Elastic vibrations of microtubules in a fluid

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We study theoretically vibrational properties of microtubules (MTs), which are long hollow cylindrical macromolecules with a diam. of the order of 25 nm and serve as a major component of cytoskeleton in eukariotic cells. Modeling MTs by thin elastic cylindrical shells, we derive the eigenfrequencies and eigenmodes of confined elastic vibrations in a shell-fluid system. Numerical calculations, based on recently obtained experimental data for Young's modulus of MT, show that MT-water system supports interface elastic waves with maximal frequencies in a gigahertz range. In a long-wavelength limit, there exist three axisymmetric acoustic waves with velocities of about 200 to 600 m/s, and an infinite set of helical waves with a parabolic dispersion law.

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I. INTRODUCTION

The increasing demand for miniaturization and enhancement of the operation speed has culminated in tremendous progress in nanostructure fabrication and the advent of the principally new microelectronic devices. Recently, much attention has been devoted to the problem of *confined* optical [1] and acoustic [2–5] vibrations in semiconductor heterostructures. Dispersion relations for acoustic waves and the effect of the phonon confinement on electron transport has been analyzed in such artificially grown objects as thin metal films [2], free-standing slabs [3] and whiskers [4], as well as buried cylindrical wires [5]. It has been suggested that such structures with confined lattice vibrations can provide an acoustic fiber for future acoustoelectronic devices [5].

On the other hand, the existence of the physical limitations for the miniaturization due to the atomic structure of matter brought about a new scientific direction, molecular electronics [6]. In contrast to the semiconductor technology that relies on artificially designed structures, molecular electronics explores the physical properties of existing organic macromolecules and their possible applications to information processing. In particular, elastic properties of biological membranes [7] and flagella [8] in an aqueous environment have been studied extensively.

From the point of view of nanophysics and molecular electronics, one of the most interesting biological objects is a cytoskeleton filamentous network existing in every eukariotic cell [9,10]. The various filaments have been classified according to their diameter and include microfilaments (5–7 nm), intermediate filaments (8–11 nm), and microtubules (24–28 nm). Though the cytoskeleton has an impact on some purely biological processes [11] (control of gene expression, protein synthesis, and cell cycle regulation), its main functions are based on the

mechanical properties such as rigidity and elasticity. The cytoskeleton is responsible for supporting the cell shape and serves as a global framework for the mechanical and functional integration of the whole cell [12]. Recently, in a series of ingenious experiments, based on the change of filament shape due to thermal (Brownian) fluctuations, the flexural rigidity and Young's elastic modulus have been measured for the intermediate filaments [15] and microtubules [16–19].

Among three major filamentous components of the cytoskeleton, microtubules (MTs) have received the most attention and are subject to intensive research [9,20–22]. MTs are hollow cylinders [13] of approximately 25 nm outer diameter, 15 nm inner diameter, and indefinite length (see Fig. 1). The wall of a MT cylinder is made
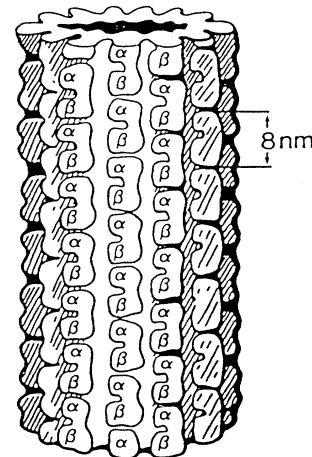

FIG. 1. Schematic drawing of a microtubule formed with protofilaments of tubulin dimers (from Ref. [14]).

up of (usually 13) linear elements termed protofilaments, which are formed of protein subunits known as tubulin dimers. Each 8-nm-long dimer consists of α and β tubulin monomers with a molecular weight of 55 kDa. Results of electron microscopy and x-ray fiber diffraction measurements demonstrate that tubulin dimers form a 120-Å pitch left-handed three-start helix set [23]. The thin-walled tubular shape of MT provides the maximal rigidity of the structure for given cross-sectional area and elastic constants of the constituent material [18].

The main directions of biophysical research on MTs include the study of their elastic properties [16–19] and the dynamical instability of assembling and disassembling [24,25]. The possibility of kinklike excitations in MTs has been investigated theoretically [26] and the experimental observation of MT disassembly due to a low-intensity ultrasound has been reported [27]. Incidentally, considerable attention in semiconductor physics has been focused on the study of electronic and vibrational properties of recently fabricated artificial counterparts of MT—graphene nanotubules [28].

In this paper, we study theoretically the confined acoustic vibrations of MT in a fluid using the formalism of the elasticity theory. The MT is modeled by a thin-walled hollow elastic cylinder immersed in liquid. This approach is similar to that used for the description of underwater acoustic scattering by thin metallic shells [29]. In Sec. II, we obtain the equations of motion for vibrations in a shell-fluid system and derive the dispersion relations for the elastic waves that are analyzed in Sec. III. The results of numerical calculations and discussion are provided in Sec. IV.

