Coupled oscillations of a protein microtubule immersed in cytoplasm: an orthotropic elastic shell modeling

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Received: 31 May 2011 / Accepted: 11 January 2012 /
Published online: 18 February 2012
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Abstract Revealing vibration characteristics of sub-cellular structural components such as membranes and microtubules has a principal role in obtaining a deeper understanding of their biological functions. Nevertheless, limitations and challenges in biological experiments at this scale necessitates the use of mathematical and computational models as an alternative solution. As one of the three major cytoskeletal filaments, microtubules are highly anisotropic structures built from tubulin heterodimers. They are hollow cylindrical shells with a ~ 25 nm outer diameter and are tens of microns long. In this study, a mechanical model including the effects of the viscous cytosol and surrounding filaments is developed for predicting the coupled oscillations of a single microtubule immersed in cytoplasm. The first-order shear deformation shell theory for orthotropic materials is used to model the microtubule, whereas the motion of the cytosol is analyzed by considering the Stokes flow. The viscous cytosol and the microtubule are coupled through the continuity condition across the microtubule–cytosol interface. The stress and velocity fields in the cytosol induced by vibrating microtubule are analytically determined. Finally, the influences of the dynamic viscosity of the cytosol, filament network elasticity, microtubule shear modulus, and circumferential wave-number on longitudinal, radial, and torsional modes of microtubule vibration are elucidated.

Keywords Cell mechanics · Microtubule-cytoplasm system · Coupled frequency · Orthotropic elastic shell

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1 Introduction

Microtubules, as the major filaments of the cytoskeleton, are known as a source of vibrations in the living cell and generate cellular activities in a wide range of frequencies [1]. These activities are connected to biological processes inside the cell and have fundamental role in cell physiology and participate in controlling the organization of living matter [2]. Microtubules are highly dynamic cytoskeletal biological nanotubes and are involved in a variety of cell functions important in the development and maintenance of cell shape, cell reproduction and division, intracellular transport, and cell movement [3]. It is worth noting that predicting the first frequencies and mode shapes of the microtubule oscillations can be used to estimate the Young's modulus of the microtubules. These modes can be observed by photonic microscopy [4]. The higher modes of microtubule vibration involve changes in the diameter of the microtubule and play a central role in the polymerization–depolymerization process or the interactions between microtubule and microtubule-associated proteins (MAPs) [4]. Microtubules also act as important targets for anticancer drugs [5]. Microtubules are built by two globular proteins, α - and β -tubulin, dimers and are long hollow cylindrical shells with outer and inner diameters of about 25 and 15 nm, respectively, and with lengths of generally 1–10 μm in the cell body and 50–100 μm or more in axons [6]. Unlike actin filaments, DNA and many other rod-like biological polymers, microtubules are hollow cylindrical tubes that exhibit many shell-like mechanical phenomena.

There exist three possible sources of energy to excite and sustain microtubule vibrations in living cells [1]: (1) Energy produced during hydrolysis of guanosine triphosphate (GTP) and delivered to microtubules; (2) Energy transferred from movement of motor proteins and their interaction with microtubules; (3) Energy released from mitochondria, which may be the most significant energy source for excitations of microtubule vibrations.

During the last decade, considerable attention has been focused on the vibration analysis of microtubules and it has been shown that a systematic investigation of microtubule vibration could strongly enhance the understanding of its biological functions [7]. Using an isotropic continuum model, the elastic vibrations of microtubules in fluid medium have been investigated by Sirenko et al. [8]. They used an isotropic membrane shell to model the microtubule and assumed the fluid around the microtubule to be an ideal fluid with a large Reynolds number. In their study, four possible vibration modes, e.g., longitudinal, circumferential, radial, and transverse bending vibrations were predicted for microtubules. One year later, Pokorný et al. [9] analyzed the vibrations of microtubules modeled as a one-dimensional chain of mass particles with translational symmetry. Kasas et al. [4] used the finite element method for free vibration analysis of microtubules without considering the effect of the surrounding cytoplasm. A two-dimensional lattice model was developed by Portet et al. [10] for longitudinal and transverse modes. An orthotropic elastic shell model has been developed to study the free vibration of microtubules [11, 12]. The oscillation frequencies and buckling load of a single microtubule have been obtained by Shi et al. [13] using a Timoshenko-beam model, classical isotropic Euler–Bernoulli beam model and two-dimensional orthotropic elastic shell model. The nonlocal continuum Euler–Bernoulli beam theory and the numerical differential quadrature method have been used by Civalek and Akgöz [14] to study microtubule vibrations. The effect of the surrounding medium has been neglected in their analysis. Recently, the vibration characteristics of microtubules have been examined based on a parabolic shear deformable beam model [15]. The electric oscillations excited by vibrations of microtubules have also been analyzed by

Cifra et al. [1]. Their model corresponds to optical branches of longitudinal vibrations. More recently, a mechanics model of microtubule vibration, considering the coupled effect of the viscoelastic surrounding cytoplasm, has been analytically investigated by Ghavanloo et al. [16]. Samarbakhsh and Tuszynski [17] presented an analytical solution for the free vibration of a microtubule. Their method is based on converting the related beam equation to an equation that allows using the method of separation of variables.

It should be noted that most research has been concentrated on the vibration characteristics of the microtubules without considering cytoplasm effects. Nevertheless, it has been shown in various experiments [18] that the cytoplasm exhibits both viscosity and elasticity from the fluid and the solid cytoskeleton networks, respectively. Moreover, in some previous works, the microtubules have been modeled as isotropic tubes with a single Young's modulus and being temperature-independent. However, experiments show that the microtubules are strongly anisotropic, whereas the longitudinal bonds between the tubulin dimers are much stiffer and stronger than the lateral bonds [19]. Therefore, the coupled effect of the microtubule-cytoplasm system and anisotropic properties of the microtubule have to be taken into account in vibration analysis of the microtubules.

To address the above-mentioned controversy in the structural role of microtubules, this paper describes a mechanics model of an anisotropic microtubule to predict the coupled frequencies of microtubule-cytoplasm system including the effect of the surrounding cytoplasm. In the present paper, the displacement representation of the first-order shear deformation shell theory for orthotropic materials is developed for modeling the microtubule. It is well known that the configuration of microtubules can be described by a pair of integers N - S , where N is the protofilament number and S the helix-start number. Most cellular microtubules have 13 protofilaments and three starts, whereas this number can vary from 9 to 17 in vitro [20, 21]. The present study considers the 13-3 microtubules since they are the majority in vivo. In order to investigate the effects of surrounding cytoplasm on the vibration of microtubules, the cytoplasm is characterized by viscous cytosol and an elastic filament network. The cytosol motion is modeled as the Stokes flow with a small Reynolds number. The surrounding elastic filament network is also included in the governing differential equations similar to what was shown by Li [22]. First, the governing equations of the microtubule elastic deformation and the cytosol equations are derived separately. Then, the stress and velocity in the cytosol induced by vibrating microtubules are analytically determined and the eigenfrequencies of the coupled cytoplasm-microtubule vibration are obtained. Finally, the effects of the dynamic viscosity of the cytosol, elastic modulus of surrounding filaments, circumferential wave-number, and microtubule shear modulus on the longitudinal, radial, and torsional modes of the microtubules are investigated.

