

WHAT IS (SCHRÖDINGER'S) NEGENTROPY?

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THERMODYNAMICS OF ORGANIZED COMPLEXITY

I attempt to outline, qualitatively, a 'thermodynamics of organized complexity' based on energy storage and mobilization in a coherent space-time structured system maintained far from thermodynamic equilibrium by energy flow. I propose that symmetrically coupled cycles will arise in open systems capable of energy storage, and that for such systems, the equal population of energy over all space-time domains (the 'k = const.' regime) is the extremum state. This regime is characterized by the maximum of the Gibbs entropy function, $S_G = -k \sum_j p_j \ln p_j$, in which the potential degrees of freedom are maximized over all space-time domains, but it is also the state of minimum entropy because the activities in all space-time domains are effectively coupled to a single actual degree of freedom.

IS IT FREE ENERGY?

The 'negentropy', or 'negative entropy', that I am thinking of, comes from Schrödinger's book, *What is Life?* [1], in which he writes, "*It is by avoiding the rapid decay into the inert state of 'equilibrium' that an organism appears so enigmatic.... What an organism feeds upon is negative entropy.*" In a footnote, later, however, Schrödinger explains that by 'negative entropy', he really means *free energy*. Many subsequent authors have taken negentropy as being simply entropy with a negative sign [2,3], as they feel it simply is erroneous to refer to 'negentropy' as free (Gibbs) energy.

Despite that, the term continues to be used by biologists to the present day, beginning with one of the most authoritative among them: "*It is common knowledge that the ultimate source of all our energy and negative entropy is the radiation of the sun*" [4]. The reason 'negentropy' continues to be used is that 'entropy with a negative sign' simply does not capture what is intended by the original term. Schrödinger uses it to identify the remarkable ability of the living system, not only to avoid the effects of entropy production - as dictated by the second law - but to do just the opposite, to increase organization, which intuitively, seems like the converse of entropy. Szent-Györgi, on the other hand, alludes to both the notions of Gibbs energy and of organization in his use of the term. Both scientists have the right intuition - energy and organization are inextricably bound up with each other. Within biological science, Gibbs energy is generally regarded the most relevant for biochemical reactions. The change in free energy being,

$$\Delta G = \Delta H - T\Delta S \quad (1)$$

The energy (enthalpy) change of the system is thereby partitioned into the entropic term, which is related to the random thermal motion (molecular chaos) of the molecules that is somehow *not* available for work, and tends to disappear at absolute zero temperature, and the Gibbs energy, which *is* somehow available for work. But as there need be no entropy generated in adiabatic processes - which occur frequently in living systems (see below) - the division into available and non-

available energy cannot be absolute: in other words, the energy associated with a molecule simply cannot be partitioned into the two categories *a priori*.

IS IT MAXWELL'S DEMON?

The second law of thermodynamics is a statistical law which applies to a system consisting of a large number of particles. A major difficulty, already noticed by Schrödinger, is that single molecules, or a very small number of them, are the active agents in living systems. Thus, each cell contains only one or two molecules of each sequence of DNA in the nucleus. Similarly, it takes no more than several molecules of a hormone to bind to specific receptors in the cell membrane in order to initiate a cascade of biochemical reactions that alter the characteristics of the whole cell. Does that mean the second law cannot be applied to living systems?

This difficulty is related to the problem of Maxwell's demon [5] - an hypothetical intelligent being who can open a microscopic trapdoor between two compartments of a container of gas at equilibrium in order to let fast molecules through in one direction, and the slow ones in the other, so that work can then be extracted from the system. It became evident in the 1950s that something like a Maxwell's demon could be achieved with little more than a trapdoor that opens in one-direction only and requires a threshold amount of energy (activation energy) to open it. This is realizable in solid-state devices such as diodes and transistors that act as rectifiers [5].

