Clustering of RNA polymerase molecules and Comorosan effect

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Abstract

Ibrahim Cisse and colleagues have made interesting discoveries about the clustering of RNA II polymerase molecules and so called mediator molecules. The clustering can be understood in terms of the notion of a tensor network formed from molecules connected by magnetic flux tubes carrying dark matter as $h_{eff} = n \times h$ phases. Dark protons are especially interesting and would form a representation of genetic code realized in water already during prebiotic phase.

A further interesting finding is that time scales coming as multiples of 5 second time scale are associated with the clustering of both RNA II polymerase molecules and mediator molecules. These time scales were discovered long time ago by Comorosan and claimed to be a universal feature of bio-catalysis. During years I have made several attempts to understand these time scales in terms of Josephson junctions between the reacting bio-molecules but failed to find a convincing explanation. The Josephson junction model combined with the notion of gravitational Planck constant and the vision about dark nuclei however leads to a correct prediction for these time scales and is consistent with several other TGD inspired hypothesis relating to quantum biology and predicts correctly the time scale of nerve pulse.

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1 Introduction

Once again I had good luck: I received a link (see http://tinyurl.com/y7bego83) to a highly interesting popular article telling about the work by Ibrahim Cisse at MIT and his colleagues [I3] (see http://tinyurl.com/y9wzt5yl) about the clustering of RNA polymerase proteins in the transcription of RNA. Similar clustering has been observed already earlier and interpreted as a phase separation giving rise to protein droplets [L6]. Now this interpretation is not proposed by experiments but they say that it is quite possible but they cannot prove it.

I have already earlier discussed the coalescence of proteins into droplets as this kind of process in TGD framework [K9] [L6]. The basic TGD based ideas is that proteins - and biomolecules in general - are connected by flux tubes characterized by the value of Planck constant $h_{eff} = n \times h_0$ for the dark particles at the flux tube. The higher the value of n is the larger the energy of given state. For instance, the binding energies of atoms decrease like $1/n^2$. Therefore the formation of the molecular cluster liberates energy usable as metabolic energy.

Remark: h_0 is the minimal value of h_{eff}. The best guess is that ordinary Planck constant equals to $h = 6h_0$ [L1, L5] (see http://tinyurl.com/goruuzm and http://tinyurl.com/y9jxyjns.

A further interesting finding is that time scales coming as multiples of 5 second time scale are associated with the clustering of both RNA II polymerase molecules and mediator molecules. These time scales were discovered long time ago by Comorosan and claimed to be a universal feature of bio-catalysis [I5, I2]. During years I have made several attempts to understand these time scales in terms of Josephson junctions between the reacting bio-molecules but failed to find a convincing explanation.

The Josephson junction model combined with the notion of gravitational Planck constant and the vision about dark nuclei however leads to a correct prediction for these time scales and is consistent with several other TGD inspired hypothesis relating to quantum biology and predicts correctly the time scale of nerve pulse. One can also understand the special role of the endogenous magnetic field $B_{end} = .2$ Gauss explaining the findings of Blackman [J1] and the relationship between dark cyclotron photons transforming to ordinary photons identifiable as bio-photons [K7] and dark Josephson photons assignable to proteins through cell membrane acting as Josephson junctions [K4, K1] associated also with reaction complexes of biomolecules.

2 TGD view about the findings

Gene control switches - such as RNA II polymerases in DNA transcription to RNA - are found to form clusters called super-enhancers. Also so called Mediator proteins form clusters. In both cases the number of members is in the range 200-400. The clusters are stable but individual molecules spend very brief time in them. Clusters have average lifetime of $5.1 \pm .4$ seconds.

Why the clustering should take place? Why large number of these proteins are present although single one would be enough in the standard picture. In TGD framework one can imagine several explanations. One can imagine at least following reasons.

