TGD interpretation of new experimental results about the mechanism of anesthesia

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Abstract

This article was inspired by an article "*Studies on the mechanism of general anesthesia*" by Lerner, Hansen and collaborators. The article told about identification of a two-step mechanism associated with the action of anesthete in lipid layer and leading to hyperpolarization. What follows is an attempt to develop in more detail earlier TGD inspired model of anesthetic action in the hope of new insights.

The new elements that TGD can provide is quantum biology relying on the predicted hierarchy of phases of ordinary matter labelled by effective Planck constant $h_{eff} = nh_0$ and zero energy ontology (ZEO) predicted that the arrow of time is reversed in ordinary state function reductions forcing to replacing the standard theory of self-organization reducing it to dissipation in non-standard time direction.

1 Introduction

I received a link to a highly interesting popular article with title "*Century-Old Scientific Debate Settled: Anesthesias Effect on Consciousness Solved*" (https://tinyurl.com/yd4ztmph). The article tells about a study from Scripps Research published in the Proceedings of the National Academies of Sciences (PNAS). The paper [J2] "*Studies on the mechanism of general anesthesia*" has appeared in PNAS (https://tinyurl.com/y8oa97eo). In addition to Lerner and Hansen, the authors are Mahmud Arif Pavel, E. Nicholas Petersen and Hao Wang, all of Scripps Research.

I have pondered possible mechanism of anesthesia in TGD framework several times earlier [K2] [L2] and it is interesting to see whether the findings allow to make earlier insights more detailed or even develop new ones.

1.1 What was observed

According to the popular article the discovery by chemist Richard Lerner, MD, and molecular biologist Scott Hansen, PhD, settles a century-old scientific debate about whether anesthetics act directly on cell-membrane gates called ion channels, or do they somehow act on the membrane to signal cell changes in a new and unexpected way. The conclusion of the researcheres is that anesthetic action is a two-step process that begins in the membrane. The anesthetics perturb ordered lipid clusters within the cell membrane known as "lipid rafts" to initiate the signal. There are two kinds of clusters involved and known with names GM1 and PIP2.

What was observed was following.

- A shift in the GM1 clusters organization, a shift from a tightly packed ball to a disrupted mess occurred first As GM1 grew disordered, it spilled its contents, among them, an enzyme called phospholipase D2 (PLD2). Melting is a good analog for what happens. Gel-to-sol transition in cytoplasm is second analogy.

- PLD2 moved like a billiard ball away from its GM1 home and over to a different, less-preferred lipid cluster called PIP2.

- This activates key molecules within PIP2 clusters, TREK1 potassium ion channels and their lipid activator, phosphatidic acid (PA) are among them. The activation of TREK1 potassium channels releases potassium hyper-polarizing the nerve and it makes it more difficult to fire. Nerve pulse generation rate becomes low and leads to a loss of consciousness - at least in clinical sense. Something analogous to this could happen when one falls in sleep.

In the sequel I try to understand in the framework provided by TGD inspired model of cell membrane and nerve pulse [K2], compare these findings to TGD inspired views about anesthesia based on hyperpolarization, and also try to build a bridge from TGD description provided by a generalization of thermodynamics forced by zero energy ontology (ZEO) predicting that in ordinary state function reduction the arrow of time changes [L8, L11].

2 TGD background

In the following Pollack effect and its generalization are discussed, ZEO based view about self-organization involving time reversal as key element is compared to the non-equilibrium thermodynamics (NET) based approach, and the TGD based view about nerve pulse generation and EEG is discussed.

2.1 Pollack effect as starting point

The generalization of Pollack effect [I3, I2, I5, I4] plays a key role in TGD inspired biology.

1. TGD based model of cell membrane relies on a generalizaton of Pollack effect so that it would allow also to other ions - at least positively charged ions inside neuronal (cell) membrane. Pollack effect occurs in presence of energy feed such as IR photons, and means charge separation in water bounded by gel so that negatively charged exclusion zone (EZ) is formed. TGD interpretation is that part of protons goes outside EZ to magnetic flux tubes and form dark proton sequences having effective Planck constant $h_{eff} = nh_0 > h$ and forming macroscopic quantum phase. Dark particles at magnetic flux tubes of magnetic body of system (MB) would control its dynamics like master and induce coherence as forced coherence.