Similar situations are associated with biological membranes, which play a major role in structuring biological systems. Typically, an electrical potential gradient of some 10^7 V/m is maintained across membranes, embedded in which are enzymes involved in the vectorial transport of ions and metabolites from one side to the other, as for example, the transport of Na^+ out of, and K^+ into the cell by the Na^+/K^+ ATPase. It has recently been demonstrated that weak alternating electric fields can drive unidirectional active transport by this enzyme without ATP being broken down. In other words, the energy from the electric field is directly transduced into transport work by means of the membrane-bound enzyme. Moreover, randomly fluctuating electric fields are also effective, precisely as if Maxwell's demon were involved in making good use of the fluctuations [6]! Of course, there is no real violation of the second law, for rectifiers and biological membranes are both non-equilibrium *structures* which can *store* energy.

The problem of Maxwell's demon is generally considered as having been 'solved' by Szilard, and later, Brillouin [2], who showed that the demon would require *information* about the molecules, in which case, the energy involved in obtaining information would be greater than that gained and so the second law remains inviolate. Perhaps, what they have failed to take account of is that the so-called information is already supplied by the special structure or *organization* of the system in which energy is stored. Biological membranes, in particular, are *excitable* structures poised for relaying and amplifying weak signals into the cell.

IS IT ORGANIZATION?

An organism is nothing if not organized heterogeneity, with nested dynamic structures over all space-time scales. There is no homogeneity, no static phase held at any level. Even a single cell has its characteristic shape and anatomy, all parts of which are in constant activity; its electrical potentials and mechanical properties similarly, are subject to cyclic and non-cyclic changes as it responds to and counteracts environmental fluctuations. Spatially, the cell is partitioned into numerous compartments by cellular membrane stacks and organelles, each with its own 'steady states' of processes that can respond directly to external stimuli and relay signals to other compartments of the cell. Within each compartment, microdomains can be separately energized to give local circuits, and single enzyme proteins, or complexes of two or more proteins function as 'molecular machines' which can cycle autonomously without immediate reference to its surroundings.

In other words, the steady 'state' is not a state at all but a conglomeration of processes which are spatiotemporally organized, *i.e.* it has a deep space-time structure, and cannot be represented as an instantaneous state or even a configuration of states [7]. Characteristic times of processes range from $<10^{-14}$ s for resonant energy transfer between molecules to 10^7 s for circannual rhythms. The spatial extent of processes, similarly, span at least ten orders of magnitude from 10^{-10} m for intramolecular interactions to metres for nerve conduction and the general coordination of movements in larger animals.

The processes are also *catenated* in both time and space: the extremely rapid transient flows (very short-lived pulses of chemicals or of energy) triggered on receiving specific signals, are propagated to longer and longer time domains of minutes, hours, days, and so on via interlocking processes which ultimately straddle generations. The processes, rather than constituting the system's 'memory' as we might think, are actually projections into the *future* at every stage. They determine how the system responds and develops in times to come. Typically, multiple series of activities are initiated from the focus of excitation. While the array of changes in the positive direction is propagating, a series of negative feedback processes is also spreading, which has the effect of dampening the changes. It is necessary to think of all these processes *cascading* in parallel in many dimensions of space and time. In case of disturbances which have no special significance for the body, homeostasis is restored sooner or later as the disturbance passes. On the other hand, if the disturbance or signal is significant enough, a series of irreversible events brings the organism to a new 'steady state' by developing or differentiating new tissues. The organism may even act to alter its environment appropriately [8]. The secret of 'negentropy' lies undoubtedly in this intricate space-time organization. But how can one describe it in terms of the second law?

As living systems consist of nested space-time compartments of various sizes, all the way down to microdomains and molecular machines, then at the very least, this implies that if thermodynamics were to apply to living systems, it must apply to individual molecules as much as to ensembles of molecules. Such is the physiologist Colin McClare's contention [9].

IS IT STORED ENERGY?

In order to formulate the second law of thermodynamics so that it applies to single molecules, McClare introduces the important notion of a characteristic time

interval, τ , within which a system reaches equilibrium at temperature T . The energies contained in the system can be partitioned into *stored* energies versus *thermal* energies. Thermal energies are those that exchange with each other and reach equilibrium in a time less than τ (so technically they give the so-called Boltzmann distribution characterized by the temperature T). Stored energies are those that remain in a non-equilibrium distribution for a time greater than τ , either as characterized by a higher temperature, or such that states of higher energy are more populated than states of lower energy. So, stored energy is any form which does not thermalize, or degrade into heat in the interval τ . Stored energy is *not* the same as Gibbs energy, as the latter concept does not involve any notion of time. Stored energy is hence a more precise concept.