1. If the initiation of transcription is quantum process involving state function reduction, clustering could allow to make this process process deterministic at the level of single gene in spite of the non-determinism of state function reduction. Suppose that the initiation of transcription is one particular outcome of state function reduction. If there is only single RNA II polymerase able to make only single trial, the changes to initiate the transcription are low. This could be the case if the protein provides metabolic energy to initiate the process and becomes too "tired" to try again immediately. In nerve pulse transmission there is analogous situation: after the passing of the nerve pulse generation the neuron has dead time period. As a matter of fact, it turns out that the analogy could be much deeper.

   How to achieve the initiation with certainty in this kind of situation? Suppose that the other outcomes do not affect the situation appreciably. If one particular RNA polymerase fails to initiate it, the others can try. If the number of RNA transcriptase molecule is large enough, the transcription is bound to begin eventually! This is much like in fairy tales about princess and suitors trying to kill the dragon to get the hand of princess. Eventually comes the penniless swineherd.

2. If the initiation of transcription requires large amount of metabolic energy then only some minimal number of N of RNA II polymerase molecules might be able to provide it collectively. The collective formed by N molecules could correspond to a formation of magnetic body (MB) with a large value of $h_{eff} = n \times h_0$ and controlling the molecules and inducing its coherent behavior. The molecules would be connected by magnetic flux tubes.

3. If the rate for occurrence is determined by an amplitude which is superposition of amplitudes assignable to individual proteins the the rate is proportional to N^2, N the number of RNA II polymerase molecules. The process for the cluster is reported to to be surprisingly fast as compared to the expectations - something like 20 seconds. The earlier studies have suggests that single RNA polymerase stays at the DNA for minutes to hours.

   Clustering could allow to speed up bio-catalysis besides the mechanism allowing to find molecules to find by a reduction of $h_{eff}/h = n$ for the bonds connecting the reactants and the associated liberation of metabolic energy allowing to kick the reactants over the potential wall hindering the reaction.

Concerning the process of clustering there are two alternative options both relying on the model of liquid phase explaining Maxwell's rule assuming the presence of flux tube bonds in liquid and of water explaining its numerous anomalies in terms of flux tubes which can be also dark (see `http://tinyurl.com/ydhknc2c`).

1. **Option I**: Molecules could form in the initial situation a phase analogous to vapour phase and there would be very few flux tube bonds between them. The phase transition would create liquid phase as flux tube loops assignable to molecules would reconnect form flux tube pairs connecting the molecules to a tensor network giving rise to quantum liquid phase. The larger then value of n, the longer the bonds between molecules would be. This kind of model [L2] (see `http://tinyurl.com/yassnhzb`) is used to explain the strange findings that a system consisting of plastic balls seems to show primitive features of life such as metabolism.

2. **Option II**: The molecules are in the initial state connected by flux tubes and form a kind of liquid phase and the clustering reduces the value of $h_{eff}/h = n$ and therefore the lengths of flux tubes. This would liberate dark energy as metabolic energy going to the initiation of the transcription. One could indeed argue that connectedness in the initial state with large enough value of n is necessary since the protein cluster must have high enough "IQ" to perform intelligent intentional actions.

Protein blobs are said to be drawn together by the "floppy" bits (pieces) of intrinsically disordered proteins. What could this mean in the proposed picture? Disorder would mean absence of correlations between building bricks of floppy parts of the proteins in translational degrees of freedom.

1. Could floppiness correspond to low string tension assignable to long flux loops with large n assignable to the building bricks of "floppy" pieces of protein? Could reconnection for these loops give rise to pairs of flux tubes connecting the proteins in the transition to liquid phase (Option I)? Floppiness would also make possible to scan the environment by flux loops to get in touch with the flux loops of other molecules and in the case of hit (cyclotron resonance) induce reconnection.

2. In spite of floppiness in this sense, one could have quantum correlations between the internal quantum numbers of the building bricks of the floppy pieces. This would also increase the value of n serving as molecular IQ and provide molecule with higher metabolic energy liberated in the catalysis.

