Aging from TGD point of view

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Abstract

This chapter written together with Reza Rastmanesh was inspired by the book "Lifespan" by Sinclair and LaPlante. The books proposed that aging is basically caused by the approach to epigenetic chaos. The book also proposesthat bio-information is not only associated with DNA and genetic code but the conformational degrees of DNA and these are crucial in epigenesis. This vision serves as the starting point of TGD (Topological Geometrodynamics) inspired view.

Negentropy Maximization principle replacing in adelic physics second law but implying it for ordinary matter is the first key notion. Magnetic body (MB)carrying dark matter as $h_{eff} = nh_0$ phases of ordinary matter implying quantum coherence in the scale characterized by h_{eff} represents the second key notion. MB is the controller of the dynamics and its quantum coherence induces the coherence of ordinary biomatter as forced coherence rather than quantum coherence.

Zero energy ontology (ZEO) predicting the occurrence of time reversal in "big" (ordinary) state function reductions is the third key notion. Time reversal forces generalization of thermodynamics and dissipation of a subsystem with a reversed arrow of time looks like self-organization from the point of view of the system. Also self-organized quantum criticality difficult to understand in ordinary thermodynamics becomes possible.

The basic idea is that at birth the MBs of information molecules are at very low temperature and gradually approach the physiological temperature, which is near to Hagedorn temperature defining the maximal temperature of MB. This thermalization leads to epigenetic chaos implying that the flux tubes carrying dark DNA and therefore also DNA become loopy. Also the control of methylation and other modifications and their reversals crucial for epigenesis is lost. In particular, demethylation fails and leads to hyper-methylation of the promoter regions of genes. This leads to the failure of the control of genes coding for housekeeping proteins and eventually the system suffers a crash down.

1 Introduction

This article was inspired by a birthday gift. The gift was a highly inspiring book "Lifespan" by David Sinclair and Matthew LaPlante [I15]. The book tells about the recent understanding concerning aging. The general vision about aging represented in the book can be summarized as follows.

1. The key idea is that genes do not determine everything. DNA has also continuum degrees of freedom characterized by its shape. These degrees of freedom are related to epigenesis which is higher level control activity controlling what genes are expressed. The basic mechanisms are prevention and allowance of gene expression. Acetylization [I2], methylation [I10] and many other modifications affect the gene expression by attaching to proteins known as histones forming kind of pearls in the necklace defined by DNA: genes follow nucleosomes in the DNa strand. Also the reversals of these processes - for instance, deacetylation [I5, I18]and demethylation [I10] are essential for the control of gene expressions.

2. Aging involves the emergence of various diseases. Usually the attention is directed to dealing with these diseases. Now the view is however more general. Aging is seen as a gradual approach to chaos manifesting as various diseases. In order to prevent the diseases one should slow down the approach to chaos.

3. Epigenetic chaos hypothesis suggests that some control systems associated with information molecules and related to the control of DNA transcription and translation by epigenesis must approach chaos. This is seen as the gradual randomization of DNA conformations causing problems in the transcription of DNA: DNA becomes loopy. The DNA coding for the ribosome acting as the translation machinery of DNA is of special importance and becomes also loopy. What comes first in physicist's mind, is an approach to thermal equilibrium. Is there some system controlling epigenesis which approaches thermal equilibrium with the environment? In standard chemistry it is difficult to identify this kind of system.

4. Biology has invented ingenious mechanisms to slow down aging. For instance, there are molecules having two functions. There are proteins making the translation of the genes related to cell replication possible.

   When the DNA coding for the ribosome gets loopy their function changes. The translation of genes ceases as the proteins leave the histone molecules and enter the damaged DNA and freeze it so that it can be prepared. This however slows down cell replication and also causes other problems leading to various diseases related to aging. One can say that a cell is like a hospitalized patient.

   The slowing down of aging would be in this framework basically fighting against the thermo-dynamical arrow of time. Is it really possible to understand the processes involved in the framework of standard bio-chemistry with a single arrow of time?

   Even the understanding of the biocatalysis is difficult: how the reacting molecules are able to find each other in the molecular soup and how the huge increase for the rate of these processes is possible. The TGD based solution of these problems will be discussed later.

What could TGD inspired theory of consciousness and quantum biology rely on zero energy ontology (ZEO) inspired biology allow to say about the mechanism behind aging?

1. Negentropy Maximization Principle (NMP) as the variational principle of consciousness replaces the second law and implies it for ordinary matter. State function reduction (SFR) means a reduction of the entanglement for a pair $S_a - S_b$ of sub-system S_a and its complement S_b in S. Measurement cascade proceeding from long to short scales decomposes at each step a system to a pair of unentangled subsystems is in question. NMP as a variational principle of consciousness states that negentropy gain in these reductions is maximized and selects the pair $S_a - S_b$ at given step.

   In adelic physics [L3, L4] the negentropy $N = -S_1 - S_2$ is sum of real and various p-adic negentropies but p-adic negentropy can be positive so that for non-trivial extensions of rationals one can have $N > 0$. This kind of entanglement is stable against NMP so that the process stops. One can assign positively colored emotions to this kind of entanglement and it distinguishes between living and inanimate matter and also between dark and ordinary matter.

2. TGD inspired theory of consciousness is basically an extension of quantum measurement theory allowing to get rid of the basic paradox of quantum measurement theory. There are two kinds of state function reductions (SFRs) "big" SFR and "small" SFR (briefly BSFR and SSFR) [L9].

   SSFRs are counterparts of "weak" measurements which are much like classical measurements and do not involve any dramatic changes. The sequence of SSFRs gives rise to a conscious entity -self - as a sequence of moments of consciousness. Subjective time as a sequence of SSFRs correlates with the geometric time. BSFRs are counterparts of ordinary quantum measurements and have a dramatic effect: in a very general sense one can say that self dies and reincarnates with an opposite arrow of geometric time.

3. There is a hierarchy of magnetic bodies carrying dark matter as phases of ordinary matter with effective value $h_{eff} = nh_0$ of Planck constant. n corresponds to the dimension of an extension of rationals. The extensions define evolutionary hierarchies with increasing complexity. n serves as a measure of algebraic complexity and as a universal IQ, and also characterizes the scale of quantum coherence. For instance, genes are characterized by the value of h_{eff} associated with their MB.

   Since MBs have higher universal IQ than ordinary biomatter, they control the biochemistry. In particular, they would control DNA and DNAs MB would actually realize genetic codons in terms of dark proton triplets. Also dark photon triplets would provide this kind of realization crucial for control of and communication with ordinary biomatter.

4. ZEO implies a theory of self-organization [L8] and of self-organized quantum criticality (SOQC) relying on time reversal [L18]. The dissipation of a system looks like in reversed

time direction extraction of energy from the environment. Also SOQC becomes possible since criticality, since a state, which is a repeller, becomes an attractor in reversed time direction. The system seems to tend to criticality for an observer with an opposite arrow of time.

5. In this framework the aging could be seen as the approach of the system formed by MBs of the information molecules and of ordinary biomatter to a thermal equilibrium. The temperature of MB gradually grows and eventually reaches a maximal temperature (due to the stringy character of flux loops) known as Hagedorn temperature and identifiable as the physiological temperature. System dies.

2 Very brief summary about some aspects of aging?

The book of Sinclair and LaPlante [I15] is about aging and how to slow down it. The basic hypothesis is that aging need not mean getting sicker and sicker all the time. Biology has developed molecular tools for slowing down aging and there are longevity genes analogs to SPs taking care of this. It might be possible to help them by a healthy lifestyle.

The books represents a vision involving the following pieces.

1. Aging is information loss and molecular level, in particular DNA level. Ribosomal DNA seems to be in a special role assignable to nucleolus. Physicist could try to understand this from the second law: entropy un-avoidably increases . Entropy increases for isolated system but it is perhaps not so simple.

