Discreteness effects on kinklike excitations in microtubules

P. Woafo, G. H. Guénoue, and A. S. Bokosah
Laboratoire de Mécanique, Faculté des Sciences, Université de Yaoundé I, Boîte Postal, 812 Yaounde, Cameroun
(Received 19 July 1995)

We show that the kink excitation in a microtubule is very narrow. The Peierls-Nabarro barrier, due to discreteness effects, and the diffusion coefficient are obtained. A discussion of the physiological implications of discretization is given. [S1063-651X(96)09912-6]

PACS number(s): 87.15.−v

I. INTRODUCTION

Recently, Sataric', Tuszyn'ski, and Zakula [1] suggested that the classical ϕ^4 model in the presence of an electric field can serve as the conceptual basis for a realistic physical picture of the energy transfer in cell microtubules. They demonstrated that kinklike excitations arise as a result of the guanosine 5′-triphosphate (GTP) hydrolysis and the electric force sustains their propagation along a microtubule. However, using the numerical values of the model parameters shows that the kink width is less than the lattice spacing. Thus the model is highly discrete.

The aim of this Brief Report is to analyze the discreteness effects on the kinklike excitations in a microtubule. The paper is organized as follows. We first give, in Sec. II, a description of a microtubule and define its Lagrangian. In Sec. III we derive the expressions of the Peierls-Nabarro (PN) barrier, the mobility, and the diffusion coefficient. We show that the discreteness effects renormalize the values of the dynamical parameters of the system. We conclude and discuss briefly the physiological implications of the discreteness effects in Sec. IV.

II. MODEL AND LAGRANGIAN

A. Description of microtubules

Neurons and other cells are comprised of protoplasm, which consists of membranes, organelles, nuclei, and the bulk interior medium of living cells: cytoplasm [2]. All cells possess delicate tubular filamentous structures called microtubules. The complex dynamic activities of microtubules and other cytoskeletal elements are essential for the molecular differentiation, formation of synapses, and dendritic spines [3,4]. In neuronal activities, it is known that the cytoskeletal elements are involved in cognitive processes: learning, experience, and memory [5]. Indeed, it has been shown that when baby rats first open their eyes, neurons in the visual cortex begin producing vast quantities of tubulin. When the rats are 35 days old and the critical learning phase is over, tubulin production is drastically reduced [6].

Of the various filamentous structures of the cytoskeleton, microtubules are the most prominent, well studied, and appear to be the best suited for dynamic information processing [3,4,7,8,10]. Microtubules are hollow cylinders, 25 nm in diameter, and formed by 13 longitudinal profilaments that are each a series of subunit proteins known as tubulin (Fig. 1). The microtubules are connected to each other by lateral cross-link filaments or synapses. Each tubulin subunit is a polar, 8-nm dimer. Each dimer consists of two slightly different classes of 4-nm, 55-kdalton (1 dalton$\simeq 2\times 10^{-27}$ kg) monomers known as α and β tubulin (Fig. 1). Within the microtubule, the tubulin dimer subunits are arranged in a hexagonal lattice. Each dimer may be viewed as an electric dipole whose dipolar character originates from the 18 calcium ions bound within each β monomer. An equal number of negative charges are localized near the neighboring α monomer.

The precise mechanism of energy transfer in microtubule is not well understood. However, following Fröhlich's ideas [9], one can assume that coherent excitations such as solitons can propagate in a microtubule provided the chemical energy, such as adenosine 5′-triphosphate and GTP, is supplied. Encouraged by the Fröhlich assumptions, Sataric', Tuszyn'ski, and Zakula considered the nonlinear dynamics