II. EQUATIONS OF MOTION

We model a microtubule with an infinitely long cylindrical shell of radius R and wall thickness h. In cylindrical coordinates (r, φ, z), the shell is chosen to be located in the region $R - h/2 < r < R + h/2$; both the inner and outer parts of the shell are filled with a fluid. The equation of motion for the displacement vector $\mathbf{u}$ of the shell is given by the second Newton's law, which in cylindrical coordinates has the form [30]

$$\sigma_{rr,r} + \sigma_{rz,z} + (\sigma_{r\varphi,\varphi} + \sigma_{rr} - \sigma_{\varphi\varphi})/r = \rho \ddot{u}_r ,$$
$$\sigma_{r\varphi,r} + \sigma_{\varphi z,z} + (\sigma_{\varphi\varphi,\varphi} + 2\sigma_{r\varphi})/r = \rho \ddot{u}_\varphi , \quad (1)$$
$$\sigma_{rz,r} + \sigma_{zz,z} + (\sigma_{\varphi z,\varphi} + \sigma_{rz})/r = \rho \ddot{u}_z ,$$

where ρ is a volume density of the shell. The left-hand sides of these equations are equal to elastic forces per unit volume and are written in terms of the stress tensor σ. The subscripts after the commas denote partial derivatives over corresponding variables. Equation (1) is subject to conditions $P_i = \sigma_{ij} n_j$ at the inner and outer surfaces of the shell, where $\mathbf{P}$ is a surface force per unit area and $\mathbf{n}$ is a unit vector normal to the boundary. Since shear forces are absent in fluids, the boundary conditions take the form

$$\sigma_{r\varphi}|_{r=R\mp h/2} = \sigma_{rz}|_{r=R\mp h/2} = 0 , \quad (2)$$

$$\sigma_{rr}|_{r=R+h/2} = p_o , \quad \sigma_{rr}|_{r=R-h/2} = p_i , \quad (3)$$

where p_0 and p_i are the pressures of fluid at the outer and inner boundaries of the shell.

In order to obtain the equations of motion for a *thin* shell ($h \ll R$), Eq. (1) is integrated over r from $R - h/2$ to $R + h/2$. Assuming that all quantities (except σ_{rr}) are practically constant with respect to r, and taking into account the boundary conditions given in Eqs. (2) and (3), we find in the lowest order in small parameter h/R:

$$-\sigma_{\varphi\varphi}/R + (p_o - p_i)/h = \rho \ddot{u}_r ,$$
$$\sigma_{\varphi\varphi,\varphi}/R + \sigma_{\varphi z,z} = \rho \ddot{u}_\varphi , \quad (4)$$
$$\sigma_{\varphi z,\varphi}/R + \sigma_{zz,z} = \rho \ddot{u}_z .$$

The stress tensor σ can be expressed in terms of strain tensor ε with the help of the Hooke's law. In the assumption of isotropic material of the shell, it is given as

$$\sigma_{ij} = \frac{E}{1+\nu} \left[\frac{\nu}{1-2\nu} \delta_{ij} \sum_l \varepsilon_{ll} + \varepsilon_{ij} \right] , \quad (5)$$

where E and ν are Young's modulus and Poisson's ratio of the material. We substitute Eq. (5) into Eq. (4), eliminate the component ε_{rr} with the help of Eq. (2), and express the remaining components of strain tensor $\varepsilon_{\varphi\varphi}$, $\varepsilon_{\varphi z}$, and ε_{zz} in terms of derivatives of the displacement vector $\mathbf{u}$ [30]. Then, the equations of motion in the lowest order in h/R may be written as

$$-\frac{u_r + u_{\varphi,\varphi}}{R^2} - \frac{\nu u_{z,z}}{R} + \frac{p_i - p_o}{\rho h s^2} = \frac{\ddot{u}_r}{s^2} ,$$

$$\frac{u_{r,\varphi} + u_{\varphi,\varphi\varphi}}{R^2} + \nu_- u_{\varphi,zz} + \frac{\nu_+ u_{z,\varphi z}}{R} = \frac{\ddot{u}_\varphi}{s^2} , \quad (6)$$

$$\frac{\nu u_{r,z} + \nu_+ u_{\varphi,\varphi z}}{R} + \frac{\nu_- u_{z,\varphi\varphi}}{R^2} + u_{z,zz} = \frac{\ddot{u}_z}{s^2} .$$

Here $\nu_\pm = (1 \pm \nu)/2$, and $s = \sqrt{E/\rho(1-\nu^2)}$ is the longitudinal "thin plate" sound speed of the shell.

To obtain the equation of motion of the fluid-shell system in a closed form, the pressure terms $p_{i,o}$ need to be related to the shell displacement vector $\mathbf{u}$. The displacement vector $\mathbf{u}_f$ of the fluid can be expressed in terms of the scalar potential Φ through the relationship

$$\mathbf{u}_f = \text{grad } \Phi ; \quad (7)$$

Φ satisfies the wave equation [32]

$$\ddot{\Phi} - s_f^2 \Delta \Phi = 0 , \quad (8)$$

where s_f is a speed of sound in a fluid. Then, using the relation between the scalar potential and pressure

$$p = -\rho_f \ddot{\Phi} ,$$

where ρ_f is a fluid density, the equation for the radial displacement u_r of the shell [given in Eq. (6)] can be rewritten as

$$-\frac{u_r + u_{\varphi,\varphi}}{R^2} - \frac{\nu\, u_{z,z}}{R} + \alpha\, \frac{\ddot{\Phi}_i - \ddot{\Phi}_o}{s^2 R} = \frac{\ddot{u}_r}{s^2}\,, \qquad (9)$$

where $\alpha = \rho_f R/\rho h$ is a dimensionless constant that characterizes the shell-fluid coupling.

