FIZIKA Volume 21, Supplement 1, 1989.
Proceedings of the XI Yugoslav SYMPOSIUM OF THE PHYSICS OF CONDENSED MATTER.
M. Davidović and M. Lj. Napijalo Editors, Donji Milanovac, October 3–7, 1988.

ON THE DESINTEGRATION OF DIMERS AT THE TUBULINE BY DEFORMABILITY LOCALIZED STATES

M. Satarić, Faculty of Technical Sciences, 21000 Novi Sad, Yugoslavia
D. Koruga, Molekular Machines Research Unit, University of Belgrade, 27. marta 80, 11000 Belgrade, Yugoslavia
Z. Ivić and R. Žakula, Boris Kidrič, Institute of Nuclear Sciences, Laboratory of Theoretical Physics, Belgrade, Yugoslavia

1. Introduction

Microtubules (MT) participate in a wide range of organized dynamical activities that apparently involve information processing [1]. Microtubules are hollow cylinders formed by protofilaments aligned parallel to the microtubule axis, fig. 1. In vivo, microtubules from most sources always have 13 protofilaments [2], which are each a series polar tubulin dimers. Each dimer consists of two slightly different classes of $55 \cdot 10^3$ molecular weight monomers. First monomer consists of α-helix curly chain and second monomer consists of β-sheet, fig. 1. Each dimer may be viewed as a electro dipole which are 4nm in diameter. The origin of dipole character is in the fact that one binds eighteen calcium ions (Ca^{++}) per dimer.

In our paper we are making the attempt to answer an interesting question related with the process of self-assembly of (MT). Namely, in the case where the (MT) are in dynamical equilibrium in the aqueons solution of disolved monomers, the next process occurs. On the one end (+) of (MT) cylinder the assembly from tubulin dimers would take place and,

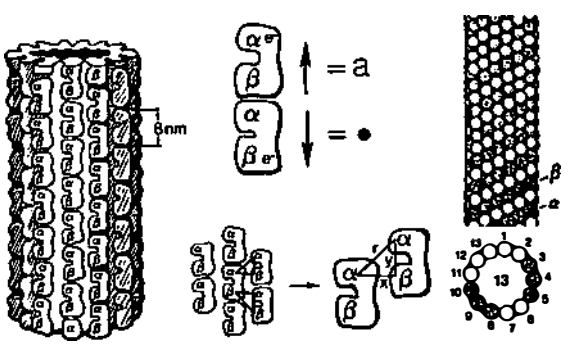

FIGURE 1. Left: MT structure from X-ray diffraction crystallography. Right top: MT-tubulin dimer subunits comprised of α and β monomers. Electron occupancy of either monomer may correlate with coherent dipole oscillations and are represented as "a" for α-monomer electron occupancy and dots connected by lines for β-monomer electron occupancy. Center bottom and right: hexagonal relations lead to neighbor rules based on lattice distances and electrostatic interactions. For neighbors shown (lower right), x = 5 nm, y = 4 nm, r = 6.4 nm.

in parallel, the disassembly at other side (-). This figure shows that if the (MT) is free in the cytoplasm, "treadmilling" will lengthen the (+) end, while the (-) end shortens that is to say, the (MT) will be moving towards the (+) end! We emphasize that during this process the length of the cylinder of a microtubule retains the constant value.

2. The Physical Model of the Process

Biological systems possess a high degree of ordering which leads to speculation on the nature of the forces responsible for this phenomenon. The cornerstone of our approach is the well known Fröhlich model [3]. Based on the Fröhlich's precepts we developed a mathematical model in which a chain (one protofilament) of coupled dipole moments is described by the so-called Θ^4 model with the potential

$$V(\Theta) = \frac{1}{2}A\Theta^2 - \frac{1}{4}B\Theta^4 \qquad (2.1)$$

where A and B are positive constant. This potential has a maximum $V(\Theta)=0$ at $\Theta=0$ and two minima $V(\Theta_0)=-A^2/4B$ at $\Theta_0 = \pm (A/B)^{1/2}$ Supposing that the interaction between two parallel protofilaments is small, let us consider just one chain of dimers as a system of quasi torsion oscilators with one degree of freedom (the torsion angle is Θ_n, where n denotes the index of dimer in the chain). Introducing a torsion constant k the Hamiltonian for the system of N dimers separated by a uniform distance R_0, so that the protofilament has a constant length L, we have

