Check Sum Computing in Doubly Frustrated Microtubule Clusters

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ABSTRACT

The hitherto unexplained presence of 12 or 13 tubulin dimmers forming parallel protofilament subunits in microtubules (MTs) is supposed to ensure sum checking in the system of two MTs, each one being a potential computing 'core'. The recently proposed, frustration – originated, double well potential is mapped, exclusively for modelling reasons, onto the Ising – type Hamiltonian acting in the rings with an intra-site nearest neighbours interaction. We infer that the final state of energetically favourable 12 qubit 'calculation' at physiological temperature is randomly 'corrected' by the conjugated nearest 13 qubit 'core' (via inter-site, as yet indeterminate, long-range interaction) in the double MT cluster. Helmholtz free energy is calculated to show that such computing cluster lowers the system demands for ATP energy while retaining the possibility of higher accuracy calculations. By performing calculation for two model systems, we find the frustration – originated energy enhancement at physiological temperatures of the human brain for the semi-classical system against the corresponding quantum one. Also, existing studies have not clearly dissociated the neural processes supporting short- and long-duration memories – we propose a possible localization of durable/flash memory in MTs, through introducing a double frustration concept. By extension to double frustration description it may be meaningful to make the next intuitive leap to the question of quantum computing and its possible function in the theory of consciousness.

Key Words: computation, Ising model, microtubule, durable memory, flash memory, neuron

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Introduction

Quantum biology is a new field of scientific exploration of quantum phenomena in biological systems (Huelga and Plenio, 2013; Piotrowski *et al.,* 2003; Piotrowski and Sladkowski, 2003 for quantum games). It may be expected that in the course of evolution Nature have learnt how to use quantum phenomena to achieve higher efficiency in these emergent cases that provide an evolutionary advantage. By the latter we mean quantitative performance improvements (e.g., Shor, 1997) over classical systems, especially in the context of their potential role in the interplay between quantum dynamics of multi-site systems.

Max Tegmark in his paper (2000) underlined the importance of quantum decoherence in brain processes (Engel *et al.,* 2007 for coherence in photosynthesis). By presenting the opposition between the classical complex neural network, that could in principle perform all cognitive processes associated with consciousness, and information processing in a quantum computer (Penrose, 1989; 1997), he concluded that environment-induced decoherence will rapidly destroy macro-superpositions in the brain. Tegmark

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introduced proper classification scheme and a subsystem decomposition in case of quantum mechanics for open systems based on density matrix ρ governed by the von Neumann equation

$$\frac{d\rho}{dt} = -\frac{i}{\hbar}[H,\rho]$$

Such system, if left in isolation, will evolve according to the deterministic, linear Schrödinger equation

$$i\hbar\frac{d}{dt}|\Psi\rangle = H|\Psi\rangle$$

where H is the full Hamiltonian of the system. However, there is no indication of a border between quantum and classical at which this equation would fail (Zurek, 2002).

In the previous paper (Pietruszka and Lipowczan, 2013) we have proposed the mechanism of geometrical frustration (Pietruszka, 2013), leading to a double well potential (Jelic and Marsiglio, 2012), as a promising explanation connected with dynamic instabilities and conformational changes characteristic in microtubules (MTs) of the neuronal system. Now, keeping in mind our previous idea, we calculate basic properties of a double MT cluster as possible candidate for a two-core processing unit (CPU), by performing a simple simulation with the Ising model as an equivalent system.

Microtubules are cylindrical protein structures that are the major part constituting the cytoskeleton in all eucariotic cells (Tipsova and Tuszynski, 1997). They have a form of hollow tubes with walls assembled from tubulins. The basic unit in microtubules is αß-tubulin, a heterodimer, approximately 8 x 10^{-9} m = 8 nm long, consisted of 2 monomers (proteins, α and β tubulin). It can make transitions between two states of polar orientation, corresponding to different electric dipole moments (Mershin *et al.,* 2004) along the axis of the tube. The tubulin dimmers, stung together out of proteins, are arranged in helical manner in MT, with a diameter of 25 nm. Each monomer is of molecular weight of m = 50 - 55 kDa ≈ 91300 x 10^{-27} kg. De Broglie wave length $\lambda = h/\sqrt{(3mk_BT)}$ = 6 x 10^{-4} nm at 310 K, which implies that some collective processes may emerge at this quantum/classical borderline for tubulin subunits, which action can be conveyed further onto MTs.