We seek the solution of the equations of motion [i.e., Eqs. (6) and (9)] as a superposition of harmonic waves with longitudinal wave vector k_z and azimuthal number m,

$$\begin{bmatrix} u_r \\ u_\varphi \\ u_z \end{bmatrix} = \begin{bmatrix} -ic_r \\ c_\varphi \\ c_z \end{bmatrix} \exp\left(im\varphi + ik_z z - i\omega t\right)\,, \qquad (10)$$

and choose the solutions of Eq. (8) for scalar potentials of fluid corresponding to the evanescent *interface* vibrations localized in the vicinity of the shell:

$$\begin{bmatrix} \Phi_i \\ \Phi_o \end{bmatrix} = \begin{bmatrix} c_i\, I_m(\kappa r/R) \\ c_o K_m(\kappa r/R) \end{bmatrix} \exp\left(im\varphi + ik_z z - i\omega t\right)\,. \qquad (11)$$

Here the inverse confinement length κ (normalized by the radius R) is given by

$$\kappa^2 = R^2(k_z^2 - \omega^2/s_f^2) \equiv k^2 - \left(\frac{s}{s_f}\right)^2 \Omega^2\,, \qquad (12)$$

where $\Omega = \omega R/s$ and $k = k_z R$ are the dimensionless frequency and wave vector, respectively. Interface vibrations of fluid, localized near the shell surface, correspond to region $\kappa^2 > 0$; in the opposite case of $\omega > s_f k_z$ the acoustic energy is radiated from the shell. The requirement of the continuity of the fluid and shell displacements at $r = R$ leads, after use of Eq. (7), to the following relation between $c_{i,o}$ and c_r:

$$\begin{bmatrix} c_i \\ c_o \end{bmatrix} = -ic_r R \begin{bmatrix} 1/\kappa I_m'(\kappa) \\ 1/\kappa K_m'(\kappa) \end{bmatrix}\,. \qquad (13)$$

Finally, substituting Eqs. (10)–(13) into (6) and (9), we obtain the eigenequation for the interface acoustic vibration in the a shell-fluid system:

$$\mathcal{D}\,[c_r,\ c_\varphi,\ c_z]^{\mathbf{T}} = 0\,, \qquad (14)$$

where the dynamical matrix $\mathcal{D}$ is given by

$$\mathcal{D} = \begin{bmatrix} \Omega^2(1 + W_{m\kappa}) - 1 & m & \nu k \\ m & \Omega^2 - m^2 - \nu_- k^2 & -\nu_+ m k \\ \nu k & -\nu_+ m k & \Omega^2 - \nu_- m^2 - k^2 \end{bmatrix}\,, \qquad (15)$$

and the coupling term between the shell and fluid is equal to

$$W_{m\kappa} = \frac{\alpha}{\kappa}\left[\frac{I_m(\kappa)}{I_m'(\kappa)} + \frac{K_m(\kappa)}{-K_m'(\kappa)}\right]\,. \qquad (16)$$

III. ANALYSIS OF DISPERSION RELATION

From Eq. (14) we find the dispersion relation for confined waves in a shell-fluid system in a form

$$\det \mathcal{D} = 0\,. \qquad (17)$$

As follows from Eqs. (15) and (16), $\mathcal{D}$ is a real symmetric 3×3 matrix depending on azimuthal number m. Therefore, for each given m the dispersion relation [Eq. (17)] specifies three positive vibrational modes $\Omega_m^{(j)}$, which are identified by $j =$ I, II, and III in decreasing order:

$$\Omega_m^{\mathrm{I}}(k) > \Omega_m^{\mathrm{II}}(k) > \Omega_m^{\mathrm{III}}(k)\,. \qquad (18)$$

The only exclusion from inequality in Eq. (18) occurs for $m = 0$, where the pure *torsional* mode,

$$\Omega_0^{\mathrm{II}}(k) = \sqrt{\nu_-}\,k\,, \qquad (19)$$

is decoupled from other modes over the entire range of k, and can cross the mode with $j =$III; a graphical illustration is given in the next section.

A. Free cylindrical shell

Let us first analyze the vibration of a *free* cylindrical shell [31] by taking the coupling constant α equal to zero. In this case, the dispersion relation defined by Eqs. (15)–(17) is reduced to a *bicubic* equation with respect to the dimensionless frequency $\Omega \equiv \omega R/s$. It is more convenient, however, to calculate the inverse relation $k_{jm}(\Omega)$ as a solution of *bi-quadratic* equation in wave vector k. Since the explicit form of the dispersion relation can be readily obtained from Eqs. (15) and (17), we present only the asymptotic values of $\Omega_m^{(j)}(k)$. For a large wavelength ($k \equiv k_z R \ll 1$), we have

$$\Omega_m^{\mathrm{I}}(k) \simeq \sqrt{m^2 + 1},\quad \Omega_m^{\mathrm{II}}(k) \simeq \sqrt{\nu_-}(m + k), \qquad (20)$$

$$\Omega_{m=0}^{\mathrm{III}}(k) \simeq \sqrt{1 - \nu^2}\,k,\quad \Omega_{m\neq 0}^{\mathrm{III}}(k) \simeq \sqrt{\frac{1 - \nu^2}{m^2 + 1}}\,\frac{k^2}{m}\,.$$

In the axisymmetric case ($m = 0$) and a long-wavelength limit, the modes I, II, and III correspond to pure *radial, torsional,* and *longitudinal* motion; for $m \neq 0$ the radial and torsional motions are coupled. In the short-wavelength limit ($k \gg m + 1$), we obtain asymptotic expressions that are not dependent on the azimuthal number m:

$$\Omega_m^{\mathrm{I}}(k) \simeq k, \quad \Omega_m^{\mathrm{II}}(k) \simeq \sqrt{\nu_- }k, \quad \Omega_m^{\mathrm{III}}(k) \simeq \sqrt{1 - \nu^2}. \quad (21)$$

Analysis of coefficients c_r, c_φ, and c_z in Eq. (14) shows that in the limit of large k the modes $\Omega_m^{\mathrm{I}}(k)$, $\Omega_m^{\mathrm{II}}(k)$, and $\Omega_m^{\mathrm{III}}(k)$ correspond to pure *longitudinal, torsional,* and *radial* vibrations. Note that for any m the minimal value of Ω_m^{I} is greater then the maximal value of Ω_m^{III}. Therefore, for given frequency Ω there exist no more than two positive wave vectors $k_m^{(j)}$, which is consistent with the availability of the *biquadratic* dispersion relation with respect to k.

