Macroscopic collectivity on microscopic base in living systems

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Abstract

The collective phenomena in living systems is discussed on the dynamic frustration basis.

The frustrated connection is introduced on all the organising levels of the living phenomenon:

- for water states (proton migration),
- for proteins and protein-structures (metabolic charge transfer),
- for cells (membrane states and ordering),
- for tissues (social signals),
- for organs and organism (overall transport problems).

It is shown, that the cancer-genesis is tightly connected with the failure of the collectivity in the system. The relevant mechanisms of the collectivity is analised in details for the better understanding the malignant tumor development.

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1. Dynamic frustration

Everybody is familiar with betting on coin-sides: when the coin is turning energeticly (we can say that it is energetic or 'hot'), the probability of the both possible sides (heat and tail) is equal. This identical betting facility lowers, when the coin collides with something, and loses its energy, became one side more possible then the other one. At the end we have a 100% probability for one side and zero for the other one. This means, that the symmetry had been broken spontaneously at the well definite energystates, starting to prefer one of the two originally identical states. (Fig. 1).

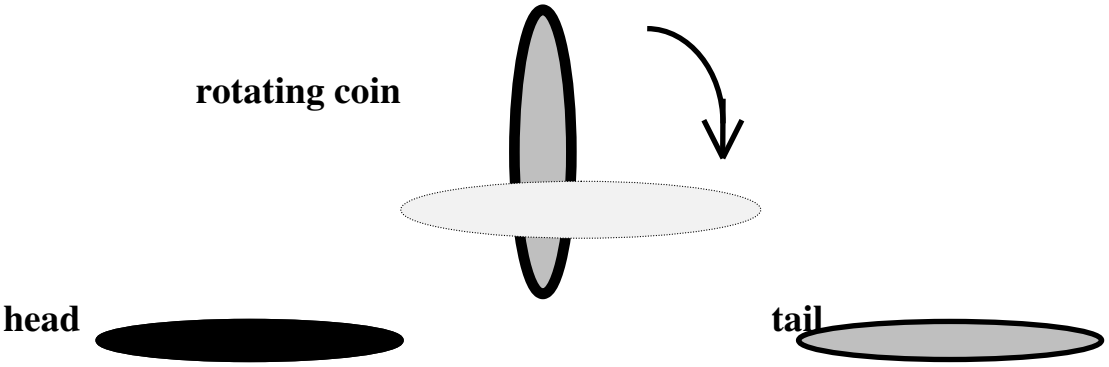

Fig. 1 Betting of a rotating coin: the basic procedure of the symmetry-brakeing

In principle this betting situation can be describe with a double-well potential, having the same depth for the two states, and the barrier between them (like a hill having two valleys at sides) isolates the states making possible a well definite states at the end (when the state occupies one of the valley). (Fig. 2)

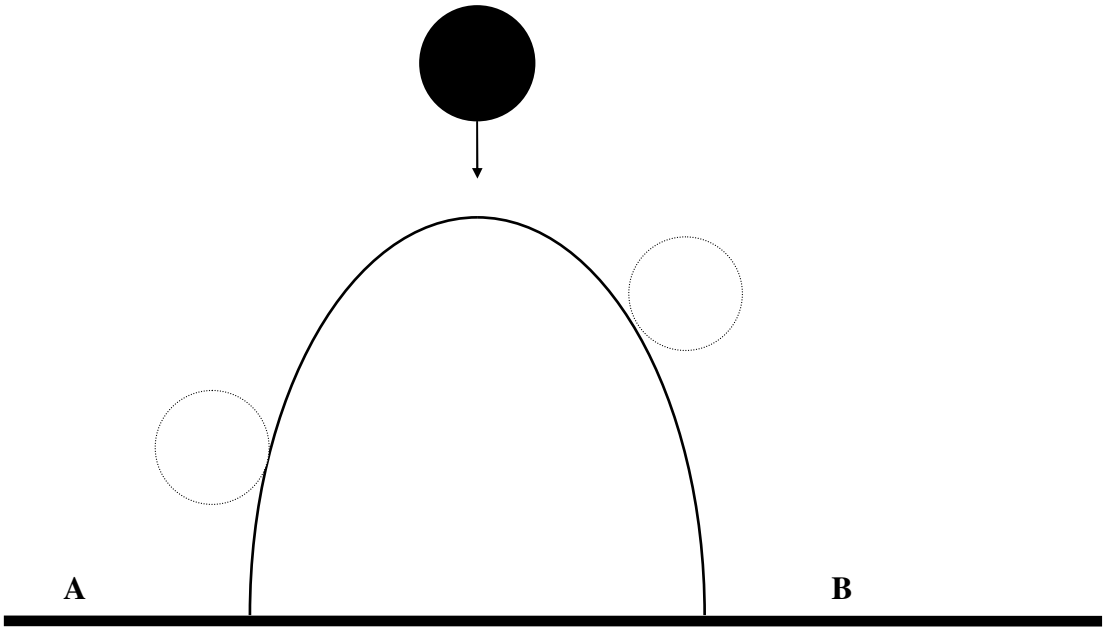

Fig. 2 The double-well potential-arrangement

Of course if the actual state has higher energy than the isolating barrier, than the probability of the occupying the states is equal. This can be formulated on the way, that when our energy is equal of the barrier's height (spontan symmetry-braking point) than the system become bifurcated, frustrated about occupying one of the possible valleys, and this frustration mechanism is the essence of our betting.

To fill up the space with equal units has some contradictory requirements. Starting the arrangement with the regular triangle in a sheet and put the forth unit on the top, forming a regular tetrahedron this is the most compact arrangement which one can ever construct. Of course this compactness accompaining with the minimal system-energy and so tjhsi is the cluster which spontaneously also appears. To continue this arrangement insisting to the most compact (lowest energy) constellation we can construct a cluster involving twenty tetrahedra sharing one vertex. This become also a regular unit (one of the five Platonic bodies) the so called icosahedron. To continue the space filling on this way unfortunately not posible in three dimension: icosahedron has five-fold symmetries, which makes it unable to fill the space properly only with its periodic repetition. But unfortunately the macroscopic energy-minimalisation requests a periodic repetition (like crystals) because the holes in between the units used for tessalation very musch increadses the system energy. (Have an experience with the ordering of the tumbs, when we try to arrange the units on the way, when the hoels in between are minimal.