The MTs are continuously growing and shrinking at both ends, which phenomenon is known as dynamic instability (Mitchison and Kirschner, 1984). Dynamic instability refers to the coexistence of assembly and disassembly at the (+) end of a microtubule. The microtubule can dynamically switch between growing and shrinking phases in this region. Tubulin dimmer can be in two states (of the same magnitude) characterized by opposite orientations with respect to the MT axis. The lateral association of the protofilaments generates an imperfect helix with one turn of the helix containing 13 tubulin dimers, each from a different protofilament. The number of protofilaments can vary. MTs, as composed of 12 or 13 such two-state dimmers, can be mapped in first approximation onto the Ising model on a ring.

Almost a century ago Bohr (1928) emphasized that even the human nervous system, treated as the "ultimate apparatus", could be analyzed as a quantum object, provided a suitable classical device could carry out the task. If macroscopic systems (like a gravity wave detector or Josephson junctions) cannot be always safely placed on the classical side of the quantum-classical boundary, then there might be no boundary at all (Zurek, 2002). According to Many Worlds Interpretation (Everett, 1957; Wheeler, 1957) each time a suitable interaction takes place between any two quantum systems, the wave vector $|\Psi\rangle$ of the universe splits, producing ever more branches. Even though the status of this theory is controversial, classicality must be an emergent property (Zurek, 2002).

Macroscopic systems are never isolated from the environment – they should not be expected to obey Schrödinger equation (Zeh, 1970), applicable only to closed systems. Classically regarded systems usually undergo the loss of quantum coherence – called decoherence, which imposes the observer to be aware of only one of the branches as the effect of interaction (Zurek, 2002). Therefore, in our approach, the initial state of a system composed of two interacting microtubules (treated as a double core processor) we describe as an isolated system, while the final state of the system ('calculation' result, corresponding to the momentary final choice of one branch) is established by decoherence.

Methods

Assume that the whole system is composed of two microtubules isolated from environment. One of them we treat as a calculating 12-site 'core', while the other 13-site 'core', as a detector recording (and checking) the result. The final state of the system is 'frozen' (recorded) in the polymerization state (with appropriate polarization) of tubulin protofilaments (Figure 1A, durable memory), while environmentally 'isolated' calculations are performed during polymerization processes (Figure 1A, flash memory).

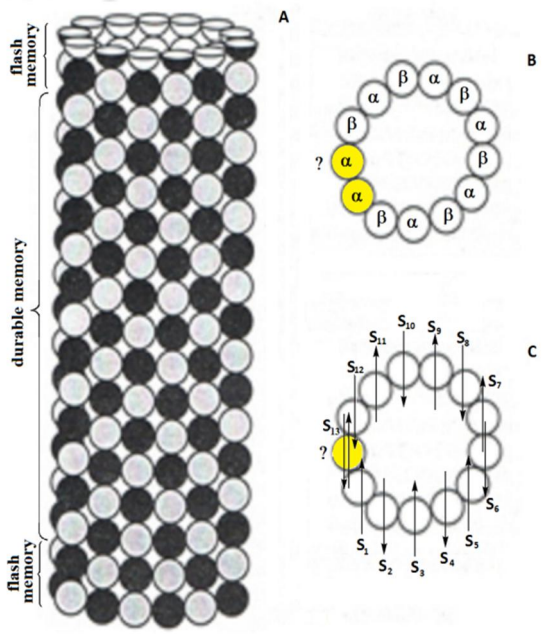

Figure 1. Microtubule (MT): (a) side view (b) top view (c) equivalent system consisted of 13 spins instead of α- and a ß-tubulin monomers (b). Note, that tubulin dimmer consisted of 13 monomers (spins) is doubly frustrated (assuming antiparallel (AF) spin arrangement). One type of frustration is avoided by the helical structure (frustration often leads to complicated noncollinear magnetic structures), while the other one can be dynamically eliminated by geometrical frustration mechanism (Pietruszka and Lipowczan, 2013). Permanent attempt of frustration removal may lead to oscillations (Pietruszka, 2013), and – consequently – 'calculations' executed in MTs double 'core' clusters. Possible locations of *durable* and *flash* memory zones (the documented propensity of MT's to undergo rapid association and disassociation in so termed "microtubule treadmilling," a process in which one end of the MT is being assembled from subunits while the other end is being disassembled producing α and ß states) are indicated. *Flash memory* is a non-volatile storage medium that can be erased and reprogrammed, in contrast to *durable memory* (compare with Craddoc *et al.,* 2012). As yet, existing studies have not clearly dissociated the neural processes supporting short- and long-duration memories (Liu *et al.,* 2013).