B. Fluid-shell system

Let us return now to the analysis of Eq. (17) for vibrations in a *coupled* shell-fluid system ($\alpha \neq 0$). Existence of a fluid in the outer part of the shell can lead to a qualitative change in the dispersion relation. Now the (ω, k_z) plane is divided to two sectors by the line $\omega = s_f k_z$. The region $\omega < s_f k_z$ (or $\kappa^2 > 0$) corresponds to the *interface* vibrations, localized at distance R/κ from the shell according to Eq. (11). The opposite case of $\omega > s_f k_z$ (or $\kappa^2 < 0$) can be described by Eq. (11), after the substitution of [33]

$$I_m(-i|\kappa|) = i^{-m} J_m(|\kappa|),$$

$$K_m(-i|\kappa|) = \frac{\pi}{2} i^{m+1} H_m^{(1)}(|\kappa|),$$

as the radiation of an acoustic wave to the outer space since the Hankel function of the first kind, $H_m^{(1)}$, corresponds to an outgoing cylindrical wave. In this situation, the eigenfrequencies $\Omega(k)$ will be complex with negative imaginary parts and, according to Eqs. (10) and (11), the amplitudes of vibrations will decay exponentially in time due to an energy loss by the system. From the discussion above, it follows that the behavior of acoustic modes depends drastically on the relation between the sound speeds in a fluid and the shell, s_f and s. Since sound speed in water is approximately 2.5 times larger than that in the MT (as discussed in the next section), $s_f > s$ is assumed throughout the rest of this paper.

To describe the spectrum of vibrations in the shell-fluid system, we derive the asymptotical expressions for the coupling term $W_{m\kappa}$ in two limiting cases of phase velocities (i) close to s_f (small κ) and (ii) much smaller than s_f (large κ). Using the expression for the Wronskian of the modified Bessel equation [33], $I_m(\kappa)K_m'(\kappa) - K_m(\kappa)I_m'(\kappa) = 1/\kappa$, and asymptotics of functions I_m and K_m, we find from Eq. (16)

$$W_{m\kappa} \simeq \begin{bmatrix} 2\alpha/\kappa^2, & \text{for } \kappa \ll 1 \text{ and } m = 0 \\ 2\alpha/m, & \text{for } \kappa \ll 1 \text{ and } m \neq 0 \quad (22) \\ 2\alpha/\kappa, & \text{for } \kappa \gg m + 1 \text{ and any } m. \end{bmatrix}$$

Since at large κ the coupling term $W_{m\kappa} \simeq 2\alpha/\kappa$ tends to zero, we deduce that in a *short-wavelength* limit ($k \gg m + 1$), the vibration spectrum of the shell-fluid system tends to that of a free shell [Eq. (21)], and classification

of modes I, II, III as pure *longitudinal, torsional,* and *radial*, is unchanged. The physical explanation for this result is that in the limit of large κ, only a fluid in the nearest vicinity, within R/κ from the shell, participates in vibration; therefore, the motion of the shell is essentially free.

In the *long-wavelength* limit, there exist two distinct cases: $m = 0$ and $m \neq 0$. For *axisymmetric* vibrations ($m=0$), the mode II with dispersion given by Eq. (19) corresponds to a pure torsional vibrations of the shell *only*, and is decoupled from the rest of the modes in the whole range of k. The frequencies of axisymmetric modes I and III should be found from the remaining 2×2 determinant involving the coupling term $W_{0\kappa}$. Since this term diverges at small κ [Eq. (22)], the frequencies $\Omega_0^{\mathrm{I}}(k)$ and $\Omega_0^{\mathrm{III}}(k)$ at small k should approach zero maintaining phase velocities less than s_f to avoid crossing the $\omega = s_f k_z$ line. Analysis shows that in the limiting case of small k the frequencies $\Omega_0^{\mathrm{I}}(k)$ and $\Omega_0^{\mathrm{III}}(k)$ are proportional to the wave vector:

$$\Omega_0^{\mathrm{I,III}}(k) \simeq \sqrt{c_{1,3}}\, k. \quad (23)$$

Substituting the expansion given in Eq. (23) into the dispersion equation, and collecting the terms of the lowest (second) order in k, the coefficients $c_{1,3}$ are found as solutions of the following quadratic equation:

$$(s^2 + 2\alpha s_f^2)c^2 - [s^2(1 - \nu^2) + s_f^2(1 + 2\alpha)]c$$
$$+ s_f^2(1 - \nu^2) = 0. \quad (24)$$

It can be shown that Eq. (24) always has two real positive roots, provided that $s_f > s$. In case of $2\alpha \gg (s/s_f)^2$ and $\nu^2 \ll 1$ the solutions of Eq. (24) are given by $c_1 \approx 1$ and $c_3 \approx 1/2\alpha$. For a coupled system (in contrast to a free shell), both modes I and III are of the mixed *radial-longitudinal* type even at $m = 0$ and small k. Note also that in the absence of fluid the frequency of the mode I would have a finite value at $k = 0$: in the case of $\alpha = 0$ we have $\Omega_0^{\mathrm{I}}(0) = 1$ in accordance with Eq. (20).

