that we agree with is that an organism actively extracts energy from the environment rather than being ordered by the energy flowing through. This property can be observed too in EZ-water that is from the very beginning more ordered and coherent than water in its environment. And this allows for the continuous existence of the gradient of energy from disordered water to EZ-water. The latter transforms it into higher potential energy that normally is converted into free energy ('work,' metabolism, etc.). If the organism is dried out or frozen, metabolism stops because the channel for free energy "dissipation" is switched off, but the potential is still there provided that its reservoir (EZ-water) is not destroyed.

Ho: In what sense does EZ water reduce oxygen, when oxygen is simply acting as a catalyst to release the stored (non-equilibrium) energy? How does infrared radiation form EZ, so that there is an excess of H+ (presumably ejected from EZ) next to it?

Voeikov and Del Giudice: Oxygen is reduced in the conventional chemical sense – EZ-water is a reducer, an ultimate donor of electrons; oxygen is the final acceptor of electrons – the ultimate oxidizer. In no sense it is a catalyst; it is first a reagent and then a product. The fact that oxygen is also the product of water oxidation is just the unique property of this redox reaction where reagents and final products are formally the same. In reality, water that is produced is the result of "free" oxygen reduction, while oxygen that is produced is the product of oxidation of water belonging to EZ-water domain. Therefore, energy released comes from the difference of energy potential between EZ-water and bulk water.

Pollack's data don't imply that EZ water is formed by IR-radiation — it responds to IR-radiation by the increase of its capacity of storing energy in the form of vortexes of quasi-free electrons in the coherent domain (see the answer to the next question). Besides, the H+ near the EZ-zone may originate not only from it, but from the bulk water as well.

Ho: To my mind, EZ is rather like a solid state, so the delocalization of its electrons would be similar to what happens in a solid-state device. But again, how would that lead to H+ being ejected?

Voeikov and Del Giudice: The coherent oscillation of water in the coherence domains involves an excited level where there is one quasi-free electron per molecule. Since the weight of the excited level in the coherent state is 0.13, there are altogether 0.13 quasi-free electrons per molecule. In a CD there are about seven million molecules so that we have about 900,000 quasi-free electrons. That is a lot! These electrons could tunnel out by quantum tunnel effect or could be extracted by small excitations. When the electron is extracted from the CD, it leaves behind an ionised molecule, which, having lost an electron, cannot join any longer the coherent oscillation and therefore reaches the non-coherent fraction of molecules that includes, as in the Landau model of liquid Helium, the molecules put out of tune by thermal collisions. The extracted electron could be captured by an oxygen molecule dissolved in water giving rise to a negative ion. The pair of ions so produced, after some chemistry elucidated in our paper, gives rise eventually to a proton and a hydroxil. The CD is therefore a donor of electrons and then a chemical reducer that, together with the non-coherent fraction, forms a redox pile.

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