$$H = \sum_n^N \left\{ -\frac{1}{2}A\Theta_n^2 + \frac{1}{4}B\Theta_n^4 - C\Theta_n + \frac{1}{2}k(\Theta_{n+1} - \Theta_n) + \frac{1}{2}\frac{\mathcal{L}_n^2}{J} \right\} \qquad (2.2)$$

where J is the moment of inertia for each dimer, $\mathcal{L}_n$ is the corresponding angular momentum, and C is the phenomenological parameter. For the sake of the convenience we can express the Hamiltonian (2.2) in the framework of second quantisation, by introducing the Bose operators (a_n^+, a_n) as follows

$$\Theta_n = \left(\frac{\hbar}{2J\Omega_A}\right)^{1/2}(a_n + a_n^+)$$
$$\mathcal{L}_n = i\left(\frac{\hbar\Omega_A J}{2}\right)^{1/2}(a_n^+ - a_n) \qquad (2.2a)$$

where Ω_A is the Einsteih s torsion frequency. The transformations (2.2a) after making the unitary transformation $(U = Y\sum_1 (a_1 - a_1^+))$ give the Hamiltonian

$$H_{ch} = \sum_n \varepsilon a_n^+ a_n + X_0 \sum_n (a_n^{+2} + a_n^2) + 12Y^2X_2 \sum_n (a_n^{+2} + a_n^2) -$$
$$- X_1 \sum_n (a_n a_{n+1} + a_n^+ a_{n+1}^+ + a_n^+ a_{n+1} + a_{n+1}^+ a_n) +$$
$$+ X_2 \sum_n (a_n^{+4} + a_n^4 + 4a_n^{+3}a_n + 6a_n^{+2}a_n^2 + 4a_n^+ a_n^3) -$$
$$- 8YX_2 \sum_n (a_n^{+3} + a_n^3) - 24YX_2 \sum_n (a_n^{+2}a_n + a_n^+ a_n^2) \qquad (2.3)$$

where we introduced a set of denotations

$$\varepsilon = -\frac{1}{2}\frac{\hbar A}{J\Omega_A} + 2X_1 + 12X_2 + \frac{1}{4}\hbar\Omega_A + 24X_2Y^2$$

$$X_0 = -\frac{1}{4}\frac{\hbar A}{J\Omega_A} + X_1 + 6X_2 - \frac{1}{4}\hbar\Omega_A \quad ; \quad X_1 = \frac{k\hbar}{4J\Omega_A}$$

$$X_2 = \frac{B\hbar^2}{16J^2\Omega_A^2} \quad ; \quad X_3 = C\left(\frac{\hbar}{2J\Omega_A}\right)^{1/2} \quad ; \quad Y = \frac{X_3}{4X_1 - \varepsilon - 2X_0} \qquad (2.3a)$$

The system evolution will be described in a quasi-classical approximation by using the coherent-state representation. The time-dependent state vector $|\Psi\rangle$ of a system with Hamiltonian (2.3) will be presented by a direct product $|\Psi\rangle = \prod_n |\Psi\rangle$ so that the time-dependent complex numbers α_n be eigenvalues of the annihilation operators a_n, $a_n|\alpha_n\rangle = \alpha_n|\alpha_n\rangle$. The functional $\mathcal{F}(\alpha, \alpha^*) = \langle\Psi|H_{ch}|\Psi\rangle$ is a Hamiltonian function in the space of coherent states and defines the equation of motion for the amplitude α_n which in a continuous limit is a form of nonlinear differential equations as follows(*)

$$\ddot{\varphi} + b_1\varphi - b_2R_0^2\frac{\partial^2}{\partial x^2}\varphi + b_3\dot{\varphi}^2 - b_4\varphi^2 + b_5\varphi^3 = 0 \qquad (2.4)$$

where the unknown function is related with coherent state, amplitude by expression