In the case of vibrations *without rotational symmetry* ($m \neq 0$), the coupling term $W_{m\kappa}$ reaches a finite value $W_{m0} = 2\alpha/m$ at $\kappa = 0$ [see Eq. (22)], and modes I and II touch the line $\omega = s_f k_z$ at finite frequencies, while the localization length R/κ will tend to infinity. However, in the case of Re $(\omega) > s_f k_z$ the frequency ω will have a negative imaginary part, and the amplitudes of vibrations will decay as a result of the radiation of acoustic energy out of the shell. The frequency of the mode III will preserve its parabolic dependence on the wave vector in the limit of small k [Eq. (20)], though with a renormalized coefficient:

$$\Omega_{m \neq 0}^{\mathrm{III}}(k) \simeq \sqrt{\frac{1 - \nu^2}{m^2 + 2\alpha m + 1}} \frac{k^2}{m}. \quad (25)$$

Thus, in the long-wavelength limit ($k_z \ll 1/R$), the shell-fluid system supports three axisymmetric interface modes with a linear dispersion law, $\Omega_0^{(j)}(k) \propto k$, corresponding to conventional *acoustic waves* with linear dis-

persion. In addition, there exists an infinite set of interface modes with a parabolic dispersion law, $\Omega_m^{III}(k) \propto k^2$ and $m = 1, 2, \ldots$, as given by Eq. (25). Since the lines of constant phases for such waves,

$$m\varphi + k_z z - \omega t = \text{const} ,$$

have the form of helices according to Eqs. (10) and (11), this set of modes can be termed as *helical waves*. In contrast to acoustic waves with constant phase and group velocities, those for helical waves tend to zero at small wave vectors k_z.

IV. NUMERICAL RESULTS AND DISCUSSION

In order to find the vibrational spectrum of the shell-fluid system in the whole range of k, we have to solve the transcendental dispersion relation given by Eqs. (15)–(17) numerically. Among the parameters required for the numerical evaluation, the most difficult to obtain are the elastic constants, E and ν, for MT, since no direct measurement seems to be possible. However, the results depend only weakly on the Poisson's ratio ν, and reliable values for the Young's modulus E has been measured [16–19] using the elegant method based on thermal fluctuations of shape of MT.

The main physical idea for the measurement of a flexible rigidity (FR) of long macromolecules is that they are subject to the Brownian motion due to interaction with the surrounding molecules of water [34,35]. Since the macromolecules are relatively heavy, the fluctuation of their center of mass is negligible, but their shape can be changed notably, depending directly on the FR for the molecule. The latter is equal to EI, i.e., the product of Young's modulus E and the geometrical moment of inertia I of a molecule's cross section.

The first determination of the MT rigidity, performed by Yamazaki, Maeda, and Miki-Noumura [16] and Mizushima-Sugano, a Maeda, and Miki-Noumura [17], were based on measurement of the thermal fluctuations of the end-to-end distance of MT; knowledge of these fluctuations and the total length of MT allows the determination of the FR [35]. However, such measurements lack a test of internal consistency, which is desirable because of the difficulty in distinguishing fluctuations from measurement noise and nonthermal bending [18]. It is believed now that the values obtained in Refs. [16,17] are almost 2 orders of magnitude smaller than the actual ones because of measurement errors and intrinsic bend of MT [18].

The first reliable data on the rigidity of MT have been obtained by Gittes *et al.* [18] using dark-field and fluorescence video-enhanced microscopy to monitor the thermal fluctuations in shape of taxol-stabilized MT free in solution. In order to overcome the problems due to the measurement noise, the FR was deduced from the Fourier decomposition of the MT shape. Results of analysis of up to the three lowest Fourier modes of the shape of MT of different length were consistent with each other and gave the value of FR corresponding to the isotropic Young's

modulus $E \sim 1.2$ GPa. Gittes *et al.* [18] have also measured the FR of actin filaments and obtained the value of the Young's modulus $E = 2.6$ GPa in good agreement with the earlier results [15]. More recently, Venier *et al.* [19] applied two independent methods to measure the FR of MT attached by one end to axonemal pieces fixed on the glass. In this study, the FR was obtained by analyzing the bending shape of MT in a hydrodynamic flow and the thermal fluctuations of the free end of MT. Both methods gave similar results for FR corresponding to an isotropic Young's modulus $E = 0.5 \pm 0.1$ GPa. The factor of 2 discrepancy with the results of Gittes *et al.* were interpreted as due to the stiffening action of taxol used in Ref. [18] to stabilize the MT.

In our numerical calculations, the most recent value of Young's modulus, $E = 0.5 \pm 0.1$ GPa from Ref. [19], is used. Another parameter needed in the calculation is Poisson's ratio ν. In general, the value for this parameter (of known materials) lies in the range $0 < \nu < 1/2$, with typical values of $\nu = 0.2$–0.3. Since our results depend only weakly on ν, we choose, for the sake of definiteness, the value $\nu = 0.3$.