   EZ has the strange property that it drives out impurities. The interpretation is that the arrow of time is change at MB controlling EZ and induces effective change of the arrow of time at EZ differing from the standard arrow of time of observer. DNA nucleotides involve negatively charged phosphate ion, which leads to the proposal that they are accompanied by magnetic flux tubes parallel to them carrying dark proton triplets as a representation of genetic codons [L3, L5].

   Negatively charge entities appear abundant in biology.

   (a) Cell interior is negatively charged, which suggests similar charge separation with positive charge assignable to dark ions at the magnetic flux tubes outside cell. Fermionic ions such as K^+, Na^+,.. could form Bose-Einstein (B-E) condensates of Cooper pairs whereas bosonic ions like such as Ca^{2+}, Mg^{2+}, Fe^{2+} could as such form B-E condensates. It is not clear whether also negatively charged ions like Cl^- form B-E condensates at flux tubes and whether they are in the interior or exterior of cell.

   (b) Microtubules carry constant negative charge density per unit length realized in terms of GTP molecules suggesting that they are accompanied by parallel flux tubes carrying say dark protons. Microtubules could be partially responsible for the negative charge of cell and could be related to the control of membrane potential.

   (c) ATP has charge -3. This forces to ask whether there is charge +3 of 3 protons associated with a magnetic flux tube accompanying ATP. Could the 3 protons form the analog of genetic codon so that information processing might take place already at this level?

2. Pollack effect would basically transform part of ordinary ions in cell interior to dark ions or their Cooper pairs outside cell at flux tubes. Note that also the analogs of 3-proton units can be considered for positive ions. This would require energy feed, which need not come from

metabolic energy. Integral proteins acting as ion channels do not require ATP to function and are a good candidate in this respect. Their opening could make possible Pollack effect for ion. Ion pumps are also integral proteins and could transfer the ions produced in the decay of Cooper pairs to ordinary ions back to cell interior.

2.2 ZEO based thermodynamical description of self-organizing cell

TGD leads to a new kind of thermodynamical description of cell as an open self-organizing system. Cell is indeed an open self-organizing system requiring metabolic energy feed. The standard description would be using non-equilibrium thermodynamics (NET). ZEO allows both arrows of time and and the arrow of time changes in ordinary ("big") state function reductions (BSFRs) possible in arbitrary long scales. This forces a generalization of thermodynamics allowing a new kind of description.

Dissipation with reversed arrow of time corresponds to generation of gradients and gradients as seen by observer with standard time direction, and energy feed needed by self-organization corresponds to dissipation of energy by self-organizing system in reverse time direction. The arrow of time could be different from standard one in long time scales only at the level of MB carrying dark matter and can induce its effective change at the level of ordinary matter.

The energy of particle increases with h_{eff} so that generation of dark phases and the preservation of h_{eff} distribution requires energy feed. Hence one can see self-organization as a direct evidence for the notions of MB and ZEO.

How does TGD description relate to the standard description of cell in terms of NET differing from the ordinary thermodynamics by the presence of energy feed?

1. In standard thermodynamical description the presence of dark matter is not assumed. Therefore the description takes into account only the ordinary matter. For living cell the differences between ion concentrations are in sharp conflict with naive expectations for ions like K^+ (concentration is considerably higher in the cell interior). They are explained by using chemical potentials μ as parameters. Their values are determined experimentally from measured ion concentrations. Their values would be basically determined by the metabolic energy feed: here NET enters the picture.

2. The basic quantity is Gibbs energy $G = E - TS$, whose minimization corresponds to second law of thermodynamics. The energy minimization and entropy maximization compete and there is a competition between energy and entropy. Giggs energy for single particle corresponds to chemical potential $\mu = e - Ts$ at single particle level. Given process is thermodynamically favored at single particle level if μ decreases in it.

3. For instance, the measured density of K^+ ions is much higher inside cell than exterior - this corresponds to the fact that dark K^+ ions or of their Cooper pairs at flux tubes are not observed. When channel is opened the K^+ ions flow to the exterior of the membrane provided this corresponds to a decrease of μ. For given ion there is also a certain value of membrane potential for which there is no flow.