2 Mechanics model

2.1 Orthotropic elastic shell model for microtubules

The configuration of a typical 13-3 elastic microtubule is shown in Fig. 1. The microtubule is modeled as an orthotropic hollow circular cylindrical shell. In the present paper, the first-order shear deformation shell theory for orthotropic materials is used for modeling the microtubule [23, 24]. We consider the microtubule as a homogeneous but anisotropic

Fig. 1 Configuration of typical 13-3 microtubule. Adopted from de Pable et al. [30] and Wang and Zhang [12]

circular cylindrical shell with Young's moduli E_x and E_θ in the longitudinal and circumferential directions, respectively, in-plane shear modulus $G_{x\theta}$, transverse shear moduli G_{xz} and $G_{\theta z}$ and Poisson's ratio along the microtubule protofilaments ν_x (Poisson's ratio along the circumferential direction is $\nu_\theta = \nu_x (E_\theta / E_x)$). It has a mean radius R , equivalent thickness h , and mass density ρ . We use x and θ as axial (longitudinal) and circumferential angular coordinates, respectively, whereas z is the distance from the microtubule axis in the radial direction, perpendicular to the microtubule axis. The microtubule displacements are denoted by U , V , and W in x , θ , and z coordinates. φ_x and φ_θ are bending slopes in the $x - z$ and $\theta - z$ planes, respectively. According to the first-order shear deformation theory, the displacement fields are of the form

$$U(x, \theta, z, t) = u(x, \theta, t) + z\varphi_x,$$

$$V(x, \theta, z, t) = v(x, \theta, t) + z\varphi_\theta,$$

$$W(x, \theta, z, t) = w(x, \theta, t). \quad (1)$$

The strain components ε_{xx} , $\varepsilon_{\theta\theta}$, $\gamma_{\theta z}$, γ_{xz} and $\gamma_{x\theta}$ at an arbitrary point of the shell are related to the middle surface strains ε_{xx}^0 , $\varepsilon_{\theta\theta}^0$, $\gamma_{\theta z}^0$, γ_{xz}^0 and $\gamma_{x\theta}^0$ and to the changes in the curvature of the middle surface κ_{xx} , $\kappa_{\theta\theta}$, $\kappa_{\theta z}$, κ_{xz} and $\kappa_{x\theta}$ by the following relationships:

$$\begin{aligned} \varepsilon_{xx} &= \varepsilon_{xx}^0 + z\kappa_{xx} & \varepsilon_{\theta\theta} &= \varepsilon_{\theta\theta}^0 + z\kappa_{\theta\theta} & \gamma_{\theta z} &= \gamma_{\theta z}^0 + z\kappa_{\theta z} \\ \gamma_{xz} &= \gamma_{xz}^0 + z\kappa_{xz}, & \gamma_{x\theta} &= \gamma_{x\theta}^0 + z\kappa_{x\theta}. \end{aligned} \quad (2)$$

Using to the first-order shear deformation shell theory, the middle surface strain-displacement relationships and changes in the curvature for a circular cylindrical shell are

$$\begin{pmatrix} \varepsilon_{xx}^0 \\ \varepsilon_{\theta\theta}^0 \\ \gamma_{\theta z}^0 \\ \gamma_{xz}^0 \\ \gamma_{x\theta}^0 \\ \kappa_{xx} \\ \kappa_{\theta\theta} \\ \kappa_{\theta z} \\ \kappa_{xz} \\ \kappa_{x\theta} \end{pmatrix} = \begin{pmatrix} \frac{\partial u}{\partial x} \\ \frac{1}{R} \frac{\partial v}{\partial \theta} + \frac{w}{R} \\ \phi_\theta + \frac{1}{R} \frac{\partial w}{\partial \theta} - \frac{v}{R} \\ \phi_x + \frac{\partial w}{\partial x} \\ \frac{1}{R} \frac{\partial u}{\partial \theta} + \frac{\partial v}{\partial x} \\ \frac{\partial \phi_x}{\partial x} \\ \frac{1}{R} \frac{\partial \phi_\theta}{\partial \theta} \\ 0 \\ 0 \\ \frac{1}{R} \frac{\partial \phi_x}{\partial \theta} - \frac{1}{2R^2} \frac{\partial u}{\partial \theta} + \frac{\partial \phi_\theta}{\partial x} + \frac{1}{2R} \frac{\partial v}{\partial x} \end{pmatrix} \quad (3)$$

where u , v , w are axial, tangential, and radial displacements, respectively. Assuming an anisotropic microtubule in a state of plane stress, the stress-strain relationships can be written as

$$\begin{Bmatrix} \sigma_{xx} \\ \sigma_{\theta\theta} \\ \sigma_{\theta z} \\ \sigma_{xz} \\ \sigma_{x\theta} \end{Bmatrix} = \begin{bmatrix} P_{11} & P_{12} & 0 & 0 & 0 \\ P_{21} & P_{22} & 0 & 0 & 0 \\ 0 & 0 & P_{44} & 0 & 0 \\ 0 & 0 & 0 & P_{55} & 0 \\ 0 & 0 & 0 & 0 & P_{66} \end{bmatrix} \begin{Bmatrix} \varepsilon_{xx} \\ \varepsilon_{\theta\theta} \\ \gamma_{\theta z} \\ \gamma_{xz} \\ \gamma_{x\theta} \end{Bmatrix} \quad (4)$$

where

$$P_{11} = \frac{E_x}{1 - \nu_x \nu_\theta}, \quad P_{12} = P_{21} = \frac{\nu_\theta E_x}{1 - \nu_x \nu_\theta}, \quad P_{22} = \frac{E_\theta}{1 - \nu_x \nu_\theta}, \quad P_{44} = G_{\theta z}, \\ P_{55} = G_{xz}, \quad P_{66} = G_{x\theta}.$$