Approximation of a microtubule by a hollow cylinder with ideal surfaces used in Refs. [18,19] to calculate the geometric moment of inertia, required the use of "contact" inner radius R_i of 11.5 nm (measured in Ref. [23]) and wall thickness h of 2.7 nm for 14-protofilament MT. Thus, the outer radius R_o of MT in our calculation is 14.2 nm and the mean radius $R \equiv (R_i + R_o)/2$ is approximately 12.8 nm. At the same time, by taking the mass of a tubulin dimer to be $M = 110$ kDa $= 1.83 \times 10^{-19}$ g, and the length $\ell = 8$ nm, we find the density $\rho = 14M/\pi(R_o^2 - R_i^2)\ell \approx 1.47$ g/cm^3 and the "thin-plate" sound speed $s = \sqrt{E/\rho(1 - \nu^2)} \approx 610$ m/s. Using the density of water ($\rho_f = 1$ g/cm^3) and speed of sound in water ($s_f = 1.50$ km/s), the value of the dimensionless coupling constant $\alpha \equiv \rho_f R/\rho h$ is found to be approximately 3.22.

We note that the calculated sound speed in MT is 2.5 times lower than in water, in contrast to that in materials with cellulose-based cell walls (e.g., wood), where the propagation speed is substantially higher. The reason for such a difference lies in the large Young's modulus of cellulose, $E \sim 100$ GPa [36], and is because of the nature of chemical binding in this polymer. In fact, glucose monomers are linked to cellulose by strong β 1,4-glicosyde (covalent) bonds, while tubulin subunits assemble into MT due to much weaker hydrophobic interaction.

The results of numerical calculations of dispersion $\Omega_m^{(j)}(k)$ for azimuthal numbers $m = 1$, 2, and 3 are presented in Figs. 2–4. Thick solid lines correspond to vibrations of MT interacting with water both *outside* and *inside* of MT. The eigenfrequencies of *free* MT are presented for comparison and are marked by thick dashed lines. The thin line is specified by $\omega = s_f k_z$ and it separates the region of interface vibrations in the MT-water system from that of radiative waves. Note that the dimensionless frequency $\Omega = 1$ corresponds to a cyclic frequency of $f_0 \approx 7.6$ GHz.

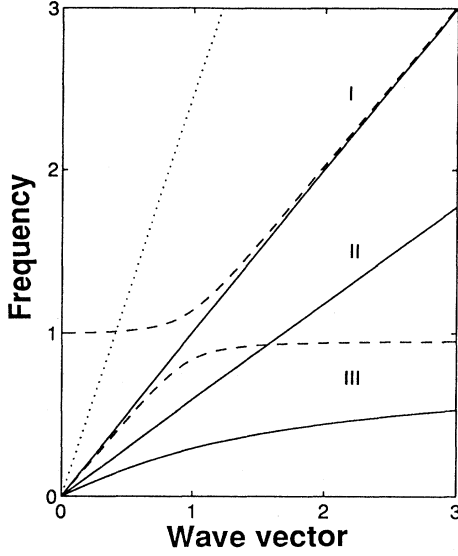As can be seen from Figs. 2–4, the frequencies of vi-

FIG. 2. Dimensionless frequency $\Omega = \omega R/s$ vs dimensionless wave vector $k = Rk_z$ for axisymmetric $(m = 0)$ vibrations of MT. $\Omega = 1$ corresponds to a cyclic frequency 7.6 GHz. Solid and dashed lines correspond to vibrations in a MT with and without water, respectively. Thin dotted line at $\omega = s_f k_z$ separates regions of interface and radiative waves.

brations for MT-water system tend to those of a *free* MT at large wave vectors $(k_z \gg m/R)$ and do not depend on the azimuthal number m. In a short-wavelength limit, the modes I and II have a linear dispersion with velocities $s \approx 610$ m/s and $s\sqrt{(1 - \nu)/2} \approx 360$ m/s, while the cyclic frequencies of the type-III modes tend to a con-
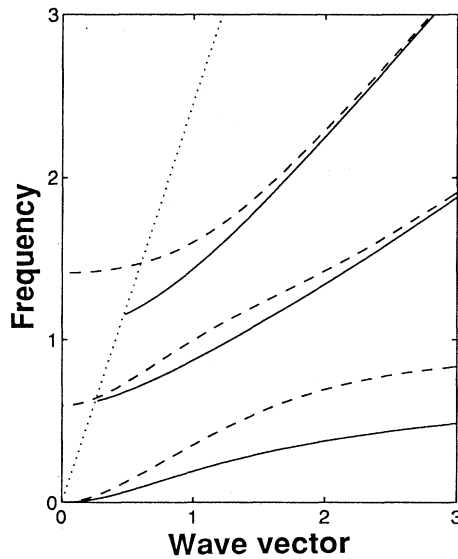

FIG. 3. Dispersion relations for vibration of MT with azimuthal number $m = 1$. Other notations coincide with those in Fig. 2.
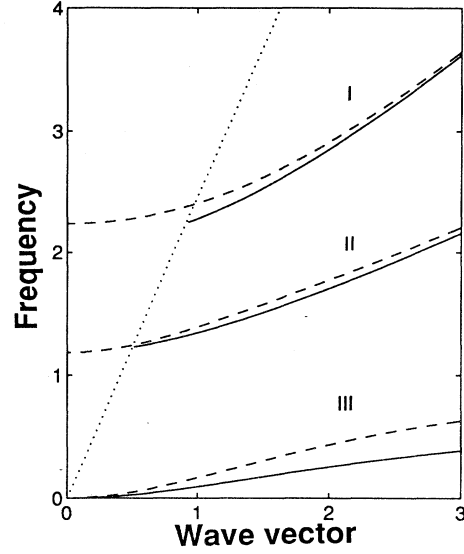
FIG. 4. Dispersion relations for vibration of MT with azimuthal number $m = 2$. Other notations coincide with those in Fig. 2.