   In TGD framework Pollack effect transforming K^+ ions to their dark variants transferred to the flux tubes outside cell and possibly forming Cooper pairs would be the description. The safest assumption is that ions are at flux tubes at both sides but that at either side the value of h_{eff} is minimal. Also phase transitions changing h_{eff} for flux tubes are expected to occur and play a key role in TGD based model for bio-catalysis.

4. An open problem is whether the phenomenological description of ordinary matter in terms of NET is equivalent with the ZEO based description in which also dark matter is taken into account. For instance, Pollack effect for protons requires energy feed. It generates charge separation, which generates negative Coulomb energy. The Coulomb repulsion between charged protons at flux tube generates positive energy. The model as dark nuclei implies that there is also scaled dow nuclear binding energy involved. The value of entropy generated in this manner depends on the scale of de-localization at MB. If macroscopic quantum phase is generated, one expects that the generated entropy is actually small.

5. It would seem that ion channels, which do not require ATP, involve the transfer of ordinary matter to dark matter at magnetic flux tubes. Could ion pumps requiring ATP be responsible for the transfer of ordinary ions between cell interior and exterior against gradient of chemical potential? Could they correspond to standard arrow of time?

2.3 EEG and nerve pulse generation in ZEO

TGD leads to a model of nerve pulse and EEG [K2, K1, K3].

1. Cell membrane is a generalized Josephson junction in the sense that there are flux tubes at both sides of the membrane connected by a flux tubes through cell membrane. The energy assignable to the ion in junction is sum of two terms. The first term is the ordinary Josephson energy given by Coulomb energy. Second terms is the difference of the cyclotron energies of ion associated with the flux tubes at the two sides of the membrane. The generalized Josephson radiation generated by this system consists of dark photons travelling along magnetic flux tubes to the part of MB much larger than the system. The Compton length of EEG radiation at Schumann frequency 7.8 Hz gives an estimate of order Earth circumference for the size scale of MB.

2. The sensory part of EEG mediating sensory information to MB would be assigned with the generalized Josephson frequencies modulated by the variation of membrane potential and in this manner coding the sensory data. If the signal is received at certain resonance frequencies it corresponds to a sequence of peaks corresponding to critical values of membrane potential.

   MB containing cyclotron B-E condensates would receive this radiation resonantly and respond by control signal consisting of dark cyclotron radiation possibly mediated through genome (and possibly also microtubuli) and inducing biological effects. They would emerge by a transition $\hbar_{eff} = h\hbar_0 = h_{gr} = GMm/v_0 \rightarrow h$ producing ordinary photons identifiable as bio-photons in visible and UV range [K4, K5]. These would induce molecular transitions.

3. h_{eff} hierarchy allows to interpret the generation of nerve pulse as a quantum jump in neuronal scale. The change of the arrow of time correspond to the change of the sign of the membrane potential temporarily. This process would liberate energy needed to preserve the thermodynamical non-equilibrium state but regeneration of standard arrow of time would require metabolic energy so that energy would be lost. For instance, generalized Josephson radiation would use part of the energy.

   Neural membrane is quantum critical against generation of nerve pulses by macroscopic quantum jump changing the arrow of time (automatically) - as a matter of fact, the Josephson energy for ion Cooper pairs is near to thermal energy. This makes cell membrane an ideal sensory receptor.

4. Quite generally motor actions correspond in TGD framework BSFRs whereas sensory perception corresponds to a sequences of "small" state function reductions (SSFRs). This would suggest that the EEG waves from the cell membrane as sensory input have standard arrow of time and control signals from MB comes as EEG waves with opposite arrow of time. One might also speak of time reflection of the positive energy signal. A detailed model for the sequence of SSFRs leads also to a model for what personal memories are [L8, L11].

What happens to GM1 fart is essentially melting.

1. Melting phase transitions - analogous to gel-sol transitions for cytoplasm - occur in the lipid layer also during the propagation of nerve pulse and has been proposed to accompany a propagation of soliton [J3] (`https://www.pnas.org/content/102/28/9790`). TGD based model of nerve pulse [K2] assumes that in the resting state of axon there is a sequence of solitons propagating along the axon mathematically. The chain of the proteins representing ion channels (and possibly also pumps) as Josephson junctions would be analogous to a chain of rotating mathematical penduli with constant phase difference.

2. Nerve pulse would correspond to a propagation of a perturbation for which some penduli oscillate rather than rotate. The local transformation of rotation to oscillation would correspond to a melting phase transition propagating along axon.

