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Information processing in brain microtubules

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Abstract

Models of the mind are based on the idea that neuron microtubules can perform computation. From this point of view, information processing is the fundamental issue for understanding the brain mechanisms that produce consciousness. The cytoskeleton polymers could store and process information through their dynamic coupling mediated by mechanical energy. We analyze the problem of information transfer and storage in brain microtubules, considering them as a communication channel. We discuss the implications of assuming that consciousness is generated by the subneuronal process.

Keywords: Microtubules; Computation; Consciousness; Subneuronal process

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1. Introduction

In recent years, many papers have addressed the problem of developing a theory of mind (Hagan et al., 2002; Hameroff and Penrose, 1996; Hameroff et al., 1998; Jibu et al., 1994; Rosa and Faber, 2004; Tuszyński et al., 1997, 1998, 1995; Tegmark, 2000; Penrose, 1989, 1994; Eccles, 1994; Watterson, 1996). Penrose and Hameroff developed a quantum model of the mind considering the cytoskeleton of neuron cells as the principal component that produces states of mind or consciousness (Hameroff and Penrose, 1996; Hameroff et al., 1998). In their model, the microtubules (MTs) perform a kind of quantum computation through the tubulins. Tubulins are proteins which form the walls of the MTs. They claim that the tubulins work like a cellular automata performing that kind of computation. In this way, the walls of the MT could be able to store and process information by using combinations of the two possible states (α and β) of the tubulins. The MT interior works as an electromagnetic wave guide, filled with water in an organized collective state, transmitting information through the brain. A gelatinous state of water in brain cells, which was observed by (Watterson, 1996), could boost these communication effects.

Using a different approach, Tuszyński et al. (1997, 1998, 1995) model the biophysical aspects of the MTs considering the following questions: What kind of computing do microtubules perform? How does a mi-

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crotubule store and process information? In order to analyze these questions they use a classical approach, studying the basic physical properties of the MTs as interacting electric dipoles.

According to Tuszyński et al. (1997, 1998, 1995), Satarić et al. (1993), Brown and Tuszyński (1997), Pokorný and Ming Wu (1998) and Kandel et al. (1991) each tubulin has an electric dipole moment $\overrightarrow{p}$ due to an asymmetric charge distribution. The microtubule is thus a lattice of oriented dipoles that can be in random phase, ferroelectric (parallel-aligned) and an intermediate weakly ferroelectric phase like a spin-glass phase. It is natural to consider the electric field of each tubulin as the information transport medium.

Therefore, the tubulin dimers would be considered the information unit in the brain and the MT subprocessors of the neuron cells. Therefore, to know how MTs process information and allow communication inside the brain is a fundamental point to understand the mind functions.

In this work, we derive some results which were not explicitly obtained in Tuszyński et al. (1997, 1998, 1995) and extend the ideas introduced by Tuszyński et al. (1997) and Pokorný and Ming Wu (1998) using the point of view of the information theory. We analyze the problem of information transfer and storage in brain microtubules, considering them as a communication channel. The electric field is the mediator of each communicator entity. We discuss the implications of assuming that the consciousness is generated by the microtubules as sub-neuronal processors.

2. Biophysical aspects of the microtubules

The cytoskeleton has a dynamical structure. It reorganizes continually as the cells change their shape, divide, and respond to their environment. The cytoskeleton is composed of intermediate filaments, actin filaments (or microfilaments), and microtubules. The filaments and the microtubules are mutually connected and form a three-dimensional network in the cell. There are many papers (Tuszyński et al., 1997, 1998, 1995) showing that the cytoskeleton is the main component which organizes the cell, mediates transport of molecules, organelles, and synaptic vesicles. The cytoskeleton possibly receives signals from the cellular environment mediated by the membrane of proteins and participates in signal transmission to the neighborhood of the cell (Pokorný and Ming Wu, 1998; Kandel et al., 1991).