The equations of motion for cylindrical microtubules with first-order shear deformation shell theory are

$$\begin{aligned} \frac{\partial N_{xx}}{\partial x} + \frac{1}{R} \frac{\partial N_{\theta x}}{\partial \theta} - N_c \frac{\partial^2 u}{\partial x^2} &= I_1 \frac{\partial^2 u}{\partial t^2}, \\ \frac{\partial N_{x\theta}}{\partial x} + \frac{1}{R} \frac{\partial N_{\theta\theta}}{\partial \theta} + \frac{Q_\theta}{R} - N_c \frac{\partial^2 v}{\partial x^2} &= I_1 \frac{\partial^2 v}{\partial t^2} - f_\theta, \\ \frac{\partial Q_x}{\partial x} + \frac{1}{R} \frac{\partial Q_\theta}{\partial \theta} - \frac{N_{\theta\theta}}{R} - N_c \frac{\partial^2 w}{\partial x^2} &= I_1 \frac{\partial^2 w}{\partial t^2} - f_r + \xi w, \\ \frac{\partial M_{xx}}{\partial x} + \frac{1}{R} \frac{\partial M_{\theta x}}{\partial \theta} - Q_x &= I_3 \frac{\partial^2 \varphi_x}{\partial t^2}, \\ \frac{\partial M_{x\theta}}{\partial x} + \frac{1}{R} \frac{\partial M_{\theta\theta}}{\partial \theta} - Q_\theta &= I_3 \frac{\partial^2 \varphi_\theta}{\partial t^2}, \end{aligned} \quad (5)$$

where f_r and f_θ are circumferential and radial external tractions as given in Section 2.3, ξ is an equivalent elastic medium constant, $\xi \approx 2.7E_c$ (E_c is the Young's modulus of the

surrounding filament network), N_c is the externally applied mid-face axial compressive force, N_{xx} , $N_{\theta\theta}$, $N_{x\theta}$, $N_{\theta x}$ are in-face stress resultants, M_{xx} , $M_{\theta\theta}$, $M_{x\theta}$, $M_{\theta x}$ are stress couple resultants and Q_x , Q_θ are transverse shear stress resultants defined as

$$\begin{aligned}\{N_{xx}, N_{\theta\theta}, N_{x\theta}, N_{\theta x}\} &= \int \left\{ \sigma_{xx} \left(1 + \frac{z}{R} \right), \sigma_{\theta\theta}, \sigma_{x\theta} \left(1 + \frac{z}{R} \right), \sigma_{\theta x} \right\} dz, \\ \{M_{xx}, M_{\theta\theta}, M_{x\theta}, M_{\theta x}\} &= \int_{-h_0/2}^{h_0/2} \left\{ \sigma_{xx} \left(1 + \frac{z}{R} \right), \sigma_{\theta\theta}, \sigma_{x\theta} \left(1 + \frac{z}{R} \right), \sigma_{\theta x} \right\} z dz, \\ \{Q_x, Q_\theta\} &= \int \left\{ \sigma_{xz} \left(1 + \frac{z}{R} \right), \sigma_{\theta z} \right\} dz,\end{aligned}\quad (6)$$

where integrations should be performed over $(-\frac{h}{2}, \frac{h}{2})$ for $P_{ij}dz$ and $(-\frac{h_0}{2}, \frac{h_0}{2})$ for $z^2 P_{ij}dz$, respectively. Moreover, h_0 is the effective thickness and I_1 and I_3 stand for the mass moment of inertia of microtubule per unit area as

$$I_1 = \int_{-h/2}^{h/2} \rho dz, \quad I_3 = \int_{-h_0/2}^{h_0/2} \rho z^2 dz. \quad (7)$$

By substituting (1–3) into (4), and then substituting the resulting equation into (6), the force and moment resultants can be derived as

$$\begin{aligned}N_{xx} &= h \left(P_{11} \frac{\partial u}{\partial x} + \frac{P_{12}}{R} \left(\frac{\partial v}{\partial \theta} + w \right) \right) + \left(\frac{h_0^3}{12} \right) \left(\frac{P_{11}}{R} \frac{\partial \phi_x}{\partial x} + \frac{P_{12}}{R^2} \frac{\partial \phi_\theta}{\partial \theta} \right), \\ N_{\theta\theta} &= h \left(P_{12} \frac{\partial u}{\partial x} + \frac{P_{22}}{R} \left(\frac{\partial v}{\partial \theta} + w \right) \right), \\ N_{x\theta} &= h P_{66} \left(\frac{\partial v}{\partial x} + \frac{1}{R} \frac{\partial u}{\partial \theta} \right) + \left(\frac{h_0^3}{12} \right) \left(\frac{P_{66}}{R} \left(\frac{1}{R} \frac{\partial \phi_x}{\partial \theta} - \frac{1}{2R^2} \frac{\partial u}{\partial \theta} + \frac{\partial \phi_\theta}{\partial x} + \frac{1}{2R} \frac{\partial v}{\partial x} \right) \right), \\ N_{\theta x} &= h P_{66} \left(\frac{\partial v}{\partial x} + \frac{1}{R} \frac{\partial u}{\partial \theta} \right), \\ M_{xx} &= \left(\frac{h_0^3}{12} \right) \left(\frac{P_{11}}{R} \frac{\partial u}{\partial x} + \frac{P_{12}}{R^2} \left(\frac{\partial v}{\partial \theta} + w \right) + P_{11} \frac{\partial \phi_x}{\partial x} + \frac{P_{12}}{R} \frac{\partial \phi_\theta}{\partial \theta} \right), \\ M_{\theta\theta} &= \left(\frac{h_0^3}{12} \right) \left(P_{12} \frac{\partial \phi_x}{\partial x} + \frac{P_{22}}{R} \frac{\partial \phi_\theta}{\partial \theta} \right), \\ M_{x\theta} &= \left(\frac{h_0^3}{12} \right) \left(\frac{P_{66}}{R} \left(\frac{\partial v}{\partial x} + \frac{1}{R} \frac{\partial u}{\partial \theta} \right) + P_{66} \left(\frac{1}{R} \frac{\partial \phi_x}{\partial \theta} - \frac{1}{2R^2} \frac{\partial u}{\partial \theta} + \frac{\partial \phi_\theta}{\partial x} + \frac{1}{2R} \frac{\partial v}{\partial x} \right) \right), \\ M_{\theta x} &= \left(\frac{h_0^3}{12} \right) \left(P_{66} \right) \left(\frac{1}{R} \frac{\partial \phi_x}{\partial \theta} - \frac{1}{2R^2} \frac{\partial u}{\partial \theta} + \frac{\partial \phi_\theta}{\partial x} + \frac{1}{2R} \frac{\partial v}{\partial x} \right), \\ Q_x &= kh P_{55} \left(\varphi_x + \frac{\partial w}{\partial x} \right), \\ Q_\theta &= kh P_{44} \left(\phi_\theta + \frac{1}{R} \frac{\partial w}{\partial \theta} - \frac{v}{R} \right),\end{aligned}\quad (8)$$

