Homeostasis as self-organized quantum criticality

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Abstract

Cold shock proteins (CSPs) and heat shock proteins (HSPs) have a great deal of similarity and have much more general functions, so it is easier to talk about stress proteins (SPs) having two different modes of operation. The attempt to understand various functions of SPs led to much more general problem: how self-organized quantum criticality (SOQC) is possible? Criticality means by definition instability but SOQC is stable, which seems to be in conflict with the standard thermodynamics. In fact, living systems as a whole are quantum critical and manage to stay near quantum criticality, which means SOQC. This is nothing but homeostasis usually understood as a complex control system needed to keep living systems in flow equilibrium.

Zero energy ontology (ZEO) forming the basics of TGD (Topological Geometrodynamics) inspired quantum measurement theory extends to a quantum theory of consciousness and living systems and predicts that the arrow of time changes in ordinary ("big") state function reductions. ZEO leads to a theory of quantum self-organization and time reversal means that dissipation in reversed direction looks like extraction of energy from the environment for the observer with standard time direction. The change of the arrow of time transforms critical states from repellers to attractors and makes SOQC possible. SOQC and homeostasis would result automatically rather than being forced. Magnetic body (MB) is another key notion. MB has a maximal temperature known as Hagedorn temperature T_H crucial for understanding SOQC and functioning of SPs. T_H would relate closely to physiological temperature in biomatter.

Quantum biology is a new research field motivated by the fact that the spatial coherence of living matter is very difficult to understand if biosystem is a mere soup of biomolecules with coherence length of order molecule size scale. Even the standard quantum biology meets this problem: Planck constant h is too small. One can ask whether the coherence of living matter might be induced by quantum coherence of something which is not ordinary biomatter:

the most natural candidate is dark matter about which only its existence is known. TGD is a proposal for a unification of fundamental interactions leading to a new view about space-time, about quantum theory, about the relation between experienced time and geometric time and also number theoretic vision allowing to identify mathematical correlates of cognition and predicting a hierarchy of Planck constants h_{eff} with arbitrary large values. Dark matter is identified as phases of ordinary matter with $h_{eff} > h$ so that quantum coherence length and time can be arbitrarily large. New view leads to a general model for quantum self-organization involving the possibility of time reversal and with dark matter acting as a master of the ordinary biomatter. In this article the key proposal is that homeostasis in living matter can be understood as self-organized quantum criticality: something emerging spontaneously rather than being forced by control.

1 Introduction

This article started as an attempt to understand the properties of cold shock proteins (CSPs) and heat shock proteins (HSPs) in TGD framework. As a matter of fact , these proteins have great deal of similarity and have much more general functions, so it is easier to talk about stress proteins (SPs) having two different modes of operation. time As we proceed, it will be revealed that this issue is only one particular facet of a much bigger problem: how self-organized quantum criticality (SOQC) is possible? Criticality means by definition instability but SOQC is stable, which seems to be in conflict with the standard thermodynamics. In fact, living systems as a whole seem to be quantum critical [Kauffman 2015] and manage to stay near criticality, which means SOQC. Note that the self-organized criticality (SOC) is generalized to SOQC.

Topological Geometrodynamics (TGD) [Pitkänen 2020_a] [Pitkänen 2014_c, Pitkänen 2016] is a 43 year old proposal for a unification of fundamental interactions. Zero energy ontology (ZEO) [Pitkänen 2020_c] is basic aspect of quantum TGD and allows to extend quantum measurement theory to a theory of consciousness and of living systems. ZEO also leads to a quantum theory of self-organization [Pitkänen 2019_a] predicting both arrows of time. Could ZEO make SOQC possible as well?

1.1 Summary of the basic properties of CSPs and HSPs

Let's consider a summary of CSPs and HSPs or briefly SPs.

1. There is a large variety of cold shock proteins (CSP) and heat shock proteins (HSPs). CSPs and HSPs are essentially the same proteins and labelled by HSPX, where X denotes the molecular weight of the protein in kDaltons. The value range of X includes the values $\{22, 60, 70, 90, 104, 110\}$ and HSPs are classified into 6 families:

small HSPs, HSPX, $X \in \{40, 60, 70, 90, 110\}$. At least HSP70 [Wikipedia$_e$] and HSP90 [Wikipedia$_f$] have ATPase at their end whereas HSP60 has ATP binding site [Wikipedia$_d$]. CSPs and HSPs consist of about $10^3 - 10^4$ amino acids so that X varies by one order of magnitude.

Their lengths in the un-folded active configuration are below 1 micrometer. CSPs/HSPs [Wikipedia$_c$, Wikipedia$_b$, Nuray and Ferhan 2001, Szaz et al 2003] are expressed when the temperature of the organism is reduced /increased from the physiological temperature. CSPs possess cold-shock domains [Wikipedia$_a$] consisting of about 70-80 amino-acids thought to be crucial for their function. Part of the domain is similar to the so called RNP-1 RNA-binding motif. In fact, it has turned that CSP and HSP are essentially the same object and stress protein (SP) is a more appropriate term.

Wikipedia article about cold shock domain [Wikipedia$_a$] mentions Escherichia Coli as an example. When the temperature is reduced from 37 °C to 10 °C, there is 4-5 hours lag phase after which growth is resumed at a reduced rate. During lag phase expression of around 13 proteins containing cold shock domains is increased 2-10 fold. CSPs are thought to help the cell to survive in temperatures lower than optimum growth temperature, by contrast with HSPs, which help the cell to survive in temperatures greater than the optimum, possibly by condensation of the chromosome and organization of the prokaryotic nucleoid. What is the mechanism behinds SP property is the main question.

2. SPs have a multitude of functions involved with the regulation, maintenance and healing of the system [Petrauskas et al 2011, Kellner et al 2019, Feidantsis et al 2019, Biter et al 2013, Szaz et al 2003]. They appear in stress situations like starvation, exposure to cold or heat or to UV light, during wound healing or tissue remodeling, and during the development of the embryo. SPs can act as chaperones [Kellner et al 2019] and as ATPAses [Fouvet et al 2018, Christopher et al].