Microtubules are hollow cylinders whose exterior surface cross-section diameter measures 25 nm with 13 arrays of protein dimers (tubulins). The interior of the cylinder contains ordered water molecules which implies the existence of an electric dipole moment and an electric field. The MTs represent a dipole due to individual dipolar charges of each tubulin monomer. The microtubule dipole produces a fast growth at the plus end towards the cell periphery and a slow growth at the minus end. The MT polarity is closely connected with its functional behavior which can be regulated by phosphorylation and dephosphorylation of microtubule-associated protein (MAP) (Tuszyński et al., 1997, 1998, 1995; Satarić et al., 1993; Brown and Tuszyński, 1997; Pokorný and Ming Wu, 1998; Kandel et al., 1991).

Guanosine triphosphate molecules (GTP) are bound to both tubulins in the heterodimer. After polymerization, when the heterodimer is attached to the microtubule, the GTP bound to the β-tubulin is hydrolyzed to the guanosine disphosphate (GDP). On the other hand, the GTP molecule of the α-tubulin is not hydrolyzed. The microtubules present a calm dynamic instability which are their principal feature (Tuszyński et al., 1997, 1998, 1995).

Many models of conformation (and polarity energy) of the microtubular protofilament were developed. These models describe the behavior of the pulses generated by the free energy in the GTP hydrolysis. The pulses propagate along the MTs using the elastic coupling or the electric field propagation between tubulin dimers (Rosa and Faber, 2004; Tuszyński et al., 1997, 1998, 1995; Satarić et al., 1993; Brown and Tuszyński, 1997). The overall effect of the surrounding dipoles on a site n can be modelled by the double-well quartic potential (Tuszyński et al., 1997, 1998)

$$V(u_n) = \frac{a}{2}u_n^2 + \frac{b}{4}u_n^4, \tag{1}$$

where u_n represents the dimer conformational change on the nth protofilament axis coupled to the dipole moment. a depends on the temperature $a = \overline{a}(T - T_c)$, T_c is the critical temperature and b is a positive parameter that does not depend on the temperature (Tuszyński et al., 1997, 1995). In Fig. 1, we plot the effective potential in terms of u_n.

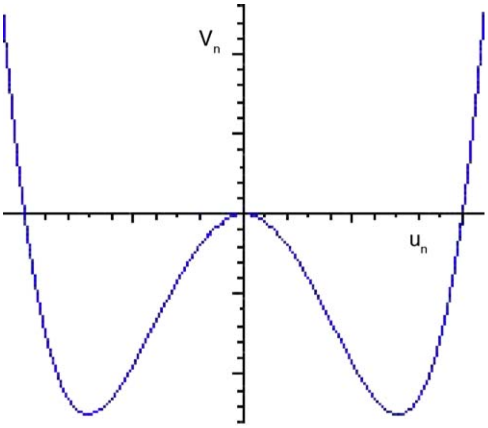

Fig. 1. Double well quartic potential model with a potential barrier $|A^2/2B|$.

In the next section, we reconsider this model taking into account the information theory, which allows us to calculate the storage and transference of information along the MT. We assume that the information is mediated by the electric field and propagates in the cellular medium. This propagation of energy can provide a communication channel.

3. Communication channels

The Shannon entropy of a random variable X is defined by (Nielsen and Chuang, 2000):

$$\langle I(X)\rangle = -\sum_i p(x_i)\log p(x_i), \tag{2}$$

where $p(x_i)$ is the probability of the outcome x_i. This definition describes the amount of physical resources required on average to store the information being produced by a source, in such a way that at a later time the information can be restored completely.