2. It has been learned that damage to DNA alone cannot explain aging. There must be additional degrees of freedom assignable to epigenesis as a control of genome. Besides genetic code there should exist additional continuous information carrying degrees of freedom.

   Epigenesis involves these degrees of freedom and DNAs conformation (involving coilings of coilings of ..) represents these degrees of freedom. Histones appear tangles along the DNA double strand selecting which genes are expressed. Acetyl tag in the histome allows gene expression to take place. When acetyl is absent, nothing happens. The effect of acetyl tag can be also silenced.

3. There are enzymes Sirn, $n = 1, 2, ..7$, called sirtuins [I12, I20] (`https://cutt.ly/Hjkh0ia`). In particular, Sir2 silences so-called mating type genes so that the cell replicates normally. If Sir2 is not present in mating type genes, they are expressed and replication does not take place normally. I understood that for yeast, the cell loses its sexual identity and does not replicate.

   During this non-replication period the cell would concentrate on maintenance. Under stress situations this would occur quite generally and make survival possible. If you cannot eat and replicate, sleep, and generate metabolic energy from thermal energy for instance. Also SPs would be at work. On the basis of [L18], one could guess that a kind of hibernation state with a reversed arrow of time could be in question. To live longer it is good to die sufficiently often!

4. This is not the only function of Sir2. When DNA double strand is broken, Sir2 must leave its job and hurry to the broken DNA and catalyze expression of SIRn coding for histone deacetylase HDAC, which removes acetyl tags from histones and deactivates DNA. After this the broken DNA is prepared. This is like putting a victim of a traffic accident to a hospital bed or even artificial coma.

   As cells get older, this kind of DNA breaks occur more often and Sir2 must leave its basic job more often and the cell loses its ability to replicate more often. It can also happen that Sir2 does not find its original position in the mating gene and starts to silence a wrong gene. This leads to epigenetic noise inducing aging.

5. In particular, ribosomal DNA in the nucleolus, the largest structure of the nucleus, can end up with chaos. Loops are formed and recombination between portions of the same

strand can occur (remember the reconnection mechanism and time reversal). Ribosome plays a fundamental role in translation so that there is no wonder that difficulties emerge. Important class of damage consists of breaking DNA double strands. This leads to a chaotic conformation involving loops. Sir2 must rush to the nucleolus and this means that mating genes activate and the replication stops. When these accidents occur too often, the cell becomes senescent.

3 Negentropy Maximization Principle (NMP) and Second Law

The natural expectation is that second law relates to aging. This motivates a section devoted to the recent view about Negentropy Maximization Principle (NMP) [K1] defining the variational principle of consciousness in the TGD framework and implying in adelic physics [L4, L3] second law in the case of non-negentropic entanglement (in standard physics entanglement is always non-negentropic).

Mathematically NMP is analogous to the second law in that it is not deterministic like the variational principles of classical physics. For a given entangled system NMP allows state function reduction (SFR) for that sub-system-complement pair for which the negentropy gain is maximal. The state function reduction can occur to any eigenstate of the density matrix of the selected subsystem in accordance with standard quantum measurement theory. This would lead to a product of pure states and the negative entanglement negentropy of the initial state would become vanishing in the final state so that negentropy would increase. The inclusion of p-adic contribution to negentropy identifiable in terms of cognitive information assignable to entanglement changes the situation and the entanglement can be stable against NMP and state function reduction cascade stops to entangled state representing cognitive fixed point. Since negentropy gain is not anymore popssible in SSFRs, death is bound to take place.

3.1 General observations about second law

First some general observations about second law.

1. Second law is an empirical fact. Second law forces the increase of entropy in statistical sense. Thermo-dynamical equilibrium is the most probable equilibrium. Second law in the standard form assumes a fixed arrow of time. Zero energy ontologuy (ZEO) forces to give up this assumption and allow both arrows of time.

2. Quantum physics is certainly behind second law. If you have an entangled system state, SFRs occur for subsystems with reduction probabilities determined by its entanglement with the environment. This eventually leads to a loss of entanglement and quantum coherence and one must apply statistical using density matrix for individual sub-system and eventually justifies thermo-dynamical description. It is important to notice that in SFR the entanglement entropy of an individual system is reduced in SFR but that in the case of ensemble of identical systems this generates entanglement entropy identical to the entanglement entropy of single particle giving thermo-dynamical entropy as a special case.

   One can consider two interpretations: a) the generation of entanglement generates single particle entropy although actually the entropy of the entire system does not increase in unitary evolution or b) the transformation of this entropy to ensemble entropy corresponds to second law. Option b) looks more realistic.

This is however only a description for what happens. One can ask what is behind second law. Is there some deeper principle as one might suspect because quantum measurement is so poorly defined theory. For instance, von Neumann proposed that only humans cause SFRs. It is often assumed that decoherence occurs without making any proposal how this happens. What is known and well-tested is that reduction probabilities for a measurement reducing the entanglement are coded by the measured density matrix, and one can say that the system goes to an eigenstate of the density matrix as the entanglement is reduced. For an ensemble of identical particles this process transforms entanglement entropy to ensemble entropy with the same value.

Negentropy Maximization Principle (NMP) is the TGD based proposal for the variational principle behind SFRs.

3.2 The new physics elements involved with NMP

NMP involves several new physics elements.

1. What is new is the hierarchy of systems having the hierarchy of space-time sheets as a geometric correlate. At the level of consciousness theory it would have self hierarchy as a correlate. Quantum measurements are assumed to correspond to SFR cascades proceeding from higher to lower levels of the hierarchy.

2. ZEO brings in the notions of "small" SFR (SSFR) as counterpart of "weak" measurement and "big" SFR (BSFR) as counterpart of ordinary quantum measurement [L9] and forces giving up the assumption about a fixed arrow of time. This modifies standard thermodynamics and leads to a new view about self-organization self-organized quantum criticality [L8, L18].

3. In the standard physics framework there is no definition of negentropy as a measure of conscious information. Negentropy can be only defined as the negative of ordinary entropy and is therefore non-positive. The best that one could have would be vanishing negentropy. This failure is understandable since standard physics does not even try to describe cognition. One manner to solve the problem is to claim that only entropy gradients, whose sign can be also negative matter and thus consider only information flows. In TGD different view is adopted.

4. To bring in conscious information one must introduce cognition. In the TGD framework it is assumed to be described by adelic physics [L3, L4]. This brings in p-adic space-time surfaces as correlates of cognition. Real space-time surfaces are replaced with their adelic counterparts forming a kind of Cartesian product of real and various p-adic space-time surfaces obeying the same algebraic equations.

   By $M^8 - H$ duality [L10, L11] one can regard space-time surfaces as surfaces in M^8 or in $H = M^4 \times CP_2$. M^8 is a subspace of the space of complexified octonions O_c and space-time surface is determined as a 4-D "root" of a real polynomial algebraically continued to an octonionic polynomial. If the coefficients of the polynomial are rational numbers, the polynomial makes sense for both real and p-adic number fields implying number theoretical universality. The dynamical principle is simple: the normal space of the space-time surface is associative/quaternionic.

   $M^8 - H$-duality maps these 4-surfaces to 4-surfaces in H. In both cases one has minimal surfaces. Also the notion of cognitive representation emerges and is essential for the number theoretical universality. It is also crucial for the construction of the scattering amplitudes [L14, L10, L11].

3.3 Detailed formulation of NMP

Consider now the formulation of NMP [K1] in this conceptual framework.

1. In adelic physics cognition is described in terms of p-adic degrees of freedom. Entropy is a sum of two terms: $S = S_1 + S_2$.

   S_1 is the ordinary entropy describing the amount of ignorance of the observer about the state of either entangled system - say Schrödinger cat and the bottle of poison.

