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Endogenous Electric Field and Organization of Living Matter

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Microtubules in eucaryotic cells form electrically polar structures, which satisfy conditions for excitation, energy condensation, and generation of endogenous electromagnetic field with strong electric near zone component. Large energy supply connected with continuous rebuilding of the microtubular structure and very likely with activity of motor proteins, and interfacial slip layer at the microtubule surface protecting vibrations in microtubules from viscous damping of the cytosol are important conditions for excitation and formation of coherent state. Generated electric field can exert a driving force for directed transport. The Wiener-Lévy process with symmetry breaking is used to describe motion of molecules and charges. Motion of molecules with diameter 1 and 5 nm at distances up to 50 nm is analysed. Transport driven by the electric field with inseparable thermal component has greater probability to reach the target than transport by thermal motion itself. Transport of electrons display similar dependence. Probability of any action depending on the ratio of the random and of the deterministic component of motion should be high enough to provide small number of errors but sufficiently low to comply with requirements for evolutionary changes.

Keywords Electromagnetic fields in biological systems; Excitation of coherent states; Microtubules.

Introduction

Organization of biological systems for a long time was understood as organization of the form, that is, morphogenesis, on the basis of chemical processes. A. M. Turing assumed that morphogenesis in living matter is not only a chemical phenomenon, but that physical processes using mechanical and electrical forces are participating in the organization [1]. A fundamentally new concept of the role of physical fields in living matter underlaying its organization was formulated by Fröhlich [2], who postulated existence of long-range quantum mechanical phase correlations and

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that biological systems exhibit relative stability in a way in which some modes of behavior remain very far from thermal equilibrium although from an atomic point of view the majority of the degrees of freedom behave like being close to thermal equilibrium. Excited longitudinal oscillations were assumed to play a role as stabilizing modes. Fröhlich's theory is based on extraordinary electrical polarity of living matter, on its nonlinear properties, and on continuous metabolic energy supply shifting important parts (modes) of the system far from thermodynamic equilibrium. Frauenfelder et al. [3] claimed that in biological physics the force is well known; It is the electromagnetic interaction. Forces of large scale electromagnetic fields are considered to mediate interactions, transfer of energy, and transmission of signals. Liboff [4] postulated essential role of macroscopic electromagnetic fields in living matter.

Our understanding of organization of biological systems includes 3 inseparable components: organization of morphological structures—a framework of each system; organization of chemical reactions—interactions of macromolecules and polymer structures and chains of reactions between them; and organization of physical fields—generation of electromagnetic fields (with dominant electrical component), important for creation of the space-time dynamic functional order. Hierarchical organization of biological systems suggests that biological electromagnetic fields might have a hierarchical structure, too.

The structures satisfying the requirements for generation of a coherent electromagnetic field must form electrically polar system (the majority of proteins are polar), exhibit spectral energy transfer by nonlinear intrinsic properties or as a result of interaction with the ambient medium, and have sufficient energy supply from metabolic sources. The microtubular structure, the main organizer of the cytoskeleton in eucaryotic cells, seems to satisfy the conditions for generation of the electromagnetic field with strong electric component [5–8]. It also is assumed that cytoskeleton including actin filaments and microtubules constitute backbone for wave propagation [9]. Electric fields can exert forces on charges, on dipoles as well as on neutral particles through dielectrophoretic effect. The electric field may be static, quasistatic, and oscillating, with amplitude that may be large if the vibrations generating the field are excited sufficiently. Attraction of small dielectric particles to living cells was attributed to the dielectrophoretic effect of the oscillating field around cells [10]. Communication between some cells may be mediated by the electromagnetic field in the near infrared region [11]. Coherent vibrations at 15 and 77 cm^{-1} [12] and coherent femtosecond processes in proteins [13, 14] were measured. Coherent oscillations of plasma membrane were measured in the frequency band 0.8–2 kHz [15].