   SPs facilitate translation, and protein folding in these situations, which suggests that they are able to induce local heating/cooling of the molecules involved in these processes. CSPs could be considered like ovens and HSPs like coolants; systems with very large heat capacity acting as a heat bath and therefore able to perform temperature control. SPs serve as kind of molecular blacksmiths - or technical staff - stabilizing new proteins to facilitate correct folding and helping to refold damaged proteins. The blacksmith analogy suggests that this involves a local "melting" of proteins making it possible to modify them.

   What "melting" could mean in this context? One can distinguish between denaturation in which the folding ability is not lost and melting in which it is lost. Either local denaturation or even melting would be involved depending on how large the temperature increase is. In a aqueous environment the melting of water surrounding

the protein as splitting of hydrogen bonds is also involved. One could also speak also about local unfolding of protein.

3. There is evidence for large change ΔC_p of heat capacity C_p ($C_p = dE/dT$ for pressure changing feed of heat energy) for formation ion nucleotide-CSP fusion [Christopher et al]. This could be due to the high C_p of CSP. The value of heat capacity of SPs could be large only *in vivo*, not *in vitro*.

4. HSPs can appear even in hyper-thermophiles living in very hot places. This suggests that CSPs and HSPs are basically identical - more or less - but operate in different modes. CSPs must be able to extract metabolic energy and they indeed act as ATPases. HSPs must be able to extract thermal energy. If they are able to change their arrow of time as ZEO suggests, they can do this by dissipating with a reversed arrow of time.

To elucidate the topic from other angles, the following key questions should be answered:

1. Are CSPs and HSPs essentially identical?

2. Can one assign to SPs a high heat capacity (HHC) possibly explaining their ability to regulate temperature by acting as a heat bath? One can also ask whether HHC is present only *in vivo* that is in a aqueous environment and whether it is present only in the unfolded configuration of HP?

1.2 The notion of quantum criticality

The basic postulate of quantum TGD is that the TGD Universe is quantum critical [Pitkänen 2014_c, Pitkänen 2016] [Pitkänen 2015_a, Pitkänen 2015_c]. There is only a single parameter, Kähler coupling strength α_K mathematically analogous to a temperature and theory is unique by requiring that it is analogous to critical temperature. Kähler coupling strength has discrete spectrum labelled by the parameters of the extensions of rationals. Discrete p-adic coupling constant evolution replacing continuous coupling constant evolution is one aspect of quantum criticality.

What does quantum criticality mean?

1. Quite generally, critical states define higher-dimensional surfaces in the space of states labelled for instance by thermo-dynamical parameters like temperature, pressure, volume, and chemical potentials. Critical lines in the (P,T) plane is one example. Bringing in more variables one gets critical 2-surfaces, 3-surfaces, etc. For instance, in Thom's catastrophe theory [Zeeman 1977] cusp catastrophe corresponds to a V-shaped line, whose vertex is a critical point whereas butterflly catasrophe to

2-D critical surface. In thermodynamics the presence of additional thermodynamical variables like magnetization besides P and T leads to higher-dimensional critical surfaces.

2. There is a hierarchy of criticalities: there are criticalities inside criticalities. Critical point is the highest form of criticality for finite-D systems. Triple point, for instance, for water in which one cannot tell whether the phase is solid, liquid or gas. This applies completely generally irrespective of whether the system is a thermo-dynamical or quantal system. Also the catastrophe theory of Thom gives the same picture [Zeeman 1977]. The catastrophe graphs available in the Wikipedia article illustrate the situation for lower-dimensional catastrophes.

3. In TGD framework finite measurement resolution implies that the number of degrees of freedom (DFs) is effectively finite. Quantum criticality with finite measurement resolution is realized as an infinite number of hierarchies of inclusions of extensions of rationals. They correspond to inclusion hierarchies of hyperfinite factors of type II_1 (HFFs). The included HFF defines the DFs remaining below measurement resolution and it is possible to assign to the detected DFs dynamical symmetry groups, which are finite-dimensional. The symmetry group in never reachable ideal measurement resolution is infinite-D super-symplectic group of isometries of "world of classical worlds" (WCW) consisting of preferred extremals of Kähler action as analogs of Bohr orbits. Super-symplectic group extends the symmetries of superstring models [Pitkänen 2014_c] [Pitkänen 2010_b, Pitkänen 2010_a, Pitkänen 2015_b, Pitkänen 2019_b].

4. Criticality in living systems is a special case of criticality - and as the work of Kauffman [Kauffman 2015] suggests - of quantum crticality as well. Living matter as we know, it most probably corresponds to extremely high level of criticality so that very many variables are nearly critical, not only temperature but also pressure. This relates directly to the high value of h_{eff} serving as IQ. The higher the value of h_{eff}, the higher the complexity of the system, and the larger the fluctuations and the scale of quantum coherence. There is a fractal hierarchy of increasingly quantum critical systems labelled by a hierarchy of increasing scales (also time scales).

   In ZEO classical physics is an exact part of quantum physics and quantum physics prevails in all scales. ZEO makes discontinuous macroscopic BSFRs to look like smooth deterministic time evolutions for the external observer with opposite arrow of time so that the illusion that physics is classical in long length scales is created.

Number theoretical physics or adelic physics [Pitkänen 2017_a] is the cornerstone of TGD inspired theory of cognition and living matter and makes powerful predictions.

p-Adic length scale hypothesis deserves to be mentioned as an example of prediction since it has direct relevance for SPs.

1. p-Adic length scale hypothesis predicts that preferred p-adic length scales correspond to primes $p \simeq 2^k$: $L(k) = 2^{(k-151)/2}L(151)$, $L(151) \simeq 10$ nm, thickness of neuronal membrane and a scale often appearing molecular biology.

2. TGD predicts 4 especially interesting p-adic length scales in the range 10 nm- 25 μ. One could speak of a number theoretical miracle. They correspond to Gaussian Mersenne primes $M_{G,k} = (1+i)^{k-1}$ with prime $k \in \{151, 157, 163, 167\}$ and could define fundamental scales related with DNA coiling for instance.