If we want to send a message X through a noisy channel, that message might be subjected to a loss of information. To correlate a sent message X with a received message Y we have to calculate the *mutual information* $I(X:Y)$ between them. The *mutual information* concept gives us how much knowledge we obtain from a message X given that we have received Y. It is defined by (Nielsen and Chuang, 2000; Preskill, 1998)

$$\begin{aligned}\langle I(X:Y)\rangle &= \langle I(X)\rangle - \langle I(X|Y)\rangle\\ &= \langle I(Y)\rangle - \langle I(Y|X)\rangle\end{aligned} \tag{3}$$

and

$$\langle I(X|Y)\rangle = -\sum_i\sum_k p(x_i, y_k)\log p(x_i|y_k), \tag{4}$$

where $p(x_i|y_k) = p(y_k, x_i)/p(y_k)$.

Nevertheless, by using a binary code to send a message M, compressed by procedure C that minimizes the use of bits in that codification, any receiver of M, using a decoding procedure D, must to be able to get all information associated to M.

Consider a symmetric memoryless channel[1] N with a binary input A_{in} and a binary output A_{out}. For n uses of the channel, the procedure C encodes the input message M such that $C^n:\{1,\ldots,2^{nR}\}\rightarrow A_{\text{in}}$ and D decodes the output such that $D^n:\{1,\ldots,2^{nR}\}\rightarrow A_{\text{out}}$, where R is the *rate of the code* (the number of data bits carried per bit transmitted) (Preskill, 1998). Therefore, if X is the encoded message M through the procedure C, Y the received message, and D is the decoding procedure for Y, then the probability of error is defined by

$$p(C^n\cdot D^n) = \max_M p(D^n(Y)\neq M|X = C^n(M)). \tag{5}$$

The principal problem of the information theory is to determine the maximum rate R for a reliable communication through a channel. When $p(C^n\cdot D^n)\rightarrow 0$ for $n\rightarrow\infty$, the rate R is said achievable. According to Shannon's theorem, given a noisy channel N, its capacity $\Omega(N)$ is defined to be the supremum over all achievable rates for this channel. That is,

$$\Omega(N) = \max_{p(x_i)}(\langle I(X:Y)\rangle), \tag{6}$$

where the maximum is taken over all input distributions $p(x_i)$ of the random variable X, for one use of the channel, and Y is the corresponding induced random variable at the output of the channel.

Eq. (6) allows us to calculate the transference of information among many physical systems. The transfer of energy may include the transfer of electrostatic energy, energy of low frequency oscillating fields, energy of light, energy of vibrations, etc. Molecules can contain energy in the chemical bonds, in the excited

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[1] The memoryless channel is the one that acts in the same way every time it is used, and different uses are independent of one another.

electron states, in the conformation states, etc. A common measure of the interaction leading to cooperative behaviour is the information transference. The electromagnetic field can transfer information through the environment among the systems like a communication channel.

4. Information processing in microtubules

Many features of the cytoskeleton support the idea that microtubules can perform computation and store information. According to Tuszyński et al. (1997), the charge separation of the MTs is wide enough to store information. Due to its dynamical coupling the information can be stored as mechanical energy and chemical events.

Changes in the opposite direction can be favorable to the SG phase over the F-phase. This change could switch from the growth mode to operational behavior. Our focus is this operational mode. Information processing is addressed by Hagan et al. (2002), Hameroff and Penrose (1996), Hameroff et al. (1998), Jibu et al. (1994) and Rosa and Faber (2004) considering the highly specialized nature of the functional proteins on the microtubules.

4.1. Microtubules as an information storehouse

The tubulins form a dipole moment net and therefore are sensitive to external electric fields. Some papers use physical models such as spin net to describe the behavior of the dipole moment net (Tuszyński et al., 1997, 1998; Dotsenko, 1994). According to those models, all tubulins are oriented to the same direction at low temperature ($\sim 200\,\mathrm{K}$) and the units of the system are organized (Fig. 2). In this case, the system is in the ferroeletric phase (F). At high temperatures ($\sim 400\,\mathrm{K}$), the system is in the paraelectric phase (P) and the polarity of the tubulins are completely disorganized (Fig. 3).