McClare goes on to restate the second law as follows: *useful work is only done by a molecular system when one form of stored energy is converted into another. In other words, thermalized energy is unavailable for work and it is impossible to convert thermalized energy into stored energy.*

The above restatement of the second law is unnecessarily restrictive, and possibly untrue, for thermal energy *can* be directed or channelled to do useful work in a cooperative system, as in the case of enzymes embedded in a membrane [7], which can undergo correlated motions. Thermalized energy from burning coal or petrol is routinely used to run machines such as generators and motor cars (which is why they are so inefficient and polluting).

A more adequate restatement of the second law, which can apply to single molecules as well as ensembles of molecules, I suggest, might be as follows [8,10]: *Useful work can be done by molecules by a direct transfer of stored energy, and thermalized energy cannot be converted into stored energy.*

The second half of the statement accounts for entropic decay as is usual in real processes both inside and outside the living system. The first half, however, is new and significant for biology.

The major consequence of McClare's ideas arises from the explicit introduction of time, and hence *time-structure*. For there are now two quite distinct ways of doing useful work, not only slowly according to conventional thermodynamic theory, but also quickly - both of which are reversible and at maximum efficiency as no entropy is generated. This is implicit in the classical formulation for an isolated system, $dS \geq 0$, for which the limiting case is $dS = 0$. But the attention to time-structure makes much more precise what the limiting conditions are. Let us take the slow process first. A slow process is one that occurs at or near equilibrium. According to classical thermodynamics, a process occurring at or near equilibrium is reversible, and is the most efficient in terms of generating the maximum amount of work and the least amount of entropy. By taking explicit account of characteristic time, a reversible thermodynamic process merely needs to be slow enough for all thermally-exchanging energies to equilibrate, *i.e.* slower than τ , which can in reality be a very short period of time, for processes that have short time constants. Thus, for a process that takes place in 10^{-12} s, a microsecond (10^{-6} s) is an eternity! So high efficiencies of energy conversion can still be attained in thermodynamic processes which occur quite rapidly, provided that equilibration is fast enough. This may be where spatial partitioning and the establishment of microdomains is crucial for restricting the volume within which equilibration occurs, thus reducing the equilibration time. This means that *local equilibrium may be achieved at least for some biochemical reactions in the living system*. We begin to see that thermodynamic equilibrium itself is a subtle concept, depending on the

level of resolution of time and space.

At the other extreme, there can also be a process occurring so quickly that it, too, is reversible. In other words, provided the exchanging energies are not thermal energies in the first place, but remain stored, then the process is limited only by the speed of light. Resonant energy transfer between molecules is an example of a fast process. It occurs typically in 10^{-14} s, whereas the molecular vibrations themselves die down, or thermalize, in 10^{-9} s to 10^1 s. It is 100% efficient and highly specific, being determined by the frequency of the vibration itself; and resonating molecules (like people) can attract one another.

Does resonant energy transfer occur in the living system? McClare [9] suggests it occurs in muscle contraction, where it has been shown that the Gibbs energy released in the hydrolysis of ATP is almost completely converted into mechanical energy in a molecular machine which can cycle autonomously without equilibration with its environment. Similar cyclic molecular machines are involved in other major energy transduction processes: in the coupled electron transport and ATP synthesis in oxidative phosphorylation and photophosphorylation, as well as in the Na^+/K^+ ATPase. Ultrafast, possibly resonant energy transfer processes are also operating in photosynthesis. There, the first step is the separation of positive and negative charges in the chlorophyll molecules of the reaction centre, which has been identified [11] to be a readily reversible reaction that takes place in less than 10^{-13} s.

McClare's ideas have been taken up and developed further [12-14], particularly in the notion of nonequilibrium, 'quantum molecular energy machines'. These ideas imply that the living system may use both means of efficient energy transfer: slow and quick reactions, always with respect to the relaxation time, which is itself a variable according to the processes and the spatial extents involved. In other words, it satisfies both quasi-equilibrium and far from equilibrium conditions where entropy production is minimum. This insight is offered by taking into account the space-time structure of living systems explicitly. Are we getting closer to the source of 'negentropy' in living systems?