Mass and charge transport in living matter conditions biological activity. Directed transport of molecules and charges (e.g. along microtubules, in the cytosol, and electron's in protein complexes) plays important role in organization [16–18]. Transport along microtubules on the cell scale distance is provided by the activity of motor proteins. Motor proteins take energy for their motion from adenosine triphosphate (ATP). Directed transport of molecules and reaction components between various compartments in cytoplasm in the space among microtubules, active transport across plasma and organelles membranes, and transport of electrons may depend on the electric field. Electrons can be carried by small diffusible molecules or transported along the molecular chains in proteins and protein complexes. The proteins and DNA have to a certain extend quasiperiodic or at least

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correlated structures. Correlation in DNA is analyzed and discussed by [19–23]. Wave functions in periodic, quasiperiodic, and random lattices were analyzed by Huang [24]. Motion of electrons may be similar to that in materials with translation symmetry but with the deformed energy band structure, formation of subbands, and with discrete levels.

The essential question of the physical basis of organization of a living cell concerns excitation of cellular structures, generation of the oscillating electromagnetic field, and directed transport of molecules and electrons by the field. Microtubules have quite extraordinary properties connected with their role in organization [6, 7]. The interfacial slip layer at the microtubule surface has exceptional properties too. Correct assessment of excitation and of the energy transfer across the solid-liquid interface cannot be made without introduction of the interfacial slip layer [25, 26]. The role of the deterministic motion in comparison with the thermal motion has to be analyzed for directed transport of molecules and charges [17, 18].

Excitation of Microtubules

Microtubules are hollow cylindrical polymer structures composed of tubulin heterodimers that are strong electric dipoles (their dipole moment is greater than 1000 Debye, i.e., 10^{-26} Cm). A schematic picture of a part of a microtubule is shown in Fig. 1a. The outer diameter of the microtubule is about 25 nm and the inner is about 17 nm. Heterodimers in the α and β states are shown in Fig. 1b (conformation and direction of the electric dipole moment are changed after hydrolysis of GTP—guanosine triphosphate to GDT—guanosine diphosphate in the β tubulin after polymerization). In the α and β states the electron charge is concentrated at the α and the β tubulin, respectively. Each heterodimer binds 18 Ca^{2+} ions. Concentration of ions in the cytosol is about 150 mM of cations and about the same concentration of anions. An ionic charge layer is formed around microtubules. A similar charge layer may be formed inside the microtubule in the cylindrical cavity too. The static electric potential around a microtubule is effectively screened within a distance of

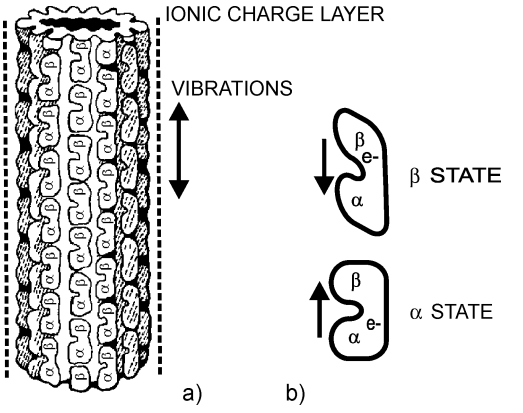


Figure 1. A part of a microtubule with tubulin heterodimers (a) and heterodimers in the α and β states. (b) Conformation change follows hydrolysis of GTP to GDP in the β tubulin after polymerization. The arrows indicate the vectors of the dipole moments [42, 43].

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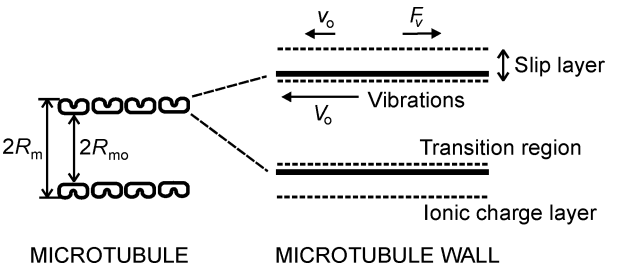


Figure 2. The microtubule wall with slip layers. A slip layer contains the charge layer of ions and the transition layer at the microtubule surface [6, 7].

