Nonlinear dynamics of microtubules — A longitudinal model

S. Zdravković\(^{(a)}\), M. V. Satarić\(^{(b)}\) and S. Zeković\(^{(c)}\)

1 Institut za nuklearne nauke Vinča, Univerzitet u Beogradu - Poštanski fah 522, 11001 Beograd, Serbia
2 Fakultet tehničkih nauka, Univerzitet u Novom Sadu - 21000 Novi Sad, Serbia

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Abstract – In the present letter we describe a model of nonlinear dynamics of microtubules (MTs) assuming a single longitudinal degree of freedom per tubulin dimer. This is a longitudinal displacement of a dimer at a certain position with respect to the neighbouring one. A nonlinear partial differential equation, describing dimer's dynamics within MT, is solved both analytically and numerically. It is shown that such a nonlinear model can lead to the existence of kink solitons moving along the MTs. The internal electrical field strength is calculated using two procedures and a perfect agreement between the results is demonstrated. This enabled the estimation of the total energy, kink velocity and kink width. To simplify the calculation of the total energy we stated and proved a useful auxiliary theorem.

Introduction. – Microtubules are major cytoskeletal proteins. They are hollow cylinders usually formed by 13 parallel protofilaments (PFs) covering the cylindrical walls of MTs. Each PF represents a series of proteins called tubulin dimers, with a length of \(l = 8 \text{ nm} \) [1–3]. They are electric dipoles whose longitudinal component of the electric dipole moment is \(p = 337 \text{ D} \) [4]. A segment of two neighbouring PFs is shown in fig. 1. One can see that there is a longitudinal shift of \(8l/13 \) between the neighbouring PFs [5,6].

A series of papers dedicated to nonlinear vibrations within MTs have been published so far [7–11]. Most of them consider MT as a mechanically shear deformable cylindrical shell, in the context of classical theories of elasticity. Results existing in these papers are important for mechanical properties of MTs in their scaffolding functions in cells. However, none of these approaches take into account either the dipolar features of tubulin dimers or the role of discrete utilization of the chemical energy released by GTP hydrolysis.

The main purpose of this work is to introduce a new model. A crucial equation is solved both analytically and numerically. We show that the kink soliton is responsible for energy transfer along MT. To calculate the total energy a useful theorem is introduced, which simplifies the calculation. On the basis of the results of this model we estimate the wave velocity and wave width. Finally, to test the model, we calculate the intrinsic electric field strength in two ways. A perfect agreement between the results suggests that the model is correct.

One can say that each dimer looks like an ellipsoid with a width of about 4 nm [12]. It has six degrees of freedom, three angular and three translational. The most general approach would be if we took all of them into consideration. Of course, this would produce an extremely complicated model and researchers have tried to study MT dynamics using only one degree of freedom per dimer. Probably the most known model so far assumes only one longitudinal degree of freedom per dimer [13]. To be more precise, the dimer performs angular oscillations...
while the coordinate $u_n$ is a projection of the top of the dimer at the position $n$ on the direction of the PF, as shown in fig. 2. Its improved and more general version was introduced recently [14]. The present model also assumes only one degree of freedom per dimer. This is $z_n$, a longitudinal coordinate of the dimer at the position $n$. Neighbouring PFs are shifted relatively to each other longitudinally, which results in a left-handed helicoid in the lateral direction. This is crucial for both the structure and energy of MT. The coordinate $z_n$ is nothing but the value of this shift. Hence, this is not a displacement in the usual sense although the dimer’s displacement is a part of this shift as the dimer oscillates around the position corresponding to the minimum of the potential energy. An important advantage of the present model is the fact that both positive and negative values of $z_n$ have a physical meaning, while the negative values of the coordinate $u_n$ in refs. [13] and [14] might be questionable. Also, this approach allows us to estimate the electric field strength, which will be explained later.

**Fig. 2: The meaning of the coordinate $u_n$, used in ref. [13].**

Model. – The starting point of the present modelling is the fact that the bonds between dimers within the same PF are significantly stronger than the soft bonds between neighbouring PFs [15,16]. This implies that the longitudinal displacements of pertaining dimers in a single PF should cause the longitudinal wave propagating along PF. The averaged impact of soft bonds with collateral PFs is taken to be described by the nonlinear double-well potential.