3. One cannot however exclude the possibility that the Josephson penduli are not kicked to oscillation but to a rotation in opposite direction. This would conform with the proposal of [J3] that nerve pulse involves propagation of some kind of soliton.

   If this is true, the ions at two sides should be at flux tubes with different values of h_{eff} and the values of h_{eff} are effectively permuted at two sides to change the sign of membrane potential. This requires transfer of energy between interior and exterior. The change of the sign of membrane potential suggests local time reversal and if BSFR occurs, this must happen. If BSFR occurs, some self - neuronal mental image - at exterior dies and re-incarnates with opposite arrow of time in the interior. The observer with standard arrow of time would see ions to flow from the MB of the neuron to interior flux tubes for which h_{eff} is increased. The naive expectation is that also the roles of channels and pumps are changed.

4. It would be natural to assign melting transition with the reduction of membrane potential and initiation of the time reversed period. The possible melting outside neuron would be accompanied by freezing in the interior. Gel-sol phase transitions in cytoplasm could accompany the nerve pulse propagation. Cavitational fluctuations of water and microtubule disassembly are known to be accompanied by gel-sol phase transitions and of emission of biophotons and IR light [I1] (`https://tinyurl.com/ya33kdzt`). Photons are indeed in central role also in the generation of Pollack effect as providers of metabolic energy to realize the transition.

   Gel like states would correspond in TGD picture states of water in which the value of h_{eff} for the flux tubes is increased and thus to ordered states with higher number theoretic "IQ" having interpretation as dimension of extension of rationals [L7, L10, L1]. The increase of h_{eff} requires energy and gel-sol phase transition would correspond to a reduction o h_{eff} and liberate stored metabolic energy. One expects gel-sol phase transitions for cellular water to accompany the propagation of nerve pulses. One can imagine that the energy liberated in gel-to-sol transition induces sol-to-gel transition. This would naturally allow interpretation also as information transfer too?

3 What could happen in anesthesia?

Anesthetes - often noble gases - are expected to have rather weak chemical effects. This suggests that the mechanism inducing hyperpolarization is not purely chemical.

1. It would seem that GM1 clusters and PIP2 clusters correspond to two different equilibria in which the dark K^+ concentrations at dark flux tubes are different and therefore also membrane potentials. The role of the anesthete and of the control step inducing sleep would be to replace GM1 with PIP2. The anesthete dissolving into lipid layers could induce its melting by lowering the density of lipids in lipid-crystal and in this manner induce the decay of GM1 clusters. The interpretation of lost coherence could be in terms of reduction of h_{eff}: if BSFR occurs, GM1 could be said to die. The decay of the GM1 clusters could be thus seen as analog of decay process in general liberating energy used in the next step of the process.

2. What could happen in the decay of GM1 cluster, which expands from tightly packed ball and looses is order? The twistor lift of TGD [L9, L6] predicts length scale dependent cosmological constant Λ characterizing various structures in all scales and the possibility of phase transitions reducing the value of Λ, scaling up the size of the structure in question, and liberating energy. Could also GM1 be characerized by Λ decreasing in the transition and could the liberated energy be used as metabolic energy in the transfer of K^+ ions?

3. The PLD2 molecules (containing phosphate) are said to move like billiard balls to PIP2 clusters, which suggests that they could travel along magnetic flux tubes connecting the two systems. PLD2 molecules act as catalysts and could help to activate TREK1 K^+ channels and their lipid activator, phosphatidic acid (PA) containing phosphate with charge -2.

All these molecules involve negatively charged phosphate ions and this could relate to the generation of charge separation by Pollack effect. PIP2 involves 3 negatively charged phosphates and it binds to the TREK1. The negative charge from phosphates bound to TRKE1 could make it part of an analog of EZ. I do not know whether one has excluded the possibility of ATP $\rightarrow$ ADP type mechanism.

4. It is not clear what happens at the level of energetics. In ZEO picture the opening of K^+ ion channels would make possible a transfer of K^+ ions by Pollack effect to their dark variants possibly forming Cooper pairs at MB at the other side of neural membrane. If this requires metabolic energy, it is not provided by ATP.