This means, we have to decide: to continue on the way when we seeking for the microscopic minimalisation of the cluster energies (regardless on the missing of the periodic repetition) so put the icosahedra into the system, or satisfy the macroscopic request and arrange the units in to crystalline structure, regardless, that the microscopic request is different, so microscopically this system will not be densest, so it will not satisfy the energy minimum in that scale. Thsu we see, that our three-dimensional space is such, when we have for every clusters in a large system a double well potential corresponding to the microscopical and the macroscopical energy minima.

To arrange the molecules in the space the energy minimisation has to be done in a clusters independently, (microscopic or short range order) or requested the energy minimum for the total system, (macroscopic or long ramge order) which means a seeking to the crystalline structure. The microscopic equilibrium requires the continuing of the started process, which has always five-fold symmetries, pentagons in the arrangement. On the other hand it must not be equivalent with the macrosccopic equilibrium, because for the proper space filling the five-fold construction is strictly prohibited.

The contradictory situation between the short- and long-range space filling leads to the so called geometrical frustration [1]. This is essentially the same effect as the proton-frustration, also a dynamic process, balancing the cluster between the short- and long-range energy-minima. To demonstrate this effect in two dimensions, we covered a sheet with regular pentagons (demonstrating that the most compact units in 3-dimensional space are icosahedra) having special rhombuses between them, Fig. 3. Non-regular pentagons, of course, are able to cover the sheet without any leaks between them, Fig. 4, but this construction is against the energy-minimisation in the cluster level (in the short-range). This is a demonstrative contradiction between the short- and long-range energy-minimisation requirements. However, there is a solution made possible by the frustrated atoms (Fig. 5) which dynamically satisfies both, statically not harmonisable, requests: the bounded atoms migrate. The same can be constructed in the real three dimensional systems: the clusters are in a dynamic equilibrium (by vibration-like breathing and/or tilting of the polyhedra, [2]).

The geometrical "frustration" of the material makes a special transport phenomenon possible [3]: if a cluster stabilises itself on microscopic level, than its neighbourhood becomes instable because of the larger fitting incompatibilities than average. In this way the stable cluster destroyed by its neighbours in order to lower the total (long-range) energy of the system. The lowered energy in the neighbourhood makes the microscopic stabilisation possible for those clusters which, in their turn, will be destroyed by their neighbours. The stable clustering is sliding towards the next cluster and pushes away

the stable cluster-bag without any particle transport. It can be visualised by the standing row of domino stones, if the first rakes than gradually all the others will be raked, falling down in a line, without any transport of the dominoes themselves, the energy is transported. Another analogy would be the moving of the wave in the wheat-field caused by the wind. A moving "stability-bag" allows a possible special transport in the cluster arrangement [4]. The phenomenon is very similar the explanation of the high-temperature superconductivity [5] and can be important for the transport and information exchange in living systems, including electron transport (charge transfer) in metabolic processes.

2. Dynamic frustration in biological systems

From the physical point of view, the life process is nothing else then lowering the average energy and increasing the average entropy in the system. In this sense, life follows the basic thermodynamic laws. This means that the living process continuously 'burns' the incoming 'nutrition' by lowering the electronic energy causing the oxidation of the outgoing final 'products'. The gradual loss of electronic energy of these molecules (the nutrition), supplies life its energy.

The oxidation process can' not be a fast process, because then the system will 'burn' itself, which terminates the continuation of this process. The process is limited by the available nutrition, which is or transported or oxidised (burned). An uncontrolled 'burning' will consume the energy in the near vicinity, not allowing it to continue the process. From the chemical point of view, the living process is a highly organised charge transfer with a sophisticated energy accumulation and self-reproduction [6]. To keep the living process going, the nutrition has to be transported to the living unit (e.g. cell) or the living system transports itself to the nutrition. For example, plants transport their nutrition by means of diffusion and osmosis. There is an other process which overcomes the barriers of fixated nutritions and that is the external energy pumps which energy is supplied by sunlight. An opposite example is the movement of the living by means of external transport processes (convective flows in the surrounding environment or by an internal mechanical unit (a muscle) which converts the chemical energy into a mechanical one.

The biological metabolism (the 'burning') is the general driving force for the evolvement to an more and more sophisticated and accommodated systems. This evolution cause the living system to be more and more independent from its environment, organising and stabilising itself.

On one side, the evolution forces the system to adapt and improve, developing a perfect 'burning' ability, but on the other hand, self reproduction is rather conservative: the systems sustains itself on the same level. Self reproduction has a sophisticated identification system which destroys the cells which are not identical. Errors in this conservative process leads to evolution, only being controlled by changing environmental demands. Only that development is honoured which satisfies the general driving force with lower energy and higher entropy. However, some serious diseases are caused by the malfunction of the controlling system of the reproduction (e.g. cancer).

2.1. Water and pH

The water is essential for the living process. It is the mother, the matrix, the fuel of life and the final product of the chemical processes [7]. The water, because of its liquid character, enhances the external transport; with its variability, promotes the evolution; with its co-operativity, promotes the self reproduction.

Every living system (irrespective of their complexity) has a considerable amount of water, in such a quantity, that the molar density of the living-systems, which is very dilute, does not reach the half mol. (The human body's molarity is definitely less than half mol, with its 60% water and its average molecular weight of more than 2000. The molarity, in average, is very close to that to sea water or the artificial infusion-solutions, which diluteness are well known.)

The life is proceeded in the dilute aqueous solution, so this aqueous electrolite is the stage and bares the essential processes of the life-phenomena.

One of the most important dynamic equilibrium is included in the hydrogen-bridges. Hydrogen bridges in the water systems are not static fixed bonds. The hydrogen oscillates by tunnelling through the bonds of the oxygen atoms. The tunnelling threshold energy depends on the distances of the oxygen atoms dividing the two states at the oxygen by a barrier which has a maximum at about 0.25 nm. If the oxygens are closer to each other, the barrier is smaller. If the distances is larger, the possibility of tunnelling sharply decreases. Every hydrogen in this meaning is 'frustrated', not fixed to one oxygen, having a double-well potential for this special bond.