The Hamiltonian for one PF is represented as

$$H = \sum_n \left[ \frac{m}{2} \dot{z}_n^2 + \frac{k}{2} \left( z_{n+1} - z_n \right)^2 + V(z_n) \right], \tag{1}$$

where dot means the first derivative with respect to time, $m$ is the mass of the dimer and $k$ is the harmonic constant describing the nearest-neighbour interaction between the dimers belonging to the same PF [13]. The first term represents the kinetic energy of the dimer, the second one, which we call harmonic energy, is the potential energy of the chemical interaction between the neighbouring dimers belonging to the same PF and the last term is the combined potential

$$V(z_n) = -Cz_n - \frac{1}{2}Az_n^2 + \frac{1}{4}Bz_n^4, \quad C = qE, \tag{2}$$

where $E$ is the magnitude of the intrinsic electric field and $q$ represents the excess charge within the dipole. It is assumed that $q > 0$ and $E > 0$. One can recognize the energy of the dimer in the intrinsic electric field $E$ at the site $n$ and the well-known double-well potential with positive parameters $A$ and $B$ that should be estimated [13]. Notice that $E$ comes from all the dimers, which means that the influence of the dimers from the neighbouring PFs is taken into consideration through this electric field.

The Hamiltonian given by eqs. (1) and (2) is rather common in physics [13,17]. The first attempt to use it in the nonlinear dynamics of MTs was done about 20 years ago [13]. To be more precise, the Hamiltonian in ref. [13] would be obtained from eqs. (1) and (2) if $z_n$ were replaced by $u_n$. Hence, we refer to these two models as $u$-model and $z$-model. However, the meanings of $u_n$ in ref. [13] and $z_n$ in the present paper are completely different. As was stated in the introduction, the $u$-model assumes an angular degree of freedom, while the coordinate $u_n$ is the projection of the top of the dimer on the direction of PF. On the other hand, the coordinate $z_n$ is the real shift of the dimer along the $x$-axis.

Using the generalized coordinates $z_n$ and $m\dot{z}_n$ and assuming a continuum approximation $z_n(t) \rightarrow z(x,t)$, we straightforwardly obtain the following nonlinear dynamical equation of motion

$$m \frac{\partial^2 z}{\partial t^2} - kl \frac{\partial^2 z}{\partial x^2} - qE - Az + Bz^3 + \gamma \frac{\partial z}{\partial t} = 0. \tag{3}$$

The last term represents the viscosity force with $\gamma$ being the viscosity coefficient [13].

It is well known that, for a given wave equation, the travelling wave $z(\xi)$ is the solution which depends upon $x$ and $t$ only through the unified variable $\xi \equiv \kappa x - \omega t$, where $\kappa$ and $\omega$ are constants. This allows us to obtain the final dimensionless ordinary differential equation

$$\alpha \psi'' - \rho \psi' - \psi + \psi^3 - \sigma = 0, \tag{4}$$

where $\psi' \equiv d\psi/d\xi$ and

$$\alpha = \frac{m\omega^2 - kl^2 \kappa^2}{A}, \quad z = \sqrt{\frac{A}{B}} \psi, \quad \rho = \frac{\gamma \omega}{A}, \quad \sigma = \frac{qE}{A \sqrt{\frac{A}{\pi}}}. \tag{5}$$

The potential $V(z_n)$, in the continuum approximation, becomes

$$V(\psi) = \frac{A^2}{B} \left( -\sigma \psi - \frac{1}{2} \psi^2 + \frac{1}{4} \psi^4 \right) \equiv A^2 \frac{f(\psi)}{B}. \tag{7}$$
The possible solutions of eq. (11) depend on the sign of the parameter \( b \). In our case \( b < 0 \), which will be shown later, and the function \( \Phi = \Phi(\xi) \) is [14,18–22]

\[
\Phi = -\sqrt{-b} \tanh \left( \sqrt{-b} \xi \right). 
\]  