where k is the shear correction coefficient. Finally, substituting (8) into (5), the equations of motion for microtubules in terms of longitudinal, circumferential, and radial displacements (u , v , w) of the mean surface of the microtubule and rotations of tangents to the reference surface (φ_x and φ_θ) are obtained as:

$$(A_{11} - N_c) \frac{\partial^2 u}{\partial x^2} + \frac{A_{66}}{R^2} \frac{\partial^2 u}{\partial \theta^2} + \frac{(A_{12} + A_{66})}{R} \frac{\partial^2 v}{\partial x \partial \theta} + \frac{A_{12}}{R} \frac{\partial w}{\partial x} + \frac{D_{11}}{R} \frac{\partial^2 \varphi_x}{\partial x^2} + \frac{D_{12}}{R^2} \frac{\partial^2 \varphi_\theta}{\partial x \partial \theta} = I_1 \frac{\partial^2 u}{\partial t^2}, \quad (9)$$

$$\left[\frac{A_{12} + A_{66}}{R} - \frac{D_{66}}{2R^3} \right] \frac{\partial^2 u}{\partial x \partial \theta} + \left[A_{66} + \frac{D_{66}}{2R^2} - N_c \right] \frac{\partial^2 v}{\partial x^2} + \frac{A_{22}}{R^2} \frac{\partial^2 v}{\partial \theta^2} - \frac{kA_{44}v}{R^2} + \left[\frac{A_{22} + kA_{44}}{R^2} \right] \frac{\partial w}{\partial \theta} + \frac{D_{66}}{R^2} \frac{\partial^2 \varphi_x}{\partial x \partial \theta} + \frac{D_{66}}{R} \frac{\partial^2 \varphi_\theta}{\partial x^2} + \frac{kA_{44}\varphi_\theta}{R} = I_1 \frac{\partial^2 v}{\partial t^2} - f_\theta, \quad (10)$$

$$-\frac{A_{12}}{R} \frac{\partial u}{\partial x} - \left[\frac{A_{22} + kA_{44}}{R^2} \right] \frac{\partial v}{\partial \theta} + (kA_{55} - N_c) \frac{\partial^2 w}{\partial x^2} - \frac{A_{22}w}{R^2} + \frac{kA_{44}}{R^2} \frac{\partial^2 w}{\partial \theta^2} + kA_{55} \frac{\partial \varphi_x}{\partial x} + \frac{kA_{44}}{R} \frac{\partial \varphi_\theta}{\partial \theta} = I_1 \frac{\partial^2 w}{\partial t^2} - f_r + \xi w, \quad (11)$$

$$\frac{D_{11}}{R} \frac{\partial^2 u}{\partial x^2} - \frac{D_{66}}{2R^3} \frac{\partial^2 u}{\partial \theta^2} + \left[\frac{D_{12}}{R^2} - kA_{55} \right] \frac{\partial w}{\partial x} + D_{11} \frac{\partial^2 \varphi_x}{\partial x^2} + \frac{D_{66}}{R^2} \frac{\partial^2 \varphi_x}{\partial \theta^2} - kA_{55}\varphi_x + \left[\frac{2D_{12} + D_{66}}{2R^2} \right] \frac{\partial^2 v}{\partial x \partial \theta} + \left[\frac{D_{12} + D_{66}}{R} \right] \frac{\partial^2 \varphi_\theta}{\partial x \partial \theta} = I_3 \frac{\partial^2 \varphi_x}{\partial t^2}, \quad (12)$$

$$\frac{D_{66}}{2R^2} \frac{\partial^2 u}{\partial x \partial \theta} + \frac{3D_{66}}{2R} \frac{\partial^2 v}{\partial x^2} + \frac{kA_{44}v}{R} - \frac{kA_{44}}{R} \frac{\partial w}{\partial \theta} + \left[\frac{D_{12} + D_{66}}{R} \right] \frac{\partial^2 \varphi_x}{\partial x \partial \theta} + \left[D_{66} \frac{\partial^2 \varphi_\theta}{\partial x^2} + \frac{D_{22}}{R^2} \frac{\partial^2 \varphi_\theta}{\partial \theta^2} - kA_{44}\varphi_\theta \right] = I_3 \frac{\partial^2 \varphi_\theta}{\partial t^2} \quad (13)$$

where $D_{ij} = P_{ij}h_0^3/12$ and $A_{ij} = P_{ij}h$ for $i, j = 1, 2, 6$ and $A_{44} = P_{44}h$ and $A_{55} = P_{55}h$. The solution of (9–13) will permit us to derive the displacement functions. For the sake of simplicity, only the microtubules with simply supported ends are considered here. The solutions of (9–13), exactly satisfying all the boundary conditions, are given in the form

$$\begin{aligned} u(x, \theta, t) &= \cos(\lambda_m x) \cos(n\theta) q_{nu}(t) \\ v(x, \theta, t) &= \sin(\lambda_m x) \sin(n\theta) q_{nv}(t) \\ w(x, \theta, t) &= \sin(\lambda_m x) \cos(n\theta) q_{nw}(t) \\ \varphi_x(x, \theta, t) &= \cos(\lambda_m x) \cos(n\theta) q_{nf}(t) \\ \varphi_\theta(x, \theta, t) &= \sin(\lambda_m x) \sin(n\theta) q_{nt}(t) \end{aligned} \quad (14)$$

where $q_{nu}(t)$, $q_{nv}(t)$, $q_{nw}(t)$, $q_{nf}(t)$ and $q_{nt}(t)$ are generalized coordinates, λ_m ($\lambda_m = m\pi/L$, m is the half-axial wave number and L is the microtubule length in micrometers) is the wave vector along the longitudinal direction (microtubule protofilaments) and n is the

circumferential wave-number. It is well known that microtubules have a large length-to-diameter aspect ratio and can usually be modeled as long shells [11, 12]. Before inserting (14) into (9–13), we need to consider the interaction tractions between cytosol and microtubule and analytically determine the stress field in the viscous cytosol. In the next section, we will formulate and obtain the stress field in viscous cytosol.