The hydrogen bridge is a special quantum-mechanical effect, based on the migration of a proton (hydrogen ion) between water molecules (Fig. 6.). The proton feels a double potential well in which it vibrates between the two energy minima. This process causes the proton to become highly delocalized which gives a well known chemical equilibrium (used for the pH definition):

$$2H_2O \Leftrightarrow OH^- + H_3O^+ \quad (1)$$

Despite that no stable state exists halfway the two oxygen atoms, the proton, averaged over a long stretch time, remains exactly in the middle, because of the equal probability of the two states in the minima of the oxygen binding potential .

2.1.1. Geometrical aspects

The situation becomes even more complicated when taking the geometrical incompatibilities of the water structure into account. The tetrahedral structure the most dense packing of the spheres possible in a small cluster [8]. Tetrahedron of water is not so dense (the oxygen atom is in the centre) but it is the most stable clustering of these molecules. Five tetrahedra sharing a common edge, constructs an almost compact polyhedra Fig. 7. The missing space for compatibility is resolved by deformation of the spheres or by the migration of the 'hard' tetrahedron (apposing the soft sphere as described in point 2, so a sphere with a fixed geometrical arrangement but now with the proton migrating). The same occurs at the next stage of the closest packing: twenty tetrahedra sharing one vertex form (by a small deformation and/or migration) an icosahedron, [9], Fig. 12. These clusters are the most dense, so they representing the smallest amount of free energy [10] among the possible clusters. These polyhedra have five fold symmetries: they have five-fold identical rotational transformation around symmetry axes through their vertexes. The icosahedral symmetry is observed indeed in the so called chlatrate structures.

A crucial problem arises when trying to continue the packing of spheres: icosahedra, despite their compactness and highest stability, do not fill the space properly, leaks (the space between the adjoining icoshedra) between the units demand an other arrangement.

2.1.2. Clusters, order

The existence of the hydrogen-bridges is the most important organising factor of the water cluster formation. The clusters will be formed in such a way as to minimise their free energy. This effect offers paths in the hydrogen network with lower energy barriers than the hydrogen bonds. This process reconstructs the actual network effectively and relatively fast [**Error! Bookmark not defined.**]. The frustration process can be so intensive that the proton migration becomes delocalised for a large area [11], giving an instability in the liquid water [12]. The structure of the water, from the point of view of the proton localisation, is similar to a gel-structure [13] which, regarding quantum mechanical effects, can be considered to be a so called quantum-gel state, [14].

Consequently, water itself is not homogeneous in this meaning of hydrogen-bond either [15].

The proton migration effectively changes the geometry of the water-tetrahedron, (recall that the angle between two bonded hydrogen connected to the oxygen is approx. 105^{o}, while between the hydrogen bridges it is approx. 110^{o} and between the lone pairs approx. 120^{o}). In this way the water-tetrahedron is not a fixed geometrical arrangement, but its edges are vibrating in accordance to the proton migrations. Consequently it can be regarded a 'smeared' or 'soft' polyhedra in the duration of a considerable longer time period than the characteristic migration time. This type of ordering appears in the structures of ice which show a significant variability. Ice has eight main and several additional structures, depending on the forming conditions. These structures can be modified by rotating of the molecules what is possible because of their V-like structure. The three characteristic formations have names I-, V- and D-forms: the I structure, which **i**nstantly changes, has a very short lifetime (10^{-14}- 10^{-16} s), compared to the intermolecular proton vibration frequency; the V-structure **v**ibrates with a medium life-time (10^{-11} - 10^{-14} s); the D-structure is changed by **d**iffusion with a relatively long life-time.

The bonding energy of the hydrogen bridges is only 0.17 - 0.29 eV/molecule (4 - 7 kJ/mol) which is only one order of the magnitude larger than the thermal energy at room temperature (~0.025 eV at 20 °C). In liquid water the order of the water molecules can not stabilise, because the thermal-energy destroys a huge fraction of the hydrogen-bridges. The cohesion effect of the hydrogen bridges in pure water is most trivial in its solid form. Ice has various structures [1] in which the water molecules are tightly bounded by the actual hydrogen bridges. The remarkable variability of the structures bonded by hydrogen bridges originate from various bonding possibilities and their geometric forms.

The molecular bond in water is 10 eV/molecule (242 kJ/mol), which is about fifty times more than the average bonding in hydrogen-bridges. However, a remarkable large part of the hydrogen-bridges exists in the liquid phase even at the temperatures as high as the boiling point. The existence of the clustering of water is revealed by the radial distribution function, measured by X-ray diffraction, (Fig. 8.). These measured hydrogen-bridges show that the "ice-structure" does not vanish at once on the melting process. The effect on the melting point is only that some domains (cluster of water) are disconnected from each other (like islands). When increasing the temperature, these domains are gradually broken down into the smaller and smaller ones. These domains are not static structures, their size fluctuates, but the average is definitely characterising

the actual state, [16], Fig. 8. This effect is well known in the solid state and statistical physics: the order does not vanish at once at the phase transition, but at the vicinity the medium-range order and, more further, the short-range order is observable, [17]. This effect is theoretically also shown in the two-dimensional Ising model (one of the rigorously solved model-systems) in the phase transition, [18]. The clustering conservation is more effective in the case of water, because the six-fold rings in the solid state (ice I) break easier at a certain point due to the incompactness of the angles of in the water tetrahedra with the six-fold ring [19]. The remaining chain appears relatively stable.

This means that the normal water, gradual melting from ice, has two structurally different phases: the monomer water-molecules and the water-clusters, Fig. 10., [20]. Moreover, the clusters of water in this phase-mixture can have a large variability depending on their actual structure and phase-transitions. This fact emphasises the complexity of normal liquid water which mostly cab be subscribed to the hydrogen-bridges.

The bonded clusters can be regarded as a huge water molecule. The estimated mean size of the cluster characteristically depends on the temperature. The mean size of the H-bonded water 'molecules' depends linearly on the inverse temperature (fig. 9,). At room temperature the average size seems to contain 300 molecules!