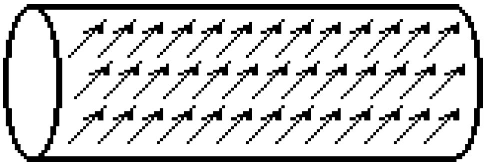

Fig. 2. Schematic picture for F-phase.

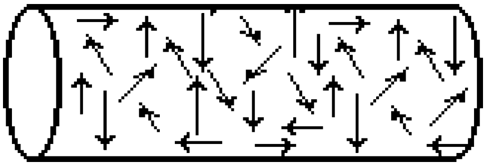

Fig. 3. Schematic picture for P-phase.

The key point is to know whether is there a phase transition from the disorder (F-phase) to order (P-phase). After this transition a new state can emerge which is known as spin-glass phase (SG) (Fig. 4). This transition is determined by the critical temperature T_c, which is estimated by some theoretical models (Tuszyński et al., 1998, 1995). Ref. Tuszyński et al. (1995) proposed a model independent of external electric fields, which is given by

$$T_c = T_c^0 \left(\frac{p}{p_0}\right)^2 \left(\frac{\epsilon_0}{\epsilon}\right), \tag{7}$$

where ϵ is the relative permittivity of the tubulin in cytosol and p is the dipole strength of the conformational states of the tubulin. The constants ϵ_0, p_0, and T_c^0 are parameters of the model estimated as 10,192 Debye and 310 K, respectively.

Eq. (7) shows the scale of the transition temperature in a MT. The main result of this model is that the MT can exist in an ordered state at the physiological temperature without an external electrical field (Tuszyński et al., 1995). Tuszyński et al. estimated that, depending on the structural disposition of the tubulins along the MT, the value of T_c can be around 300 K which is near to the human body temperature (Tuszyński et al., 1998, 1995).

We analyze the propagation of information along MTs considering the above phases with $T_c^0 = 310\,\mathrm{K}$. Assuming an energy approximation dependent on the mean polarity described by the Landau theory of phase transitions, the total energy is given by (Tuszyński et al., 1997; Pokorný and Ming Wu, 1998; Haken, 1990)

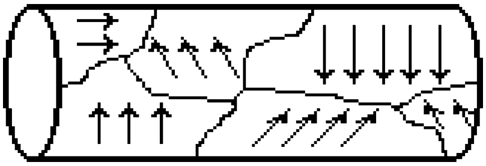

Fig. 4. Schematic picture for SG-phase.

$$E=\left(\frac{a}{2}\wp^2+\frac{b}{4}\wp^4\right)N_0, \tag{8}$$

where $\wp$ represents the continuous variable for the mean polarization at each site and N_0 is the total number of sites. The parameter a depends linearly on the temperature $a=\bar{a}(T-T_c)$, where $200\,\mathrm{K}<T_c<400\,\mathrm{K}$ and $b>0$ (Tuszyński et al., 1997, 1998, 1995). E will be minimized by $\wp=0$ for $T>T_c$ and by $\wp=\pm\sqrt{-\bar{a}(T-T_c)/b}$ for $T<T_c$. We use the Boltzmann distribution $g(\wp)$ to weight the energy distribution as a function of the mean polarity

$$g(\wp)=Z^{-1}\exp(-\beta E), \tag{9}$$

where $\beta^{-1}=kT$, Z is the normalization, and k is the Boltzmann constant. Substituting (9) into (8) we get

$$g(\wp)=Z^{-1}\exp\left(\frac{\bar{a}(T-T_c)}{2kT}\wp^2+\frac{b}{4kT}\wp^4\right). \tag{10}$$

Because $\wp$ is a continuous variable, we need to use the continuous counterpart of (2) in order to calculate the information mean value of the system. Replacing $p(x)$ by $g(\wp)$ in (2), we obtain the following expression for the information storage capacity:

$$\langle I\rangle=\frac{\ln Z}{\ln 2}-\frac{\bar{a}(T-T_c)}{2kT\ln 2}\langle\wp^2\rangle-\frac{b}{4kT\ln 2}\langle\wp^4\rangle. \tag{11}$$

The average of $\wp$ over the whole MT, considering all domains, is obtained from

$$\langle\wp^n\rangle=\int_{-\infty}^{\infty}g(\wp)\wp^n\,\mathrm{d}\wp. \tag{12}$$

After substituting (7) into (11), we plot the information storage capacity against the temperature and p^2/ϵ for some values of $\bar{a}$ and b. Using these plots we estimate the best value of p^2/ϵ when T_c is around 310 K (Figs. 5–7).