stant value of 7.2 GHz [see Eq. (20)]. In the limit of large k, modes I, II, and III correspond to pure longitudinal, torsional, and radial vibrations. Note that because of our assumption of homogeneous MT walls, the results at $k \gtrsim 1$ are only of qualitative character (the length of the tubulin dimer, 8 nm, is comparable to the radius of MT, 13 nm). Moreover, since our derivation was based on the assumption of thin MT walls $(h \ll R)$, the results are even qualitatively wrong for $k > R/h \approx 5$. The assumptions made do not modify the long-wavelength $(k \ll 1)$ part of the spectrum, which is of prime importance for the study of conformational changes in proteins [37,38].

The behavior of the eigenfrequencies at intermediate and small values of wave vector k depends essentially on whether the azimuthal number m is equal to zero.

For axisymmetric vibrations $(m = 0)$, the mode $\Omega_0^{\mathrm{II}}(k) = \sqrt{(1 - \nu)/2}\,k$ with the velocity 360 m/s (see Fig. 2) involves the pure torsional vibrations of the shell *only* and is decoupled from other modes [cf. Eq. (19)]. The other two modes in Fig. 2 (I and III) cannot touch the line $\omega = s_f k_z$, because the shell-fluid coupling term $W_{0\kappa}$ [given by Eq. (22)] diverges when phase velocity of a wave approaches sound speed in a fluid s_f. At large wavelength, the radial-longitudinal modes I and III depend linearly on k and are characterized by speeds of propagation 614 and 225 m/s according to Eqs. (23) and (24). The linear dependence of Ω_0^{I}, Ω_0^{II}, and Ω_0^{III} on k in the long-wavelength limit allows us to identify them with conventional *acoustic* modes, in contrast to other elastic modes that also could be called acoustical. For vibrations without rotational symmetry, two modes $(\Omega_m^{\mathrm{I}}$ and $\Omega_m^{\mathrm{II}})$ for each given $m \neq 0$ cross the line $\omega = s_f k_z$ and become *radiative* modes at small k. Continuation of their dispersion curves is not shown at $k_z < \mathrm{Re}\,(\omega/s_f)$ in Figs. 3 and 4, since in this region the eigenfrequencies

are complex. The *helical* mode III remains real at all wavelengths, and $\Omega_m^{III} \propto k^2$ in agreement with Eq. (25).

V. CONCLUSION

We have investigated the existence of interface elastic vibrations of MT immersed in water. It is found that this system supports nonradiative elastic waves localized in the vicinity of the MT wall with maximal frequencies of order of tens of gigahertz. In the long-wavelength limit, there exist three axisymmetric *acoustic* waves with propagation speed of approximately 200–600 m/s and an infinite set of *helical* waves with a parabolic dispersion law.

Our results draw attention to a parallel existing be-tween recent studies of acoustic phonon quantization in artificially grown semiconductor nanostructures [2–5,28] and vibrations of their biological counterparts, micro-tubules. On other hand we hope that our analysis of large-scale collective motions of MT based on elasticity formalism complements molucular dynamics simulations of vibrational spectra of globular proteins [37–39].

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[1] L. Wendler, Phys. Status Solidi (b) **124**, 513 (1985); N. Mori and T. Ando, Phys. Rev. B **40**, 6175 (1989); M. A. Stroscio, *ibid.* **40**, 6428 (1989); K. W. Kim *et al.*, J. Appl. Phys. **72**, 2282 (1992).

[2] N. Perrin and M. N. Wybourne, Phys. Rev. B **43**, 9511 (1991); J. C. Nabity and M. N. Wybourne, *ibid.* **44**, 8990 (1991); K. Johnson, M. N. Wybourne, and N. Perrin, *ibid.* **50**, 2035 (1994).

[3] N. Bannov, V. Mitin, and M. Stroscio, Phys. Status Solidi (b) **183**, 131 (1994); N. Perrin, Phys. Rev. B **48**, 12 151 (1994); N. Bannov, V. Aristov, and V. Mitin, Solid State Commun. **93**, 483 (1995).

[4] A. K. Viswanath *et al.*, Microwave Optical Technol. Lett. **7**, 94 (1994); M. A. Stroscio and K. W. Kim, Phys. Rev. B **48**, 1936 (1993); S. Yu *et al.*, *ibid.* **50**, 1733 (1994); M. A. Stroscio *et al.*, J. Appl. Phys. **76**, 4670 (1994).

[5] N. Nishiguchi, Jpn. J. Appl. Phys. **33**, 2852 (1994); Phys. Rev. B **50**, 10 970 (1994).

[6] *Molecular Electronics — Science and Technology*, edited by A. Aviram (Engineering Foundation, New York, 1989); D. Koruga and J. Simić-Krstić, J. Mol. Electron. **6**, 167 (1990).

[7] R. Lipowsky, Festkörperprobleme **32**, 19 (1992); H. Bolterauer, J. A. Tuszyński, and M. V. Satarić, Phys. Rev. A **44**, 1366 (1991).

[8] R. Rikmenspoel, in *Dynamics in Fluids and Plasmas*, edited by S. I. Pai (Academic, New York, 1966), p. 9.