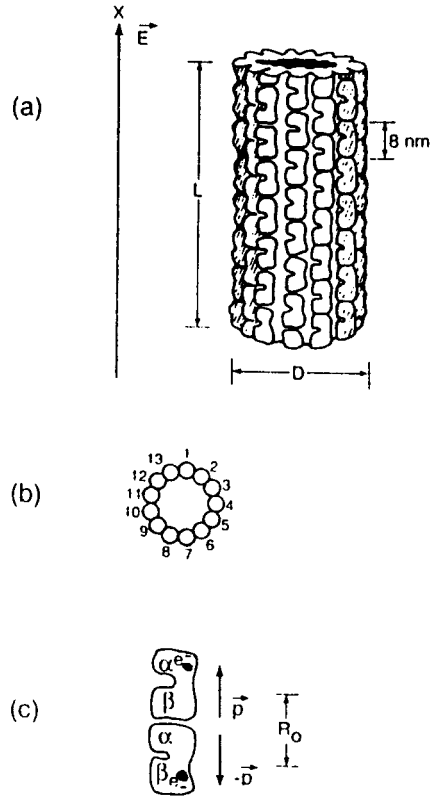

FIG. 1. (a) Structure of a microtubule, (b) its cross section, and (c) two neighboring dimers (from Ref. [1]).

of dimer dipoles in one protofilament of a microtubule in terms of the well-known double-well or ϕ^4 potential model. The essential argument in favor of introducing the double-well model stems from the fact that the longitudinal projection of the dimer displacement interacts with the rest of the lattice through a mean-field force due to an anharmonic lattice field potential as in ferroelectrics such as $Pb_5Ge_3O_{11}$ and antimony sulphoiodide SbSl [11,12]. This is validated by the fact that the mobile electron on each dimer can be localized closer to either the α monomer or the β monomer, resulting in changes in dimer conformation.

B. Model Lagrangian

Thus the Lagrangian of one profilament of a microtubule can be defined as

$$L=\sum_{n=1}\left\{\frac{1}{2}my_n^2-\frac{c}{2}(y_{n+1}-y_n)^2-V(y_n)\right\}, \tag{1}$$

where y_n is the longitudinal displacement of the n dimer and c is the stiffness parameter resulting from strain and electrostatic interactions between two neighboring dimers. m is the effective mass of a dimer. The dot on y_n stands for the time derivative.

The overall effect of the surrounding dimers on a chosen dimer n can then be qualitatively described by the double-well ϕ^4 potential, which is extended to include an electric field E

$$V(y_n)=\frac{-A}{2}y_n^2+\frac{B}{4}y_n^4-qEy_n, \tag{2}$$

where A and B are the model parameters. $B>0$ and A is a linear function of the temperature that may change its sign at an instability temperature T_c, that is,

$$A(T)=A_0(T_c-T), \tag{3}$$

with $A_0>0$. In this model, the temperature T varies below T_c. The electric field E is due to the fact that the microtubule cylinder can be taken as a giant dipole, and q represents the effective mobile charge of a single dimer.

Since the dimers move in a sort of solvent, one must take into account the force

$$f_\nu=-m\lambda\dot{y}_n \tag{4}$$

associated with the viscosity of the solvent (λ is the damping coefficient). We therefore have to deal with a ϕ^4 model plus dissipation and an external field. This model has been studied extensively both in the continuum limit [11–13] and in the discrete limit [14,15]. Some applications of the model in the context of hydrogen-bonded systems such as ice and ferroelectrics of order-disorder types have also been considered [16].

III. PN BARRIER AND DIFFUSION COEFFICIENT FOR A KINK IN MICROTUBULES

A. Theoretical expressions

In the continuum limit, the model Lagrangian (1) with Eqs. (2) and (4) possesses an asymmetric kink solution [11,15] defined as

$$y(x,t)=\mp y_0\left\{\eta_1+\frac{\eta_2-\eta_1}{1+\exp[(x-vt)/L]}\right\}, \tag{5}$$

where

$$y_0=(A/B)^{1/2}$$

and

$$L=[2m(c_0^2-v^2)/A]^{1/2}/(\eta_1-\eta_2). \tag{6}$$

The coefficient c_0, known as the speed of sound, is defined as

$$c_0^2=\frac{cb^2}{m},$$

where b is the lattice spacing. The coefficients η_1 and η_2 are the extreme zeros of the polynomial

$$P(\eta)=\eta-\eta^3+qEB^{1/2}A^{-3/2}$$

and are given by

$$\eta_1=\frac{2}{\sqrt{3}}\cos\left(\frac{\theta}{3}+\frac{2\pi}{3}\right), \tag{7a}$$

$$\eta_2=\frac{2}{\sqrt{3}}\cos\frac{\theta}{3}, \tag{7b}$$

with

$$\theta=\arccos\left[\frac{3qE}{2A}\left(\frac{3B}{A}\right)^{1/2}\right]. \tag{7c}$$