   S_2, as the p-adic variant of entropy (also real valued) assignable to cognitive information has an analogous formula and similar defining properties but can be *negative*(!) and is interpreted as a measure for the information carried by entanglement.

   Thr possibility of having negative sign is basically due to the fact that the logarithms $log(p_k)$ of probabilities p_k in the Shannon formula $S = -\sum_k p_k log(p_k)$ for entropy are replaced by the logarithms of their p-adic norms $|p_k|_p$ given by p^{-n} for $p_k = p^n(a_0 + a_1 p + ...)$ (note that

the exponent changes sign!): $log(p_k) \to log(|p_k|_p)$. Entropy remains additive since the p-adic norm of product is product of p-adic norms.

A more general formula for the real Shannon entropy S_1 is as $S_1 = -Tr(\rho log(\rho))$ (ρ is the density matrix). Even in the case that the matrix elements of ρ are in the extension of rationals used, this formula need not generalize for S_2 since also $log(\rho)$ should have this property. The manner to avoid the problem is to diagonalize ρ. This is possible if the eigenvalues of ρ - having an interpretation as entanglement probabilities p_k (equivalently reduction probabilities) - belong to the extension of rationals considered.

At the fundamental level this extension is defined by the space-time surface determined by a polynomial with rational coefficients (M^8-H duality [L10, L11]): the roots of the polynomial determine the extension and space-time surface (number theoretic holography). If the entanglement probabilities are not in the extension, one might argue that the entanglement is stable - note however that NMP alone could make it stable.

Quantum coherence involves stable entanglement carrying cognitive information measured by S_2. The destruction of coherence if allow by NMP destroys information defined as the sum $N = -S = -S_1 - S_2$. In absence of cognition one would have $N = -S_1$ and NMP would transform to second law.

2. The cascade of "small" state function reductions (SSFRs) eventually leads to a state in which the remaining entanglement is stable. There is no subsystem-complement pair for which SSFR could take place in such a manner that negentropy $N = -S = -S_1 - S_2$ would increase. The resulting states are analogous to bound states.

3. Remarkably, in its adelic formulation NMP states that the total entropy, which tends to be negative for extensions of rationals, gets smaller and negative: information is generated! The pessimistic second law transforms to an optimistic NMP! The gloomy character of second law would be due to the neglect of cognition from physics.

   Cognitive entropy gets more and more negative but real entropy which is closely related to it but tending to have a smaller magnitude than p-adic entropy for extensions of rationals also increases [K1] [L9]. Hence their sum tends to increase with the dimension $n = h_{eff}/h_0$ of the extension.

What makes entanglement stable against SSFR? One can consider two mechanisms.

1. Adelic physics allows negentropic entanglement, which tends to be stable against SSFRs since it can only become even more negentropic.

2. One can also consider another stabilization mechanism. The rule would state that if the density matrix of the subsystem-complement pair does not allow eigenvalues in the extension of rationals considered, the reduction is not possible. For a stable entanglement density matrix would not allow eigenvalues in the extension of rationals considered. One can of course criticize this rule as somewhat *ad hoc* and the first option might be enough. One can also ask whether this mechanism is equivalent with the first mechanism.

3. What could be the interpretation of the negentropic entanglement? I have assigned positive emotions like love to this entanglement, also experience of understanding, etc...

3.3.1 NMP implies increase of ordinary entanglement entropy

NMP implies increase of the ordinary entanglement entropy. The hasty conclusion would be that this implies also increase of thermal entropy and thus second law. Here one must be however cautious.

1. Second law as an increase of ordinary entropy would still hold true but the increase of cognitive information would be larger than the increase of the real entropy for non-trivial extensions of rationals (this is always the case).

   The asymptotic states with maximum negentropy and with stable entanglement would have maximal real and minimal p-adic entanglement entropy and their sum would be negative - and $N = -S$ would therefore serve as a measure for the amount of conscious information.

2. One might argue that intelligent systems tend to pollute their environment: they are entanglement entropy generators and by witnessing what has been happening to our environment, it would be easy to agree.

   One must be however extremely cautious with formulas. The stability of negentropic entanglement means that the real entanglement entropy cannot transform to ensemble entropy and cannot therefore actualize! Is this what distinguishes loving attention as something unique and positive: the entanglement is stable and cannot transform to ordinary entropy?

3.3.2 Could NMP allow the failure of second law in some situations?

The dream about eternal youth seems to be in conflict with the second law. For physicist second law is usually the absolute authority. Working with the details of NMP however force to challenge this view.

A generalization of second law taking into account time reversals is required in ZEO and already this implies apparent breakings of second law. Furthermore, NMP implies second law as the increase of entanglement entropy. NMP does not allow SFRs transforming negentropic entanglement entropy to thermodynamic ensemble entropy unless the SFRs occurs at higher level of hierachy so that the local reduction of negentropy is compensated by its increase in a longer scale. The implications of this fact remain to be understood.

Could NMP break the second law? Can this be consistent with empirical facts? Could the breaking of second law occur at the level of dark matter only? Second law would apply only to the entropy transformable to thermal entropy. The sum $N = -S_1 - S_2$ is what matters: for a trivial extension one has $N = 0$ so that this transformation is possible. $N = 0$ can be however true also for non-trivial extensions. Could the total entanglement negentropy assignable to the ordinary matter satisfy $N = 0$ and be therefore transformable to thermal entropy whereas "dark" entanglement negentropy satisfying $N > 0$ would not allow this. Could one identify dark/living matter as negentropic matter and ordinary/inanimate matter as non-negentropic thermalizable matter? Note that also the phases with $h_{eff}/h_0 = n$ could in principle have $N = 0$. The stability of dark entanglement could directly relate to the failure to observe dark matter.

3.3.3 Comparison with the proposal of Jeremy England

Jeremy England [I23] has noticed that living systems increase entropy and has proposed it as a basic principle of biology. England's proposal is discussed from TGD point of view in [L2]. I did not however realize in this article the fact, that negentropic entanglement entropy need not allow a transformation to thermal entropy.

One can represent several objections against England's idea.

1. Second law cannot force or even allow the generation of life. Second law relates to the occurrence of SFRs but we do not have a real theory of quantum measurement.

2. Second law assumes preferred arrow of time and there is a lot of support for its violation in living matter as realized first by Fantappie [J4]: in particular, self-organization processes could involve dissipation with reversed arrow of time.

3. To understand life one must take it seriously. Living system is somehow different from inanimate matter. The emergence of life means the generation of conscious information but in the framework of standard physics there is no definition of conscious information.

These objections raise several questions. Why the emergence of life would be accompanied by a generation of entropy? What could serve as a measure for conscious information? How to describe cognition? To these questions adelic physics provides a possible answer. If entropy that England talks about is identified as the entropy produced in SFRs of systems having $N = 0$, TGD view is consistent with the proposal of England.

3.3.4 Cognitive fixed point instead of thermal equilibrium?

The analogy with the second law strongly suggests that the system approaches a cognitive fixed point (negentropy maximum) during the sequence of SSFRs followed by the analog of unitary time evolution. SSFRs cannot generate negentropy anymore. Since the system does not learn anymore, BSFR is bound to occur. A possible number theoretic formulation for the fixed point could be following.

1. The time evolution following SSFR generates entanglement. This entanglement is maximally reduced in measurements of observables, which correspond to operators, whose action does not affect the states at the passive boundary.

2. Cognitive measurements define an important class of such measurements [L13]. The cognitive quantum states correspond to wave functions in the Galois group G of the extension - that is elements of the group algebra $F(G)$ of G. G can be decomposed to a product $G = \prod G_i$ of subgroups defined by the hierarchy of normal subgroups of G defined by the representation of the extension as an extension of an extension of ... of rationals.