3 About Comorosan effect and clustering of RNA II polymerase proteins

What about the interpretation of the time scales τ equal 5, 10, and 20 seconds appearing in the clustering of RNA II polymerase proteins and Mediator proteins? What is intriguing that so called Comorosan effect [I5, I1] involves time scale of 5 seconds and its multiples claimed by Comorosan long time ago to be universal time scales in biology. The origin of these time scales has remained more or less a mystery although I have considered several TGD inspired explanations for this time scale is based on the notion of gravitational Planck constant [K6] (see `http://tinyurl.com/yb8fw3kq`).

One can consider several starting point ideas, which need not be mutually exclusive.

1. The time scales τ associated with RNA II polymerase and perhaps more general bio-catalytic systems as Comorosan's claims suggest could correspond to the durations of processes ending with "big" state function reduction. In zero energy ontology (ZEO) there are two kinds of state function reductions [L3]. "Small" state function reductions - analogs of weak measurements - leave the passive boundary of causal diamond (CD) unaffected and thus give rise to self as generalized Zeno effect. The states at the active boundary change by a sequence of unitary time evolutions followed by measurements inducing also time localization of the active boundary of CD but not affecting passive boundary. The size of CD increases and

gives rise to flow of time defined as the temporal distance between the tips of CD. Large reductions change the roles of the passive and active boundaries and mean death of self. The process with duration of τ could correspond to a life-time of self assignable to CD.

Remark: It is not quite clear whether CD can disappear and generated from vacuum. In principle this is possible and the generation of mental images as sub-selves and sub-CDs could correspond to this kind of process.

2. In [K6] I proposed that Josephson junctions are formed between reacting molecules in bio-catalysis. These could correspond to the shortened flux tubes. The difference $E_J = ZeV$ of Coulomb energy of Cooper pair over flux tube defining Josephson junction between molecules would correspond to Josephson frequency $f_J = 2eV/h_{eff}$. If this frequency corresponds to $\tau_J = 5$ seconds, h_{eff} should be rather large since E_J is expected to be above thermal energy at physiological temperature.

   Could Josephson radiation serve as a kind of of synchronizing clock for the state function reductions so that its role would be analogous to that of EEG in case of brain? A more plausible option is that Josephson radiation is a reaction to the presence of cyclotron radiation generated at MB and performing control actions at the biological body (BB) defined in very general sense. In the case of brain dark cyclotron radiation would generate EEG rhythms responsible for control via genome and dark generalized Josephson radiation modulated by nerve pulse patterns would mediate sensory input to the MB at EEG frequencies.

   A good guess motivated by the proposed universality of the Comorosan periods is that the energy in question does not depend on the catalytic system and corresponds to Josephson energy for protein through cell membrane acting as Josephson junction and giving to ionic channel or pump. The flux tubes themselves have universal properties.

3. The hypothesis $\hbar_{eff} = \hbar_{gr} = GMm/\beta_0 c$ of Nottale [E1] for the value of gravitational Planck constant [K5, K2, K10, K9] gives large $\hbar$. Here $v_0 = \beta_0 c$ has dimensions of velocity. For dark cyclotron photons this gives large energy $E_c \propto \hbar_{gr}$ and for dark Josephson photons small frequency $f_J \propto 1/h_{gr}$. Josephson time scale τ_f would be proportional to the mass m of the charged particle and therefore to mass number A of ion involved: $f_J \propto A$ possibly explaining the appearance of multiples of 5 second time scale. Cyclotron time scale does not depend on the mass of the charged particle at all and now sub-harmonics of τ_c are natural.

The time scales assignable to CD or the lifetime-time of self in question could correspond to either cyclotron of Josephson time scale τ.

1. If one requires that the multiplies of the time scale 5 seconds are possible, Josephson radiation is favoured since the Josephson time scale proportional to $h_{gr} \propto m \propto A$, A mass number of ion.