STORED ENERGY VERSUS GIBBS ENERGY

It is of interest to compare the thermodynamic concept of 'free energy' (Gibbs energy) with the concept of 'stored energy'. The former cannot be defined *a priori*, much less can it be assigned to single molecules, as even changes in free energy for an ensemble cannot be defined unless we know how far the reaction is from equilibrium. 'Stored energy', as defined by McClare with respect to a characteristic time interval, can readily be extended, in addition, to a characteristic spatial domain. We can generalize it to *stored energy within a characteristic space-time*. As such, it is explicitly dependent on the space-time structure of the system, and hence, it is a precise concept which can be defined on the space and time domain of the processes involved. Indeed, stored energy has meaning with respect to single molecules in processes involving quantum molecular machines as much as it has with respect to the whole organism [8]. For example, energy storage as bond vibrations or as strain energy in protein molecules occurs within a spatial extent of 10^{-9} to 10^{-8} m and a characteristic timescale of 10^{-9} to 10^{-8} s [20]. In terms of a whole organism such as a human being, the overall energy storage domain is in metre-decades.

Can one now offer a tentative answer to the question. 'What is negentropy?' Isn't 'negentropy' simply *stored, mobilizable energy*? To work out how energy is

stored and mobilized is the beginning of a 'thermodynamics of organized complexity' which could be applied to living systems. I shall sketch out a few preliminary, qualitative ideas in the last section, some of which are dealt with in greater detail in my recent book [8].

TOWARDS A THERMODYNAMICS OF ORGANIZED COMPLEXITY

Coupled cycles

Significant advances in our understanding of living systems began with the thermodynamics of open systems. The quasi-equilibrium approximations of the steady state developed by Onsager and Denbigh show how symmetrical *coupling* of linear processes can arise naturally in a system under energy flow [15,16]. A system of many coupled processes can be described by a set of linear equations,

$$\mathbf{J}_i = \sum_k L_{ik} \mathbf{X}_k \quad (2)$$

where \mathbf{J}_i is the flux of the i^{th} process ($i = 1, 2, 3, \dots, n$), \mathbf{X}_k is the k^{th} thermodynamic force ($k = 1, 2, 3, \dots, n$), and L_{ik} are the proportionality coefficients (where $i = k$) and coupling coefficients (where $i \neq k$). Onsager showed that for such a multicomponent system, the couplings for which the \mathbf{X}_k s are invariant at microscopic level with time reversal (*i.e.* velocity reversal) will be symmetrical; in other words,

$$L_{ik} = L_{ki} \quad (3)$$

The mathematical entities of the Onsager's thermodynamic equations of motion can all be experimentally measured and verified, although the approach has not yet been systematically applied to the living system. Nevertheless, it captures a characteristic property of living systems: the reciprocal coupling of many energetically efficient processes: for example, ATP synthesis from ADP and P_i is coupled to electron/proton transport in oxidative phosphorylation, and ATP splitting is coupled to the translational movements between myosin and actin binding sites in muscle contraction [8]. In both cases, the reactions are completely reversible: ATP can be split into ADP and P_i by the ATP synthesizing enzyme when the electron/proton gradients are run in reverse. Similarly, ATP is synthesized by the myosin ATPase when ADP and P_i is supplied.

Another important development in the thermodynamics of the steady state came from Morowitz, who derived a theorem showing that at steady state, the flow of energy through the system from a source to a sink will lead to at least one cycle in the system [17]. For a canonical ensemble of systems at equilibrium with i possible states, where f_i is the fraction of systems in state i (also referred to as occupation numbers of the state i), and t_{ij} is the transition probability that a system in state i will change to state j in unit time. The principle of microscopic reversibility requires that every forward transition is balanced in detail by its reverse transition, *i.e.*,

$$f_i t_{ij} = f_j t_{ji} \quad (4)$$

If the equilibrium system is now irradiated by a constant flux of electromagnetic radiation such that there is net absorption of photons by the system, *i.e.* the system is capable of *storing* energy, a steady state will be reached at which there