The kink solution (5) exists under the condition

$$E<E_{\max}=\frac{2A}{3q}\left(\frac{A}{3B}\right)^{1/2}, \tag{8}$$

The velocity v, the damping coefficient λ, and η_1 and η_2 are related by the equation

$$v^2=[9A\eta_3^2/(2m\lambda^2+9A\eta_3^2)]c_0^2, \tag{9}$$

where $\eta_3=-(\eta_1+\eta_2)$ is the third zero of $p(\eta)$.

Structurally, for $E>0$, the position $y_0\eta_1$ corresponds to a metastable position, while $y_0\eta_2$ is a stable state. A kink with a positive velocity displaces progressively the particles from the right well $y_0\eta_2$ of the substrate potential $V(y)$ to the left one $y_0\eta_1$. For a kink with a negative velocity, the opposite happens. When $E<0$, the first process is energetically difficult, contrary to the second process. For $f<0$, the oposite happens. We consider hereafter the case $f>0$ and a kink

with positive velocity. This corresponds to the most probable state where all the particles are lying in the stable equilibrium position $y_0\eta_2$.

In the discrete lattice, one can use the projection operator method with Dirac's second class constraints to show that the dynamics of the kink coordinate X [$X(t)=vt$ in the continuum limit] can be described by the equation (see Ref. [15])

$$M\ddot{X}+M\lambda\dot{X}=\frac{\pi E_{\mathrm{PN}}}{b}\sin(2\pi X/b)-F_a, \tag{10}$$

where

$$M=\frac{my_0^2(\eta_1-\eta_2)^2}{6bL} \tag{11}$$

is the effective mass of the kink. The quantity E_{PN} can be seen as the Peierls-Nabarro barrier occurring in the dislocation theory of crystals [17]. Its expression is given here as [15]

$$E_{\mathrm{PN}}=\frac{2mc_0^2y_0^2(\eta_1-\eta_2)^2\pi^2}{180L^2\sinh(2\pi L/b)}\left(1+\frac{4\pi^2L^2}{b^2}\right)\left(3+\frac{8\pi^2L^2}{b^2}\right). \tag{12}$$

The term F_a in Eq. (10) is an average force depending on E.

The interactions between the kink and phonons give rise to a new mechanism of energy loss. Moreover, due to thermal fluctuations, the right-hand side of Eq. (10) may contain an additional term $R(t)$, obeying the correlativity

$$\langle R(t)\rangle=0, \quad \langle R(t)R(t')\rangle=2\lambda MT\delta(t-t'). \tag{13}$$

The angular brackets denote the equilibrium average and δ is the Dirac function. The kink motion is therefore diffusive and its diffusion coefficient is given by [18]

$$D=D_0\exp(-E_{\mathrm{PN}}/k_BT), \tag{14}$$

where

$$D_0=(k_BT)/M\lambda \tag{15}$$

is the diffusion coefficient in the continuum limit (e.g., $E_{\mathrm{PN}}\Rightarrow 0$). The diffusion coefficient D_0 is thus weighted by an Arrhenius factor due to discreteness effects.

B. Numerical values

To estimate the values of E_{PN} and D in the microtubule, we have used the following set of parameters reported in Ref. [1]: $m=10^{-22}$ kg, $q=6\times10^{-18}$ c, $b=80\times10^{-10}$ m, $\lambda=5.6\times10^{11}$ s^{-1}, and $c_0=1.7\times10^{3}$ ms^{-1}. For the parameters A and B, in the absence of any hard data for the microtubule, we assume typical values for filamentous ferroelectrics such as $Pb_5Ge_3O_{11}$. This assumption is due to structural similarity between microtubules and filamentous ferroelectrics. Thus $A(T)=10(320-T)$ J m^{-2}, where the critical temperature for the microtubule is set $T_c=320$ K and $B=1.6\times10^{24}$ J m^{-4}. Although the electric field sharply increases as one approaches the end points of the profilament, we assume that its magnitude is approximately constant in the hole protofilament.