In our case a measurement is done on a two-state system S (with total "spin" ½) in which another quantum effectively one bit detector D records the result (Zurek, 2002). Two orthonormal states $|S\,☺\rangle$ and $|S☹\rangle$ span the Hilbert space of the investigated system (one core), while $|D☺\rangle$ and $|D☹\rangle$ span the Hilbert space of the detector (second core). We shall assume that before the interaction, the system was in a pure state $|\psi_S\rangle=a|S☺\rangle+b|S☹\rangle$, where complex a and b satisfy the equation $|a|^2+|b|^2=1$. The whole (composite) system initial state is given by $|\Phi_i\rangle=|\psi_S\rangle|D☹\rangle$. Evolution of $|\Phi_i\rangle$ into a correlated state $|\Phi_c\rangle$ takes the form $|\Phi_i\rangle=|\psi_S\rangle|D☹\rangle= (a|S☺\rangle+b|S☹\rangle)|D☹\rangle \Rightarrow a|S☺\rangle|D☺\rangle + b|S☹\rangle|D☹\rangle=|\Phi_c\rangle$, since the detector "clicks" only when the spin is in the state $|S☺\rangle$: $|S☺\rangle|D☹\rangle \Rightarrow |S☺\rangle|D☺\rangle$. The correlated state vector implies that for the detector in the state $|D☺\rangle$ the system is to be found in the state $|S☺\rangle$. However, to receive the full menu of possibilities in the double MT cluster, a density matrix approach should rather be used. The latter can be employed to describe the probability distribution over the alterative outcomes

$$\rho_c=|\Phi_c\rangle\langle\Phi_c|=\sum_{i=1}^{12}\sum_{j=1}^{13}\left(a|S:)\rangle_i|D:)\rangle_j\right)\left(a_i\langle S:(|_j\langle D:(|\right)$$

where after cancelling the off diagonal terms representing quantum entanglement (e.g., Horodecki *et al.,* 2007) the reduced density matrix ρ_r of classical correlations remains. Our further calculation will remain in the framework of this general outline.

Model 1

Let us consider the 1-dimensional Ising model on a ring, which is a simple equivalent model for a microtubule with 'inter-tubulin interactions'. In what follows, first we compute the canonical partition function Z by using the transfer matrix technique (e.g. Batista[2]), next we calculate the entropy S and the energy E of the system. Eventually, the energy difference for two 12 and 13 tubulin dimmers (represented by the Ising sites) is calculated, being in α and β tubulin states (corresponding to 'spin up', 'spin down' states, respectively, instead of a double well potential, which can also describe an electric dipole (Tripsowa and Tuszynski, 1997), as a function of temperature.

[2]Batista VS group
http://xbeams.chem.yale.edu/~batista/vaa/node37.html

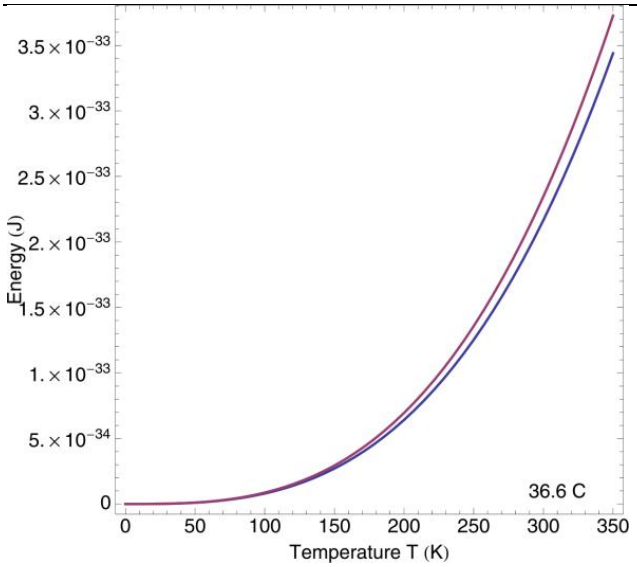

Figure 2. Energy of two MT rings consisted of 12 (lower plot) and 13 (upper plot) tubulin dimmers. The energy difference for the model parameters (Ising model) at 310 K required for the transition (check sum operation) equals 1.9918 x 10^{-34} J and is the least quanta of the energy in the system that can propagate (note, this is a value close to the Planck constant). The calculated energy fluctuation (variance) at physiological temperature of 310 K equals 1.10772 x 10^{-63} (1.20003 x 10^{-63}) J for 12 (13) - site rings, respectively. Note, there is no indication of a local extremum at the physiological temperature for this model.