is a flow of heat out into the reservoir (sink) equal to the flux of electromagnetic energy into the system. At this point, there will be a different set of occupation numbers and transition probabilities, f_i' and t_{ij}' ; for there are now both radiation induced transitions as well as the random thermally induced transitions characteristic of the previous equilibrium state. This means that for some pairs of states i and j ,

$$f_i' t_{ij}' \neq f_j' t_{ji}' \quad (5)$$

For, if the equality holds in all pairs of states, it must imply that for every transition involving the absorption of photons, a reverse transition will take place involving the radiation of the photon such that there is no net absorption of electromagnetic radiation by the system. This contradicts the original assumption that there is absorption of radiant energy (see previous paragraph), so we must conclude that the equality of forward and reverse transitions do not hold for some pairs of states. However, at steady state, the occupation numbers (or the concentrations of chemical species) are time independent (*i.e.* they remain constant), which means that the *sum* of all forward transitions is equal to the *sum* of all backward transitions, *i.e.*,

$$df_i'/dt = 0 = \sum (f_i' t_{ij}' - f_j' t_{ji}') \quad (6)$$

But it has already been established that some $f_i' t_{ij}' - f_j' t_{ji}'$ are non-zero. That means other pairs must also be non-zero to compensate. In other words, members of the ensemble must leave some states by one path and return by other paths, which constitutes a cycle. Hence, *in steady state systems, the flow of energy through the system from a source to a sink will lead to at least one cycle in the system.*

The two results - Onsager's reciprocity relationship and Morowitz' theorem of chemical cycles - I believe, imply a third: that *symmetrically coupled cycles* will arise in open systems which are capable of storing energy under energy flow [8]. Coupled cycles are the stuff of living organization, as a most cursory glance at a metabolic chart of 'biochemical pathways' will immediately reveal to us. It is how living systems store and mobilize energy: the energy yielding cycles are almost always coupled to energy requiring ones so that energy can be transferred to larger and larger space-time domains. (And as mentioned above, *symmetrical* coupling is indeed the rule for the energetically most efficient processes in the living system.) Thus, the energy of the photon absorbed by chlorophyll in green plants goes to reduce NADP and to make ATP, which in turn goes to make carbohydrates, fats, proteins and nucleic acids with increasingly longer turnover times and wider distributions.

Dissipative structures are coupled cycles

Coupled cycles actually also appear in the nonlinear regime [8], in dissipative structures, arising in systems maintained far from thermodynamic equilibrium by energy flow. A nonlinear generalization of the Onsager reciprocity relation has recently been obtained by Sewell for a class of irreversible processes in continuum mechanics [18], suggesting that symmetrical coupling may also be important for dynamical stability in the far from equilibrium regime. A well-studied example of a dissipative structure is the Bénard convection cells which form in a shallow pan of water, heated uniformly from below, as a critical temperature difference is reached

between the top and the bottom of the pan. At that point, the hotter, and therefore, lighter water at the bottom rises to the top while the denser water at the top sinks to the bottom, and so on in a cyclic manner, resulting in a convection flow cell. Soon, the water in the entire pan become convection cells, all of the same size and cycling together, giving a regular honey-comb appearance when viewed from the top. The resulting dissipative structure represents a nonequilibrium phase transition to macroscopic order. It has a dynamic stability suggestive of that in living systems, which depends on the coupling of cyclic processes, in this case, heat flow being coupled to the convective movement of molecules.

Dissipative structures are coherent structures

Dissipative structures are also *coherent* structures in which a system with an astronomical number of *potential* degrees of freedom settles into a single *actual* degree of freedom. It is anti-statistical, collective activity generating long-range dynamical order.

Laser action is yet another example of condensation into a collective mode of activity when energy pumping into the system exceeds a certain threshold. Based on these analogies, Fröhlich [19] predicts that as a living organism is made up predominantly of dielectric molecules packed rather densely together, it may represent a special solid state system where electric and viscoelastic forces constantly interact. Under those conditions, metabolic pumping results in condensation to collective modes of activity or 'coherent excitations', giving macroscopic order and coordination to the living system. Fröhlich's hypothesis has been developed by others since [20,21]. Duffield [21], in particular, proves that the 'Fröhlich state' is an asymptotically stable global attractor. There is, indeed, a growing body of experimental evidence for coherence and cooperativity at different levels within living systems: from the action of enzymes [22], to whole organisms [23] and populations of organisms [24,25].