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two Debye lengths (the Debye length is about 0.8 nm in cytosol). The ionic charge layer schematically shown in Figs. 1 and 2 effectively screens the static electric field around microtubule. Due to hydration the ions are surrounded by bound water molecules up to a distance of about 0.5 nm. Charged proteins of considerably greater size than hydrated ions screen the static potential too. The majority of water molecules in the screening layer around the microtubule surface are not free and the viscous properties of this layer are different from those of cytosol in more distant regions from the microtubule. Some water molecules and ions can penetrate inside the tubulins and behave like an integral part of them. Ions in the cytosol have small mobility and there is a slip in vibrations between the charge layer and the microtubule surface [6–8].

Microtubules have extraordinary elastic properties—extremely large elastic deformability at low stress [27, 28]. When the strain exceeds about 50–60% the microtubule loses its elasticity and flows without limit [28]. Figure 3 shows strain versus stress of the cytoskeleton microtubules, intermediate filaments, and actin filaments. The dynamic shear modulus G determined from the Janmey's measurements is smaller than $5\,Nm^{-2}$. The dynamic shear modulus was measured in a medium corresponding to cytosol including concentration of ions [28, 29]. The

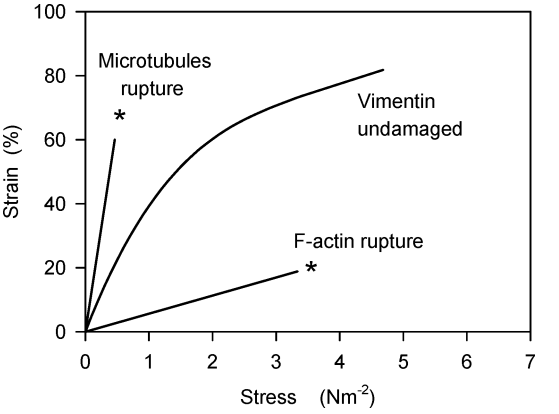


Figure 3. Strain as a function of stress of vimentin, actin, and tubulin filaments. Microtubules have extraordinary elastic deformability [28].

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interfacial slip layer consists of the microtubule surface layer and of the ions and protein layer at the surface (Fig. 2).

Assessment of interfacial slip layer is not complete without taking into account the whole cytoskeleton structure. C termini of microtubules protruding from the outer surface exhibit strong interaction with the heterodimer surface and with other proteins [30]. Microtubule associated proteins MAP-1 and MAP-2 form sidearms and connect microtubules to actin filaments [31]. Motor proteins and microtubule associated proteins contribute to the separation of the microtubule surface from the cytosol. Effects of the layers of organized water suggested by [32] are assessed in the following discussion.

The interphase and *M* phase structures of microtubules are in Figs. 4a and b. Cytoskeleton is a mutually connected structure subdividing the cytoplasm space into small regions. For a cell with diameter of 10 μm and with 500 microtubules the distance between microtubules at the plasma membrane (a) and in the center of the metaphase plane of the mitotic spindle (b) may be about 1 μm. The distance is much smaller near the centrosomes. Therefore, the oscillating electric field can have effect on a considerable part of cytosol. Dynamic instability (polymerization and depolymerization of microtubules) in the interphase and treadmilling (polymerization from one side and depolymerization from the other side) in the M phase exchange heterodimers with exhausted energy (with GDP in the β tubulin) for energy rich ones. From energy released by hydrolysis 7.1 $kJmol^{-1}$ is stored in the microtubule [33, 34]. Power supplied to a microtubule 1 cm long is about 10^{-14} Wcm^{-1} [6–8]. In the M phase of the cell cycle the rate of exchange of heterodimers is more than one order of magnitude greater than in the interphase and energy supply is correspondingly increased too.