2.2 Dynamic equations of cytosol motion

Cytosol is the liquid component of the cytoplasm surrounding the organelles and other cytoplasmic structures in a cell where a wide variety of cell processes take place and it can be modeled as a viscous fluid. Both the viscous effects of the surrounding filament network and the cytosol are assumed to be included in μ . We use the Navier-Stokes equations for incompressible fluids in cylindrical coordinates to obtain the cytosol equations of motion. It has been shown by several researchers that the Reynolds number is very low for cytoplasmic streaming, for instance, $Re = 10^{-3}$ [25] and the inertia terms in the Navier-Stokes equations are negligible. With these approximations and neglecting the axial motion of the cytosol, the momentum-balance equation for the cytosol motion can be described by the well-known Stokes equations as

$$\frac{\partial p}{\partial r} = \mu \left(\frac{\partial^2 v_r}{\partial r^2} + \frac{1}{r^2} \frac{\partial^2 v_r}{\partial \theta^2} + \frac{1}{r} \frac{\partial v_r}{\partial r} - \frac{v_r}{r^2} - \frac{2}{r^2} \frac{\partial v_\theta}{\partial \theta} \right) \quad (15)$$

$$\frac{1}{r} \frac{\partial p}{\partial \theta} = \mu \left(\frac{\partial^2 v_\theta}{\partial r^2} + \frac{1}{r^2} \frac{\partial^2 v_\theta}{\partial \theta^2} + \frac{1}{r} \frac{\partial v_\theta}{\partial r} - \frac{v_\theta}{r^2} + \frac{2}{r^2} \frac{\partial v_r}{\partial \theta} \right) \quad (16)$$

whereas the continuity equation takes the form

$$\frac{\partial v_r}{\partial r} + \frac{v_r}{r} + \frac{1}{r} \frac{\partial v_\theta}{\partial \theta} = 0. \quad (17)$$

To obtain the cytosol stress field, the continuity and momentum equations must simultaneously be solved for velocity. To reduce the general formulations given in (15–17) to a single governing equation in terms of a single unknown variable, we use the stream function ψ , where

$$v_r = \frac{1}{r} \frac{\partial \psi}{\partial \theta}, \quad v_\theta = -\frac{\partial \psi}{\partial r}. \quad (18)$$

After substituting the stream function ψ from (18) into (15–17), the following relation can be obtained,

$$\nabla^4 \psi = 0 \quad (19)$$

where ∇^4 is the biharmonic operator. It should be noted that satisfactory results have been obtained in the literature by considering the no-slip condition between the microtubule and the cytosol interface [21, 26]. Therefore, we assume that the cytosol moves with the same velocity as that of microtubule at $r = R_o$, so that

$$v_r(R_o, \theta) = -\frac{\partial w}{\partial t}, \quad (20)$$

$$v_\theta(R_o, \theta) = -\frac{\partial v}{\partial t}. \quad (21)$$

In addition, the induced viscous flow of the cytosol decays spatially away from the microtubule and vanishes far from the microtubule:

$$\lim_{b \rightarrow \infty} v_r(b, \theta) = \lim_{b \rightarrow \infty} v_\theta(b, \theta) = 0. \quad (22)$$

The boundary value problem (19–22) is solved analytically by using the Michell solution [27] to determine the stream function ψ as

$$\psi = \begin{cases} \left[b_{11}r + b_{12}r \ln r + \frac{b_{13}}{r} + b_{14}r^3 \right] \sin \theta & \text{for } n = 1 \\ \left[b_{n1}r^n + b_{n2}r^{2+n} + b_{n3}r^{-n} + b_{n4}r^{2-n} \right] \sin n\theta & \text{for } n \geq 2 \end{cases} \quad (23)$$

where b_{ni} ($i = 1, 2, 3$ and 4) are coefficients to be determined ($\partial b_{ni}/\partial r = \partial b_{ni}/\partial \theta = 0$). Substituting (23) into (18), we obtain

$$\begin{cases} v_r = \left[b_{11} + b_{12} \ln r + \frac{b_{13}}{r^2} + b_{14}r^2 \right] \cos \theta \\ v_\theta = - \left[b_{11} + b_{12} (\ln r + 1) - \frac{b_{13}}{r^2} + 3b_{14}r^2 \right] \sin \theta \end{cases} \quad \text{for } n = 1 \quad (24)$$

and

$$\begin{cases} v_r = n \left[b_{n1}r^{n-1} + b_{n2}r^{n+1} + b_{n3}r^{-(n+1)} + b_{n4}r^{-(n-1)} \right] \cos n\theta \\ v_\theta = - \left[nb_{n1}r^{n-1} + (2+n)b_{n2}r^{n+1} - nb_{n3}r^{-(n+1)} + (2-n)b_{n4}r^{-(n-1)} \right] \sin n\theta \end{cases} \quad \text{for } n \geq 2. \quad (25)$$

Substituting (24) into the boundary conditions (20–22), the coefficients b_{1i} can be obtained as

$$b_{11} = b_{12} = b_{14} = 0, \quad b_{13} = -R_o^2 \frac{dq_{1w}}{dt} \sin(\lambda_m x) = -R_o^2 \frac{dq_{1v}}{dt} \sin(\lambda_m x). \quad (26)$$

Similarly, the coefficients b_{ni} are obtained as

$$b_{n1} = b_{n2} = 0, \quad (27)$$

$$b_{n3} = \frac{R_o^{n+1}}{2} \left(\frac{n-2}{n} \frac{dq_{nw}}{dt} - \frac{dq_{nv}}{dt} \right) \sin(\lambda_m x). \quad (28)$$

$$b_{n4} = \frac{R_o^{n-1}}{2} \left(\frac{dq_{nv}}{dt} - \frac{dq_{nw}}{dt} \right) \sin(\lambda_m x). \quad (29)$$

The stress components are related to the velocities by

$$\begin{cases} \sigma_{rr} = \frac{4\mu}{r} \cos \theta \frac{dq_{1w}}{dt} \sin(\lambda_m x) \\ \tau_{r\theta} = \frac{4\mu}{r} \sin \theta \frac{dq_{1v}}{dt} \sin(\lambda_m x) \end{cases} \quad \text{for } n = 1 \quad (30)$$

$$\begin{cases} \sigma_{rr} = \frac{2\mu n}{r} \sin(\lambda_m x) \left[\frac{dq_{nv}}{dt} + \frac{1}{n} \frac{dq_{nw}}{dt} \right] \cos n\theta \\ \tau_{r\theta} = \frac{2\mu n}{r} \sin(\lambda_m x) \left[\frac{dq_{nv}}{dt} + \frac{1}{n} \frac{dq_{nw}}{dt} \right] \sin n\theta \end{cases} \quad \text{for } n \geq 2. \quad (31)$$

2.3 Coupled elastic deformation and viscous flow

To investigate the coupling effects of the elastic deformation of the microtubule and the viscous flow of the cytosol, we assume that the surface traction of the cytosol along the interface is equal and opposite to external tractions exerted on the microtubule

$$\begin{aligned} f_\theta &= -\tau_{r\theta}(R_o, \theta), \\ f_r &= -\sigma_{rr}(R_o, \theta). \end{aligned} \quad (32)$$

It should be noted that the hydrodynamic stresses given in (32) are based on two-dimensional theory. In the case of a cylinder vibrating in the fluid, the fluid field is not two-dimensional. However, the three-dimensional effect is very small for large wavelengths [28, 29]. Consequently, the hydrodynamic tractions based on the two-dimensional theory are applicable.