These graphs corroborate with the results of Tuszyński et al. (1997, 1995), which show that, at the physiological temperature with $p^2/\epsilon\sim 3600$ Debye^2, we can have a mode of information storage in MTs. This is the most important feature for finding another subunit of information processing inside the brain. It could show us new perspectives for cognitive aspects.

However, according to these graphs, the maximum information storage is obtained at the spin-glass phase, therefore we need to make some assumptions. In this phase, there are domains with many energy levels which can store information. The interaction among the domains, due to the electric field generated by the oscillating dipoles, must be considered. This electric field is emitted to the neighborhood area producing many channels among the domains in MT.

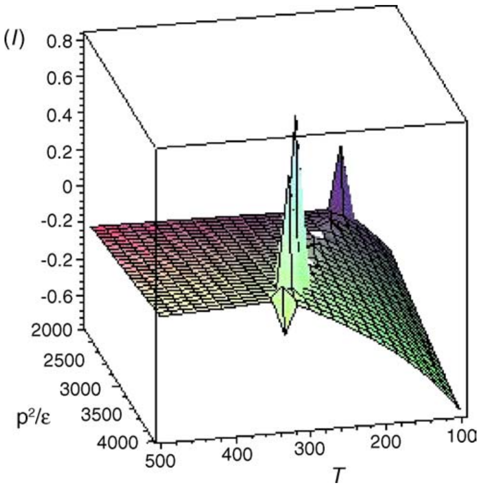

Fig. 5. Information storage capacity of MT when $\bar{a}=0.5\times 10^{-5}$, $b=0.5$.

4.2. Microtubules as a communication channel

Given the capacity of information storage of MTs, the issue now is to know whether there exist some kind of information processing on them. To study any kind of processing, it is necessary to describe how the infor-

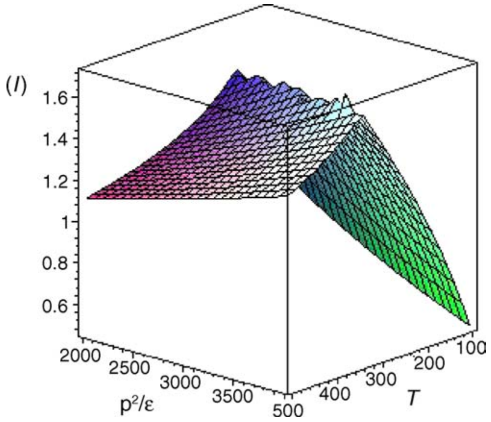

Fig. 6. Information storage capacity of MT when $\bar{a}=0.5\times 10^{-6}$, $b=0.5\times 10^{-3}$.

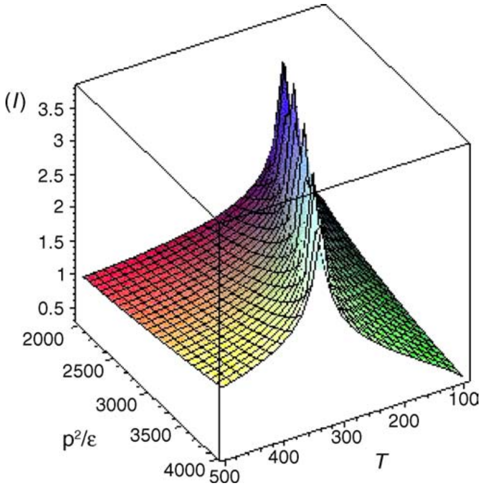

Fig. 7. Information storage capacity of MT when $\bar{a} = 0.5 \times 10^{-6}$, $b = 0.5 \times 10^{-8}$.

mation is stored in the MT walls, and how the information propagates along the MT. We learned that the SG phase has the maximum capacity of information storage. Therefore, we will restrict to this phase in order to describe the communication among the domains. Here, we are assuming that the electric field generated by the MT dipoles is the main mediator which allows the communication among the domains.