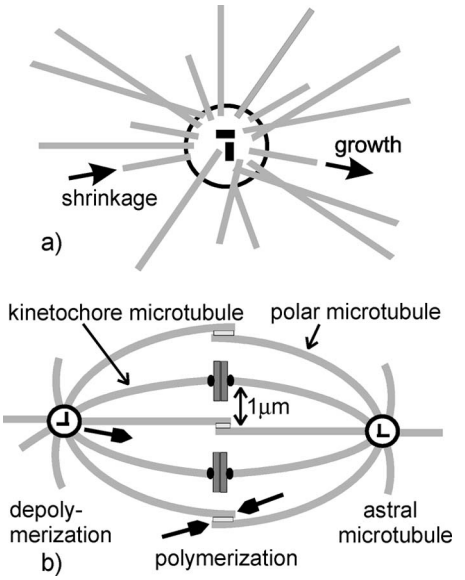


Figure 4. The microtubular structures: a centrosome with attached microtubules in the interphase (a) and the mitotic spindle in the M phase (b). The heterodimers are exchanged by the mechanism of dynamic instability (a) and treadmilling (b). Polymerization and depolymerization are indicated by arrows [6, 7].

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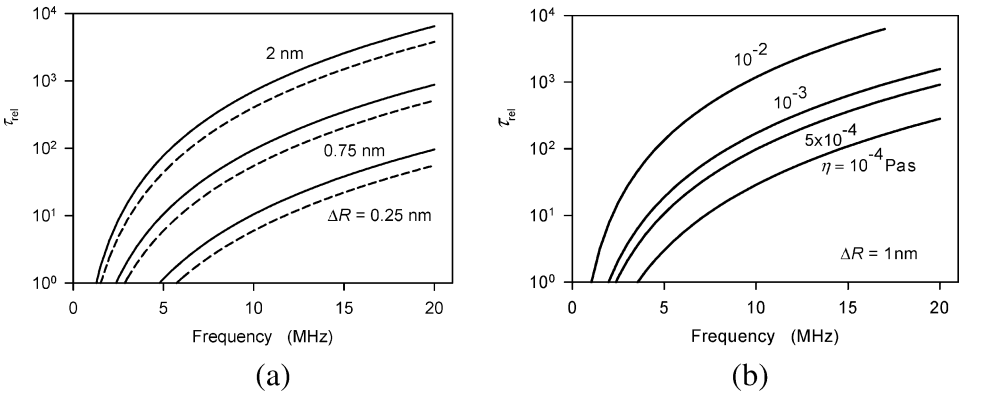


Figure 5. Relative relaxation time, τ_{rel}, as a function of frequency. Shear modulus $G = 5\,\mathrm{Nm}^{-2}$ [6, 7]. a) Effect of thickness ΔR of the slip layer on viscous damping; the dashed and solid lines denote viscosity, η, of the cytosol 0.5×10^{-3} and 10^{-3} Pa s, respectively. b) Effect of viscosity η on damping; thickness ΔR of the slip layer is 1 nm.

The relative relaxation time, τ_{rel} (ratio of the relaxation time of damping caused by viscosity effects to the period of vibrations in microtubule), is shown in Figs. 5a and b as a function of frequency [6, 7]. Parameter is the thickness ΔR (0.25, 0.75, and 2 nm) of the slip layer (η is 0.5×10^{-3} = the dashed lines and 10^{-3} Pa s = the solid lines) (a) and the dynamic viscosity η (10^{-4}, 0.5×10^{-3}, 10^{-3}, and 10^{-2} Pa s) of cytosol ($\Delta R = 1$ nm) (b). The curves in Fig. 5 are evaluated for the greatest value of the shear modulus $G = 5\,\mathrm{Nm}^{-2}$ and amplitude of vibration inside the microtubule 0.5 nm. Power loss at 10 MHz per 1 cm length and $\eta = 5 \times 10^{-4}$ Pa s is $3.3 \times 10^{-14}\,\mathrm{Wcm}^{-1}$ (this value is of the same order of magnitude as the power supplied from hydrolysis of GTP to GDP). Assuming that the shear modulus may be about $1\,\mathrm{Nm}^{-2}$ and thickness of the slip layer greater than 1 nm, then the values of the relative relaxation time are more than 2 orders of magnitude greater.