Substituting (14) and (30–32) into (9–13), one can obtain a microtubule-cytoplasm system of equations,

$$\begin{aligned} -\left[\lambda_m^2(A_{11}-N_c)+n^2\frac{A_{66}}{R^2}\right]q_{nu}+\left[\frac{(A_{12}+A_{66})n\lambda_m}{R}\right]q_{nv}+\left[\frac{A_{12}\lambda_m}{R}\right]q_{nw}-\left[\frac{D_{11}\lambda_m^2}{R}\right]q_{nf} \\ +\left[\frac{D_{12}n\lambda_m}{R^2}\right]q_{nt}=I_1\ddot{q}_{nu} \end{aligned} \quad (33)$$

$$\begin{aligned} \left[\left(\frac{A_{12}+A_{66}}{R}-\frac{D_{66}}{2R^3}\right)n\lambda_m\right]q_{nu}-\left[\left(A_{66}+\frac{D_{66}}{2R^2}-N_c\right)\lambda_m^2+\frac{n^2A_{22}}{R^2}+\frac{kA_{44}}{R^2}\right]q_{nv}-\left[\frac{A_{22}+kA_{44}}{R^2}n\right]q_{nw} \\ +\left[\frac{D_{66}n\lambda_m}{R^2}\right]q_{nf}-\left[\frac{D_{66}\lambda_m^2}{R}-\frac{kA_{44}}{R}\right]q_{nt}=I_1\ddot{q}_{nv}+\frac{2\mu n}{R}\left[\dot{q}_{nv}+\frac{1}{n}\dot{q}_{nw}\right] \end{aligned} \quad (34)$$

$$\begin{aligned} \left[\frac{A_{12}\lambda_m}{R}\right]q_{nu}-\left[\frac{A_{22}+kA_{44}}{R^2}n\right]q_{nv}-\left[\lambda_m^2(kA_{55}-N_c)+\frac{A_{22}}{R^2}+\frac{kn^2A_{44}}{R^2}\right]q_{nw}-[kA_{55}\lambda_m]q_{nf} \\ +\left[\frac{knA_{44}}{R}\right]q_{nt}=I_1\ddot{q}_{nw}+\frac{2\mu n}{R}\left[\dot{q}_{nv}+\frac{1}{n}\dot{q}_{nw}\right]+\xi q_{nw} \end{aligned} \quad (35)$$

$$\begin{aligned} -\left[\frac{D_{11}\lambda_m^2}{R}-\frac{D_{66}n^2}{2R^3}\right]q_{nu}+\left[\frac{2D_{12}+D_{66}n\lambda_m}{2R^2}\right]q_{nv}+\left[\left(\frac{D_{12}}{R^2}-kA_{55}\right)\lambda_m\right]q_{nw} \\ -\left[D_{11}\lambda_m^2+\frac{D_{66}n^2}{R^2}+kA_{55}\right]q_{nf}+\left[\frac{D_{12}+D_{66}n\lambda_m}{R}\right]q_{nt}=I_3\ddot{q}_{nf} \end{aligned} \quad (36)$$

$$\begin{aligned} \left[\frac{D_{66}n\lambda_m}{2R^2}\right]q_{nu}-\left[\frac{3D_{66}\lambda_m^2}{2R}-\frac{kA_{44}}{R}\right]q_{nv}+\left[\frac{knA_{44}}{R}\right]q_{nw}+\left[\frac{D_{12}+D_{66}n\lambda_m}{R}\right]q_{nf} \\ -\left[D_{66}\lambda_m^2+\frac{D_{22}n^2}{R^2}+kA_{44}\right]q_{nt}=I_3\ddot{q}_{nt} \end{aligned} \quad (37)$$

which can be written as

$$[\mathbf{M}] \{\ddot{\mathbf{q}}\} + [\mathbf{C}] \{\dot{\mathbf{q}}\} + [\mathbf{K}] \{\mathbf{q}\} = \{0\} \quad (38)$$

where $\{\mathbf{q}\}$ is a vector of the microtubule generalized coordinates and $[\mathbf{M}]$, $[\mathbf{C}]$ and $[\mathbf{K}]$ are mass, non-proportional damping and stiffness matrices of the microtubule immersed in cytoplasm. The elements of these matrices are given in Table 1.

For complex modal analysis, it is assumed that $\{\mathbf{q}\}$ is a harmonic function of time and expressed as

$$\{\mathbf{q}\} = \begin{bmatrix} U \\ V \\ W \\ \varphi_x \\ \varphi_\theta \end{bmatrix} \exp(i\omega t). \quad (39)$$

Table 1 The elements of stiffness, damping and mass matrices

Stiffness Matrix	
$K_{11} = \left[\lambda_m^2 (A_{11} - N_c) + n^2 \frac{A_{66}}{R^2} \right]$	$K_{12} = - \left[n \lambda_m \frac{(A_{12} + A_{66})}{R} \right]$
$K_{13} = - \left[\frac{\lambda_m A_{12}}{R} \right]$	$K_{14} = \left[\frac{\lambda_m^2 D_{11}}{R} \right]$
$K_{15} = - \left[\frac{n \lambda_m D_{12}}{R^2} \right]$	$K_{21} = - \left[\left(\frac{A_{12} + A_{66}}{R} - \frac{D_{66}}{2R^2} \right) n \lambda_m \right]$
$K_{22} = \left[\left(A_{66} + \frac{D_{66}}{2R^2} - N_c \right) \lambda_m^2 + \frac{n^2 A_{22}}{R^2} + \frac{k A_{44}}{R^2} \right]$	$K_{23} = \left[\frac{n(A_{22} + k A_{44})}{R^2} \right]$
$K_{24} = - \left[\frac{n \lambda_m D_{66}}{R^2} \right]$	$K_{25} = \left[\frac{\lambda_m^2 D_{66}}{R} - \frac{k A_{44}}{R} \right]$
$K_{31} = \left[- \frac{\lambda_m A_{12}}{R} \right]$	$K_{32} = \left[\frac{n(A_{22} + k A_{44})}{R^2} \right]$
$K_{33} = \left[\lambda_m^2 (k A_{55} - N_c) + \frac{A_{22}}{R^2} + \frac{n^2 k A_{44}}{R^2} \right]$	$K_{34} = [k \lambda_m A_{55}]$
$K_{35} = - \left[\frac{k n A_{44}}{R} \right]$	$K_{41} = \left[\frac{\lambda_m^2 D_{11}}{R} - \frac{n^2 D_{66}}{2R^3} \right]$
$K_{42} = - \left[\frac{n \lambda_m (2D_{12} + D_{66})}{2R^2} \right]$	$K_{43} = \left[\left(k A_{55} - \frac{D_{12}}{R^2} \right) \lambda_m \right]$
$K_{44} = \left[\lambda_m^2 D_{11} + \frac{n^2 D_{66}}{R^2} + k A_{55} \right]$	$K_{45} = - \left[\frac{n \lambda_m (D_{12} + D_{66})}{R} \right]$
$K_{51} = \left[\frac{n \lambda_m D_{66}}{2R^2} \right]$	$K_{52} = \left[\frac{3 \lambda_m^2 D_{66} - 2k A_{44}}{2R} \right]$
$K_{53} = - \left[\frac{k n A_{44}}{R} \right]$	$K_{54} = - \left[\frac{n \lambda_m (D_{12} + D_{66})}{R} \right]$
$K_{55} = \left[\lambda_m^2 D_{66} + \frac{n^2 D_{22}}{R^2} + k A_{44} \right]$	
Mass Matrix	
$\mathbf{M} = \begin{bmatrix} I_1 & 0 & 0 & 0 & 0 \\ 0 & I_1 & 0 & 0 & 0 \\ 0 & 0 & I_1 & 0 & 0 \\ 0 & 0 & 0 & I_3 & 0 \\ 0 & 0 & 0 & 0 & I_3 \end{bmatrix}$	
Damping Matrix	
$C_{22} = \begin{cases} \frac{4\mu}{R_0} & n = 1 \\ \frac{2\mu n}{R_0} & n \geq 2 \end{cases}$	$C_{23} = \begin{cases} 0 & n = 1 \\ \frac{2\mu}{R_0} & n \geq 2 \end{cases}$