The enzyme molecule is now known to be much more mobile than previously thought: with peptide bond vibrating, deforming, hydrogen bonds breaking and forming, entire domains of the protein macromolecule contracting and expanding, and the polypeptide chain unfolding and refolding over a wide range of time-scales from 10^{-14} s to seconds and even minutes. Enzyme catalysis depends on the very rapid 'fluctuations' as the protein samples its 'conformational space' in the context of its micro-environment, so that the single trajectory corresponding to efficient enzyme action can be readily accessed in a coherent, or highly cooperative way over the whole of the macromolecule. (For details, readers should consult the excellent collection of papers in ref.[26].)

One of the predictions of Fröhlich's hypothesis of coherent excitations is extreme sensitivity to weak electromagnetic fields, which can precipitate specific coherently excited states or interfere with their formation at phase transition. In my laboratory, we have found that brief exposures of early fruitfly embryos to weak static magnetic fields cause characteristic global perturbations to the segmental body pattern of the larvae emerging 24 hours later [27,28]. The abnormalities are reminiscent of the fluid dynamical patterns obtained in a typical Couette-Taylor experiment, and also similar to the pattern defects that can arise in phase ordered liquid crystals (I thank Ian Stewart for pointing this out to me). Indeed, we have recently succeeded in imaging live organisms by visualizing coherent liquid crystalline mesophases of molecules making up the living tissues [8,29,30]. A particularly interesting finding is that for all organisms, from protozoa to vertebrates

without exception, the anterior-posterior axis of the body is also the major polarizing axis for all of the tissues. This is quite compelling evidence for some kind of globally coherent polarizing field, which not only gives rise to the major body axis, but also phase-order the molecules all over the body.

Coupled cycles, space-time structure, energy storage and coherence

Coupled cyclic processes structure space and time for energy storage and mobilization. In the Bénard convection cells, thermal energy is stored in the hot water at the bottom, which is used to perform the 'work' involved in bulk flow. By extrapolation, we can think in terms of the organism as a nested structure of coupled cycles within coupled cycles spanning the entire range of characteristic space-time domains. One of the most distinguishing feature of the organism - of 'living stuff' as opposed to a 'man-made machine' such as a computer - is that it is thick with activities over all space-time scales (*cf.* Havel's concept that the density of interacting levels is a distinguishing feature of organisms [31]). Its energy storage is correspondingly distributed over the entire range of space-time domains in a readily mobilizable form through coupled, catenated cycles. The reason organisms can respond so promptly and mobilize energy at will is because energy is instantly available in the short-term stores. The ATP 'energy debt' in our muscles, for example, is seldom allowed to accumulate, as it is immediately replenished by creatine phosphate and by breaking down glycogen, these latter energy stores taking increasingly longer times to replace. It is in this way that the organism can effectively achieve a single degree of freedom as consistent with coherence and living organization.

Coherence in a space-time structured system is a transparency of energy and information transfer throughout the entire system. It has many interesting implications [8]. The most obvious implication is that our actions are invariably space-time cascades differing in extents and durations from the microscopic through the mesoscopic to the macroscopic. It is an intriguing thought that the usual distinction between quantum and classical (or microscopic versus macroscopic) phenomena may only be a illusion of scale. The so-called 'collapse of the wave function' associated with a macroscopic measurement process may be the result of a space-time cascade reaching the characteristic dimensions of our everyday awareness, which, nevertheless, remains 'quantum' to an observer of galactic dimensions. The possibility for observing 'macroscopic quantum coherence' has been considered by a number of physicists who question the usual distinction between the quantum and the classical domains (see [32]).

k=const. regime and extremum state for organized open systems

The thermodynamics of organized complexity thus involves energy storage and mobilization spanning the entire nested hierarchy of space-time domains. I have arrived at this conjecture via another route, but it is, in effect, a generalization of Popp's discovery, from his many years of experimentation on light emission from living organisms: that photons are stored in living organisms with equal population over all frequencies, for which he proposed the ' $f=const.$ rule' [33]. All organisms emit light ('biophotons') at ultraweak intensities from a few photons per cell per day to several hundred photons per organism per second, which are strongly correlated with the cell cycle and other functional states [34]. The emitted light typically covers a wide band (200 nm to 900 nm) around the optical range - the limitation being usually set by the photon-detecting device - with approximately

equal number of photons throughout the range, thus deviating markedly from the Boltzmann distribution characteristic of a system at thermodynamic equilibrium.