$$\varphi_n = \frac{1}{2}(\alpha_n + \alpha_n^*) \qquad (2.4a)$$

and we have a new set of parameters

$$b_1 = \frac{1}{\hbar^2}\left[\varepsilon^2 - (2X_0 + 48Y^2X_2)^2\right] - 4\frac{X_1}{\hbar^2}\Phi$$

$$b_2 = \frac{2X_1}{\hbar^2}\Phi \quad ; \quad b_3 = 48YX_2\Phi^{-1} \quad ; \quad b_4 = \frac{48YX_2}{\hbar^2}\Phi$$

$$b_5 = \frac{32X_2}{\hbar^2}\Phi \quad ; \quad \Phi = \varepsilon - 2X_0 - 48Y^2X_2 \qquad (2.4b)$$

We simply look for a travelling-wave solution of equation (2.4) and apply boundary conditions for soliton with velocity v. Using $\xi = x - vt$, the solution describing a soliton-like excitation of dimer's dipols is found as normalizing function of time and space

$$\alpha(x,t) = U_0\left\{\left(1 - \frac{1}{2}\frac{1}{ch^2\tau}\right) - i\frac{v\hbar f}{\Phi}\frac{th\,\tau}{ch^2\tau}\right\} \qquad (2.5)$$

where

$$\tau = (\xi - \xi_0)f \quad ; \quad f = \frac{b_3v^2}{v_0^2\left(1 - \frac{v^2}{v_0^2}\right)} \qquad (2.5a)$$

the constant of normalization has the form

$$U_0 = \left\{\frac{1}{2}\left[\frac{5(3Lf-5)}{4v^2\hbar^2f^2} + \left(1 + \frac{48R_0\hbar^2v^2f^2\Phi^2}{5(3Lf-5)^2}\right)^{1/2}\right]\right\}^{1/2} \qquad (2.5b)$$

(*) Throghout this paper the dots will be used to denote the derivation with respect to time

$v_0 = R_0\sqrt{b_2}$ is the velocity of longitudinal torsion waves, and ξ_0 is the center of soliton.

3. Soliton Relaxation at the end of the (MT) Protofilament

We supposed that in the process of self-assembly, the attaching of one dimer at the (+) end of a protofilament produces one torsion solitonic impuls. This soliton propagates through corresponding protofilament. When soliton reaches the (-) end its energy can be employ in the process of detaching of uttermost dimer in protofilament. The aim of this chapter is that, starting from mentioned picture, enables us with a statistical approach giving the reaction rate of the dimer detachment caused by solitonic mechanism, fig. 2.

In the other words, the detachment of a dimer at the end of the (MT) cylinder can be consider as the following reaction

soliton + bound uttermost dimer = free dimer

Moreover, the surplus of solitonic energy can be employed for the excitation of internal degrees of freedom in the detached dimer (for example this energy can induce the hydrolysis of ATP and its transformation into ADP).

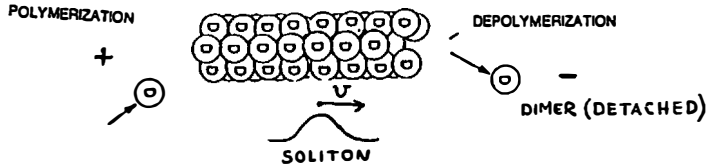

figure 2.

Using the metod of the non-equilibrium statistical mechanics [4] we will study the role of solitonic mechanism in the process of dimer s detachment.

Let us now introduce the complet Hamiltonian of such a system in the form

$$H_{tot} = H_{ch} + H_D + H_{int} \qquad (3.1)$$

where H_{ch} is the Hamiltonian of protofilament chain (2.5). The uttermost dimer is treated as Fermi-subsystem with energy of excitation E_D

$$H_D = E_D D_L^+ D_L \qquad (3.1a)$$

D_L^+, D_L are the Fermi operators describing presence and absence of the dimer at the (-) end.