Substituting (39) into (38) yields a set of algebraic equations for U , V , W , φ_x , and φ_θ as

$$H(n, \lambda, w)_{5 \times 5} \begin{bmatrix} U \\ V \\ W \\ \varphi_x \\ \varphi_\theta \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix} \quad (40)$$

where $\lambda = R\lambda_m$ is non-dimensional wave vector. For non-trivial solutions, one sets the determinant of the characteristic matrix in (40) to zero

$$\det(H(n, \lambda, w)) = 0. \quad (41)$$

Expansion of the determinant of above equation provides the system's characteristic equation

$$F(n, \lambda, w) = 0 \quad (42)$$

where $F(n, \lambda, w) = 0$ is a polynomial function. This characteristic function can be used to investigate the frequencies of the cylinder-fluid system. Solving (42), one obtains five pairs of roots of frequencies with different combinations of wave vector λ and circumferential mode n .

3 Results and discussion

A single microtubule is analyzed to determine the vibration characteristics of microtubules immersed in cytoplasm. To model the microtubule geometry, the cross section of a microtubule is treated as an equivalent annular shape with an equivalent thickness $h = 2.7$ nm [8]. According to the experimental data on shell-like buckling of individual microtubules, the bending stiffness of microtubules can be estimated by an effective thickness h_0 , which was determined as 1.6 nm [30]. In our numerical calculations, the mass density is $\rho = 1.47 \text{ g/cm}^3$, the outer radius is $R_o = 14.2$ nm and the mean radius R is 12.8 nm. The value of $\pi^2/12$ is also used for the shear correction coefficient. Since our results depend only weakly on Poisson's ratio, the values $\nu_x = 0.3$ and $\nu_\theta = 0.3 \times 10^{-3}$ are used in the present calculations. The effects of the other main parameters are studied below.

3.1 Effect of circumferential wave-number

Three different modes are given by (38) for each wave vector, λ , and circumferential wave-number, n . Two modes are predominantly radial and torsional ('circumferential') and the third one is mainly longitudinal (Fig. 2). The longitudinal and torsional vibrations propagate along microtubule protofilaments and helical pathway, respectively. The variations of the torsional, radial and longitudinal frequencies of the microtubule, without considering the cytoplasm effects, are shown in Fig. 3a–c, respectively, for $0 \leq \lambda \leq 0.8$, $n = 1, 2, 3, 4, 5$, longitudinal Young's modulus $E_x = 1$ GPa, circumferential Young's modulus $E_\theta = 1$ MPa and shear modulus $G_{x\theta} = 1$ MPa. As seen from Fig. 3a, for $\lambda \geq 0.1$, all frequencies increase considerably with increasing λ . By increasing axial wavelength (decreasing λ) for $\lambda < 0.1$, the lowest frequency with $n = 1$ decreases and goes to zero at $\lambda = 0$, while those of torsional modes ($n = 2$ to 5) become almost independent of axial wavelength and approach a nonzero asymptotic value at infinite axial wavelength ($\lambda = 0$). It can be shown by a simple

Fig. 2 Mode shapes along the circumferential (torsional) and longitudinal directions

mathematical analysis that the lowest frequency leads to a transverse bending mode with a rigid body motion of the circular cross-section. Moreover, the asymptotic value rises rapidly with growing circumferential wave number n . It should be noted that the lowest torsional frequencies are not necessarily associated with the lowest n . As shown for the example in Fig. 3a, for $\lambda \geq 0.35$, the minimum torsional frequency occurs for $n = 2$. It can also be seen from Fig. 3b that the radial frequencies are not sensitive to the wave vector and increase very slightly with increasing wave vector. This means that the microtubule radial frequencies are length-independent. Figure 3c shows the longitudinal frequency varying

Fig. 3 The dispersion curves of the microtubule frequencies with $n = 1 - 5$, $E_x = 1$ GPa, $E_\theta = 1$ MPa and $E_{x\theta} = 1$ MPa; **a** torsional (circumferential) mode, **b** radial mode and **c** longitudinal mode

with the wave vector with circumferential wave-number n . This is seen that the longitudinal frequencies are sensitive to the circumferential wave-number for small values of the wave vector ($\lambda < 0.4$) whereas the effect of the circumferential wave-number on the longitudinal frequencies seems to be small for ($\lambda > 0.4$). It is worth noting that the longitudinal motions have higher natural frequencies and smaller amplitudes than those of the torsional motions of the microtubule. In other words, the vibrations which propagate along the protofilaments do so significantly faster than those along the microtubule helix since the longitudinal bonds between the tubulin dimers are much stiffer and stronger than the lateral bonds. These results are in good agreement with previous studies investigating the vibrational properties of microtubules with different approaches such as two-dimensional lattice model [10], continuum approach [11] and elastic network model [7].

Finally, it should be noted that the low elastic modulus along the microtubule helix, E_θ , and small equivalent thickness for bending h_0 lead to low bending stiffness, D_{22} , of microtubule. It physically means that the torsional (circumferential) vibration could result in the large deformation on cross sections of microtubules and thus significantly affect the mechanical performance and structural integrity of microtubules.