   The problem is that the values $A = 2, 3, 4, 5$ are not plausible for ordinary nuclei in living matter. Dark nuclei at magnetic flux tubes consisting of dark proton sequences could however have arbitrary number of dark protons and if dark nuclei appear at flux tubes defining Josephson junctions, one would have the desired hierarchy.

2. Although cyclotron frequencies do not have sub-harmonics naturally, MB could adapt to the situation by changing the thickness of its flux tubes and by flux conservation the magnetic field strength to which f_c is proportional to. This would allow MB to produce cyclotron radiation with the same frequency as Josephson radiation and MB and BB would be in resonant coupling.

Consider now the model quantitatively.

1. For $\hbar_{eff} = \hbar_{gr}$ one has

$$r = \frac{\hbar_{gr}}{\hbar} = \frac{GM_D m}{c\beta_0} = 4.5 \times 10^{14} \times \frac{m}{m_p}\frac{y}{\beta_0} \quad .$$

   Here $y = M_D/M_E$ gives the ratio of dark mass M_D to the Earth mass M_E. One can consider 2 favoured values for m corresponding to proton mass m_p and electron mass m_e.

2. $E = h_{eff}f$ gives the concrete relationship $f = (E/eV) \times 2.4 \times 10^{14} \times (h/h_{eff})$ Hz between frequencies and energies. This gives

$$x = \frac{E}{eV} = 0.4 \times r \times \frac{f}{10^{14}Hz} \ .$$

3. If the cyclotron frequency $f_c = 300$ Hz of proton for $B_{end} = .2$ Gauss corresponds to bio-photon energy of x eV, one obtains the condition

$$r = \frac{GM_D m_p}{\hbar\beta_0} \simeq .83 \times 10^{12} x \ .$$

Note that the cyclotron energy does not depend on the mass of the charged particle. One obtains for the relation between Josephson energy and Josephson frequency the condition

$$x = \frac{E_J}{eV} = 0.4 \times .83 \times 10^{-2} \times \frac{m}{m_p} \times x\frac{f_J}{Hz} \ , \ E_J = ZeV \ .$$

One should not confuse eV in ZeV with unit of energy. Note also that the value of Josephson energy does not depend on h_{eff} so that there is no actual mass dependence involved.

For proton one would give a hierarchy of time scales as A-multiples of $\tau(p)$ and is therefore more natural so that it is natural to consider this case first.

1. For $f_J = .2$ Hz corresponding to the Comorosan time scale of $\tau = 5$ seconds this would give $ZeV = .66x$ meV. This is above thermal energy $E_{th} = T = 27.5$ meV at $T = 25$ Celsius for $x > 42$. For *ordinary* photon ($h_{eff} = h$) proton cyclotron frequency $f_c(p)$ would correspond for $x > 42$ to EUV energy $E > 42$ eV and to wavelength of $\lambda < 31$ nm.

   The energy scale of Josephson junctions formed by proteins through cell membrane of thickness $L(151) = 10$ nm is slightly above thermal energy, which suggests $x \simeq 120$ allowing to identify $L(151) = 10$ nm as the length scale of the flux tube portion connecting the reactants. This would give $E \simeq 120$ eV - the upper bound of EUV range. For $x = 120$ one would have $GM_E m_p y/v_0 \simeq 10^{14}$ requiring $\beta_0/y \simeq 2.2$. The earlier estimates [K9] for the mass M_D give $y \sim 2 \times 10^{-4}$ giving $\beta_0 \sim 4.4 \times 10^{-4}$. This is rather near to $\beta_0 = 2^{-11} \sim m_e/m_p$ obtained also in the model for the orbits of inner planets as Bohr orbits.

   For ion with mass number A this would predict $\tau_A = A \times \tau_p = A \times 5$ seconds so that also multiples of the 5 second time scale would appear. These multiples were indeed found by Comoran and appear also in the case of RNA II polymerase.