As \( \Phi^{-1} \) diverges for small \( \xi \) we look for the biophysically tractable solutions for which \( a_1 \neq 0 \) and \( b_1 = 0 \) in eq. (10). All this brings about the following system of equations for the unknown parameters \( a, a_1, a_2 \) and \( \alpha \):

\[
\begin{cases}
-2a_0 + 8a_0^3 + \sigma = 0, \\
-1 + 3a_0^2 + 2\alpha b = 0, \\
\rho = 3a_0a_1, \\
2\alpha = -a_1^2.
\end{cases}
\]  

Notice that \( a_0a_1 > 0 \) and \( \alpha < 0 \). Negative \( \alpha \) means that the harmonic energy in the Hamiltonian (1) is larger than the kinetic energy. This may indicate a small velocity of the wave and/or a big \( k \), which can be seen from eq. (5). As the neighbouring dimers are not connected by strong chemical bonds, we expect a very small wave velocity.

Three real values of \( a_0 \) satisfy the first of eq. (13) for \( \sigma < \sigma_0 \). They describe the system in the states corresponding to the right and left minimum and the maximum [14] (see fig. 3). For example, the function \( \psi_1(\xi) \), describing the system which is initially in the right minimum, is

\[
\psi_1(\xi) = a_0 - b_0 \tanh \left( \frac{3a_0b_0}{\rho} \xi \right),
\]  

where

\[
a_0 \equiv a_{01} = \frac{1}{2\sqrt{3}} \left( \cos F + \sqrt{3} \sin F \right), \quad b_0 = \sqrt{1 - 3a_0^2}.
\]  

We can see that \( \psi_1(\xi) \) is an antikink soliton depending on both \( \rho \) and \( \sigma \), as \( a_{01} \) is a function of \( \sigma \). Its asymptotic values are \( \psi_1(-\infty) = \psi_R \) and \( \psi_1(+\infty) = \psi_M \). Notice that the jump of the function \( \psi_1(\xi) \) depends on \( \sigma \) only, while the solitonic width, \( \xi \), its slope, depends on both \( \rho \) and \( \sigma \). It is obvious that the solitonic width is proportional to viscosity. According to eqs. (13) and (15) we can easily check that \( b < 0 \) holds for \( \sigma < \sigma_0 \) in eq. (9).

The same solution of eq. (4), \( i.e., \) eqs. (14) and (15), can be obtained using Jacoby elliptic functions [23].

It is very important to keep in mind that the solution given by eqs. (14) and (15) is different from what was offered before [13,17]. To study two ground states of a proton the asymptotic values \( \psi_2(-\infty) = \psi_R \) and \( \psi_2(+\infty) = \psi_L \) were assumed [17]. Of course, both states \( \psi_R \) and \( \psi_L \) are stable. However, the fact that the state \( \psi_M \) is unstable has an important biophysical meaning. Suppose that a dimer obtained a portion of energy released by guanosine triphosphate (GTP), which results in its displacement. This displacement affects the surrounding dimers causing the wave creation. If the dimer moves from \( \psi_R \) to \( \psi_L \) it needs one more portion of energy to escape
ψ

from ψL. We do expect that the rational Nature offers only one energy supply and that the system moves from the bottom of fig. 3 to a value that is close but below the maximum value. In other words, the transition from ψL to any state close to ψM is enough for the soliton creation and allows a spontaneous return to the ground state ψ.

The function ψ in fig. 4 together with the results of the numerical solutions of eq. (4).

In what follows we will estimate the kink’s velocity and some other parameters. For this purpose we should calculate a projection of the electric field on the x-axis in the point A in fig. 1, which is denoted as E. One way to calculate this internal electric field is straightforward but tedious. We can calculate the components coming from all the excess charges in MT. For example, the electric field from the denoted charge −q in fig. 1 is

$$E_{1x} = \frac{q}{4\pi \varepsilon_0 \varepsilon_x} \left( \frac{8l}{13} - \frac{d}{2} \right) \left[ \left( \frac{8l}{13} - \frac{d}{2} \right)^2 + a^2 \right]^{-\frac{3}{2}}. \quad (26)$$

The total energy, in continuum approximation, can be calculated as

$$\varepsilon = \frac{1}{t} \int_{-\infty}^{\infty} \varepsilon dx, \quad (20)$$

where

$$\varepsilon = \frac{m}{2} \left( \frac{\partial q}{\partial t} \right)^2 + \frac{k^2}{2} \left( \frac{\partial q}{\partial x} \right)^2 + f(q) \equiv \varepsilon_1 + \varepsilon_2 + \varepsilon_3. \quad (21)$$