Transport of Molecules

Motion driven thermally has random character. The thermal motion is isotropic with small random steps. A molecule, which is within a small space with a probability near one in the beginning, may be found with equal probabilities in any region after elapse of sufficiently long time. Symmetry braking condition changes random isotropic motion to random anisotropic motion (in preferential direction). The Wiener-Lévy process [35] also may be used for description of the motion with a symmetry breaking condition [17, 18]. Probability density of the Wiener-Lévy process with a symmetry breaking term in the one-dimensional approximation is given by the relation

$$f(x;t) = \frac{1}{\sqrt{2\pi\alpha t}} \exp\left[-\frac{(x-\gamma)^2}{2\alpha t}\right], \tag{1}$$

where t is time, x is distance, α is variance parameter, and γ is symmetry breaking term which is given by $\gamma = vt$ for deterministic force F. Using the Stokes' law we

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get $v = F/(6\pi\eta r)$ and $\alpha = k_B T/(3\pi\eta r)$, where η is dynamic viscosity, r is radius of a spherical particle, k_B is the Boltzmann constant, and T is temperature in K.

Probability density $f(x; t)$ of finding a molecule at a distance x (in a small region of space along the x axis at time t) is evaluated from Eq. (1). The deterministic force acting on the particle may depend on the intensity of the electric field and on the charge of the particle; on the intensity and on its gradient and on the dipole moment of the particle; and in the case of dielectrophoresis, on the polarizability of the particle. Fig. 6a shows $f(x; t)$ of a molecule with a diameter $\Phi = 5\,\text{nm}$ as a function of distance x for time 0.1, 0.7, and 3 μs. The dashed lines and the full lines denote motion driven thermally and motion driven thermally together with a deterministic force, respectively. The maximum of the $f(x; t)$ curve of the motion driven thermally remains at $x = 0$. The $f(x; t)$ curve spreads with increasing time. Action of the deterministic force shifts the $f(x; t)$ curve along the x axis but it does not change its form. Different shift effects of the forces with different magnitudes after elapsed time 0.5 and 10 μs are shown in Fig. 6b (the dashed and the solid lines holds for the force 0.3 and 1 pN, respectively). The magnitude of the force is decisive for sufficiently high probability to reach the target within given time. The effect of the variance parameter on spreading is given by the dotted curve in Fig. 6b. The solid lines are evaluated for $\alpha_5 = 226\,\text{nm}^2\text{s}^{-1}$ and the dotted line for $\alpha = 3\alpha_5$. Figs. 7a and b show probability P (distribution function) versus time t that a particle will reach the target at a distance 10, 25, and 50 nm. Diameter Φ of the particle is 1 nm and variance parameter $\alpha_1 = 1130\,\text{nm}^2\text{s}^{-1}$ (a) and $\Phi = 5\,\text{nm}$ and $\alpha = \alpha_5$ (b). The dashed and the solid lines are evaluated for the thermal motion and for motion driven by a deterministic force (0.1 and 1 pN) together with thermal one, respectively. The dotted lines are determined for $\alpha = 3\alpha_1$ (a) and $\alpha = 3\alpha_5$ (b). Increase of random component of motion caused e.g. by external disturbances changes probability of directed motion. In the range $0.5 < P \leq 1$ the P values are smaller for greater α that those for smaller α. External disturbances can decrease probability of required action.