3. The p-adic length scale $L(k = 167) = 2^{(167-151)/2}L(151) = 2.5$ μ m so that SPs could correspond to $k \in \{165, 167, 169\}$. $L(167)$ corresponds to the largest Gaussian Mersenne in the above series of 4 Gaussian Mersennes and to the size of cell nucleus. The size scale of a cold shock domain in turn corresponds to $L(157)$, also associated with Gaussian Mersenne. Note that the wavelength defined by $L(167)$ corresponds rather precisely to the metabolic currency .5 eV.

4. HSPX, $X \in \{60, 70, 90\}$ corresponds to a mass of X kDaltons (Dalton corresponds to proton mass). From the average mass 110 Dalton of amino acid and length of 1 nm one deduces that the straight HSP60, HSP70, and HSP90 have lengths about .55 μm, .64 μ, and .8 μm. The proportionality of the protein mass to length suggests that the energy scale assignable to HSPX is proportional to X. (HSP60, HSP70, HSP90) would have energy scales (2.27, 1.95,1.5 eV) for $h_{eff} = h$ naturally assignable to biomolecules. The lower boundary of visible photon energies is a 1.7 eV.

   Remark: One has $h = h_{eff} = nh_0$ for $n = 6$. What if one assumes $n = 2$ giving $h_{eff} = h/3$ for which the observations of Randel Mills [Mills et al 2003] give support [Pitkänen 2017_b]? This scales down the energy scales by factor 1/3 to (.77,.65,0.5) eV not far from the nominal value of metabolic energy currency of about .5 eV.

   There are strong motivations to assign to HSPs the thermal energy $E = T = .031$ eV at physiological temperature: this is not the energy $E_{max} = .084$ eV at the maximum of the energy distribution, which is by a factor 2.82 higher than E. The energies above are however larger by more than one order of magnitude. This scale should be assigned with the MBs of SPs.

5. The wavelengths assignable to HSPs correspond to the "notes" represented by dark photon frequencies. There is an amusing co-incidence suggesting a connection with the model of bio-harmony [Pitkänen 2014_a, Pitkänen 2014_b]: the ratios of energy scales of HSP60 and HSP70 to the HSP90 energy are 3/2 and 1.3, respectively. If HSP90 corresponds to note C, HSP60 corresponds to G and HSP70 to note E with ratio 1.33. This gives C major chord in a reasonable approximation! Probably this is an accident. Note also that the weights X of HSPXs are only nominal values.

1.3 Hagedorn temperature, HHC, and self-organized quantum criticality (SOC)

Self-organized criticality (SOC) is an empirically verified notion. For instance, sand piles are SOQC systems. The paradoxical property of SOQC is that although criticality suggests instability, these systems stay around criticality. In standard physics SOQC is not well-understood. TGD based model for SOQC involves two basic elements: ZEO and Hagedorn temperature.

1. ZEO predicts that quantum coherence is possible in all scales due to the hierarchy of effective Planck constants predicted by adelic physics. "Big" (ordinary) state function reductions (BSFRs) change the arrow of time [Pitkänen 2020_c]. Dissipation in reversed arrow of time looks like generation of order and structures instead of their decay - that is self-organization. Hence SOQC could be made possible by the instability of quantum critical systems in non-standard time direction. The system paradoxically attracted by the critical manifold in standard time direction would be repelled from it in an opposite time direction as criticality indeed requires.

2. Surfaces are systems with infinite number of DFs. Strings satisfy this condition as also magnetic flux tubes idealizable as strings in reasonable approximation. The number of DFs is infinite and this implies that when one heats this kind of system, the temperature grows slowly since heat energy excites new DFs. The system's maximum temperature is known as Hagedorn temperature and it depends on string tension for strings.

   In the TGD framework, magnetic flux tubes can be approximated as strings characterized by a string tension decreasing in long p-adic length scales. This implies a very high value of heat capacity since very small change of temperature implies very large flow of energy between the system and environment.

   T_H could be a general property of MB in all scales (this does not yet imply SOQC property). An entire hierarchy of Hagedorn temperatures determined by the string tension of the flux tube, and naturally identifiable as critical temperatures is predicted. The temperature is equal to the thermal energy of massless excitations such as photons emitted by the flux tube modellable as a black body.

   Remark: If the condition $h_{eff} = h_{gr}$ [Pitkänen 2018], where h_{gr} is gravitational Planck constant introduced originally by Nottale [Nottale an Da Rocha 2003], holds true, the cyclotron energies of the dark photons do not depend on h_{eff}, which makes them an ideal tool of quantum control.

   Hagedorn temperature would make them SOQC systems by temperature regulation if CSP type systems are present they can serve as ovens by liberating heat energy and force the local temperature of environment to their own temperature near T_H. Their own temperature is reduced very little in the process. These systems can

also act as HSP/CSP type systems by extracting heat energy from/providing it to the environment and in this manner reduce/increase the local temperature. System would be able to regulate its temperature.

A natural hypothesis is that T_H corresponds to quantum critical temperature and in living matter to the physiological temperature. The ability to regulate the local temperature so that it stays near T_H has interpretation as self-organized (quantum) criticality (SOC). In the TGD framework these notions are more or less equivalent since classical physics is an exact part of quantum physics and BSFRs create the illusion that the Universe is classical in long (actually all!) scales.

Homeostasis is a basic aspect of living systems. System tends to preserve its flow equilibrium and opposes the attempts to modify it. Homeostasis involves complex many-levels field back circuits involving excitatory and inhibitory elements. If living systems are indeed quantum critical systems, homeostasis could more or less reduce to SOQC as a basic property of the TGD Universe.

2 The basic ideas about SPs

The TGD based model for SPs relies on the notion of MB carrying dark matter as $h_{eff} > h$ phases and the notions of heat transfer and heat capacity. The basic idea is that at least in aqueous environment the MBs of biomolecules in general have a large number of DFs and act as heat reservoirs with a stable temperature near a Hagedorn temperature. MBs of SPs have also high heat transfer rates between the thermal environment of the ordinary matter. ZEO - in particular time reversal - makes it possible to realize thermal regulation in terms of SOQC. On the other hand, information carrying biomolecules cannot have high heat transfer rate with environment.