The graphs of the previous section show that near to the critical temperature T_c the information capacity has the maximum capacity of storage. Following Tuszyński et al. (1997), we assume in this phase a partition of lattices by local domains (see Fig. 4). Therefore, the previous prescription is valid only on the local domains. In this way, a domain j has a polarization $\wp_j$ with probability $g_j(\wp_j)$. If we make these assumptions, the total probability is given by

$$g = \prod_{j=1}^{r} g_j(\wp_j), \tag{13}$$

where r is the number of domains (Tuszyński et al., 1997).

As a consequence of (13) we have for the spin-glass phase

$$\langle I \rangle = \sum_j \langle I_j \rangle \tag{14}$$

with j in the set of domains.

Now, we need to calculate the amount of information transferred through the channels among the domains (Tuszyński et al., 1997; Pokorný and Ming Wu, 1998). The domains will communicate only if they interact. If we consider two domains, the communication is mediated by the electrical interaction between them. In order, to calculate the capacity of this communication channel, we use the mutual information concept.

From (6), we know how much information is transferred from an event x_k (of an ensemble X) to another event y_j (of an ensemble Y). The term $p(x_k|y_j)$ imposes the dependence among the systems. Assuming a Boltzmann distribution, we want to know the dependence between the *domain k*, with polarization $\wp_k$, and the *domain j*, with polarization $\wp_j$. This dependence is described by the distribution $g(\wp_k|\wp_j)$ which imposes a connection between the domains. Following Pokorný and Ming Wu (1998), we will assume that the output energy is expressed as a function of the electric field energy and of the mean polarization energy. Therefore, in the thermodynamic equilibrium, we have the average of the output energy E^{out} of a *domain j* as

$$\langle E_j^{\text{out}} \rangle = \langle E_j^{\text{signal}} \rangle = \langle E_j^{\text{flow}} \rangle + \langle E_j^{\text{noisy}} \rangle, \tag{15}$$

where E_j^{signal} is the energy of the coherent signal, E_j^{noisy} the noisy energy, and E_j^{flow} is the energy of the flow along the system. The energy E_j^{flow} is responsible for the interaction between the domains. Therefore, supposing that the *domain j* emits E_j^{flow}, we can express the dependence of a *domain k* as

$$g(\wp_k|\wp_j) = Z^{-1} \exp[-\beta(E_k + E_j^{\text{flow}} + E_j^{\text{noise}})], \tag{16}$$

where E_k is the correspondent energy of the *domain k*.

The information entropy depends on the amount of energy in the system and on the noisy energy E_j^{noisy}. The noisy energy is a function of the temperature of noise T_n (which is taken around 400 K), and it is given by (Pokorný and Ming Wu, 1998)

$$\langle E_j^{\text{noisy}}(T_n) \rangle = Z^{-1} \exp(A\langle \wp_j^2 \rangle + B\langle \wp_j^4 \rangle), \tag{17}$$

where $A = a(T_n - T_c)/2kT_n$ and $B = b/4kT_n$.

To evaluate the communication channel capacity, each domain is approximated by a unique dipole. The information transference will be mediated by a radiation of the electric field in the equatorial region of an oscillating dipole.