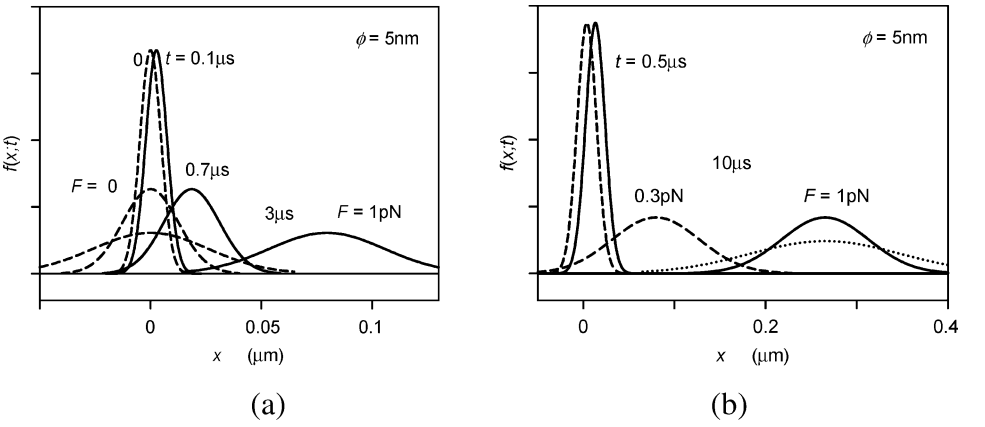


Figure 6. Probabilty density $f(x; t)$ as a function of distance x. a) Dependence of spreading on time; the dashed and solid lines denote thermal motion without any force and with a deterministic force, respectively. b) Effect of different forces on shift of the $f(x; t)$ curve.

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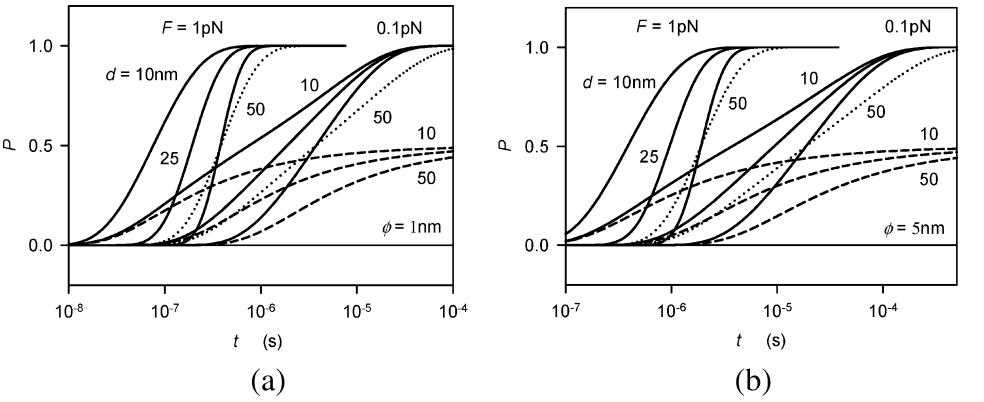


Figure 7. Motion of mass particles. Distribution function P as a function of time, t. The dashed and solid lines are used for thermal motion and for motion driven by deterministic force together with thermal motion, respectively. Force, F, is 0.1 and 1 pN and distance d is 10, 25, and 50 nm. Diameter, Φ, of the spherical molecule is 1 (a) and 5 nm (b).

Transport of Electrons

The molecular chains of proteins and DNA in living matter display quasitranslation symmetry or correlation of the potential profiles along the chain. The energy band structure may be similar to that of solids with perfectly periodic lattice but with the conduction band split into subbands and discrete levels. Generally, the greater disturbance of the perfect translation symmetry, the greater deformation of the band structure. Electron transport may be described by transmission coefficients for DNA molecules [36]. Electron transport with donor-acceptor tunneling and hopping is assumed to exist in periodic nucleotide base stacks [37]. Potential profile properties of the polypeptide chains in proteins depend on the amino acid sequence (on the primary structure). In proteins the position of the C_α atom is a position of disturbances in the periodicity of the potential profile due to different amino acid residua. Different conformations of the polypeptide chain (such as α helix or β sheet) can inscribe their influence into the band structure, too. We will assume that disturbances of translation symmetry and of the energy band structure are not great and that the Bloch-like electronic states can exist. Besides the assumption that the Wiener-Lévy process describes the thermal and the deterministic motion we will assume that the Bloch theorem may be used in its standard form [38]. The variance parameter $\alpha = s^2/\Delta t$, where s is the length and Δt is the time interval for elementary step of random walk which is equal to the mean free path of electrons. The variance parameter for electron motion is given by $\alpha = sv = s\hbar|k|m^*$ where v is velocity of an electron, m^* is its effective mass, $\hbar$ is the Planck constant, and $|k| = k = 2\pi g/(aG)$ is the absolute value of the reduced wave vector (a is period of the lattice, G is number of particles in the lattice, and g is an integer). The probability density that the electron is at x is given by [18]