The total Hamiltonian of the system (we abandon the 'magnetic field' term, and replace the helical arrangement of a MT that consists of 12 (or 13) protofilaments by anti-parallel 'spin' orientation for α- and β-tubulin states) can be decomposed into 3 parts

$$H = H_1 + H_2 + H_{\text{int}} \tag{1}$$

where

$$H_1 = -J \sum_{j,k=1}^{12} S_j S_k \tag{2}$$

$$H_2 = -J \sum_{j,k=1}^{13} S_j S_k \tag{3}$$

The H_1 operator affects only the first subsystem and H_2 affects only the second subsystem. The interaction Hamiltonian H_{int} is the remaining inseparable part, defined as

$$H_{\text{int}} = H - H_1 - H_2 \tag{4}$$

Such decomposition is always possible, although it is generally only useful if H_{int} is 'small'.

In Eqs (2) and (3) parameter J is the coupling constant in the each subsystem (the subsystem – subsystem interaction term is momentarily neglected). The sum of products S_jS_k defines the interaction between spins, including only nearest neighbours. The canonical partition function Z, which describes the statistical properties of either subsystem in thermodynamic equilibrium, is given by the trace

$$Z_{1(2)} = Tre^{-\beta H}{}_{1(2)} \tag{5}$$

And $\beta=1/k_BT$, where T stands for absolute temperature and k_B for the Boltzmann constant.

In order to perform calculations in the absence of an external field a transfer function can be defined (ibid.)

$$T(S_iS_{i+1}) \equiv \exp(\beta J S_i S_{i+1}) \tag{6}$$

Calculations with the use of the transfer matrix yields the exact partition function

$$Z_{1(2)} = 2^N \left(\cosh^N(\beta J) + \sinh^N(\beta J)\right) \tag{7}$$

where N is the number of sites (tubulin dimmers in the MT) in the ring.

The ensemble average for the energy of a single subsystem equals (we omit the subsystems' indices)

$$\langle E \rangle = -\frac{\partial \ln Z}{\partial \beta} = k_B T^2 \frac{\partial \ln Z}{\partial T} \tag{8}$$

and the result of calculations is presented in Figure 2.

The variance in the energy (energy fluctuation in the ring) is given by

$$\left\langle (\Delta E)^2 \right\rangle = -\frac{\partial^2 \ln Z}{\partial \beta^2} \tag{9}$$

and the entropy of the subsystem equals

$$S = \frac{\partial}{\partial T}(k_B T \ln Z) \tag{10}$$

For brevity the explicit form of the final expression for energy, identical for both subsystems, we convey to the Appendix. Now, we may proceed to the alternative description based on the double-well potential.

Model 2

Let us consider the 1-dimensional Ising model on a ring consisted of single tubulin dimmers located at each site. Hamiltonian of the system of 12 dimmers communicating by nearest

neighbors interaction is given by (we put the constant exchange integral under the sum)

$$H = -\sum_{i=1}^{12} J_i J_{i+1} \qquad (11)$$

where J_i is the projection operator dependent on the curvature of the symmetry transition region designated in our previous papers as Γ (Pietruszka *et al.*, 2012; Pietruszka, 2013) acting on a single site i in the ring. The state of the single site in microtubule ring is given by the state vector $|JM\rangle$ (Pietruszka and Lipowczan, 2013) resembling the total momentum and its projection in case of magnetic systems (Nolting, 2009). $J_i = \{K_s + K_c, K_s - K_c\}_i$, where K_s corresponds to the spherical symmetry and K_c corresponds to the cylindrical one. Hence, the parameters K at a given site (the meaning will be given later) for different symmetries can be added or subtracted. The projection of the curvature – dependent parameter K can be chosen from the following set $M_i = \{K_s + K_c, K_s - K_c, -K_s + K_c, -K_s - K_c\}$. Hence, the explicit single site matrix in energy units is given by

$$\begin{bmatrix} e^{\beta(VK_s+VK_c)^2} & e^{\beta(VK_s+VK_c)(VK_s-VK_c)} & 0 & 0 \\ e^{\beta(VK_s-VK_c)(VK_s+VK_c)} & e^{\beta(VK_s-VK_c)^2} & 0 & 0 \\ 0 & 0 & e^{\beta(-VK_s+VK_c)^2} & e^{\beta(-VK_s+VK_c)(-VK_s-VK_c)} \\ 0 & 0 & e^{\beta(-VK_s-VK_c)(-VK_s+VK_c)} & e^{\beta(-VK_s-VK_c)^2} \end{bmatrix} \qquad (12)$$

where V is the volume of a tubulin dimmer.