   Elements of $F(G)$ decompose to superpositions of products of functions in G_i and the factors are entangled. Note that the order of G_i matters and is induced by the inclusion hierarchy for the extensions considered: the largest extension is at the top of the hierarchy. One has "ordered" entanglement. This is analogous to the directedness of attention which is difficult to understand in the standard physics framework.

   Eastern philosophies speak also of states of consciousness in which there is no distinction between observer and observed and not division. Could this kind of attention involve negentropic entanglement between systems, which correspond to the same extension of rationals so that the. attention cannot be directed? Or could it correspond to negentropic cognitive entanglement allowing cognitive SSFRs?

   The first cognitive measurement leads to a product decomposition in $F(G/(G_2...G_n)) \times F(G_2..G_n)$ if the entanglement coefficients between $G_1 = G/(G_2...G_n)$ and $F(G_2..G_n)$ are in the extension of rationals considered. Same can happen at the next step and leads to a similar decomposition of $F(G_2, ...G_n)$. The maximal cognitive measurement cascade leads to a product of wave functions in $F(G_i)$ but it can happen that there is no measurement cascade at all.

3. The picture leads to ask whether one could speak of cognitive analogs of particle reactions representing interactions of thoughts. Finite group G has always a decomposition in terms of simple factors G_i induced by the hierarchy of normal subgroups. The simplest situation corresponds to a Cartesian product of simple subgroups: $G = \prod_i^{\times} G_i$. In this composition the order of factors does not matter and the situation is analogous to a many particle system without interactions.

   The group algebra of G is a Cartesian product of group algebras of G_i and the natural group representations are unentangled tensor products as analogs of free many-particle states. One might say that there are no cognitive interactions. This situation is representable as a product $P = \prod_i P_i$ of polynomials P_i assignable to the factors. This polynomial is not irreducible. Note that the polynomial associated with a given Galois group is highly non-unique and that cognitive representations are discrete and preferred ones correspond to algebraic integers [L10, L11].

   An irreducible polynomial representing a composite of polynomials with Galois group G having composition in terms of Galois groups of extension of extension of ... with extension at level i having Galois group G_i. Functional composition $P_{n_1} \circ P_{n_2} \circ ...$ can produce a decomposition of Galois groups G_i identified as Galois group of E_i as extension of E_{i-1}. It is not clear to me whether any composition is possible. For a given ordering of the G_i there can be several decompositions. Could non-trivial decompositions, which do not reduce to a Cartesian product, represent cognitive interactions?

   The intuition about what happens in particle reactions suggests that the reduction of cognitive entanglement could correspond at space-time level a process in which incoming cognitive

many-particle state is represented by a product of polynomials P_{n_i} and outgoing many particle state by the product of polynomials Q_{m_i} such that conservation of degree holds true: $\sum n_i = \sum m_i$. In the interaction region defined by CD, the polynomial would be some irreducible polynomial constructed as a functional composite of polynomials R_i. Do the continuity conditions at the boundaries of CD allow nontrivial interactions not requiring $P_i = Q_i$? Cognitive dynamics based on the representations of the Galois group assignable to cognitive representations would define a number theoretical analog of topological quantum field theory.

4. Suppose that the time evolution following SSFR for individual mutually unentangled subsystems is in good approximation unitary (their interactions with other such subsystems can be neglected) so that they do not entangle, the density matrix of an individual system suffers a unitary automorphism so that entanglement entropies remain unaffected and the negentropy gain vanishes. One could speak of "asymptotic freedom" as a condition for the cognitive fixed point.

   The cognitive fixed point would define the "silent wisdom" of the re-incarnate having the formerly active boundary of CD as a passive boundary of CD. What would be learned during life would help during the next life cycle.

4 TGD based model for aging

In this section the TGD based view about aging is discussed. The king idea is that the magnetic bodies (MBs) of information molecules and linear molecules formed from them (DNA,RNA, amino-acids,tRNA) are at very low temperature in the beginning. The temperature of MB starts to raise and approach the physiological temperature. The entropy of MB increases. Since the MB of the molecule controls the molecule, the control by MB starts to fail and this leads to the diseases accompanying aging.

4.1 Aging as approach of MB and BB to thermal equilibrium

Ordinary entropy increases for an isolated system, it approaches thermal equilibrium - thermalizes. Aging must correspond to thermalization in some sense. There are two views about this.

1. The weak form of the proposal making sense in the standard physics context would identify aging as thermalization. For ordinary biomatter, which already is in thermal equilibrium in good approximation, this idea does not lead to anything interesting.

2. Ordinary matter and the dark matter at MBs carrying dark matter as phases of ordinary matter with $h_{eff} = nh_0$ have widely different temperatures at the moment of birth. Aging means that these systems approach thermal equilibrium in the sense that temperatures become identical . MB has infinite number of degrees of freedom and therefore maximal temperature known as Hagedorn temperature identifiable naturally as physiological temperature [L18]. This option will be considered in the sequel.

Consider the situation in TGD.

1. What are the continuous degrees of freedom whose entropy growth would lead to aging. In the TGD framework they would be naturally the geometric degrees of freedom associated with the flux tubes of dark DNA controlling ordinary DNA. Their number is infinite implying that temperature is below Hagedorn temperature around physiological temperature. One can assign a temperature to the flux tubes and also to these degrees of freedom and this is below Hagedorn temperature. When temperature at flux tubes increases, the geometric shape starts to thermally fluctuate and the overall size increases. Cells indeed increase in aging as do also we!

2. For information molecules the temperature of MB must be very low: dark DNA flux tubes have a very precise shape and therefore also ordinary DNA. For SPs the situation is different and this makes possible their basic functions.

3. Aging could simply mean that the dark genome approaches thermal equilibrium with ordinary biomatter at physiological (Hagedorn) temperature and entropy of dark genes and magnetic flux tubes increases. Flux tubes get more and more irregular shaped and induce a development of loops for ordinary DNA and breaks DNA double strand. Nucleosomes are loop like structures associated with histones and also these are known to be lost. Epigenetic chaos is induced. When thermal equilibrium is achieved death as heat death occurs and changes the arrow of time at the level of the entire body which is left in the geometric past of the standard observer to continue life with an opposite arrow of time.

   Remark: ELF em fields at EEG frequency range have quantal effects affecting the behavior and physiology of vertebrate [J3]. EEG photons however have energies many orders of magnitude below thermal energies so that effects should be completely masked. My first proposal for explanation was that the temperature at the space-time sheets of ions is extremely low and below the energy of EEG photons. Later I gave up this option in favor of h_{eff} hypothesis.The two explanations are actually consistent. Thermal energy is proportional to the temperature. For an n-sheeted structure one has by the additivity of thermal energy for different identical sheets $T_H = nT_H(sheet)$ implying $T_H(sheet) = T_H/n$. For the huge values of h_{eff} and thus of n, $T(sheet) \leq T_H(sheet)$ is indeed extremely small!

4. There is a connection to the article [L16] about DNA and arrow of time. One can argue as follows. As the electric field along DNA double strand decreases by the shortening of the sticky ends, the string tension as density of electric energy per length decreases, the stiffness of DNA decreases, and the fluctuations start to develop. Second possibility is that the shortening of telomeres and sticky ends is a controlled process causing a programmed aging.

5. There are molecules devoted to preparation of the damaged DNA. The epigenetic tags on histones of mating genes could control the arrow of time for the gene involved. If the tag is present, the gene is expressed. If not or if inhibited by say Ser2, the arrow of time is reversed.