Using eq. (17) we easily obtain

$$\varepsilon = \left( \frac{m\omega^2}{2} + \frac{k^2\kappa^2}{2} \right) \left( \frac{dq}{d\xi} \right)^2 + f(q). \quad (22)$$

as well as

$$\frac{d\varepsilon}{d\xi} = \left[ (m\omega^2 + k^2\kappa^2) \frac{d^2 q}{d\xi^2} + \frac{df}{dq} \frac{dq}{d\xi} \right]. \quad (23)$$

Equations (19) and (23) give

$$\frac{d\varepsilon}{d\xi} = 2k^2\kappa^2 \frac{d^2 q}{d\xi^2} \frac{dq}{d\xi} = k^2\kappa^2 \frac{d}{d\xi} \left( \frac{dq}{d\xi} \right)^2. \quad (24)$$

If we set a constant of integration to be zero, for the integral (20) to converge, as required by the point five of the theorem, we obtain

$$\varepsilon = k^2\kappa^2 \left( \frac{dq}{d\xi} \right)^2 = 2\varepsilon_2, \quad (25)$$

which proves the theorem.

Estimations. – Electric field strength. We want to calculate a projection of the electric field on the x-axis in the point A in fig. 1, which is denoted as E in eq. (2). One way to calculate this internal electric field is straightforward but tedious. We can calculate the components coming from all the excess charges in MT. For example, the electric field from the denoted charge −q in fig. 1 is

$$E_{1x} = \frac{q}{4\pi \varepsilon_0 \varepsilon_x} \left( \frac{8l}{13} - \frac{d}{2} \right) \left[ \left( \frac{8l}{13} - \frac{d}{2} \right)^2 + a^2 \right]^{-\frac{3}{2}}. \quad (26)$$

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Non-negligible contributions are from PF including the dimer with the point A and from the two neighbouring pairs of PFs. For \( \varepsilon_r = 8.41, \quad q = 1.75e, \quad d = 4.04\, \text{nm} \) and for \( \alpha = 0.60\lambda \), which comes from the geometry of MT as the inner and the outer diameters are 15 nm and 25 nm [5], we finally obtain

\[ E = 1.7 \times 10^5 \, \text{N/C}. \]  
(27)

Another way to estimate \( E \) is related to the meaning of \( z_n \). This estimate is extremely important, representing one of the tests of the model introduced in this paper. It was pointed out that \( z_n \) is the longitudinal coordinate of the dimer. This should be understood as the shift of the dimer with respect to its neighbour from the neighbouring PF (see fig. 1). This, practically, means that the two dimers, as \( 8/13 \) and \( -5/13 \) (see fig. 1), yielding the following system of equations:

\[ \sqrt{A/B} \psi_R = \frac{8l}{13}, \quad \sqrt{A/B} \psi_L = -\frac{5l}{13}. \]  
(28)

A solution of this system is \( \sigma = 0.91\sigma_0 \) and \( \sqrt{A/B} = 4.31 \, \text{nm} \). Unfortunately, this is not enough to calculate \( E \) as the value of the parameter \( A \) should be known, which can be seen from eq. (6). Notice the rather large \( \sigma \), which brings about the negligible left minimum (line c in fig. 3).

A next step is to calculate \( A \). It is well known that MTs serve as a “road network” for motor proteins (kinesin and dynein) dragging different “cargos” such as vesicles and mitochondria to different sub-cellular locations. The antikink soliton from above should be understood as a signal for the protein to start moving along PF. The required energy for the soliton creation comes from hydrolysis of GTP. When the system obtains the portion of energy it moves from the bottom in fig. 3 to a higher energy level. If we suppose that the energy released by GTP, which is \( 0.25 \, \text{eV} \), matches the difference between the minimum and maximum, i.e.,

\[ |V(\psi_R)| + V(\psi_M) = 0.25 \, \text{eV}, \]  
(29)
we obtain the value

\[ A = 3.1 \times 10^{-3} \, \text{N/m}. \]  
(30)

This brings about exactly the same value for \( E \) as already calculated, i.e., the value given by eq. (27), which indirectly validates our model.