   In NET picture Gibbs free energy should decrease if the process is spontaneous as suggested by the absence of ATP. This could be the case also now at least approximately. There could be quantum criticality in the sense that there is large number of states of neuron with essentially same energy or with energies differing only slightly but with different membrane potential.

   The increase of the membrane potential reduces the rate for the spontaneous generation of nerve pulses. Nerve pulse generation is expected to release energy but the regeneration of membrane potential back to its original value requires energy. Hence one expects that the anesthetic state saves metabolic energy as also sleep state is expected to do. Note that the feed of metabolic energy could corresponds quite generally to dissipation in opposite time direction. Could the MB of PIP2 cluster live in opposite time direction - as also GM1 cluster when active - and get its metabolic energy making possible the transfer of K^+ ions in this manner?

5. What is the role of the anesthete? Meyerton-Overton hypothesis states that the potency of anesthete correlates with its liquid solubility. The anesthete dissolved into the 2-D liquid-crystal formed by lipid layer should somehow induce the decay of GM1 cluster: the dissolved anesthete could force the reduction of density of 2-D liquid crystal if the total pressure is preserved. Could this decay liberate provide the metabolic energy needed in Pollack effect? Anesthete dissolves spontaneously. In standard picture the interpretation would be that this reduces Gibbs energy G. Does this liberate energy or is the increase of entropy enough to reduce G?

4 Questions

The foregoing speculative picture raises several questions.

1. The falling to sleep could involve similar transition. What happens to conscious experience in anesthesia and sleep. Sensory input from cell membranes to MB disappears and also motor control from MB becomes impossible but does this really mean loss of consciousness? Could the experience be nearer to a meditative state?

2. The arrow of time changes inside EZs assignable to negative charge in Pollack effect. Could PIP2 cluster be contained in EZ and thus have also reversed arrow of time. Could EZ property be tested? Could also the GM1 cluster have reversed arrow of time and be responsible for the transfer of different kind of ions?

   In ZEO "big" (ordinary) state function reduction (BSFR) corresponds quite universally to death and re-incarnation with opposite arrow of time for conscious entity involved. Could falling asleep be BSFR at some level of self hierarchy. Could GM1 clusters as conscious entities die and could their decay be analogous to ordinary decay process and provide both building bricks (PLD2) and metabolic energy for PIP2 clusters? Could this be interpreted as a kind of birth or wake-up for PIP2 clusters? Could the re-incarnated GM1 clusters live in opposite arrow of time?

3. K^+ channels represent only one particular kind of ion channel and there are many manners to control the ion flux. Could all ion channels rely to Pollack effect? What about on pumps. Could ion pumps be channels but with opposite arrow of time?

4. Quantum consciousness theorists like Hameroff have speculated about the role of microtubules in the action of anesthetes. The proposal is that the anesthete could bind in the hydrophobic pocket of microtubule. The recent findings seem to exclude this option.

   Microtubules however carry large negative charge density due to the presence of GTP molecules (analogous to ATP molecules), which strongly suggests the existence of magnetic flux tubes parallel to them and carrying dark protons or possibly some other positive ions. Microtubules are highly dynamical in quantum critical phase. Could their varying negative charge control the membrane potential by generating opposite varying charge at MB outside cell membrane by Pollack effect (I have discussed anesthetes in several sections of [K2]). Could the transition to sleep be controlled by the microtubular level using a variant of the mechanism discussed as a tool?

   Concerning the possible the source of metabolic energy, it is known that $GTP \to GDP$ cycle occurs [J1] (`https://tinyurl.com/yapdcotf`). Could this mechanism serve as an analog of $ATP \to ADP$ with metabolic energy stored in metabolites replaced with the metabolic energy carried by dark photons transforming to bio-photons?

5. What is interesting is that at the endogoneous magnetic field with value $B_{end} = .2$ Gauss assigned with monopole flux tube part of Earth's magnetic field with nominal value of $B_E = .5$ Gauss the cyclotron frequency of K^+ ion (and Cooper pair) is 7.5 Hz. Could dark Schumann resonance photons induce cyclotron transition of B-E condensate of K^+ Cooper pairs? A magnetic field oscillating frequency of with 7 Hz frequency not too far from the lowest Schumann resonance frequency and cyclotron frequency of K^+ ions appears also in the experiment of Montagnier et al [L4] strongly suggesting remote replication of DNA.

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