4.1.1 Objections related to metabolism

Metabolic energy feed is needed to keep the distribution of h_{eff}:s and even increase the values of h_{eff} - defining universal IQ and characterizing quantum coherence scale. This relates to the second important aspect of life: quantum coherence in long length scales is needed to generate the coherent behavior of ordinary biomatter and is not possible in standard bio.chemistry framework. Ageing would be a gradual reduction of this quantum coherence by thermalization of MBs of the basic information molecules, in particular the dark variants of the basic biomolecules. If you want to live long, take care of your personal quantum coherence!

One can develop some objections against the vision about ageing as thermalization of the MBs of information molecules.

1. Aging is viewed as changes of the body after birth. What about the processes before birth? When sperm and gametes inoculate and divide and divide and form some distinguished organs, this process needs a high amount of energy; that is why mothers get to eat more during pregnancy.

   Fetus generates new structures - parts of MBs containing dark matter as $h_{eff} = n \times h_0$ phases of ordinary matter with increasing value of h_{eff}. This requires high metabolic energy feed provided by mother. Information molecules are however still very far from thermal equilibrium and the gradual increase of the temperature of MBs has practically no effects. The situation remains the same also at the young age. At later age MBs approach thermal equilibrium and problems with the bio-control by MB emerge.

2. Reactive Oxygen Species (ROS) cause also damage for DNA: the more ROS, the shorter the life of the cell. That is why food with low calories content or fastings or low carbohydrates (which need less oxygen to burn) diets are good for longevity.

   ROS have been also seen as a cause of aging and one could argue that they should cause a lot of damage during the fetus period involving intense metabolism. The repair

mechanisms of MB work almost optimally for fetus and at young age and allow handling of the problems due to ROS. The authors of [I15] argue that it is now known that ROS are not the basic reason for aging. As a matter of fact, ROS are essential for the demethylation [I7].

4.1.2 Is apoptosis as programmed cell death consistent witht he proposal?

Also programmed cell death - apoptosis - could be treated as an objection against aging as approach to thermal equilibrium. Apoptosis as a programmed cell death cannot be purely thermal event. It could be induced by MB at the higher level of hierarchy as BSFRs. Perhaps by MB of cell group as in the development of fingers from the cell mass. Apoptosis could have several motivations.

1. The basic prediction is that giving systems are intentional systems having free will at all levels. MB at the higher level could act like dictator and destroy quantum coherence locally leading to the death of the cells but generating quantum coherence and generation of structures in longer scales which would also take the metabolic energy resources used by the dead cells.

   Negentropy Maximization Principle (NMP) would be the deeper principle behind the second law. Apoptosis would be consistent with the NMP which implies second law as a by-product and as its name tells, implies negentropy increase. Therefore thermalization would not the only cause of cell death.

   Apoptosis would indeed generate more complex structures when fingers develop from tissue. Destruction of lower level structure would be the price paid for the generation of a higher level structure and negentropy gain in longer scales.

2. Evolution means steps in which h_{eff} increases in BSFRs and longer scales of quantum coherence at the level of MB emerge. Extinction of cells and sauri would be part of evolution.

A controlled BSFR causing the analog of death/hibernation of a subsystem could be also represented as an objection. The BSFR would have the survival of a larger system as a motivation [L18]. In fact, all motor actions can be seen as BSFRs at some lower level so that life is continual dying! Death/hibernation of a subsystem means savings of metabolic energy and can be seen as one manner to fight against second law since the dead subsystem lives with the opposite arrow of time: living system is basically 4-D entity in ZEO - not just the time slice which corresponds to conscious experience!

4.1.3 Is the biochemical approach trying to describe dissipation as a controlled process?

A general comment related to the distinction of the standard approach and the TGD approach relying on ZEO is in order. Standard approach does its best to identify control mechanisms leading from state A to state B. Huge amount of information exists about reaction pathways and one can only admire these data mountains.

This approach is very natural as long as time reversal is not involved. If this is the case, there are processes, basically healing and repair processes, that occur in a reversed time direction as dissipative processes and each BSFR leading to a time reversed state involves its own reaction pathways. The tragedy would be that the standard approach tries desperately to understand loss of order as a controlled process inventing endlessly reaction pathways!

Of course, this work would not be useless. The problem is however that a deeper understanding is missing and prevents seeing how incredibly simple the picture is at the fundamental level.

1. The increase of entropy in reverse time direction apparently breaks second law in the standard time direction. Stress proteins (SPs) discussed in [L18] are involved with this battle. The magnetic bodies of SPs can extract heat energy from the environment in heat shock and heat DNA and proteins in cold shock, and also act as heat engines for molecular motors.

2. As also the authors of [I15] emphasize: diseases are a consequence of a loss of information. Disorder increases as quantum coherence is lost, and manifests as numerous diseases. Quite concretely, the h_{eff} distribution flattens in the sequence of SSFRs. System gets less intelligent and is unable to cope with the hard reality! Second law would eventually win although this process can be slowed down by BSFRs of subsystems.

3. Things can go wrong in very many manners: as Tolstoy said, families can be unhappy in myriads of different ways but there are very few ways to be a happy family! Therefore the disease centered thinking of medicine is perhaps not the best approach. One should do something which helps to prevent all diseases simultaneously. One can avoid diseases by choosing a healthy lifestyle. Also a medicine relying on the idea that BSFRs for subsystems could help. BSFR could be seen also as falling sleep and resting and gathering metabolic energy - even from thermal energy.

4. Time reversed dissipative evolution looks like healing in the reversed arrow of time. If this is the case, the tragedy of biology would be the attempt to understand time reversed dissipation in terms of complex control actions based on complex reaction pathways or even as some kind of computer programs.

5. MB would be in a key role since most diseases would be problems in the control performed by MB and basically due to the reduction of h_{eff} and therefore of information contents. About detailed criteria for when one has a disease this approach cannot say much.

4.1.4 Loss of the control of housekeeping genes causes vicious circle leading to death

The basic problem from the point of view of longevity would be that during aging MB gradually loses control of not only methylation, acetylation and their reversals but also other modification processes.

A possible explanation for hypermethylation is that the control actions inducing demethylation fail. The observed hypomethylation in the complement of CpG islands could be due the failure of methylation so that the state becomes stable. More generally, this suggests that the loss of control of all modifications is the mechanism leading to the situation in which the modifications cannot be changed. For instance, the differential methylation of hippocampus is known to be relevant for memory recall, which could relate to the emergence of memory problems at the old age.

CpG:s which are hypermethylated appear in the promoter regions of almost all housekeeper genes so that housekeeping [I8] (`https://cutt.ly/2jQgOSD`), in particular transcription and translation machineries, metabolism, functioning of stress proteins, etc.... becomes difficult.

The enzymes responsible for the methylation and demethylation are especially important for housekeeping genes [I8] whose promoter regions contain CpG islands. Metabolism related enzymes like Cytochrome P450 are involved also with demethylation as enzymes. Methylation of the promoter region of housekeeping genes means also methylation of genes coding for demethylase. This vicious circle - not so positive positive feedback - leads to death.

What causes the loss of the control of these modifications? The mechanisms leading to the loss of control would relate to modifications of the chromatin and DNA organization. These include reduced global heterochromatin, nucleosome remodeling and loss, changes in histone marks, global DNA hypomethylation with CpG island hypermethylation, and the relocalization of chromatin modifying factors [I22, I13, I19]. In the TGD framework these changes would be caused by the thermalization of the MBs of DNA and chromosomes.

Also cancer induces these changes about which the appearance of additional chromosomes in the mitochondrial DNA in cancer is an example. It has been found that a very weak oscillating magnetic field with strength in nanotesla range and with oscillation frequency around 60 Hz (Schumann frequency) leads to the disappearance of additional chromosomes [I26]. The loss of quantum coherence is the general explanation but it is not clear whether this can be due to thermalization at the level of DNA in this case. A possible explanation is that the control by MB at a higher level of hierarchy is lost and the presence of magnetic field re-establishes a connection with this MB in turn re-establishing quantum coherence [L5].