Biophotons can also be studied as stimulated emission after a brief exposure to light of different spectral compositions. It has been found, without exception that the stimulated emission decays, not according to an exponential function characteristic of non-coherent light, but rather, to a hyperbolic function which is a sufficient condition for a coherent light-field [35]. What this implies is that photons are held in a coherent form in the organism, and when stimulated, they are emitted coherently, like a very weak, multimode laser. Such a multimode laser has not yet been made artificially, but it is at least not contrary to the theory of coherence in quantum optics [36], *so long as the modes are coupled together*.

There is, indeed, evidence that the modes within the visible range are coupled together. Spectral analysis of the emission stimulated by monochromatic light or light of restricted spectral compositions show that the hyperbolic decay kinetics is uniform throughout the visible spectrum [37]. The stimulated emission always covers the same broad range, regardless of the composition of the light used to induce it, and furthermore, can retain its spectral distribution even when the system is perturbed to such an extent that the emission intensity changes over several orders of magnitude. These observations are consistent with the idea that the living system is one coherent 'photon field' bound to living matter. This photon field is maintained far from thermodynamic equilibrium, and is coherent simultaneously in a whole range of frequencies that are nonetheless coupled together to give, in effect, a single degree of freedom. This means that random energy input to any frequency will become delocalized over all frequencies, precisely as predicted in a system in which energy is stored and mobilized over all space-time domains.

The equal population of space-time photons (or energy) may be referred to as the ' $k=\text{const.}$ regime'. The significance of this regime is that *it may be the extremum state towards which all open systems - capable of storing energy - evolve*. The Gibbs entropy function of the system,

$$S_G = -k\sum_j p_j \ln p_j \quad (7)$$

reaches a maximum when all the p_j s become equal.

Let us dwell on this further, as it may be the key to living organization and 'negentropy'. The $k=\text{constant}$ regime is the maximum entropy state in which the *potential* degrees of freedom are maximized over all space-time domains, but, for living systems, it is also the state of minimum entropy because the activities in all space-time domains are effectively coupled so there is only a single actual degree of freedom [33]. Formally, it has the characteristics of the '1/f noise' identified in systems exhibiting so-called 'self-organized criticality' [38], and large interactive dynamical systems typically self-organize into a globally correlated 'critical' state far from equilibrium [38]. This critical state is highly sensitive, in that a small local event can lead to large 'avalanches' of activity spreading throughout the system, when self-similarity in activities occur over all space and time scales. The theory claims to provide a natural explanation of a number of physical and geophysical intermittent phenomena, including earthquakes, volcano eruptions, solar flares, noise in electronic circuits, economics and patterns of species extinction in evolution. The parallel with the picture of the living system that we have described is striking. This very same state can also be described in terms of the *coherent*

quantum state or 'pure' state in which all possibilities are superposed and immediately accessible [8,39]. The adaptability of the organism depends on just this seemingly paradoxical property. For, only by maximizing the potential degrees of freedom is it possible to access the single degree of freedom that is required for coherent action.

'Negentropy', as *stored mobilizable energy in a space-time structured (organized) system*, can be intuitively understood as follows. In an equilibrium system, energy is fixed, which in turn fixes the population of energy levels characteristic of the temperature of the system. In a nonequilibrium system such as the organism, energy is stored over all space-time domains. For a given temperature, the energy stored is no longer fixed, but on account of efficient coupling, becomes transferred to ever larger space-time domains (starting from the photon trapped in photosynthesis, or the energy in food) until all characteristic domains are equally populated. This implies that the organism itself has no preferred levels, its activities spanning the 'quantum' to 'classical', from the 'microscopic' through 'mesoscopic' to the 'macroscopic' in a quasi-continuum of self-similar patterns.

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