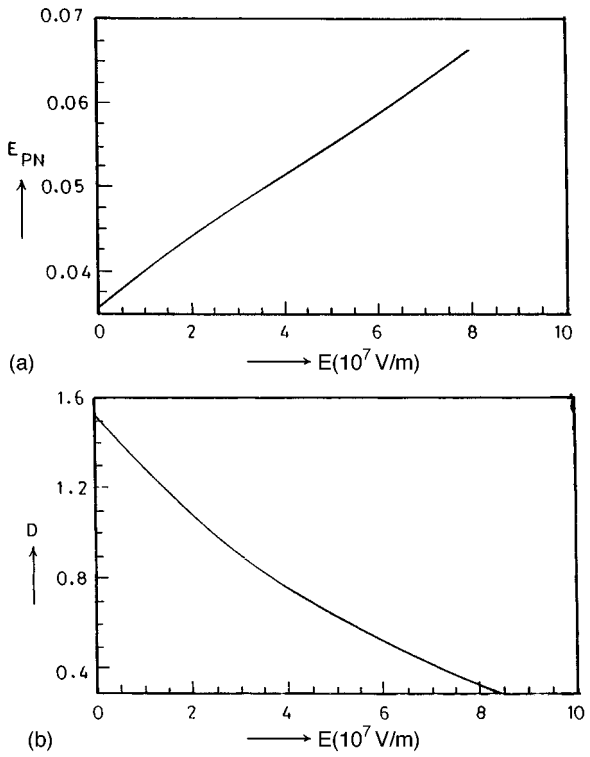

FIG. 2. (a) Peierls-Nabarro barrier E_{PN} (in eV) versus the electric field E and (b) diffusion coefficient D (in 10^{-2} cm^2/s) versus E.

We first analyze the variations of E_{PN} and D as functions of the electric field E at the physiological temperature $T=300$ K. We thus obtain $E_{\max}=14.3\times10^{7}$ V/m and $y_0=1.12\times10^{-11}$ m. The kink width L decreases as E increases and consequently E_{PN} increases [Fig. 2(a)]. This is due to the relativistic effects. Indeed, the kink velocity increases with E, the kink becomes more narrow, and the discreteness effects are dominant. The diffusion coefficient decreases with E [Fig. 2(b)]. The kink mobility can easily be deduced from Eq. (9). It increases with E.

We have also analyzed the variations of E_{PN} and D as functions of T for the electric field $E=10^5$ V/m. The kink width increases with T but remains less than the lattice spacing. For instance, for $T=300$ K, $L=8.5\times10^{-10}$ m. Thus the kink in the microtubule is so narrow that it considerably suffers the effects of the discrete nature of the protofilament. Thus it cannot propagate freely unless its motion is sustained by additional external forces such as thermal fluctuations. E_{PN} decreases when T increases. This is understandable if we appeal to the fact that L increases with T. Moreover, this can be related to the lowering of the substrate potential barrier $V_{\max}=A^2/4B$ since A decreases with T. A comparison of E_{PN} and $v_{\max}$ leads to the conclusion that the kink facilitates the transfer of charge and energy in the microtubule. The temperature dependence of the diffusion coefficient shows that it increases with T. At the physiological temperature, we obtain $D=2.80\times10^{-5}$ cm^2/s ($D_0=4.78\times10^{-2}$ cm^2/s).

As concerns for force F_a in Eq. (10), it increases with the electric field E. For instance, for $E=10^5$ V/m,

$F_a = 1.07 \times 10^{-10}$ N; for $E = 10^6$ V/m, $F_a = 10.7 \times 10^{-10}$ N; and for $E = 10^7$ V/m, $F_a = 107 \times 10^{-10}$ N.

IV. CONCLUSION

We have analyzed the discreteness effects of the motion of kinklike excitations in microtubules, the prominent and the best suited filamentous structures for dynamic information processing in neurons. With the approximated values of model parameters, it is seen that the kink in the microtubule is so narrow that the discreteness effects cannot be neglected. The potential barrier that modulates the kink motion and the diffusion coefficient have been obtained. Their dependence on the electric field and on the temperature has been sketched.