Using the complex Poynting vector and taking the real part, we get an expression for the mean value of the energy E_j^{flow}. The amount of energy absorbed by the oscillating charged units depends directly on their effective cross-section and on the intensity of the flow of energy. We can calculate it considering the radiation flow of energy through the cross-section D over a spherical surface of radius R, where D is a rectangle whose sides are x and z. Hence, the expression for the flow of energy towards the dipole axis is given by

$$\langle E_j^{\text{flow}} \rangle = 2\pi^2 S_j \arcsin \frac{x}{2R_x} \left[\frac{z}{2R_z} - \frac{1}{3} \left(\frac{z}{2R_z} \right)^3 \right], \tag{18}$$

where $S_j = \wp_j^2 \sqrt{\eta^3 \varepsilon \nu_j^4}$, ν_j the dipole frequency, ε the permitivity, η the permeability of the medium, R_x and R_z are the perpendicular distances from the dipole to the z and x sides, respectively (Pokorný and Ming Wu, 1998).

Using (3) and (4), and the previous relations, we can derive an expression for the capacity of communication between two domains. The channel between two domains j and k will be denoted by N_{jk}, hence,

$$\Omega(N_{jk}) = \langle I(E_k) \rangle - \langle I(E_k | E_j) \rangle, \tag{19}$$

where $\langle I(E_k) \rangle$ is given by an expression similar to (11). The conditional information $\langle I(E_k | E_j) \rangle$, for a specific polarity $\wp_j$, can be calculated by a continuous version of (4), that is,

$$\langle I(E_k | E_j) \rangle = \frac{\ln Z}{\ln 2} - \beta \int g(\wp_k, \wp_j)(E_k + E_j^{\text{signal}})\, \mathrm{d}\wp_k. \tag{20}$$

Through those calculations we can infer that there is an inter-dependence among the domains in the SG phase. Each domain communicates to other domain the value of its polarity. It transforms the MT in a net of communication units (in this case the units are the domains—see Fig. 8). Besides, as each domain has a particular polarity, in the context of the information theory, we can interpret each polarity representing a type of symbol. It would build a kind of alphabet along the whole MT, where each domain represents a letter. However, since the polarity $\wp$ is a continuous variable, we have a kind of continuous alphabet.

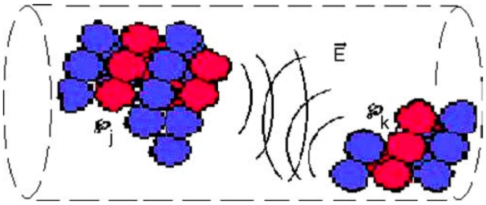

Fig. 8. A representation of the communication between domains accomplished by the electromagnetic field on the MT.

Considering the case $x = z$, we plot the capacity of information transference between each domain as a function of the distance and frequency (Figs. 9–11).

The graphs show that the best conditions to have a communication among the domains are at the

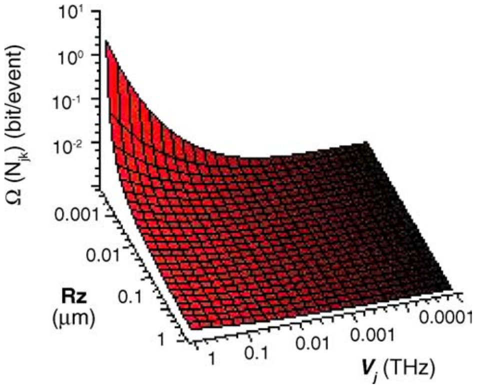

Fig. 9. Communication capacity: frequency $\upsilon_j \times$ distance R_z when $T \sim 300K$.

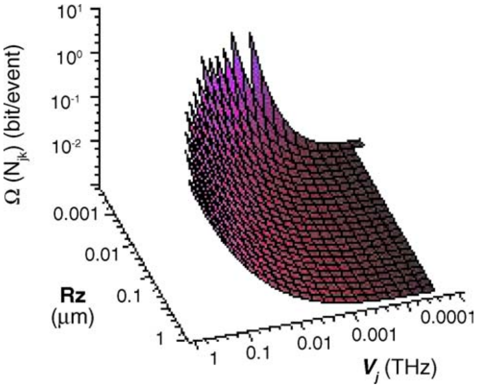

Fig. 10. Communication capacity: frequency $\upsilon_j \times$ distance R_z when $T \sim 100K$.