MB controls the conformations of DNA and chromosomes. MB is identifiable as a flux tube network and its control relies on its motor actions involving reconnections and shortenings of the flux tubes by a temporary reduction of h_{eff}. These motor actions of MB would become fuzzy by the thermal motion. The precise motor performance of MB is crucial for the realization of modifications occurring at the promoter regions near histones and at histone tails. Therefore the thermalization of the flux tube degrees of freedom of MB could be the basic reason for the problems.

4.1.5 When does death occur?

Aging could simply mean that the dark genome approaches thermal equilibrium with ordinary biomatter at physiological (Hagedorn) temperature [L18] and entropy of dark genes and magnetic flux tubes increases. Flux tubes get more and more irregular shaped and induce a development of loops for ordinary DNA and breaks DNA double strand. Epigenetic chaos is induced. When thermal equilibrium is achieved death as an analog of heat death occurs and changes the arrow of time at the level of the entire body which is left in the geometric past of the standard observer to continue life with an opposite arrow of time.

BSFR means death and death is bound to occur. But when? TGD proposes a general criterion: at a given step either SSFR or BSFR occurs and the SFR that means maximum negentropy gain takes place. This SFR is not unique. It can be either SSFR or BSFR and in both cases there are a lot of options for the final state.

When would BSFR win in the comparison?

1. Total entropy can be defined as the sum of p-adic and real Shannon entropies. p-Adic Shannon entropies involving p-adic norms $N_p(p_k)$ of probabilities p_k in the logarithmic factors $log(N_p(p_k))$ can be negative. In this case they characterize the information (associated with cognition) assignable to the entanglement.

2. Real entropy characterizes the lack of information about the state of either entangled system and is associated with sensory input (is the cat dead or alive?). The sum of the real and p-adic entropies can be negative for non-trivial extensions of rationals so that one would have genuine cognitive information. One could also speak of mere cognitive information as the p-adic contribution to the entropy and this can be negative.

3. Intuitively it seems obvious that thermalization meaning that the temperature difference between MBs and systems such as genes is reduced, means loss of information defined in this manner. Information molecules cease to be information molecules at least in the geometric degrees of freedom.

4. BSFR becomes the winner if SSFRs can give only very small negentropy gain or if the negentropy gain becomes negative. The fact that we do not learn much anymore at the old age, could reflect the reduction of the negentropy gain in SSFRs.

Also the distribution of $h_{eff} = n \times h_0$ values could reduce IQ. As found in [L13], a complete cognitive measurement inducing maximal reduction of entanglement for an extension with dimension n would reduces the state to a product state with state space with dimensions n. which are factors of n and thus smaller than n: instead of single MB with high IQ several with lower IQs. It might happen that the next SSFRs are not anymore able to regenerate larger values of n and the system becomes less intelligent.

An objection against this picture is that there are also situations when resurrection seems to occur: this has happened for people having had near-death experiences. One can also slow down the process of aging by a appropriate diet.

1. The slowing down of the aging process is possible by the reversal of the arrow of time at lower levels so that time reversed dissipative processes at these levels look like self-organization and generate order from the point of view of the organism. This would be a general. mechanism used by living matter to slow down the approach of MB to thermal equilibrium with MB.

2. This does not however explain resurrection. The opposite BSFR can however occur at the level of the entire organism but with a suitable stimulation like resuscitation opposite BSFR can take place. Taking into account the fact that also the organism is only one level in the hierarchy of conscious entities, this reduces to the first option.

   The analog of resuscitation occurs at the atomic level in the experiments of Minev et al [L7]. Although the deterministic process apparently leading to the final state of BSFR had already occurred, it could be stopped by a suitable stimulus. In TGD framework the interpretation is that the BSFR had already occurred and the time reversed time evolution apparently leading to the final was observed. A suitable stimulation however induced the opposite BSFR so that the process apparently stopped [L7].

4.1.6 DNA and the arrow of time

There is a connection with the article about DNA and arrow of time by Rastmanesh and Pitkänen [L17]. The proposal is as follows. As the electric field along DNA double strand (with dark DNA strands included) decreases by the shortening of the sticky ends, the string tension as density of electric energy per unit length decreases, the stiffness of DNA is reduced, and thermal fluctuations start to develop.

Biologist might wonder how various biological and homeostatic maneuvers like weakening of acetylation/phosphorylation/methylation eventually translate to a decrease of the electric field strength along DNA! In the TGD framework one can see the situation in a different manner: chemistry is not the boss now but is controlled by MB.

1. Modifications (or rather, the loss of the control of modifications) are not the primary cause of the weakening of the electric field. What happens at the control level, at MB, is the primary cause. The weakening of the electric field along DNA would correlate with the shortening of the sticky ends carrying electric charges creating the longitudinal electric field.

   This would also correlate with the reduction of the level of consciousness at the level of DNA if one is ready to generalize Becker's findings [J2] about the correlation of the strength of the longitudinal electric field along the body axis with the level of consciousness. Similar correlation with consciousness can be assigned to the electric field directed from visual cortex to frontal lobes.

2. The reduction of the electric field strength reduces energy density of DNA and therefore string tension. DNA begins to fluctuate geometrically, which generates epigenetic noise. Initially dark DNA is like a tense guitar string but transforms gradually to spaghetti. Basically the reduction of string tension reflects the dissipation accompanying the approach of MB to thermal equilibrium with the ordinary bio-matter.

   One could perhaps say that the reduction of string tension of MB flux tubes forces the reduction of electric field strength and the internal consistency (Maxwell equations) requires reduction of the sticky end lengths proportional to the charges generating the electric field along DNA. Note that also charge separations tend to disappear in the approach to thermal equilibrium.

3. An interesting question is whether hyper-methylation accompanying aging [I17, I25, I24] could be seen as an attempt to minimize the effects of DNA damage - analogous to an amputation of a leg to prevent necrosis. Hyper-methylation accompanies also cancer [I14, I21].

   Second view is that hypermethylation is due to the loss of control of MB caused by the approach to thermal equilibrium. Hyper-methylation could be seen as the failure of demethylation caused by the low level of demethylase activated by MB and caused by methylation of the genes coding for demethylase! This positive feedback loop would lead to the failure of the control of MB.

Is the shortening of the telomeres a controlled process or due to thermalization? The first option could be argued to be realistic since otherwise the population would end up to fight about metabolic resources. Second law could of course solve the problem without any need for a controlled

action. If the length of telomeres correlates with the charges of the sticky ends proportional to its length which in turn would be proportional to the length of the telomere as proposed in [L17], the conclusion would be that the shortening is not a controlled process.

5 Epigenesis and aging in TGD framework

In the TGD framework epigenesis would be control of the biological body by MB consisting of ordinary biomatter. The basic control tool would be dark photon 3N-plets coupling resonantly to the dark proton sequences of proteins serving as enzymes and RNAs serving as ribozymes. The coupling would be precise and based on the addresses defined by dark proton 3N-sequences defining emitting dark 3N-photons.

These would in turn catalyze the basic biochemical processes and here TGD suggests a mechanism explaining why the reactants find each other and where the energy needed to overcome the energy barrier to make reaction fast enough come. The reduction of h_{eff} for flux tubes would be the needed mechanism.

Also other catalysts than enzymes and ribozymes can be considered. For these catalysts and organic and non-organic molecules in general, the coupling with MB could be single photon resonant coupling transforming 3N-photon to bio-photon.

5.1 How MB could control biochemistry

How does the general biochemistry picture involving biomolecules and reaction pathways relate to the multi-resonance vision about how MB controls ordinary biomatter? Can one reduce this picture to a description in terms of multir-resonance frequencies - that is to the level of MB and MB-BB communications alone.