$$f_e(x;t) = \frac{R}{A}\sum_k \frac{1}{\sqrt{2\pi\alpha t}} \exp\left(-\frac{\hbar^2 k^2}{2m^* k_B T}\right) \exp\left[\frac{(x-\gamma)^2}{2\alpha t}\right] \tag{2}$$

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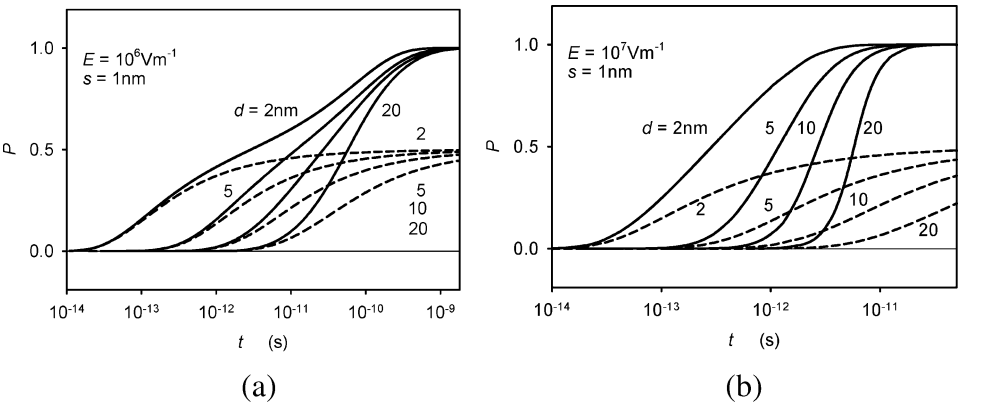


Figure 8. Motion of electrons. P as a function of t. The dashed and solid lines are used for thermal motion and for motion driven by deterministic force together with thermal motion, respectively. Distance d is 2, 5, 10, and 20 nm. Intensity, E, of the electric field is 10^6 (a) and $10^7\,\mathrm{Vm}^{-1}$ (b) [18].

where A is normalization factor. We replaced the Fermi-Dirac distribution by the Boltzmann one. As the velocity $v = \mu E$ where E is intensity of the electric field we have to determine the mobility μ. Using the Einstein relation for the diffusion coefficient we may evaluated μ from the relation [18]

$$\mu = \frac{se}{2k_B TA} \sum_k \frac{\hbar k}{m^*} \exp\left(-\frac{\hbar^2 k^2}{2m^* k_B T}\right) \tag{3}$$

where e is elementary charge.

Figures 8a and b show the probability versus time that electron can reach the required target space at a distance d (2, 5, 10, and 20 nm). Intensity of the electric field is 10^6 (a) and $10^7\,\mathrm{Vm}^{-1}$ (b). The dashed lines and the solid lines denote thermal motion and thermal motion together with deterministic force, respectively. Large effect of thermal motion on the transport is visible for intensity of the electric field $10^6\,\mathrm{Vm}^{-1}$ (Fig. 8a). Electron may be transported over a path 20 nm long within about 10 ps with probability near one (Fig. 8b).