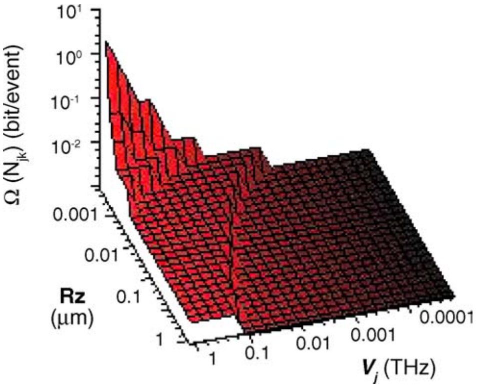

Fig. 11. Communication capacity: frequency $\upsilon_j \times$ distance R_z when $T \sim 600K$.

physiological temperature, with frequency of the conformational changes of the tubulin dimer protein around to $10^{12}\,\mathrm{s}^{-1}$. The relative permitivity and permeability in the neighborhood of the oscillating units is assumed to be 1 (Satarić et al., 1993; Brown and Tuszyński, 1997; Pokorný and Ming Wu, 1998). The distance z between the protein molecules is adopted to be around to 1–0.1 μm. At 300 K the information transference is suppressed over a distance R_z equal to 0.1 μm, and frequency around to 0.1 THz (Fig. 9). At a distance smaller than 0.1 μm the communication does not depend on the frequency. Finally, at a distance greater than 0.1 μm the high frequency of the electric field plays a fundamental role in the transference of information. For the other regimes of temperature, the system is not in the SG-phase and the graphs show the loss in performance (Figs. 10 and 11).

According to Fröhlich (1986), biological molecules with dipolar vibrational activity could manifest a quantum coherent mode. Those systems could have some isolating effect from thermal environments. The frequency range of that quantum mode (also known as Fröhlich systems), is around 10^{11}–$10^{12}\,\mathrm{s}^{-1}$ (Hagan et al., 2002; Jibu et al., 1994). Therefore, the high frequency regimes obtained above, besides providing a communication along the MT, and also maintain some quantum coherent regime.[2]

5. Conclusions

This work confirms the results of Hagan et al. (2002), Hameroff and Penrose (1996), Hameroff et al. (1998), Jibu et al. (1994), Rosa and Faber (2004) and Tuszyński et al. (1997, 1998, 1995) which consider microtubules as a classical subneuronal information processor. Using information theory, we calculate the information capacity of the MTs, and using the models of Hagan et al. (2002), Hameroff and Penrose (1996), Hameroff et al. (1998), Jibu et al. (1994), Rosa and Faber (2004), Tuszyński et al. (1997, 1998, 1995) we estimate that the favorable conditions for storage and information processing are found at temperatures close to the human body. These results corroborate the possibility of communication among the domains (where each energy level corresponds to some kind of symbol). This communication is mediated by the dipole electric field, and this interaction is necessary to describe some processing or computing on MT. Through this communication, each domain (or symbol) presents some dependence with another. Therefore, there are storage as well as processing of information associated to the dimers. Besides, from the information theory point of view, the formation of domains creates some redundancy for storage or representation of these symbols. This redundancy is important for error correction and information protection. However, some points still need further investigations. To mention at least two: (1) the direction of the propagation of the information under the influence of the environment is an interesting point to be analyzed, (2) according to (Hagan et al., 2002; Hameroff and Penrose, 1996; Hameroff et al., 1998; Jibu et al., 1994; Rosa and Faber, 2004) there is some water ordination inside MTs which could increase the quantum processes in MTs. These points deserve to be analyzed using the information theory point of view.

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[2] Some papers show that the tubulin vibration frequency is in this regime (Pokorný and Ming Wu, 1998; Haken, 1990).

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