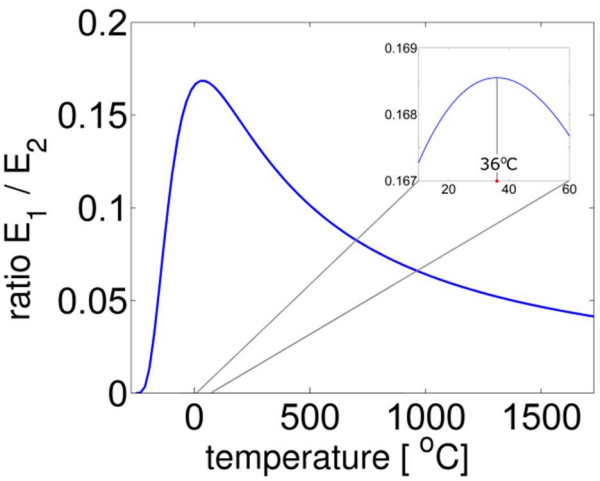

Figure 3. The plot of the ratio of the calculated energy levels in the symmetry frustration scheme in the diagonal base. A clear maximum at physiological temperature 36 – 37 °C exists (inset), for the resolution of 1 K. Simulation parameters read: K_s = 3.99 x 10^{12} Pa and K_c= 3.90 x 10^{12} Pa (data obtained from the scaling considerations ($p_{PT}V_{PT}/T = p_{MT}V_{MT}/T$) with pollen tubes (PTs), Pietruszka at al., 2012). For the assumed radius of the tubuline dimmer r = 6.5 nm, the approximate volume equals V ~ 8.7 x 10^{-24} m^3.

Let us consider the first block 2 x 2 of the matrix. Because K_s and K_c are associated with stress/strain properties resulting from the curvature of the actual symmetry chosen by the system, we may assume $K_i = \sigma_i V$, where σ denotes radial stress in a tubulin dimmer, and V is the conserved volume. The symmetry (curvature) – dependent interaction strengths K_i (energy units) are determined with the aid of the radial stress on the surface of the tubulin (Pietruszka *et al.*, 2012).

The eigenstates and energies are calculated and the ratio of the two energy levels is plotted as a function of temperature in Figure 3. It is worth noting that the maximum appears at physiological temperature of T= (273.16 + 36) K or ~ 36 in Celsius scale. At the peak value of the energy ratio we have

$$|\Phi_1\rangle = 0.38\,|K_s\rangle - 0.92\,|K_c\rangle$$
$$|\Phi_2\rangle = -0.92\,|K_s\rangle - 0.38\,|K_c\rangle \qquad (13)$$

where the $|K_s\rangle$ and $|K_c\rangle$ states represent curvature dependence at a given symmetry.

Conclusions

Since the advent of quantum computing by Feynman (1982), Deutsch (1985) and others, many interesting proposals have been put forward (Piotrowski and Sladkowski, 2003; Miakisz *et al.*, 2006; Pawela and Sladkowski, 2013). Penrose (1989; 1997) and Hameroff and Penrose (2003) considered MTs as a possible 'localization' of memory, and a place relevant for quantum computation (in the framework of string theory), which approach was disproved by Tegmark (2000), who discussed system-observer-environment triad for fundamental reasons (ultra-short decoherence times). In contrast, in the system discussed by us, the

correlated state of the system can be preserved for the characteristic time scales of conformational changes in the system. In addition, the collective state of 13 interacting tubulin dimmers on a ring (2^{13} states) can in fact perform energetically favorable random corrections over more common 12 (2^{12} states) tubulin objects in MTs (checksum computing), however as yet the source of this interaction is unknown. Nonetheless, the comparison of the quantum Model 1 against semi-quantum Model 2, where the interesting maximum naturally appears at physiological temperatures, give hope that the new kind of semi-classical interaction leading to enforced oscillations (and hence calculations) in this doubly frustrated system (MT) may be responsible for performing basic operations and data storage in our neuronal system.

Appendix

The explicit expression for the subsystems' energy reads (Model 1):

$$\langle E \rangle = T^2 \frac{JN \cosh\left(\frac{JT}{k_B}\right)^{N-1} \sinh\left(\frac{JT}{k_B}\right) + JN \cosh\left(\frac{JT}{k_B}\right) \sinh\left(\frac{JT}{k_B}\right)^{N-1}}{\cosh\left(\frac{JT}{k_B}\right)^{N} + \sinh\left(\frac{JT}{k_B}\right)^{N}}$$

where N is a number of sites (tubulin dimmers) in a ring and J is the inter-tubulin interaction constant.

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