2.1 Conditions on the heat transfer rates between the systems involved

To avoid lengthy explanations, it is appropriate to introduce some shorthand notations. Denote by $j_H(X-Y)$ heat transfer rate between systems X and Y. Denote by E. Denote BB(X) the biological body of system X. X can denote the ordinary biomolecule (DNA,RNA,protein) denoted by BM or stress protein SP.

There are several conditions on the model explaining the HHC

1. $j_H(MB(SP)-E)$ should be high so that the MB of SP can rapidly adapt to temperature changes and extract thermal energy from the environment and act as an oven or a coolant. $j_H(MB(SP)-BM$ should be high so that CSPs could rapidly warm up BMs for processes like translation, transcription and folding.

$j_H(MB(SP)-BM$ can be also high if heat transfer occurs indirectly via $MB(BM)$. This requires that both $j_H(MB(BM)-BM$ and $j_H(MB(SP)-MB(BM)$ are high. However, the large value of $j_H(MB(BM)-BM$ implies that BMs can take care of temperature regulation without the help of SPs. Hence this option does not seem to be consistent with empirical facts. Hence $j_H(MB(BM)-BM$ must be low.

There is also a deeper rational for this. The MBs of ordinary bio-molecules must carry information and cannot be thermalized so that the energy transfer rate between them and their BB and between them and the environment must be low.

2. In CSP mode the MBs of SPs should actively extract energy from fats. The BMs should extract thermal energy from MBs of SPs. In HSP mode MBs of SPs at temperature than that of the local thermal environment (including BMs) should cool it by absorbing thermal energy from it.

The following table summarizes the constraints on the symmetric matrix of heat transfer rates $j_H(A,B)$ for various combinations of subsystems X and Y. The shorthand notations are (SP, BM, E) for (stress protein, basic biomolecule, environment) and $MB(X)$ for the MB of molecule X. Environment E is taken as the thermal environment at the level of ordinary matter. The diagonal heat transfer rates are not considered. H/L for the matrix element $j_H(X,Y)$ of the table means that its value can be large/small. The symbol "*" means that this particular transfer is not relevant.

X/Y	SP	$MB(SP)$	BM	$MB(BM)$	E
SP	$*$	**H**	$*$	$*$	$*$
$MB(SP)$	**H**	$*$	**H**	$*$	**H**
BM	$*$	**H**	$*$	**L**	$*$
$MB(BM)$	$*$	$*$	**L**	$*$	$*$
E	$*$	**H**	$*$	$*$	$*$

(2.1)

In the minimal scenario the only constraints are on $j_J(SP, MB(SP)$ (H), $j_J(BM, MB(SP)$ (H), and $j_J(BM, MB(BM)$ (L).

The natural question is what makes it possible for the MBs of SPs to gain energy.

1. The first manner to get energy is heat transfer from the environment. Passive heat transfer would involve either ordinary photons transformed to dark photons and absorbed by MB(SP) or active heat extraction in time reversed mode involving emission of dark photons transformed to ordinary photons and absorbed by ordinary matter. The energies should be in the range of thermal energies at physiological temperatures.

2. The negative energy photons from the MB of biomolecule can be also received by other MBs acting as analogs of population reversed laser. Thermalisation is expected

to occur if there is large number of this kind of states. MB should allow almost continuum of cyclotron energy state in the energy resolution defined by the size scale of the molecules.

3. At least some SPs such as HSP70 and HSP90 could act as ATPases providing the heat energy at their MBs to drive ADP $\rightarrow$ ATP process. They would act as general purpose quantum heat engines with MB acting as a heat bath running the ATPase machinery. Heat engine function requires a heating of the MB SP to a temperature above the local physiological temperature but below the Hagedorn temperature: in ZEO time reversal for the MB of SP allows this: it would look like extraction of thermal energy from the environment. Part of the energy heating MB of SP could come from the binding of ATP to ATPAse part of PS. This energy is in the range of 3-7 eV for nucleotides and could heat the MB of SP.

   One could also consider remote metabolism for the molecules receiving the metabolic energy quantum with a negative energy photon inducing $ATP \rightarrow ADP$. Note that the metabolic energy quantum .5 eV is in infra-rede (IR) range and corresponds to 2.4 μm wavelength very near to the largest p-adic length scale $L(167)$ in the quadruplet of primes $k \in \{151, 157, 163, 167\}$ defining four Gaussian Mersennes and defining the size scale of nucleus.

Now, consider the extraction of heat energy from the environment:

1. The energies assignable to the photon wavelengths defined by the lengths of HSPX proteins are proportional to 1/X and above 1.5 eV, which is considerably above the energy of thermal photon at the maximum of Planck distribution for energy is $E_{max} = .084$ eV).

2. The energy transfer would be based on energy resonance and is possible only if the cyclotron frequency spectrum of dark particles contains energies possessed by molecules in their spectrum in infrared range. This poses a condition on the cyclotron energies $E = \hbar_{eff} eB/m$ assumed to be in bio-photon energy range: this requires that $h_{eff} = nh_0 = \hbar_{gr} = BMm/v_0$ is large: one has $E = GMB/v_0$ does not depend on the mass of charged particle. Cyclotron energies involve also the contribution from a longitudinal motion along the flux tube. The energy scale for dark photon is now $\hbar_{eff}/L$ and also universal since L scales as $\hbar_{gr}$. If L is small the energy scale is so large that longitudinal DFs are not excited and thermalization does not occur. Same is true if B is large enough.

   Magnetic field strength is expected to scale like $1/L^2(k)$, where $L(k)$ is the p-adic length scale characterizing the molecule. The endogenous magnetic field $B_{end} = 2B_E/5$ identified as the monopole flux part of the Earth's magnetic field is expected to define an important value in the spectrum of magnetic fields. The corresponding p-adic length scale corresponds to the length scales assignable to SPs. Also

octaves of this value are expected and the model of bio-harmony [Pitkänen 2014$_a$, Pitkänen 2014$_b$] suggests that the preferred values are given by 12-note scale.