Water interacts with the surfaces, creating at the vicinity well structured water agglomerates, [21]. This surface structured water, many times observed as bound water or close water, has a low dielectric constant and more limited absorption of the microwave and radio-frequency radiation. This water shows a shorter relaxation time during NMR investigations. The temperature dependent structural phase transition is also observed in these structures [21], showing a highly co-operative order-disorder phenomenon. The hydration orientation of protein surfaces is well established in the literature [22]. These type of waters have similar "polymeric" structures as so called "polywater" [23], [24], but have an entirely different origin and was later proved to be an artefact [25].

2.2. Proteins and stability

The living process causes a gradual loss of the electron energy of incoming compounds (nutriments, foods) by a multi-step oxidation, having very little energy changes in one step. The typical metabolic energy-step is in the range of the hydrogen-bridge bond.

Consequently there is a possibility energetically to rearrange the water structure [26] and with this drastically change the physical properties (for example the dielectric constant) of the material without changing the composition (only the microscopic ordering) of the medium itself.

The function, or rather, combustion, of biological organic material is defined by a definite chemical balance. This balance is fundamentally an energy-balance acting between solar energy on the one hand (as a source) and vital energy on the other (as the absorber or user) (figure 4). In essence, both sides of the chemical reactions

Fig. 4. The balance between life processes and solar energy

take place through electromagnetic interactions, either in the generation or combustion of organic material. The energy domain in which the energy transfer, resulting from these processes, fall is that of electromagnetic interactions, which do not fall within the domains of non-ionising radiation.

Thus, the frequency equivalent to electromagnetic radiation taking part in 0.0001-0.1 eV biological energy transfers is $\nu_{biol} \cong 10^{10}$-10^{13} Hz (10-10,000 GHz). (Naturally, the actual frequency depends on the energy transfer involved (biological metabolism and information exchange), as every type is different).

In essence, the formation - or, rather, decomposition - of water works as the two basic pillars of the energy equation in life processes but these are not immediate processes which are completed in only one step. Of course, in the decisive majority of cases, other elements apart from hydrogen and oxygen take part in the process, which means that we need to direct our attention towards other processes as well.

Biological systems cannot withstand this type of energy release and so, activation energy - the release of energy - proceeds step by step in these systems (figure 7).

Fig. 7. The mechanism of the small steps (For brevity's sake, we have depicted only one of the 'small steps').

The mechanism by which these steps are taken is one of the most characteristic biological properties. By categorising energy transfers in a different way from that in which pure chemistry would, it brings them about in steps which utilise a fundamentally small amount of energy (characteristically falling within the 10-100 GHz radiation frequency band) and see to the system's continuous operation [10]. This gives a very interesting recognisation of the different metabolistic properties in a given living

system, because the energy-loss of tyhe electronic energy creates definite radiations in the 100 Ghz region. (see later).

2.2.1. Stability of the protein molecule

The protein is a huge molecule. It is difficult to interpret its living state, because it is dynamic and "screaming and kicking....." [27]. However, the dynamic motion of the proteins has been proven both theoretically [28], [29], [30], and experimentally [31], [32].

The protein in-vitro is an insulator in which electrons are at the lowest possible energy filling up the closed common electron-shells (valence-bands). The protein in-vitro, in an insulating state, is not able to transfer any information, having only coupled electrons in almost localised bonds. The protein in-vitro has no ESR signal, [33], while the protein in-vivo is different: it has a strong ESR signal [33] representing uncoupled electrons; it is a conductor, having a common band with other proteins nearby; the cohesion forces in this system are strongly enhanced in comparison to their in-vitro counterpart. Due to the inert protein in-vitro the cohesion forces between these molecules are not as large as in-vivo, the system can in fact relatively easily decay to its non-living form.

The isolation of protein islands is enhanced by the adsorbed water [34]. The adsorbed water coverage in-vitro (and also in the cancer tissues) is almost randomly distributed on the boundary of the protein molecule, producing an insulating layer with large dielectric permeability, [35]. To make a material have a collective intermolecular transport, the disordered structure must be rearranged.

In the living state there is a considerable smaller dielectric permeability around the proteins because of the ordered adsorbed water [35], while much larger cohesion forces were observed [35]. In the living state the strict isolation as well as the electronic saturation of the macromolecule has been lost desaturated proteins do appear. The system that is insulator in-vitro, becomes semiconducting in-vivo. The desaturation is produced by an electron acceptor, tuning away the molecule from the stable, static equilibrium. We suggest a strong charge transfer which driving force is the metabolic process itself. That is responsible for the living state, giving the possibility for a special type of collectivity and co-operativity in the system.

The essential mechanism of the life in this submolecular level, is the electron-desaturation of proteins by various reagents due to the metabolistic processes. The

desaturation is going through the electron acceptors. The living process is realised in a charge flow making the final oxidation through various steps by different reagents (oxidation process). The oxidation goes step-by-step transferring only a fraction of the electron-charge in each step. This mechanism of the charge transfer is life itself on micromolecular level. The collectivity appears in the conduction chain of information between the protein molecules. The stable non-conducting protein-state has been destabilised in-vivo and the molecules try to stabilise themselves seeking to fill up their shells to an electronically closed, stable situation. The non-saturated macromolecules seek to reach their stable, saturated form. The molecules in the neighbourhood of the one which saturates itself will be more unstable due to the missing charge. (The charges that are transported here can be very small. They are not like a ball jumping from protein to protein, but only a fraction of the charge can move in this process. The process can be visualised by the standard quantum mechanics where an electron is 'smeared' between the atoms involved in molecules, compounds and alloys, the electron wave functions overlap each other.)

Seeking stability on microscopic level (seeking a molecule configuration for stable insulation state) contradicts the global (macroscopic) stability requirements. These are stablised by the transported charge (semiconductor) due to the metabolic process which causes, by its nature, non-corresponding electronic charges in the process. Consequently the non-stable, saturated molecules produced in this process. In the living system, the local and global energy requirements compete with each other resulting in a geometrical frustration. It is supposed that their balance has a central role in the formation of the actual phase [3].