A careful reader may notice that the GTP energy affects the total energy rather than the potential energy \( V \) only. The maximum of \( V \) corresponds to the zero value of the kinetic energy, but the harmonic term, being essentially the potential energy, deserves a comment. In our approach the first two terms in eq. (3) yield the first term in eq. (4) as both of them are proportional to \( \partial^2 z/\partial q^2 \). This practically means that the harmonic term should be treated as the kinetic energy and that our estimation (30) is correct.

Kink velocity and kink width. From eq. (14) we can recognize the solitonic width \( \Lambda \equiv Nl \), with \( N \) being a number of dimers, as [24]

\[ \frac{2\pi}{Nl} = \frac{3a_0k}{\rho} b_0, \]  
(31)

which, together with the first of eq. (6), gives

\[ v \equiv \frac{\omega}{k} = \frac{3a_0l}{2\pi\gamma} b_0 AN. \]  
(32)

Also, according to the expressions for \( \alpha \) and \( \rho \) in eqs. (5) and (6) and the last two of eq. (13) we easily obtain

\[ k = \frac{v^2}{l^2} \left( m + \frac{\gamma^2}{18Aa_0^2} \right) \equiv \frac{v^2}{l^2} (m + M) \approx \frac{v^2}{l^2} M. \]  
(33)

For the viscosity coefficient \( \gamma \) we use \( \gamma = 5.3 \times 10^{-11} \, \text{kg/s} \) [13], which is still a disputable value.

Using the theorem proved above we can derive the following expression for the total energy:

\[ \mathcal{E} = \frac{4klsa_0}{\rho} \frac{A}{B} b_0^2. \]  
(34)

Equations (32)–(34) and (6) yield the value

\[ \mathcal{E} = \frac{1}{3\pi} \frac{A}{B} b_0^2 \, AN = 4.70 \, AN, \]  
(35)

where the units \( \varepsilon_u = eV \) and \( A_0 = N/m \) are assumed. To derive eq. (34) we incorporated the following constant value to the potential \( V \), initially given by eq. (2), which is convenient for integration:

\[ \Delta V = qE \sqrt{A/B} a_0 + \frac{A^2}{2B} (a_0^2 + b_0^2) - \frac{A^2}{4B} \left( a_0^2 + 6a_0^2b_0^2 + b_0^4 \right). \]  
(36)

This ensures the point five in the theorem from above to be satisfied. The minimum of \( V \) is \( V(\psi_R) = -0.125 \, eV \). The GTP energy is delivered to a single dimer and is transferred to \( N \) of them due the interactions between the dimers. Therefore, we can write

\[ 4.70 \, AN + 0.125 = 0.25. \]  
(37)

The obtained value for \( AN \), together with eqs. (30) and (32), gives

\[ v = 0.54 \, \text{m/s}, \]  
(38)

and

\[ N = 8.6, \]  
(39)

which means that about nine dimers are covered by the kink.

The value for the velocity is at least one order of magnitude smaller than the estimated value in ref. [14]. It is very likely that the assumed values for the parameter \( k \) in ref. [14] were overestimated. This, practically, means that this model could be used to determine the values of the parameters existing in other models and vice versa. Of course, this requires further research.
Concluding remarks. — According to our model the kink soliton is responsible for the energy transfer along the MT. Such wave can be utilized by a cell for some important mechanisms underlying its functional dynamics. As MTs serve as a “road network” for motor proteins it is very likely that the cell’s compartment which needs the specific cargo will launch the soliton of the above kind sending it as a signal along the closest MT. The soliton will activate proper motors being close to MT along which the soliton propagates.

Our model allows us to make some estimates. The small value for \( v \) was anticipated when we discussed the negative sign of \( \alpha \). One should keep in mind that the forces responsible for the soliton creation are not strong covalent bonds, which would provide big \( v \). According to the model the kink covers about nine dimers. This result is reasonable as very small \( N \) would be in contradiction with the continuum approximation. To test the validity of this approximation a discrete counterpart of eq. (3) should be solved numerically and the results should be compared. This research is in progress and will be submitted soon for publication.

It would be very good if the kink excitations along MT were identified experimentally. For this goal we suggest the neutron scattering strategy explained in ref. [25].

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