For short linear molecules the energy scales would be too high to allow thermalization so that these molecules can serve as information molecules. For long DNA one has length scale hierarchy and thermalization can occur only in long enough length scales. Human DNA has total length of order 1 meter but if the size of DNA defines the p-adic length scale, then DNA does not thermalize since the size of nucleus is not larger than $L(167) = 2.5$ μm. Note that DNA defines a length scale hierarchy in codons, genes, and also coiling scales define hierarchy levels. When the length of the molecules is longer than the wavelength of thermal photon at room temperature, one expects thermalisation to occur. SPs have lengths below 1 μm.

3. The thermalization should take place for the MBs of SPs. There are two energy scales associated with the cyclotron energies and the free motion along the flux tube respectively. Thermal energy scale could correspond to either of these length scales.

   (a) Cyclotron energy scale is given by $E_c = GMB/v_0$ for $h_{eff} = h_{gr}$ and the scales are proportional to B. Longitudinal energy scale dose not depend on h_{eff} since the flux tube length scales like h_{eff}. Since B scales like $1/L^2(k)$, cyclotron length scale increases for small protein sizes. This suggests that thermalization is associated with the cyclotron DF and appears for large enough p-adic length scales characterizig protein size.

   (b) Longitudinal energy scale naturally corresponds to the lengh of protein for $h_{eff} = n$. The energy scale of longitudinal excitations is consirably above the thermal energy scale so that thermalization would not be possible. It might be however possible to transfer energy from these DFs to the MB of SP where it is transformed to thermal energy.

2.2 A new physics model for HHC

Now, consider a more concrete new physics model for HHC:

1. HHC suggests the existence of new DFs to which energy is stored so that temperature is not raised as new DFs become available.

2. In the theory of extended objects like strings, the very large number (infinite) of degress of freedom (DFs) implies a maximal temperature T_H known as Hagedorn temperature. Flux tubes are extended objects. This suggests that the MBs of SPs are near to the Hagedorn temperature defining the maximal temperature for their MBs. Also the assumption that the physiological temperature is near but usually below T_H: this condition allows SP to act as heat engine. This cannot be true for the information carrying biomolecules such as DNA, RNA and proteins since

thermalization destroys information. Therefore they must have a temperature much below T_H.

3. In a hot environment the existence of Hagedorn temperature T_H for the MB of HSP means that the thermal energy is transferred from the environment to the MB of HSP. This tends to reduce the local temperature of the environment towards T_H. HSP would act as an ideal coolant. Their presence would faciliate the basic functions of cells.

4. CSP and its MB would be at temperature near T_H and could act as an oven. Their presence around DNA, RNA, and proteins would raise their temperature locally and facilitate transcription, translation and protein folding and unfolding otherwise prevented by a low temperature.

5. SPs could act as heat engines providing heat energy to molecular motors [Wikipedia$_g$]. This entails SP to have a temperature higher than the temperature of environment. In ZEO this is possoble by using a time reversed mode for SP to extract energy from the environment. Many SPs have ATPase at their end and this would make them universal heat engines providing the work as metabolic energy currency for any molecular user.

6. Quite generally, by their ATPase property, many SPs could act as metabolic energy sources in stressful situations - this comprises many other situations in addition to low and high temperatures. Metabolic energy feed increases h_{eff} and would increase the scale quantum coherence reduced in the damage of DNA, proteins and tissue, for instance. After this, the system could self-organize to the healed state. For instance, CSPs could induce local melting of misfolded proteins leading to a repair. CSPs act as chaperones and their basic tool would be local "melting" (remind our operational definition of "melting") by feeding heat energy - allowing to establish a correct conformation.

7. The MBs of SPs could extract their thermal energy from the thermal energy of the environment in time reversed mode allowed by ZEP allowing the temperature of SP to even exceed that of environment in the final state of BSFR.

Consider a quantitative estimate.

1. For a typical flux tube length is larger than the radius of the flux tube. The critical temperature identified as Hagedorn temperature corresponds to a typical thermal energy of the flux tube and is determined by flux tube length and its string tension. The critical temperature is inversely proportional to the length of the flux tube.

2. Critical temperature T_H roughly corresponds to the energy of a photon with wavelength equal to the flux tube length L : $E = T_H \sim h_{eff}/L$. For $h_{eff} = h$ the flux

tube length corresponds to the length scale of CSP but for large values of $h_{eff} = h_{gr}$ it corresponds to a scale of even Earth. The energies and temperature T_H are however the same irrespective of the value of h_{eff} and thus length of flux tube.

3. The rough estimate is that for physiological temperatures T_{ph} around T_H, the length for $h_{eff} = h$ the wave length for a thermal photon at temperate 310 K the maximum of energy distribution is around 14.7 μm: note that the sizes of most animal and plant cells are oin the rage of 10-100 μm. For the wavelength distribution the wavelength for the maximum is roughly 7 μm. CSPs and HSPs consist of about 100-1000 amino acids or so. Length would be in the range .1-1 μm. The energies of photons with a wave length of straight SP are definitely above thermal energy range.

Some questions are in order.

1. If the new DFs are associated with MB, what can one say about the value of h_{eff} serving as IQ could be? SPs are possessed already by bacteria which suggests that the value of h_{eff} cannot be very large. Acting as a chaperon is a control function, which suggests a higher than normal value of h_{eff}. Higher than normal value ignites intriguing question whether they have higher IQ (as a value of h_{eff} characterizing number theoretic complexity) than other proteins helping to survive in difficult situations. On the other hand, the thermalization means that SP flux tubes cannot carry information unlike the flux tubes of basic bio-molecules with their MBs at very low temperature.

2. Cell membrane must stay flexible as temperature is lowered. This is known to be achieved by a generation of unsaturated bonds to lipids. This involves desaturase enzyme creating C-C double bond. Desaturase enzymes are not SPs. SPs can however faciliate the transcription and translation of desaturase enzymes.