However, the dynamics of kink and soliton excitations in microtubules is still an open and important problem. Indeed, with the numerical values of model parameters assumed for microtubules, preliminary results of a direct numerical simulation show that such narrow kink excitations cannot propagate over long distances whatever the value of the electric field satisfying the condition $E < E_{\max}$. They can move only because of external fluctuations, so that the motion has an activated character, showing hopping from one PN well to another.

Discreteness effects and the resulting type of motion analyzed here have some physiological implications. It can be stated that the transfer of energy or charges in microtubules has a Brownian and stochastic character. Consequently, this can explain the well-known erratic process of assembly and disassembly at the ends of microtubules. Indeed, one can relate the rate of assembly and disassembly of microtubules to the stochastic rate of kink excitations arriving at their ends [1]. Moreover, the diffusive nature and the pinning effects characterizing the kink motion in microtubules can help in the understanding of the dynamic instability of the velocity of microtubules growth [19] and the rate of microtubules nucleation [20].

ACKNOWLEDGMENTS

P.W. would like to thank the International Centre for Theoretical Physics (ICTP), Trieste, Italy where an important part of the work was done. He is also indebted to the Swedish Agency for Research Cooperation with Developing Countries for financial support for his visit to ICTP.

[1] M. V. Sataric', J. A. Tuszyn'ski, and R. B. Zakula, Phys. Rev. E **48**, 589 (1993).
[2] S. Rasmussen, H. Karampurwala, R. Vaidyanath, K. S. Jensen, and S. Hameroff, Physica D **42**, 428 (1990).
[3] P. Dustin, in *Microtubules*, 2nd ed. (Springer, Berlin, 1984), p. 442.
[4] D. Soifer, Ann. N.Y. Acad. Sci. **466**, 1 (1986).
[5] R. Mileusnic, S. P. Rose, and P. Tillson, Neur. Chem. **34**, 1007 (1980).
[6] J. Cronly-Dillon, D. Carden, and C. Birks, J. Exp. Biol. **61**, 443 (1974).
[7] P. Vassilev, M. Kanazirska, and H. T. Tien, Biochem. Biophys. Res. Commun. **126**, 559 (1985).
[8] J. S. Becker, J. M. Olivier, and R. D. Berlin, Nature **254**, 152 (1975).
[9] H. Fröhlich, Nature **228**, 1093 (1970); Proc. Natl. Acad. Sci. U.S.A. **72**, 4211 (1975); in *Modern Bioelectric Chemistry*, edited by F. Gutmann and H. Keyzer (Plenum, New York, 1986), p. 241.
[10] M. P. Barnett, in *Proceedings of the Third Molecular Electronic Device Conference*, edtied by F. Carter (Naval Research Laboratory, Washington, DC, 1987).
[11] M. A. Collins, A. Blumen, J. F. Currie, and J. Ross, Phys. Rev. B **19**, 3630 (1979).
[12] J. F. Currie, A. Blumen, M. A. Collins, and J. Ross, Phys. Rev. B **19**, 3645 (1979).
[13] St. Pnevmatiks, N. Flytzanis, and A. R. Bishop, J. Phys. C **20**, 1030 (1987).
[14] P. Woafo, T.C. Kofane, and A. S. Bokosah, Phys. Lett. A **160**, 237 (1991).
[15] P. Woafo and T. C. Kofane, J. Phys. Condens. Matter **5**, 7063 (1993).
[16] A. Gordon, Physica B **146**, 373 (1987); **150**, 319 (1988); Solid State Commun. **69**, 1113 (1989); Nuovo Cimento **12**, 229 (1990).
[17] F. R. N. Nabarro, in *Theory of Crystal Dislocations* (Clarendon, Oxford, 1967).
[18] J. A. Combs and S. Yip, Phys. Rev. B **29**, 438 (1984).
[19] D. K. Fygensen, E. Braun, and A. Libchaber, Phys. Rev. E **50**, 1579 (1994).
[20] D. K. Fygensen, H. Flyvbjerg, K. Sneppen, A. Libchaber, and S. Leibler, Phys. Rev. E **51**, 5058 (1995).