1. Suppose that MB of DNA, RNA, or protein controls DNA, RNA or protein by signals from dark genes using multi-resonance mechanism allowing to select the target and use modulation of dark photon signal to code control signals. Also the MB of DNA, RNA, or protein can be controlled by a higher level of the hierarchy.

   If all control takes place in this manner, epigenetic control would be control of proteins acting as enzymes, of RNA, in particular ribozymes, and of DNA. MB would also activate genes coding for various enzymes, in particular housekeeping enzymes.

   The controlled proteins would be naturally enzymes catalyzing various biochemical reactions.

2. Could the MB of DNA just change its geometric conformation inducing change of DNA conformation and changing also the epigenetic patterns determined by methylation, etc...? This would represent something new: in TGD one has a network of molecules connected by flux tubes, in biochemistry approach one has only molecules.

   The first basic mechanism for the change of the conformation would be the reduction of h_{eff} leading to the shortening of the flux tubes and liberation of energy and its reversal. The reduction of h_{eff} is crucial in the TGD based model of bio-catalysis. The opposite process would feed metabolic energy to MB. The formation of reconnection would be another key process and allow to change the topology of the flux tube network. This would be the basic mechanism of the immune system and also of biocatalysis in which the U-shaped flux tubes associated with the reacting molecules would reconnect.

   For instance, the actions of cells during say catastrophic events mean typically that proteins like Sir2 come in rescue by travelling along flux tubes or pairs of them serving as highways: these highways do not exist in standard biology. The existing pattern of flux tubes determines the road network. MB would control the topology of this network by reconnecting and by controlling the lengths of the flux tubes by h_{eff} changing transitions: motor actions of MB would be in question.

3. TGD leads to a view about emotions as sensory perceptions of MB. The model for genetic code emerging from a model of bio-harmony [L1, L6, L12, L15] based on icosahedral and

tetrahedral geometries and the observation that music expresses and induces emotions leads to the proposal that the bio-harmony characterized by 64 allowed 3-chords in one-one correspondence with DNA codons has 3N-resonances assignable to the 3-chords of the harmony as a correlate. These resonant interactions induce transitions of selected bio-molecules and possibly also specific transitions of a given biomolecule characterizing the harmony. Could epigenesis be regarded as expressions of emotions by music of light?

BSFR would create a superposition of deterministic time evolutions leading to the geometric past. It would define an average time evolution described in terms of reaction pathways. Could the final state of MB in BSFR dictate also the epigenetic patterns - say bio-harmony determined by frequencies of cyclotron transitions of protons? They are indeed determined by the strengths of the magnetic fields at flux tubes. This would conform with the proposal that the outcome of volitional action as BSFR dictates what happens in the brain of geometric past explaining the findings of Libet [J1] [L7].

SSFRs give rise to an approximately classical time evolution and generation of entropy, and therefore aging. h_{eff} distribution becomes flatter and MBs of information molecules and ordinary matter approaches thermal equilibrium. The distribution for the conformations of the magnetic flux tubes thermalizes and cell size increases. Basically string tensions decrease since the electric fields involved weaken and the electric and also magnetic contribution to the tension weakens.

What could be the general mechanism of bio-catalysis? The MB of the enzyme could activate the enzyme when the value of h_{eff} of a flux tube connecting it to other reactants is reduced and induces the shortening of the flux tube and liberation of energy.

Depending in what direction energy flows, one can imagine two scenarios for what happens.

1. The energy could flow from higher levels of hierarchy to lower levels. The flux tube at the highest level would be shortened and liberate energy transferred to a lower level. At the lowest level enzyme would be excited and return to the ground state and liberate the energy needed to overcome the potential wall making reaction slow. Now the shortening of the flux tube of enzyme's MB does not seem to be necessary energetically.

   The process would proceed from higher to lower levels in the hierarchy of MBs by this kind of excitations and de-excitations transferring the energy to the lower level, somewhat like in photosynthesis. The flow of money from top towards bottom in a big project serves as a second metaphor for the course of events.

2. If the process is a generalized motor action involving BSFRs and time reversals, the higher levels in the hierarchy of MBs extract energy from shorter scales (very much like higher levels extract work of lower levels in the social hierarchies!). One could also say that negative energy is sent to the lower levels of the hierarchy.

   The lower level would provide the energy by reducing its h_{eff} so that its energy is reduced and energy is liberated and taken by the higher level. This would induce the shortening of magnetic flux tubes at all levels. The cascade would proceed down to the level of MBs of proteins and also the U-shaped flux tubes connecting the protein to the other reactants would shorten and bring the reactants together. The reduction of the flux tube length should provide energy to overcome the potential wall, not only the energy going to the higher level of hierarchy.

It is not quite clear which option is realized. Motor actions involve transfer of metabolic energy from short to length scales giving rise to macroscopic coherent motion: time reversal would be natural from this point of view.

5.1.1 Methylation and acetylation

The figures of `https://cutt.ly/Qjgrko3` illustrate the effect of methylation and acetylation of DNA or of histone tail.

1. The nucleosomes [I9] surround a given gene but nucleosomes can roll along DNA downstream towards the gene to be transcribed and opens the DNA double strand. The modification of the histone tail can prevent or facilitate the opening of the double strand.

2. The portion of DNA between the nucleosome and gene corresponds to the promoter part of DNA initiating the gene expression. Proteins initiating the transcription bind to it or alternatively it can be transcribed to RNA.

The methylation [I9] and acetylation [I1] of the histone tail serves as the first example. The binding of the methyl, acetyl, or some other group to the histone tail has an indirect effect on the gene. Histone is positively charged. Since DNA is negatively charged, DNA and histone bind together.

The addition of a modifier can increase or reduce the charge of the histone and tighten or loosen the binding between histone and DNA. Methyl is positively charged and tightens the binding and makes the opening of DNA necessary for transcription more difficult. Acetyl is negatively charged and loosens the binding so that the transcription becomes easier.

Consider next the methylation of a promoter region (`https://cutt.ly/3jj8ohZ`).

1. A promoter is a sequence of DNA to which proteins bind that initiate transcription of a single RNA from the DNA downstream of it. This RNA may encode a protein, or can have a function in and of itself, such as tRNA, mRNA, or rRNA. Promoter region has therefore two - it seems alternative - functions.

2. The methylation of cytosin occurs at CpG islands associated with the promoter region of gene. Promoter region is the region to which proteins initiating the transcription of gene bind. Methylation occurs also for the promoter regions of CpG-islands [I16].

3. How methylation silences the gene transcription? Methylation decreases the charge of DNA locally and loosens the binding to histone. This would favor the transcription of the promoter region instead of the transcription of the gene requriing the binding of RNA polymerase to the promoter region.

4. If methyl is always positively charged, the direct binding to DNA reduces DNA charge locally and reduces the interaction between histone and help opening of DNA in the promoter region: this would not facilitate the transcription of gene but transcription of non-translated RNA or protein. The binding would also prevent the binding of RNA polymerase to the promoter region. The start codon of the non-protein coding gene could be in the promoter region.

More facts about DNA methylation [I10] (`https://cutt.ly/pjj3G45`) are needed to develop a TGD based view about the situation.

1. DNA methylation reprogramming occurs during gameto-genesis and early embryogenesis. The methylation patterns are erased and regenerated. This requires that the memory about the methylation pattern is stored. In the TGD framework MB could serve as the temporary information storage.

2. DNA methylation occurs also in highly transcribed gene bodies and must be distinguished from the methylation of promoter regions. The methylation of gene bodies seems to relate to splicing and could prevent the transcription of intronic portions of the gene.

3. In general, the level of DNA methylation is very low. The level of methylation is however high in promoter regions. In particular, in CpG islands [I3] (`https://cutt.ly/sjj3STW`) accompanying the promoter regions of genes, especially those coding for housekeeping proteins.