The high electronic stability is connected with the perfect saturated state which is missing a small amount of charge because the electron acceptors, responsible for the oxidation driving force in living state, transport this charge. On the other hand, the long-range requirements are opposite: the effective long-range could be created only by the large correlation length which requires non-saturated, well-interacting molecules. The momentarily optimal short-range order cannot be frozen in because its neighbourhood becomes more instable by the stabilisation of the given short-range unit (protein). The incompatibility of energy minima of the short and long-range orders creates an instable situation. The material (on this level too) has to be frustrated. The non-saturated proteins fit the long-range requirements well, but in the short-range the search for the saturated situation will dominate, contradicting the global tendencies. Again a 'stability-bag' (a so called 'soliton') will be formed, moving through the material [4]. This is one of the forms of frustration discussed before. If the short-range forces are favoured in the total system, the long-range order does not have a balance, (or vice

versa) then the life would disappear. A delicate balance in the effective interaction length stabilises the dynamic frustration, which is, we suggested [36], the basic behaviour of life. The dynamic frustration of the living protein is a possible explanation for the "screaming and kicking ...." [27], but in any case responsible for the long-range interactions, the co-operative and collective behaviour of the living processes. The transported charges in the frustration are one of the important components of the cohesion forces and without it the life itself vanishes.

2.2.2. Protein structure

breathing-like protein vibrations...

internal H-bonds, frustrtaed (bifurcated) vibration by internal H-bonds, Figure!!

many hydrogen-bridges (harp model),

On microscopic level of protein arrangements, the geometrical organisation is trivial: octahedron and even icosahedron are constructed (Fig. 10., [37]). These structures are very similar to the clusters observed in amorphous materials (so called ´Bernal holes [38], Fig. 11.), which are created, under influence of the effective short-range interactions, to obtain a closest packing. But it is possible that the long-range interactions are not effective enough to build up a long-range order and thereby to occupy the space properly with ordered structures.

The protein clustering well shows the search for closest packing in short-range-order well, causing the above described conditions. This geometrical contradiction between the five-fold symmetry in closest packing and the prohibited five-fold symmetry in proper space occupation is a very nice solution of nature to solve the problem of free surfaces, avoiding the enticement of the living material in a genuine crystalline form. The closest packing has always free surfaces and does not fit the order which kills the internal dynamism without the direct contact with the metabolistic transport lines and water transmission of the living dynamism. This is exactly the point why the DNA also has five-fold helixes (α and β forms) and inside these molecule, some five-fold rings as well. The macroscopic chains of polyhedral protein units (Fig. 12., [39]) offer a soliton transfer mechanism through the linear-arrangements with aid of the above discussed breathing and tilting distortions of the polyhedra. According to this well known geometrical incompatibility to occupy the space, ([37], [40], vibrations caused by the frustration occur and can cause the so called 'bioconductive connectional system' [41], [42] which had been introduced due to other reasons, but are in good agreement with our assumptions.

..protein chains similar to pentagons

2.3. Cells

2.3.1. Membrane stability

double dipole layer

2.3.2. Through-membrane oscillation

osmotic oscillations

2.3.3. Arrangement frustration

Organisation of the larger units (cells) also shows the importance of the five-fold arrangements which already had been indicated theoretically [43], [44], [45], [46]; numerically [47], [48], [49], [50], [51], [52], [53], [54], and even experimentally [55], [56], [57], [58]. The enigma about the mystic five in the average co-ordination number of the cells [59] is in the light of these observations trivial: the five fold symmetry is the closest packing, which minimises the energy in a short range (the same as in solids, called Frank-Kasper phases, [8], Fig. 13.) and creates the five-fold co-ordination (the so called Aboav-Weaire law) in the cell-arrangements. The two-cell correlation function [59] can also be seen from the point of view of the search of the closest packing. This arrangement gives also frustration possibility in dynamic way.

2.4. Tissue, organ, organism

Collectivity.....

3. Collectivity and life

On every level in the living system, water provides the transmission of the dynamism, that is the effective media to settle the total living process.

The important balance between the short and long-range effects, controlled by the energetic situation, is that the system always tries to realise the lowest available energy which is in the cluster (in microscopic range) appears in a five fold symmetry, while on the macroscopic scale it is the ordered occupation of space which eliminates the five fold symmetries and therefore contradicts with the microscopic requirements. This delicate balance leeds to dynamic vibrations, which can be easily frozen in by domination of one of the forces in the system. The protein, with its saturated-desaturated states in the living process (balancing between the low energy state in microscopic level, which is the saturated molecule, and the low energy state demanded by the metabolism, which is a not-saturated state), also manifestates this basic dynamic construction and builds a system called life, built up by this dynamical equilibrium in all the organising levels from the water-transfer through the proiteins and up to the organism as well. The dynamical vibration is effective for the overall living organism. It has effect on every level of organisation of the system: starting from the protein building up the total unity:

protein → protein-agglomerates → cells → tissues → organs → organism.

Accordingly, the system creates a balance between nutrients and end-products which breaks down the energy stored in chemical bonds in the nutrients and creates end-products in which the chemically stored energy is low. At the same time, certain biological systems (plants) are capable of executing this process in reverse, for which they receive their energy from solar energy and electromagnetic radiation. (This process is a fundamental conversion which makes the nutrients available to the other life processes which are not capable of such a conversion).

Photosynthesis utilises the low-energy lower half of the near infrared and visible spectrum. The characteristic green colour of plants indicates that the chlorophyll which executes this conversion reflects green from the sun's so-called A15 spectrum (which includes all visible frequencies (white light)), while it absorbs and utilises its complementary colour. This conversion is capable of producing a relatively high-energy (and thus, high-frequency) radiation (in the 100,000 GHz [=100 THz] band!).

In life-characterising conversion transformations,

(**chlorophyll-type formation ⇔ metabolic combustion**)

In essence, charges flow from one location to the other, since the change in the chemical bonds is also that of the electrons'state. Charge-transfer is, in essence, the existence of microscopic electric charges which, either on an entirely local scale, or spread out over

a larger field-section, ensure the energy exchange between the molecules.In figure 8, we demonstrate the energy scale for the changes which take place during these oxidation processes in three different acids.

Fig. 8. The energy scale of biological processes

As we mentioned, the end-product of the combustion process is a charge transfer, a charge flow or, simply, currents. These currents basically appear in the microscopic currents of different systems, but there are several macroscopic currents which have their place in the living body. These currents, for the most part, can be divided as follows (see figure 9):

Fig. 9. The division of currents which occur in living organism's system.