2.3 Physiological temperature as Hagedorn temperature, local temperature regulation, and self organized quantum criticality

The notions of quantum criticality, self-organized quantum criticality (SOC) and Hagedorn temperature leads to a new physics based model for the explanation of SP functions.

1. Hagedorn temperature T_H as a maximal temperature of MB of stress protein would be crucial for its functioning. Why the physiological temperature is around 310 K is one of the puzzles of biology. The work of Kauffman [Kauffman 2015] suggests that the interpretation as a quantum critical temperature is appropriate. TGD predicts a hierarchy of quantum critical temperatures. The natural guess would be that this

quantum critical temperature is Hagedorn temperature realized at the level of MB asymptotically: in practice, the temperature of MB would be somewhat below T_H.

This would facilitate temperature regulation or perhaps even make it possible. At quantum criticality also long length scale quantum fluctuations are possible and this makes modifications of the system possible - say damaged proteins. If the temperature T of the environment at BB is above T_H, the thermal energy flows to MB of SP and its temperature T is reduced. MB can also make BSFR reversing the arrow of time and extract thermal energy from the environment.

2. Self-organized criticality (SOC) generalizes to self-organized quantum criticality (SOQC) in the TGD framework. SOC is well-known but it is not understood. For instance, sand piles are SOC systems. They tend to approach a critical state, which looks paradoxical since just the opposite should hold for critical systems by their defining property which makes them unstable! Critical system is optimal for measuring and representing since it has a large number of different states with roughly the same energy. Therefore biosystems should be critical systems.

   The basic objection against SOC and SOQC is that SCs are unstable by definition. In ZEO this objection can be circumvented. Quantum coherence is possible in all scales and in BSFRs the arrow of time is changed. This transforms the critical manifold from a repeller to an attractor and time reversals make SOQC possible. The occurrence of SOQC would be direct empirical proof for the ZEO and its most dramatic predictions.

What is the distinction between CSP and HSP modes of SPs? SOQC according to ZEO suggests that time reversal could explain this difference. How do the time reversals for CSP and HSP modes differ? The following picture is suggestive.

1. The time reversal occurs for the MB of SP in HSP mode so that they extract thermal energy from environment.

2. The time reversal occurs for the MBs molecules interacting with SPs in CSP mode so that they can extract heat energy from the MB of CSP.

It has been already told that homeostasis in presence of quantum criticality is essentially quantum critical SOC.

2.4 $\Delta C_p > 0$ for HSP90-nucleotide binding as support for the model

Chistopher et al have studied enthalpy driven reactions involving nucleotide or ansamycin bimnding to HSP90: the title of the article [Christopher et al] is "*StructuralThermodynamic Relationships ofInteractions in the N-Terminal ATP-Binding Domain*". These

reactions occurring in constant pressure are enthalpy driven meaning that heat is liberated in these reactions - the second option would be entropy driven reaction in which the large entropy gain makes reaction possible. The formation of a bound state means a reduction of DFs suggesting a decrease of the heat capacity C_p of the combined system.

Researchers however find $\Delta C_p > 0$ when another reactant is nucleotide but not for the ansamycin case. Intuitively, the number of DFs should increase to explain this. The authors of the article discussed a number of explanations for their unexpected finding.

The presence of MB means new hidden DFs and the neglect of its presence could lead to thermo-dynamical anomalies. Could $\Delta C_p > 0$ in an enthalpy driven reaction leading to a formation of bound state be such an anomaly?

1. Suppose HSP90 has MB can have large C_p and that it is at the temperature of the environment. The temperature varies in the range 2-25 °C being considerably below the physiological temperature 37 C proposed to correspond to a maximal temperature - Hagedorn temperature - for the magnetic flux tubes of SPs. C_p for the MB of SP is expected to increase as the temperature rises since new DFs are thermally excited.

   C_p could be rather high already for the initial state if it corresponds to the sum of heat capacities for nucleotide/ansamycin and HSP90. The size of the MB of nucleotide for $h_eff = h$ should be small if it correlates with the size of nucleotide/ansamycin. Nucleotide is an information molecule and therefore its MB should be at a low temperature and have low C_p (thermal energies cannot excite the states at low temperature).

2. Since binding reaction is in question, C_p for the combined system should be reduced unless something happens at the level of MBs. Could the heat capacity of MB of HSP90 increase for nucleotide binding? Could even the value of ΔH for the nucleotide case be larger than thought due to the fact that part of ΔH is transferred to MB of HSP90?

   (a) A lot of heat is liberated in the exothermic binding reaction in both cases. The measure part of the liberated heat goes to the standard DFs discussed in the article. Part of ΔH is transferred to the MB of HSP90 and can heat it to a higher local temperature. New DFs open and heat capacity of MB of CPS90 increases so much that the net heat capacity can increase despite the reduction of ordinary contribution to C_p.

   This would happen for the nucleotide but not for ansamycin. Why would the fraction of liberated heat going to the MB of HSP be so small for ansamycin that ΔC_p remains negative?

   (b) Could the heat ΔH liberated in the nucleotide case be considerably larger than assumed and larger than for ansamycin plus CSP. This is quite possible since

only the fraction going to the environment is measured, not that transferred to MB. Theoretical estimates do not of course take the possible presence MB into account. If ΔH for the nucleotide case is larger than believed, then MB of HSP90 can be heated more and $\Delta C_p > 0$ is possible.

(c) The inspection of tables of [Christopher et al] shows that the values of ΔH for the nucleotide case are in the range 3-8 eV *per* reaction and correspond to UV energies. For reactions $\Delta C_p < 0$ the values of ΔH are of order .3 eV and correspond to IR photons but with energies larger than thermal energies. The difference is more than order of magnitude and suggests a similar difference for ΔH transferred to MB, which supports the proposed explanation.

2.5 Some functions of SPs in TGD perspective

2.5.1 SPs as heat baths for molecular heat engines and providers of heat energy to ATPs

Heat is produced as a side effect of metabolism and HSPs could extract this heat using remote metabolism and transform it to heat energy resourses liberated when needed.