[9] M. Schliwa, *The Cytoskeleton. An Introductory Survey* (Springer, New York, 1986).

[10] P. Traub, *Intermediate filaments. A Review* (Springer, New York, 1985); K. C. Holmes *et al.*, Nature (London) **347**, 44 (1990).

[11] U. Z. Littauer and I. Ginsburg, in *Gene Expression in Brain*, edited by C. Zomzely-Neurath and W. A. Walker (Wiley, New York, 1985).

[12] K. Luby-Phelps, Current Opinion Cell Biol. **6**, 3 (1994).

[13] L. Beese, G. Stubbs, and C. Cohen, J. Mol. Biol. **194**, 257 (1987).

[14] S. Rasmussen *et al.*, Physica (Amsterdam) **42D**, 428 (1990).

[15] T. Takebayashi, Y. Morita, and F. Oosawa, Biochem. Biophys. Acta **492**, 357 (1977); H. Nagashima and S. Asakura, J. Mol. Biol. **136**, 169 (1980); T. Yanagida *et al.*, Nature (London) **307**, 58 (1984).

[16] S. Yamazaki, T. Maeda, and T. Miki-Noumura, in *Biological Functions of Microtubules and Related Structures*, edited by H. Sakai, H. Mohri, and G. G. Borisy (Academic, New York, 1982), p. 41.

[17] J. Mizushima-Sugano, T. Maeda, and T. Miki-Noumura, Biochem. Biophys. Acta **755**, 257 (1983).

[18] F. Gittes, B. Mickey, J. Nettleton, and J. Howard, J. Cell. Biol. **120**, 923 (1993).

[19] P. Venier, A. C. Maggs, M.-F. Carlier, and D. Pantaloni, J. Biol. Chem. **269**, 13 353 (1994).

[20] P. Dustin, *Microtubules* (Springer, Berlin, 1984).

[21] *Microtubules*, edited by K. Roberts and J. S. Hyams (Academic, New York, 1979).

[22] N. Hirokawa, Current Opinion Cell Biol. **6**, 71 (1994); H. C. Joshi, *ibid.* **6**, 55 (1994).

[23] D. Chrétien and R. H. Wade, Biol. Cell. **71**, 161 (1991).

[24] T. Mitchison and M. Kirschner, Nature (London) **312**, 232 (1984); D. K. Fygenson, E. Braun, and A. Libchaber, Phys. Rev. E **50**, 1579 (1994).

[25] P. M. Bayley, M. J. Schilstra, and S. R. Martin, J. Cell. Sci. **95**, 33 (1990); S. R. Martin, M. J. Schilstra, and P. M. Bayley, Biophys. J. **65**, 578 (1993).

[26] M. Satarić *et al.*, J. Mol. Electron. **6**, 63 (1990); M. V. Satarić, J. A. Tuszyński, and R. B. Žakula, Phys. Rev. E **48**, 589 (1993).

[27] J. Adler, O. Necas, and I. Hrazdira, Folia Biol. (Prague) **39**, 55 (1993).

[28] S. Iijima, Nature (London) **354**, 56 (1991); M. F. Lin and K. W.-K. Shung, Phys. Rev. B **47**, 6617 (1993); R. A. Jishi, M. S. Dresselhaus, and G. Dresselhaus, *ibid.* **48**, 11 385 (1993).

[29] R. D. Doolittle and H. Überall, J. Acoust. Soc. Am. **39**, 13 (1966); J. D. Murphy, E. D. Breitenbach, and H. Überall, *ibid.* **64**, 677 (1978); E. D. Breitenbach, H. Überall, and K.-B. Yoo, *ibid.* **74**, 1267 (1983); M. Talmant and G. Quentin, in *Progress in Underwater Acoustics*, edited by H. M. Merklinger (Plenum, New York, 1987), p. 137.

[30] K. F. Graff, *Wave Motion in Elastic Solids* (Clarendon, Oxford, 1975).

[31] S. Markuš, *The Mechanics of Vibrations of Cylindrical Shells* (Elsevier, Amsterdam, 1988).

[32] L. D. Landau and E. M. Lifshits, *Fluid Mechanics* (Pergamon, Oxford, 1987).

[33] I. S. Gradshtein and I. M. Ryzhik, *Tables of Integrals, Series, and Products* (Academic, Boston, 1994).

[34] R. A. Harris and J. E. Hearst, J. Chem. Phys. **44**, 2595 (1966).

[35] L. D. Landau and E. M. Lifshits, *Statistical Physics, Part 1* (Pergamon, Oxford, 1980).

[36] S. A. Wainwright, W. D. Biggs, J. D. Currey, and J. M. Gosline, *Mechanical Design in Organisms* (Princeton University Press, Princeton, 1982).

[37] M. M. Tirion, D. ben-Avraham, and K. C. Holmes, in *Actin: Biophysics, Biochemistry, and Cell Biology*, edited by J. E. Estes and P. J. Higgins (Plenum, New York, 1994), pp. 3–12.

[38] D. ben-Avraham, Phys. Rev. B **47**, 14 559 (1993); M. Tirion and D. ben-Avraham, J. Mol. Biol. **230**, 186 (1993).

[39] M. Levitt, J. Mol. Biol. **168**, 595 (1983); M. Levitt, C. Sander, and P. S. Stern, *ibid.* **181**, 423 (19985); B. Brooks and B. Karplus, Biophys. **80**, 6571 (1983); N. Go, T. Noguti, and T. Nishikawa, Proc. Natl. Acad. Sci. USA **80**, 3696 (1983).