There are tiny, practically molecular, charge transfers which are catalysed by enzymes, enzymes being, in essence, those things which aid in electron transfers and bring the microscopic currents into existence - in the simplest terms, they are microscopic conductors (figure 10, [11]).

Fig. 10. A diagram of enzymes' operation [11].

The charges transmitted during microscopic (vibration) processes cover a somewhat larger scale and are manifested in a soliton transfer based on the domino theory. This soliton transfer is no more than the sort of information and expansion which, for instance, we find in falling dominoes (figure 11). In the case of living systems, it is only

Fig. 11. The domino-effect of soliton transfer.

modified to the extent that biological units, during these vibration processes, stabilise - or, rather, destabilise with them - their environment. In this way, the following vibration unit, as the result of this environmental destabilisation, starts to stabilise and thus destabilises its predecessor - in other words, a 'stability focal point' runs through the material, something which is one of the most basic form of charge flows or information flows in living systems. This 'social signal' makes connections between proteins, cells, tissues and organs possible, too. Certain varieties of these social signals trigger off chemical processes and their local production increases the social signals' effectiveness (for example, the largest of this kind of production is nitrogen-monoxide

production in pericellular systems [12]). During division, the cell isolates itself from its tissular environment and breaks the social signal [13]. After division, the signal's broken path can even be geometrically re-established (figure 12, [14]).

Fig. 12. The arranged rebuilding of the intercellular collective signal [14].

- Dynamic frustration is the essence of life, a special instability which makes the body's dynamic equilibrium possible. Looking at it from this point of view, the Popp's biophoton theory [15] and the Szász's frustration theory [16] basically describe the same sort of functions, only in different terms. The vibration process can be discussed on different levels :
- the unstable potential-valley of hydrogen bridges
- protein instability (metabolism)
- cluster instability
- structural frustration, *e.g.*, the protein-chain signal and, in certain cellular relationships, in the discussion of the social signal (figure 13).

Fig. 13. A summary of frustration.

The frustration process arises on every level of organisation in living material, from water proton-frustration to intercellular frustration, which is what produces the social signal.

The frustration process which arises in pure water and, in essence, derives from the proton's double potential-valley is considered in figure 14.

Fig. 14. Protein frustration between two water molecules.

Examples of different hydrogen bonds occurring in different biological systems are given in figure 15 [2]. An entire system of hydrogen-

Fig. 15. An example of hydrogen bridge bonds in biological systems [2].

bridge bonds can arise in structures which, in theory, the so-called 'hydrogen-harp' model [17] summarises (figure 16).

Fig. 16. The hydrogen harp model in DNA systems [17].

The above vibrations were measured together with the proteins' internal vibrations [18]; the resulting frequencies fell within quite a narrow range and quite close to one another - proton vibration fell within the 100 GHz band, as did protein vibration and most globular proteins' vibrations [19]. To this we must add that the polyhedral structures derived from globular proteins are not the sort to fill fields (for instance, there are also icosahedra between them (figure 17, [20],

Fig. 17. The arrangement of globular proteins in cluster or chains [20], [21].

[21])) and, deriving from this characteristic of theirs, the chains create geometric frustrations within themselves [22], [23]. This frustrated chain is similar to the frustration chain suggested in high-temperature ceramic super-conductors [24], [25], [26]. Cells and the vibration processes which bind together intercellular participants can also be described in a similar way [27].

The forming concentration elements create significantly more macroscopic currents within the vibration currents which form a part of the body's biological functions. In essence, these concentration elements can also, with the formation of internal surfaces (membranes), cause high electric fields. For instance, a simple membrane has a field strength of approx. 2 million V/m as a result of the ordered double-layer's extraordinary thinness and relatively high-tension voltage [28].

In essence, the system works like a concentration element: if we bring together an acidic and an alkaline medium together in some way or another (tap, membrane, etc.), a potential difference arises between the two (this being the concentration element) which then acts as a driving force among the different ions and the charged particles in general. This concentration element is capable of producing general currents which then act as the basic tools within living systems which function on metabolism (figure 18).

Fig. 18. The concentration cell as a vital sign.

Depolarisation currents work on even larger scale and are capable of limiting the operation of certain organs (*e.g.*, the heart, muscles, etc.) (figure 19). These depolarisation currents surface in different ways and, with certain injuries ('wound current') (figure 20, [30]) and in the case of broken bones (figure 21, [31]), play a delimiting role in the acceleration of cell growth.

Fig. 19. The generation of depolarisation currents [29].

Fig. 20. The formation of the 'wound current' [30].

Fig. 21. Electrostatic field changes in the immediate vicinity of bone fractures [30].

Different global currents come into being in the body along with those already mentioned, caused by the flow of aqueous solutions within the body. The aqueous solutions which play a part in the body are: the blood stream, the lymphatic flow, the kidney or other water-filtering systems' flows and other liquid streams, such as saliva or other secretory products.

The bloodstream, which contains 8g salt per litre (essentially sodium, chlorine, calcium and magnesium ions), undergoes a complete blood exchange every 23 seconds. Thus, in a given cross-section of the main blood vessels, not only is its salt content totally dissociated 0.8%, but an ion migration of a magnitude of 10^{22} also takes place every second. If we were to deal with only one type of ion, this would then be equivalent to a current of 1000 A! As a result, this current's effect, since it is a magnetic field, can't be measured, which essentially means that the ions all move together - in other words, the resultant current is nil. The bloodstream does not produce electromagnetic effects, which means that these ions, in moving together, signify a contrary current or, rather, disable each other's effects (said effects being currents). These currents are not parallel, moving within a complicated network (that of the blood vessels) (figure 22), and this network operation also contributes to the

Fig. 22. Typical currents and the characteristics of the blood-vessel network.

produced fields' mutual destruction. At the same time, it should be clear that, in systems where the ions separate or, rather, where they are limited by homogenous ion currents, we must count on there being serious current effects and thus, electric effects.