SPs could be used for heating as in the basic biological processes like transcription and transcription. SPs could also act as heat engines transforming heat energy to work in the case of molecular motors [Wikipedia$_g$].

There are reports about the role of HSPs in doing molecular work [Kellner et al 2019, Bonventre et al 1999, Biter et al 2013]: the new element would be heat energy coming from the MB of SP. At least SPs such as HSP60, HSP70, HSP90, HSP104 binding to ATP could serve as general purpose heat engines transforming heat energy at their MB to metabolic energy currency used in various biological processes.

1. All processes produce heat and the very idea of HSPs would the that HSPs gather this heat energy and act as heaters as in the case of transcription, translation, and replication or as heat engines liberating the heat energy as ordered energy. Action as ATPase would make HSP a general purpose molecular heat engine. Currently, we know that HSPX for $X \in \{60, 60, 90, 104\}$ at least act as ATPases.

   Very important question: Is ATPase property a general property of HSPs?*

   By the second law of thermodynamics these heat engines have some maximal efficiency proportional to the difference of the temperatures for heat bath - now MB - and the system receiving the energy. Hence HSP MBs must be at a temperature higher than the systems receiving the energy. The formation of HSP90-ATP bound state would liberate binding energy about 3-7 eV *per* reaction (metabolic energy quantum is .5) eV and this heats MB of HSP and would lead to the reported increase of heat capacity.

2. There is, however, a reason to worry. By Carnot's law maximal effectiveness is proportional to $\Delta T/T$, where ΔT is the temperature difference between the system receiving the work and heat bath, now the MB of SP, and T the temperature of the heat bath. Is the temperature difference high enough to give a reasonable effectiveness?

   ZEO provides a quantum manner to get rid of worries. Time reversal could make possible for the MB of HSP to develop a temperature higher than that of environment by what looks for an observer extraction of thermal energy from the environment but is actually BSFR leading to final state which dissipates in reverse time direction to a state in which the temperatures are equal. T_H should be however somewhat higher than the physiological temperature.

2.5.2 Heat shock protein 70 and ATP in homeostasis

ATP depletes in stress situations due to the lack of ordinary metabolic energy feed as in ischemia. The role of HSP70 and its co-function with ATP in this kind of situation is discussed in [Bonventre et al 1999] . Also HSP70 involves ATPase and the lack of the ordinary metabolic energy could be replaced by thermal metabolic energy feed from the MBs of say HSP70.

2.5.3 SPs and infection

One can distinguish between immune response, which is specific to the invader organism (say bacterium or virus) or molecule and non-specific immune response involving inflammation and fever. Infection includes both the effects of the invader and those caused by the non-specific immune response.

1. The invader specific immune response would be basically an action of the MB: this is the basic vision of TGD. Already the MB of water recognizes the invader molecules by the cyclotron energy spectrum of their MBs: this is just water memory [Smith 2001, Ho 2011, Montagnier et al 2009] discussed from TGD point view in [Pitkänen 2011]. "Homeopathy" is he ugly synonym for "water memory" and involves mechanical agitation feeds energy to the MBs of water clusters forming a population mimicking invader molecules.

   MBs of water clusters are varying its flux tube thicknesses and in this manner changing corresponding cyclotron frequencies to get in tune with possible invaders: this is similar to what we do when we search for a radio station. When a hit occurs, MB of the water cluster fixes the flux tube thickness. After getting to resonance, the MBs of water molecules clusters can reconnect with U-shaped flux tubes to corresponding bacterial flux tubes: a pair of flux tubes connecting the water cluster MB to the invader molecule is formed. Invader is caught. The chemical side of the

immune system emerged later and would involve sequences of dark proton triplets associated with proteins as addresses - 3N-fold resonance.

2. When bacteria infect cells, they induce inflammation and fever by raising the body temperature as a non-specific immune response. Inflammation can be seen as the body's protective response against infection. The fever helps immune cells to migrate to infection by a process known as chemotaxis. What fever and inflammation could mean in the proposed picture about SPs?

A possible explanation is as follows.

1. Quite generally, the loss of quantum coherence as a reduction of h_{eff} induced by the attack by bacteria should transform ordered energy to heat and produce entropy and also raise the temperature inducing fever. One possible mechanism producing heat in the loss of quantum coherence could be the decay of dark cyclotron condensates and dark photon states to biophotons with $h_{eff} = h$ and with energies around Hagedorn energy of order the energy associated with the physiological temperature. Also the decay of dark proton sequences in the reduction $h_{eff} \to h$ to ordinary protons would liberate energy as photons: Pollack's experiments show that IR irradiation produces exclusion zones (EZs) most effectively so that the energy would be in IR range.

2. Inflammation involves HSPs, in particular HSP70 [Krause et al 2015]. If the heat produced by the infection causing the fever can be seen as an entropic waste energy, SPs such as HSP90 would do its best to transform it to ordered energy realized as metabolic energy quanta with the nominal value around .5 eV. As discussed, this would mean a formation of bound states liberating energy - for instance, HMP90-ATP bound state would liberate energy with part going to the MB of HSP70/90 and part to a local environment.

   HMP70/90 acting as ATPases in the bound state and generate metabolic energy quanta by the ADP $\to ATP$ process. The liberated binding energy could cause the observed raise of C_p of the MB of HMP90 and allow it to absorb more effectively heat energy from the environment by temporary time reversal and transform it to metabolic energy quanta. HSPs would be thus generated to absorb the surplus heat to be used as a metabolic energy resource and fever would be reduced as a consequence.

3 Speculative mechanisms explaining some biological observations

In the sequel some speculative applications will be considered.

3.1 Obesity, failing diets, and SPs

The effects of diets on HSP expression and activation have recently been studied, see for instance [Feidantsis et al 2013, Renes et al 2016, Habich et al 2017, Saad, Sabbah and Rezk 2019]. During the initial phase of diet the weight is lost. After that the weight often starts to regain. Does a new energy source emerge or is the level of metabolic energy consumption reduced so that the weight regain starts although the nutrient feed stays at the same albeit reduced level?