Discussion

Fröhlich postulated existence of coherent physical fields in biological systems generated by electrically polar systems and excited by metabolic energy supply. Microtubular cytoskeleton structures satisfy requirements of the Fröhlich theoretical model. Supply of energy from hydrolysis of GTP to GDP in heterodimers after polymerization seems to be sufficient for excitation of vibrations in the structures. Supply of energy to microtubules from activity of motor proteins transporting cargo along proteins or generating shifts between structures by exerted force is not analyzed yet. But we assume that contribution to energy supply from activity of motor proteins is significant. Damping of vibrations by energy transfer from a microtubule to the cytosol due to viscosity effects is very small due to properties of the interfacial slip layer that includes the surface layer of the microtubule,

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attached proteins, and the charge layer of attracted ions. Any analysis that does not take into consideration the interfacial boundary conditions cannot yield correct results. Electric field generated by the microtubular structure can interact with molecules of water. Until quite recently these effects were neglected. Layers of organized water inside cell are discussed by [32]. Physical essentials for explanation of special properties of water are in [39]. As the 4 poles of the electric charges of a water molecule are concentrated at the corners of a space structure only slightly different from a tetrahedron water molecules can form tetrahedron frames. Water molecules are always distributed between 2 loosely connected systems: the quasiamorphous nonstructured water and quasicrystalinne structured system of clathrate hydrates. Energy supply to water can change proportion between these structures [39]. Ultraviolet luminescence measurements of water confirm existence of various structures with stereo chemical parameters of hydrogen bonds [40]. Computer modeling supports possibility of formation of various parametric structures. Lobyshev [40] claims that water previously exposed to electric, magnetic, electromagnetic, acoustic, or vibration fields acquires biological activity that it keeps for considerably long time. Viscosity of water depends on the amorphous quasicrystalinne structure ratio too [39]. Electric field generated by microtubules may strongly influence surrounding water. The role of activated water on vibrations in microtubules and damping may be assessed after reliable data on the activated water will be measured.

Transport of molecules and charges contains random component driven thermally and deterministic component driven by a coherent force. Energy of thermal noise is many orders of magnitude greater than energy of deterministic motion but due to randomness the motion is isotropic. Thermal motion can help to overcome potential barriers. Coherent processes driven by deterministic force have high probability of required action regardless of the small energy content in comparison with energy of thermal processes. Decrease of deterministic and increase of random component results in smaller probability of required action. Deterministic and random processes may have an optimal proportion for biological function. If the probability is small, the system is liable to be disturbed under external fluctuations but the disturbances may be important for evolutionary changes. The great probability provides resistance against disturbances and against making errors. Transport of reaction components and building blocks for polymerization is very likely one of the functions of the generated electromagnetic field. Besides the transport the lines of force of the electric field may serve as a directing channels in which the structures are built.

Coherent vibrations very likely have an important role in protein reactions. Proteins have special properties based on their nuclear dynamics. Nuclear motion influences protein conformation resulting in different biological functions. Excitation by energy supply alters nuclear dynamics. Vos and Martin [41] claim that on the time scale up to 1 ps coherent vibrational motion conserving the phase for several periods of oscillations may be a general property of proteins and their fundamental functional feature.

Conclusions

Microtubule structures in the cytoskeleton of eucaryotic cells satisfy conditions for excitation of vibrations and generation of electromagnetic field with dominant

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electrical component in their vicinity. Microtubules are highly dynamic structures in which their subunits—tubulin heterodimers—are exchanged continually by the mechanism of dynamic instability and treadmilling. Energy supply is provided by hydrolysis of GTP to GDP in the tubulin heterodimers after polymerization. Energy supply from motor proteins is not analyzed yet. Interfacial slip layer at the microtubule surface prevent vibrations in microtubules from damping by viscous effects of cytosol.

Electric field generated by polar structures in a cell can provide driving force for directed transport of molecules and charges. Random thermal motion has smaller probability to reach the target than motion driven by a deterministic force together with thermal motion. Effect of deterministic force on the directed transport is dominant.

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