Ordered water can probably function as an information exchanger between molecules and even partly between the larger units (e.g. cells) by means of the hydrogen-bridges. The measured protein vibration frequencies are quite high (10 - 1000 GHz, the corresponding lifetime is 10^{-10} - 10^{-12} s) [60], [61]. This range is basically in agreement with the measured (Brillouin- and Raman-scattering) and calculated water vibration

frequencies, at about 200 cm^{-1} and 30 cm^{-1} (2000 GHz, stretching mode, 900 GHz torosional mode, respectively) [62], [63], which (first of all the torosional mode at 30 cm^{-1}, i.e. at 900 GHz) is tuneable by an external electric field, [64]. The intercellular communications (introduced by Frölich [66]) and the Becker postulates on the "secondary nervous system", [65]) are also in this regime (100 GHz, [66]), while the proton oscillation (hydrogen bridge, generating solitons [67]) is also in the range of 100 GHz. The optical radiation in infrared (1 - 1000 THz [1 THz = 1000 GHz]), in far infrared (100 GHz) [39] and even in the range of visible and ultraviolet [39] supprort the imposed role of water as transmitter in the cellular system well. The intercellular communication [68] and the social signal between the cells [69], can be easily explainabled in this way.

The ordered water is very usefull and able to switch quickly, transferring some energy, with time constants in a rang up to 10^{-12} sec [70]. The quick energy (and/or disturbance) transport is mainly connected to the tetrahedral structure of water molecules [**Error! Bookmark not defined.**] and, consequently, to the geometrical frustration, as was discussed before.

Biological charge transfers require that the donor and acceptor are in close range of each other: if they are 2 nm from each other, the charge-donation effectivity could decrease by 10^{-12} [71]. In the case the proteins are in close vicinity, the ordered water makes the charge transfer between them possible, [72]. Just very recently it was observed that haemoglobin bonds 60 water molecules during the oxygen transport [73]. This picture is expanded to some other switching system [74]. It is not known yet [75], why there are a definite number of water molecules connected to a certain biological process, but the only explanation can be found in the connections with ordered water. Note that the very small energetic effect in the haemoglobin action (8 kcal/mol) [76] is exactly in the range of the hydrogen-bridge energies as well as in the range of the water cluster melting energy, [63].

Dielectric permitivity is drastically lowered in the ordered state, arranged by the protein surface. Consequently the information exchange, due to the enhanced proton-migration, is promoted. The importance of the change of dielectric permitivity was at first pointed out by Szent-Györgyi [33], who proved this fact experimentally, which had been postulated much earlier [77], [78]. (Note that some of the actual switching mechanisms (for example the function of the black-melanin) are also based on water [34] and connected with its reordering [79].)

From the former Sovietunion, a large amount of information was released about the frequency-specific effects of microwaves in the 39-60 GHz frequency range, [80],

which was later very intensively investigated by other laboratories over the world, [81], [82], [83], [84], [85]. The effect is remarkable and amazing. There are a lot of models introduced to understand the problem, but not one is widely accepted yet. Our position in this question is that the radiation as a funstion of the frequency, which corresponds with the actual problematic transmission in the living system (i.e. in the hydrogen-bridge, cell signalization or others), can be helpful in the healing process. Instead of healing these radiations can be a very useful indication of abnormal, unhealthy processes in the living system and thus be used as a tool of diagnosty. There are very interesting investigations comparing the effect of healing radiation of extrasense-people with those of the artificially applied radiations [86]. They had amazing results: the effect of the extrasense radiation can be replaced by the artificial radiation and applied in therapies [87].

The characteristic radiation of the metabolistic processes can give a good identification of the tissues as well. Every tissue of course works among well definite circumstances, which can be immediately recognised by pathologycal identification. Followingly the tissues haqve a definite radiated frequency if they are working well. If the niormaql work-distribution is hurted somehow, than the radietive frequenbcy is also tuned away from the normal one. This effect can be useful not only for diagnosty but for the active therapies also applicable (for example the Rife method).

4. Carcinogenesis in dynamic basis

The living processes, in the view of our interpretation, is very depending on the order-disorder phenomenon. The ordered state (if it is not frozen in by long-range forces) is necessary for the transmission of solitonic signals, which is the basic of the metabolism. That is why it is so important to control the order and repair if it is possible.

Standard food, normal nutrition that is, has a preordered state, because most of them are aqueous solutions or water-solvable salts, which are, or partly are, ordered as they were part of a living system, or because of simple standard electric forces (by the available surfaces), the hydration processes can effectively order them.

Of course, a check is needed for both possiblities: what happens if only disordered states are incorporated by a living system and what happen if we force the ordering artificially? A sample of forced disorder is microwave cooking, while the ordered option is vegetarianism (more precisely not cooked, natural food). After the death of a living system, the ordered system wil disappear beacuse there is no metabolic process to sustain the ordering. However, the membranes around the cells keep a potential due to the double lipid layer causing still a small ordering. The water molecules, because of

their dipole effect will 'dismantle' the membrane slowing by forming hydogen-jackets around the charged membrane. After this stage the system will become liquid. This is the rotting process. This means that plants, with a different (tougher) cell mebrane than animals, will sustain the after-death odering a bit longer than animals.

4.1. Cancer and life

The ground state of life processes is the massive proliferation, a state where cooperativity and work-division have no role and the reproduction is the only form of continuity. (This stage was called the alpha stage of life by A. Szent-Györgyi [i].) More complicated and sophisticated are the more evolved life forms which can be characterised by the ability to differentiated and adapt. This stage must have cooperativity, a well determined active information exchange between the units (cells) to control the proliferation. Growth must satisfy the requirements of the total cluster: the tissue, the organs or the organisms. At this stage the adhesion capability of the cells is remarkable large. The system is definitely compact, the dilute aqueous solution is not liquid-like anymore but a semi-crystalline [ii, iii], having well ordered bonds and dipoles. (This is the stage Szent-Györgyi calls the beta stage [24].)

4.2. Cancer and living system

The intercellular communication is the basic of the cooperativity which only just recently became a popular topic in the scientific communities [iv],[v],[vi]. In [5] we have suggested a special mechanism which is obviously connected to the water and to the balance of the short-range and long-range requests in living matter.