1. The fractality of TGD Universe suggests an analogy to our society. Living organism is a molecular society, and the fractality of the TGD Universe encourages looking at the situation from the point of view of our own society. Our energy resources have been depleting and we have learned to save energy, and also to recycle thermal energy to increase thermal efficiency. Could the organism learn to use remote metabolism to extract thermal energy from the environment besides SPs. Note that the thermal energy of a thermal photon at room temperature is rather near to the Coulomb energy of a unit charge assignable to the cell membrane voltage perhaps defining another metabolic energy currency.

2. The TGD explanation relies on the proposed ability of at least some SPs to act as ATPases transforming heat energy of their MB to ordered energy realized as metabolic energy quanta. The binding of SPs to ATP [Christopher et al] would also liberate binding energy transformed to heat, which is partially transferred to MB as heat energy serving as an additional metabolic energy source. Also the reduction of heat losses would mean more effective use of metabolic energy.

   People having obesity predisposition might generate HSP60 or HSP70 and HSP90 even in situations without stress. Also psychological stress such as depression might generate HSPs [Bahrami et al 2019]. HSP60 is known to be associated with obesity [Habich et al 2017]. HSP60 is associated with mitochondria and has ATP binding site but does not have ATPase. Could ATP binding site give HSP60 a role analogous to that of ATPase using heat energy of MB of HSP70 to generate ATP from ADP? A more plausible option is that the binding of ATP provides energy for HSP60 and only HSP70 and HSP90 act as ATPases.

   HSP70 [Mayer et al 2019] expression is considerably higher in obesity without metabolic syndrome but lower in obesity with metabolic syndrome [Saad, Sabbah and Rezk 2019]. This would suggest that the diet induces expression of HSP70 and therefore brings an additional metabolic energy source available. In metabolic syndrome the level of HSP70 utilizing thermal energy and reducing entropy of the system would be abnormally low. Besides the expression of HSP70, also its activation is needed [Wang et al 2017]. If the activation takes a considerable time, one could understand why it takes time for the additional metabolic energy source to emerge.

3. The ability to act as heat engines and ATPases relies on ZEO: the MBs of SPs could extract thermal energy from the environment in a mode with reversed arrow of time: instead of a disappearance of the necessary temperature gradient it would be generated. One can also say that system learns during diet to use remote metabolism.

   The phenomenon of remote metabolism or quantum credit card has been previously proposed by Pitkänen [Pitkänen 2013]: system would actively extract energy rather than receive it passively. The receiver of effective negative energy signal would be analogous to a population reversed laser assignable to MB. Quantum credit card would facilitate rapid access to energy via bypassing "bureaucratic formalities". This mechanism applies also to information transfer and makes communications possible with effective signal velocity exceeding the maximal signal velocity.

   Quite recently, it has been learned that quite simple physical systems can "breathe" by extracting the energy of Brownian motion [Kuzkin,Krivtsov 2020]: the finding is discussed from the point of view of ZEO in [Pitkänen 2020_d].

4. The utilization of metabolic energy becomes more effective during diet and there is less waste of energy. Less nutrients would be required and if the dietary consumption stays at the same albeit reduced levels, fat begins to be regenerated. Dietary stress would induce the generation of SPs. SPs acting as APTases would extract thermal energy from the environment and also from the liberated binding energy in the formation of SP-ATP complex and liberate it as ordered energy by ADP$\rightarrow$ ATP process. The slow rate for the generation of enzymes needed to generate and activate SPs might be the reason for the slow response

5. One could see the situation also in the following manner. ZEO and time reversal are involved with the extraction of thermal energy from the environment by the MBs of SPs. One can also say that the system learns during the diet to use remote metabolism. The time reversal would be the analog of sleep period. Also we get metabolic energy resources during sleep and the same mechanism could be involved. This could be also seen as hibernation/sleeping at the molecular level and the hibernation/sleep even at the level of organisms could rely on the same mechanism.

3.2 Sleigh dogs which run for days without eating, and starving bacterial colonies

Suppose that the general view about SPs is correct. Assume also there is a fractal hierarchy of MBs. Not only those of biomolecules and of smaller systems, but also of cells, organelles, organs, bodies, larger units like populations...

Assume also that $h_{eff} = h_g r$ holds true so that the cyclotron energy spectrum does not depend on the mass of the dark charged particle. This implies that MBs at all levels

of the hierarchy can communicate with the lowest level and also exchange energy and serve as metabolic energy sources. SPs would thus allow the transfer of energy to all these levels.

This admittedly speculative picture could explain the reported ability of sled dogs to run several days without eating [Robson 2008]: they could store the energy to their MBs and use it during substrate lack. A possible storage to their collective MB would increase further the energy storage ability. This would mean a connection to collective levels of consciousness predicted by TGD and receival of metabolic energy feed as dark photons from these levels [Pitkänen 2013]. h_{eff} hierarchy indeed makes possible energy transfer and communications between widely different scales characterizing a hierarchy of conscious entities.

This picture could partially explain also why bacteria in media lacking substrate form tightly bound colonies looking like multicellulars. They could store energy to their MB and use it during its substrate lack. Perhaps also the dissipation is reduced because h_{eff} increases.

The cells could also learn to extract thermal energy of the cellular environment besides the thermal energy of SPs, which is more or less another manner to say the same. Starvation could have been the evolutionary pressure leading to the formation of multicellulars. Indeed, the embryos of multicellulars are found to form tightly bound bacterial colonies [Yin et al 2019]: the TGD based model is discussed in [Pitkänen 2020_b]. There is also anecdotal evidence about analogous abilities of Tibetan monks and people regarded as saints.

To summarize, the proposed general model involves several new physics elements. the new view about space-time and fields, the new view about quantum theory based on ZEO predicting time reversal in BSFRs and a new view about self organization and a realization of SOQC, the h_{eff} hierarchy labelling dark matter as phases of ordinary matter predicted by number theoretic vision about TGD, and the hierarchy of collective levels if consciousness having as a correlate the hierarchy of MBs carrying dark matter in TGD sense. This vision can be defended only by its internal consistency and ability to solve a long list of deep problems of recent day physics.

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