The interaction between subsystems is represented with H_{int}

$$H_{int} = V_{nL} a_n^+ D_L + h.c. \qquad (3.1b)$$

By using the well-known procedure of non-equilibrium statis-

tical operator technique following [5, 6] we can calculate the average value of energy current from the protofilament chain to the uttermost dimer in the chain

$$\langle \dot{N}_{ch} \rangle = Sp(\dot{N}_{ch}\hat{\rho}) \tag{3.2}$$

where

$$N_{ch} = \sum_n a_n^+ a_n \quad ; \quad i\hbar\dot{N}_{ch} = [N_{ch}, H_{tot}] \tag{3.2a}$$

and the non-equilibrium statistical operator $\hat{\rho}$ is given by

$$\hat{\rho} = Q^{-1}\exp(-\hat{M} + \delta\hat{M}) \tag{3.2b}$$

where we introduced the set of denotations

$$M = \beta\left(\sum_k \gamma_k a_k^+ a_k + \gamma_D D_L^+ D_L\right) \quad ; \quad \beta = (k_B T)^{-1}$$

$$\gamma_k = (\Delta_k - \mu_{ch}) \quad ; \quad \gamma_D = E_D - \mu_D$$

$$\tilde{\Delta}_k = \Delta_k\left[1 + \frac{9}{2}\left(\frac{W_k}{\Delta_k}\right)^2\right] \quad ; \quad \frac{W_k}{\Delta_k} < 1$$

$$\Delta_k = \varepsilon - 2X_1\cos kR_0 \quad ; \quad W_k = X_0 - X_1\cos kR_0 + 12X_2Y^2 \tag{3.2c}$$

The deviation of the system from the equilibrium state is embraced by the small operator $\delta\hat{M}$ defined as follows

$$\delta\hat{M} = (\mu_{ch} - \mu_D)\beta\int_{-\infty}^{0} dt\,(e^{\varepsilon t}\dot{N}_{ch}) \tag{3.2d}$$

μ_{ch} and μ_D are the chemical potential of the torsion chain excitation and of detaching dimer at the end of protofilament; t is time and ε is small parameter.

After very long evaluations of corresponding integrals the expression (3.2) leads to the final result for dimer current.

$$\langle \dot{N}_{ch} \rangle = -\frac{\beta(\mu_{ch} - \mu_D)\,|V_{LL}|^2 U^2}{16\hbar^2}\,\frac{\left(1 + \frac{\pi\hbar\omega_D}{\Phi}\right)}{\pi^2 N^2 f v}\,\frac{\exp[-\beta(\tilde{\Delta}_k - \mu_{ch})]}{ch^2\left(\frac{\pi\omega_D}{2vf}\right)}\,Z(v,\omega_D) \tag{3.3}$$

where

$$Z(v,\omega_D) = \left[\frac{1 - n_D}{\gamma_D + \gamma_k}\left(\frac{W_k}{\Delta_k}\right) + \frac{n_D}{\gamma_k - \gamma_D}\left(1 + \frac{3}{2}\,\frac{W_k^2}{\Delta_k^2}\right)\right]\delta\left(k - \frac{\omega_D}{v}\right) \tag{3.3a}$$

where $\hbar\omega_D = E_D$ and n_D is the Fermi distribution population of detached dimer

$$n_D = \left\{\exp\left[\beta(E_D - \mu_D)\right] + 1\right\}^{-1} \tag{3.3b}$$

From final expression (3.3) follows that the contribution of solitonic mechanism strongly depends on the ratio ω_D/v, where $\hbar\omega_D$ is energy of excitation of uttermost dimer in the chain, and v is the solitonic velocity. The mentioned contribution grows with increasing of soliton velocity.

[1] S.R. Hameroff and R.C. Watt, J. Theor. Biol. **98**, 549 (1982)
[2] R. Dustin, Microtubules, Springer-Verlag, Berlin, Heidelberg, New York (1978)
[3] H. Fröhlich, Rev. Nuovo Cimento **7**, 416 (1977)
[4] D.N. Zubarev, Non-Equilibrium Statistical Thermodinamics pp 216, 330, 344 Nauka, Moscow (1971) in Russian
[5] Z. Ivić, M. Satarić and R. Žakula, Phys. Stat. Sol. (b) **129**, 221 (1985)
[6] M. Satarić, Z. Ivić and R. Žakula, Physica Scripta Vol **34**, 283 (1986)