2. For proton one would thus have 2 biological extremes - EUV energy scale associated with cyclotron radiation and thermal energy scale assignable to Josephson radiation. Both would be assignable to dark photons with $h_{eff} = h_{gr}$ with very long wavelength. Dark and ordinary photons of both kind would be able to transform to each other meaning a coupling between very long lengths scales assignable to MB and short wavelengths/time scales assignable to BB.

   The energy scale of dark Josephson photons would be that assignable with Josephson junctions of length 10 nm with long wavelengths and energies slightly above E_{th} at physiological temperature. The EUV energy scale would be 120 eV for dark cyclotron photons of highest energy would be fixed by flux tube length of 10 nm.

   For lower cyclotron energies forced by the presence of bio-photons in the range containing visible [K7, K8] and UV and obtained for B_{end} below .2 Gauss, the Josephson photons would have energies below E_{th}. That the possible values of B_{end} are below the nominal value $B_{end} = .2$ Gauss deduced from the experiments of Blackman [J1] does not conform with the earlier ad hoc assumption that B_{end} represents lower bound. This does not change the earlier conclusions.

   Could the 120 eV energy scale have some physical meaning in TGD framework? The corresponding wavelength for ordinary photons corresponds to the scale $L(151) = 10$ nm

which correspond to the thickness of DNA double strand. Dark DNA having dark proton triplets as codons could correspond to either $k = 149$ or $k = 151$. The energetics of Pollack effect suggests that $k = 149$ is realized in water even during prebiotic period [L4] (see `http://tinyurl.com/yalny39x`). In the effect discovered by Blackman the ELF photons would transform dark cyclotron photons having $h_{eff} = h_{gr}$ and energy about .12 keV. They would induce cyclotron transitions at flux tubes of B_{end} with thickness of order cell size scale. These states would decay back to previous states and the dark photons transformed to ordinary photons absorbed by ordinary DNA with coil structure with thickness of 10 nm. Kind of standing waves would be formed. These waves could transform to acoustic waves and induce the observed effects. Quite generally, dark cyclotron photons would control the dynamics of ordinary DNA by this mechanism.

It is natural to assume that $B_{end} = .2$ Gauss corresponds to the upper bound for B_{end} since magnetic fields are expected to weaken farther from the Earth's surface: weakening could correspond to thickening of flux tubes reducing the field intensity by flux conservation. The model for hearing [K3] requires cyclotron frequencies considerably above proton's cyclotron frequency in $B_{end} = .2$ Gauss. This requires that audible frequencies are mapped to electron's cyclotron frequency having upper bound $f_c(e) = (m_p/m_e)f_c(p) \simeq 6 \times 10^5$ Hz. This frequency is indeed above the range of audible frequencies even for bats.

For electron one has $h_{gr}(e) = (m_e/mp) \times h_{gr}(p) \simeq 5.3 \times 10^{-4} h_{gr}(p)$, $\hbar_{gr}(p)/\hbar = 4.5 \times 10^{14}/\beta_0$. Since Josephson energy remains invariant, the Josephson time scales up from $\tau(p) = 5$ seconds to $\tau(e) = (m_e/m_p)\tau(p) \simeq 2.5$ milliseconds, which is the time scale assignable to nerve pulses [K4, K1].

To sum up, the model suggests that the idealization of flux tubes as kind of universal Josephson junctions. The model is consistent with bio-photon hypothesis. The constraints on $h_{gr} = GM_D m/v_0$ are consistent with the earlier views and allows to assign Comorosan time scale 5 seconds to proton and nerve pulse time scale to electron as Josephson time scales. This inspires the question whether the dynamics of bio-catalysis and nerve pulse generation be seen as scaled variants of each other at quantum level? This would not be surprising if MB controls the dynamics. The earlier assumption that $B_{end} = 0.2$ Gauss is minimal value for B_{end} must be replaced with the assumption that it is maximal value of B_{end}.

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