4. Usually the methylation of C in CpG leads to a mutation replacing C with T. This could have led to CpG loss in DNA except in CpG islands, where some stabilization mechanism should prevent the mutations: presumably an energy barrier somehow caused by CpG is involved.

   Hypermethylation accompanies cancer and also aging [I24, I25] and could be seen in the TGD framework as reflecting the approach to epigenetic chaos basically due to the reduction of the scale of quantum coherence in turn caused by the reduction of the values of h_{eff}.

5. CpG loss is believed to be induced by transposable elements (TEs) attaching to DNA and hopping around it. TEs are methylated and lose CpG as C transforms to T.

6. So called housekeeping proteins [I8] are enzymes crucial for various functions including general gene expression, and the control of various housekeeping functions takes place via the control of the expression of housekeeping genes. Therefore CpG islands, which are stable against mutations and allow both methylation and demethylation are needed. Dynamical and differential methylation is also known to relate to memory recall in the case of hippocampus.

   For CpG islands $C \to T$ the mutations induced by methylation are prevented by some mechanism. The loss of CpG makes sense outside CpG islands since this stabilizes the genes against C $\to$ T mutations.

MB uses enzymes and ribozymes as a tool in the control of the basic biochemical processes. DNA methyltransferases [I11] catalyze methylation and MB would control the process by activation of this enzyme. In the case of demethylation the enzymes used are demethylases [I6].

The mechanism of demethylation can be taken as an example since the failure of demethylation might lead to hypermethylation of CpG islands known to accompany aging [I24, I17] and in TGD framework it could be due to the approach of the dark genome and proteome to thermal equilibrium.

1. Oxidative demethylation [I7] (`https://cutt.ly/Gjj2Ilz`) replaces CH_3 group with hydrogen. This requires the presence of a reactive oxygen species (ROS). ROS include superoxide O_2^-, hydrogen peroxide H_2O_2 and hydroxyl radical OH.(`https://cutt.ly/yjj2Ubv`).

   Superoxide is produced in aerobic metabolism via $O_2 + e^- \to O_2^-$. This in turn leads to reactions $2H^+ + 2O_2^- \to H_2O_2 + O_2$ followed by $H_2O_2 + e^- \to HO^- + OH$ and $2H^+ + 2e^- + H_2O_2 \to H_2O$.

2. Demethylation is catalyzed by demethylases in presence of O_2. N-methyl groups are oxidized with oxygen coming from ROS O_2 and CH_2O splits out so that the net reaction is $R_2N - CH_2 \to R_2N - H + CH_2O$.

   Enzymes known as alpha-ketoglutarate-dependent hydroxylases act as DNA demethylases. Also Cytochrome P450 [I4] (`https://cutt.ly/ujj2OuK`) catalyzes demethylation in histones and some forms of DNA (cytocine associated with CpG). "450" refers to "450 nm"", which is the wavelength at which cytochrome P450 has maximum absorption. The wavelength corresponds to blue light near UV range and the photon energy is 2.76 eV. CYPs is a very large class of enzymes catalyzing metabolic processes.

What TGD view could be?

1. Suppose that MB controls bio-matter by expressing its moods coded by bio-harmonies in terms of dark photons 3N-plets (say) with the frequency patterns correlating with mood and affecting matter in mood dependent manner via a transformation to bio-photons.

2. 60 per cent of promoter regions of human genes contain CpG islands of length about 100-1000 codons and almost all housekeeping genes have CpG islands in their promoter regions. Why?

3. MB would induce both methylation and demethylation and other modification using various enzymes which they could activate by dark 3N-photons using as address the dark proton sequence associated with the enzyme. After activation the reaction would proceed by the proposed general mechanism of biocatalysis.

4. One can imagine several alternative courses of events after the activation. Even the question whether the energy transfer is from short to long length scales associated with MB or vice versa is not fully settled: this depends on the arrow of time assignable to this process.

   In the case of CYP450, one cannot avoid the temptation to ask whether a biophoton with 450 nm wavelength could be formed in a decay of 3N-dark photon to ordinary photon.

5.1.2 Methylation, aging, and memory

According to [?]https://cutt.ly/njAKgFy), the general trends, supported by an increasing body of both in vitro and in vivo work, are the establishment of global hypomethylation (non-CpG islands) and regions of hypermethylation (primarily CpG islands) with age. CpG islands are located in the promoter regions of genes, in particular those of housekeeping genes.

Hypomethylation outside CpG islands could be due to the spontaneous mutation $C \to T$ but also the failure of the control of the methylation by MB could be involved. Hypermetylation of promoter regions implies that the promoter region transcribing RNA is transcribed instead of gene. This could be due to the failure of demethylation caused by the loss of the control.

In both cases the loss of control could have the same reason. The MBs of the genes coding for housekeeping genes and possibly also the MBs of the housekeeping enzymes approach thermal equilibrium with the ordinary bio-matter.

How methylation could relate to aging in TGD framework?

1. Methylation could become irreversible during aging and lead to hypermethylation if MB loses the control of demethylation. If enzymes are the control tools of MB, the reduced transcription of DNAs coding for demethylases would lead to a failure of the control. The approach of MBs of DNA and enzymes to thermal equilibrium with ordinary biomatter could be the basic reason for the failure.

2. Housekeeping proteins are an especially important class of proteins since they catalyze basic biological functions necessary for the transcription of genes - also the genes coding form them. Their promoter regions are also almost always CpG islands. Therefore one can say that the methylation of their promoter regions would be a natural cause of various problems with housekeeping activities caused by aging.

3. CYP450 catalyzes generation of ROS in turn catalyzing demethylation and a large number of metabolic processes crucial for the functioning of the organism. In particular, demethylation could become less effective with aging due to the reduced level of CYP450. CYP450 is a housekeeping protein and the promoter regions of genes coding for CYP450 would be methylated. Methylation slows down transcription of CYP450 and this in turn slows down demethylation. This positive feedback loop eventually leads to a kind of death spiral.

4. Differential methylation of the hippocampus is known to be crucial for the memory recall (here memories are understood as learned behaviors rather than episodal memories) [J5]. Differential methylation is not possible without demethylation. If methylation becomes irreversible the formation of recallable memories becomes more difficult. Short term memory recall as also memory recall in longer time scales indeed become less effective during aging.

5.2 How epigenetic information is inherited?

There is evidence for the inheritance of epigenetic information.

1. Epigenetic inheritance takes place in mitosis and sometimes also in meiosis. The methylation related epigenetic disorder increases with aging.

2. How could the epigenetic information be inherited in this picture? It could be represented by the geometry of MB - flux tube network - and at the genetic level by both control genes. Emotional aspects, something new, would have bio-harmony as a correlate, and bio-harmony is determined by cyclotron frequencies determined by the magnetic field strengths of the flux tubes. Not only cell but also MB replicates and the replication of MB induces replication at cell and DNA level.

   Both genetic and epigenetic information could be inherited in the replication if MB replicates geometrically like a particle in the decay A$\to$ A+A. Usually particles are regarded as pointlike and Feynman diagram expresses this. The line A decays to two lines A+A. This makes sense also for 3-surfaces, in particular magnetic bodies, replacing the point like particles. That replication occurs at the fundamental physics is a new element in TGD based vision.

At the level of causal diamonds (CDs) A→A+A would look like follows. The CD of A in the initial state and the CDS of A+A in the final state would intersect and contain the vertex region. Could the moods of A be inherited by A:s in A+A under some conditions - in other words, are cyclotron frequency spectra of flux tubes of A inherited?: this is true i the flux tubes would replicate as such.

Some methylation patterns are inherited in meiosis but not all. If these patterns are determined by the bio-harmony, magnetic flux tubes are copied faithfully in some cases even in meiosis but not always.

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