The cells are tightly connected, 'glued' the hydrogen bridges. This adhesion makes cooperativity in tissue possible. Here every cell receives a defined signal from the organised system, from near or far. Every cell (or group of cells) has a typical characteristic in the tissue. The cell membrane is the actual controller of the charge transport, manifested in different molecules and ions. The membrane charge is arranged in a double-layer which is able to order the outside water by its electric field and making the structure adequate for the dynamic frustration processes [5]. (Note that the ions in the intercellular water disturb the ordered structure and because of their destroying effect, the geometrical frustration is supported.

Finishing the proliferation, the cell-membrane builds up the hydrogen bridges once more [30], increases the adhesion and recreates the long-range order function. At the same time, this process creates the typical shape of the actual cell through the ordering-control of the cell membrane. The total process is collective and co-operative [31], for which the driving force is the gradual loss of the incoming electron energy in the living system [[vii]], forcing the dynamic equilibrium into action., the frustration, which makes the living system "screaming and kicking...".

This proliferation is a healthy, standard process, which is in a balance with the normally functioning long-range forces, keeping the system living. The clue for the balance in a statistical point of view, is to have a recreation of the long range forces after the cell proliferation. The system becomes intact again. The cell proliferation is biologically programmed. The devided and renewed cell switches itself into the collectively organised tissue, satisfying the common long-range requests. The dividing of the cells is statistical in the tissue with the co-operative forces preserving its history. The mutual long-range signal fits the units back later into the tissue. However, the cluster size of the proliferated area can be so large, that the signal can't overcome the critical interaction distance. The cooperativity in the tissue can not be reconstructed any more. The cooperativity and therefore the history of the cell are demolished. This is point when the system can not turn back to its standard balance. The cells are not controlled by the system any more, they live independently and divide unlimited, out of control. This is cancer. The cohesive forces are low enough for the delocalisation of the cells which causes the well known metastasises. In this context the cancer itself is not a decease of the cells, but a missing of cooperativity, defecting the well balanced dynamic equilibrium. In the cancer development in the initial period is normal. However, when the velocity of the rapid proliferation exceeds the rate at which the chromatin material can be transformed into normally functioning genes, gene defects are formed. Cell mutations appear and the process eventually produces the malignant tumour. The process decreases the cohesion, the cells metastasises.

The hydrate-jacket of the ions affect the short range which contradicts the requirements of long range ordered water. The cell, during normal action, is well fitted in the long-range order requirements by the dynamic frustration. However, if the cell (due to an other biological signal [31]) starts dividing, the cell's vicinity drastically changes. The water around it becomes disordered, the adhesion forces lower by destruction of the hydrogen bridges and the cell gets isolated by the larger dielectric permitivity. The cell now is out of the long-range control and divides alone, independently of its function in the tissue. The living matter becomes fixed in its stable state (the alpha stage).

The dynamic alternation of the beta and alpha states is the origin of growth of the living systems. A so called "Social controls on cell survival and cell death" [31] for which the molecular mechanism is unknown at this moment. Cells usually kill themselves by activating a suicide program [viii],[ix],[x]. The 'activation' signal comes from the other cells [xi] (a 'social' control) which is in fact a cooperativity of the cells, activating not only death, but proliferation as well, eliminating the unwanted cells [35] and producing new by proliferation, or keeping the existing ones with "survival signals" [xii],[xiii],[xiv],[xv],[xvi],[xvii]. These observations on some competitive signals [31], and some competition between the cell survival and cell proliferation [xviii],[xix],[xx], as well as on different other growth factors [xxi],[xxii], emphasises the importance of the cooperativity which is the key of the sophisticated living systems. The actual central effect is conducted by the electronic transport (Krebs-Szent-Györgyi cycle, the basic metabolism) which effects the roots of the life-processes. It means that the mitochondrion inside of the cell must be the general controller of the process.

4.3. Influences for cancer-genesis

Fat food can destroy the useful water structures in the nutrition. Fat, by being hydrophobic, breaks the chain of hydrogen bridges needed to transport charges from protein to protein, which contributes to an healthy metabolism. Fat works as an isolator in the energy distribution network. In this process fats breaks the normal electro-chemical reactions and first of all effects the resistivity as was defined by Vincent.

An abundance of fat in the body can cause fatal performance problems of the living system (the human body). We consider cancer linked to the disorder in living systems. It is not surprising that fat effects the development of cancer as well as disorder of the water structure. It is remarkable that cancer is formed in those places where fat tends to accumulate (see fig 14) [xxiii]. In this last era there has been a significant increase of mortality due to cancer. If we look at the nutrition habits throughout the history of civilisation, we can see that only the last decades there has been an increase in fat food production and consumption. Looking at today, we see that in Western societies there is in percentage more deaths caused by cancer than in other parts of the world. The geographical distribution mortality caused by cancer shows a remarkable and strict correlation which supports the above ideas well (fig. 15). Breast cancer, for instance, shows well the influence of fat food. It not only increases the possibility to get breast cancer, but it decreases the age where one can possibly get cancer.

Not only food but the environment as well has an important impact on the living systems. Pollution can destroy the hydrogen bridges between the water molecules and thus corrupt the energy transport.

An other and new kind of destruction source is *electro-smog* [56]. All electronic machines spread around electrons, bombarding the water molecules, upsetting the water structures. This "pollution" not only poses serious danger to the living system but it destroys the order in nutrition as well, causing defects and disorder. This electro-smog is not neglectable in this society [xxiv] accumulating more and more electronic equipment. Its danger lies mainly in that:

- the living system can not directly sense electro-smog
- electro-smog effects the structures in the total body, not necessarily effecting a special part of the body.

According to our opinion this danger is not realised well yet, despite the fact it is one of the most rapidly growing pollution in our society.

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7. Figure captions

Fig. **Error! Bookmark not defined.** Schematic picture of the water tetrahedron.

Fig. **Error! Bookmark not defined.** Schematic coupling of two water molecules by a hydrogen-bridge.

Fig. **Error! Bookmark not defined.** Different types of water-orders in a ring arrangement.

Fig. 11 Bernal-holes in amorphous structures.

Fig. 12 Chains of the protein polyhedra to build up larger, macrosopic units.

Fig. 13 Packing density and the coordination numbers. The optimal packing is at about five, corresponding to the Frank-Kasper phases.

Fig. 16

Fig. 17

Fig. 18

Fig. 19

Fig. 20

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