3.2 Effect of cytosol dynamic viscosity

Viscous damping by the surrounding cytosol may quench excitation of vibrations. The role of the surrounding cytosol is characterized by the cytosol dynamic viscosity (μ). In order to estimate the effect of the cytosol, dynamic viscosity on the coupled microtubule-cytosol frequencies, a dimensionless frequency is defined by $R\omega/S_L$, where $S_L = \sqrt{E_x/\rho}$. The predicted coupled microtubule-cytosol frequencies are shown in Fig. 4a–c for cytosol dynamic viscosity $\mu = 0.001$ Pa.s and $n = 1, 3$ and 5 , respectively. The eigen-frequencies of a free microtubule with no cytosol are also plotted in this figure for comparison. The results are obtained by using the following parameters: axial Young's modulus $E_x = 1$ GPa, circumferential Young's modulus $E_\theta = 1$ MPa, shear modulus $G_{x\theta} = 1$ MPa and elastic modulus of surrounding network $\xi = 0$. It is seen from Fig. 4a ($n = 1$) that the microtubule-cytosol system only supports a longitudinal mode, whereas no visible discrepancy can be found between the longitudinal mode of the free microtubule and that immersed in cytosol. In contrast, the radial and torsional modes observed for a free microtubule vanish when the microtubule is immersed in cytosol. This means that the motion of a microtubule immersed in cytosol in the radial and torsional directions is an exponentially decreasing function of time, which corresponds to an overdamped vibration where only non-oscillatory motion is allowed. In particular, the exponential decay of transverse bending has been observed experimentally for microtubules by Felgner et al. [31].

The coupled microtubule-cytosol frequencies obtained from the first-order shear deformation shell theory for $n = 3, 5$ are also shown in Fig. 4b–c. It can be seen that the coupled torsional and longitudinal modes for all values of λ approximately coincide with those of a free microtubule without considering the surrounding cytosol. The results for coupled microtubule-cytosol frequencies by using Sanders-Koiter classical shell theory are also presented in Fig. 4d–f for comparison. By comparing the radial mode in both theories, it can be concluded that the results deviate as the wave vector increases. For wave vectors less than 1.5, the results almost match; however, by increasing the wave vector, the radial mode increases rapidly in classical theory while showing a smooth increase in first-order shear deformation theory. Considering the torsional mode without cytosol effects, the results are almost similar for wave vectors less than 2. However, for larger values of the wave vector,

Fig. 4 The dispersion curves of the microtubule frequencies with $E_x = 1$ GPa, $E_\theta = 1$ MPa, $G_{x\theta} = 1$ MPa and $\xi = 0$; **a** $n = 1$, **b** $n = 3$ and **c** $n = 5$; panels **d** through **f** show results obtained with the Sanders-Koiter classical shell theory

it grows more rapidly in classical theory rather than first-order shear deformation theory. Considering the cytosol effects, in the first-order shear deformation theory, the results are more or less the same (with a little difference); however, in the classical theory, it depends on the wave vector value. It can be seen that the results deviate rapidly from a specific wave vector, while such behavior is not seen in the first-order shear deformation theory. Moreover, both theories show that the radial mode observed for a free microtubule vanish for all circumferential modes numbers ($n = 1 - 5$) when the microtubule is immersed in cytosol.

The longitudinal mode is the same with or without fluid effects in both theories. It should be noted that the cytosol dynamic viscosity has been obtained by different biophysical methods in previous studies. However, because of methodological uncertainties, reported values of cytosol viscosity vary across a wide range of magnitudes [32]. Therefore, more attention should be paid to the study of cytosol viscosity variation in vibration analysis of a microtubule-cytoplasm system. To elucidate the effect of cytosol viscosity on the dynamic behavior of the microtubule in cytosol, the torsional microtubule frequencies are plotted in Fig. 5 for $n = 2$, $E_x = 1$ GPa, $E_\theta = 1$ MPa, $G_{x\theta} = 1$ MPa, $\xi = 0$ and four different cytosol viscosity values, $\mu = 0, 0.001, 0.005$ and 0.01 Pa.s. These results are obtained by using first-order shear deformation and Sanders-Koiter shell theories. It can be seen that for a free microtubule, without considering fluid effects, the result varies a little when changing the theory used. However, those obtained by first-order shear deformation theory are smoother and less than those obtained by classical shell theory. Moreover, it is seen that frequencies predicted are very close to each other for large values of μ ($\mu \geq 0.001$).

Fig. 5 Effect of the cytosol viscosity on the torsional microtubule frequency for $n = 2$, $E_x = 1$ GPa, $E_\theta = 1$ MPa, $G_{x\theta} = 1$ MPa, $\xi = 0$ and four different cytosol viscosities, $\mu = 0, 0.001, 0.005$ and 0.01

Considering fluid effects, the results differ little until the wave vector is less than 2. After that, the results predicted by classical theory grow rapidly while those obtained by first-order shear deformation theory grow more gradually. Finally, although it is not shown here, the effect of the cytosol viscosity on the radial and longitudinal modes is small and negligible. To analyze the damping effects of the surrounding cytosol, we have to note that the major constituent of the cytosol is water. It should also be noted that the ordering of the water molecules in the form of layers parallel to the surface is a crucial phenomenon influencing elasto-electrical properties and damping of the cytoskeleton vibration system. It has been experimentally proven that organized water has different physical properties compared to bulk water [35–38]. Recently, it has been reported by Pokorný et al. [39] that zones of layered water cause a significant reduction in the microtubule vibration damping due to reduced thermal motion of water molecules, reduced energy transfer across the layers, and viscoelastic transition of hydrated water. A better insight can also be obtained by considering the quality of microtubule vibrations. The quality factor (Q) determines the qualitative behavior of simple damped oscillators. Physically speaking, Q is 2π times the ratio of the total energy stored divided by the energy lost in a single cycle per radian of oscillation. The value of the quality factor determines the underdamped, critically damped and/or overdamped regime of an oscillator. However, increasing in the value of the quality factor leads the relative amount of damping to decrease. Pokorný et al. [39] studied the dependence of the microtubule Q factor on the level of water ordering. They reported an increase in the Q factor as a function of the water ordering level and a value of 50 for the quality factor of a microtubule with an ordering level of 99%. If a microtubule is considered in direct contact with normal water (not ordered), the quality factor would be about 0.5.

3.3 Effect of the shear modulus

The shear modulus $G_{x\theta}$ is an independent material constant of the orthotropic microtubules. Since the value of the shear modulus $G_{x\theta}$ of microtubules ranges from 1 KPa to 1 MPa in

Fig. 6 The dependence of the microtubule frequency on The shear modulus with $n = 1$, $E_x = 1$ GPa, $E_\theta = 1$ MPa, $G_{x\theta} = 1$ MPa, $\xi = 0$ and $\mu = 0$; **a** torsional mode and **b** longitudinal mode

the literature [19, 33, 34], it is necessary to examine its effect on microtubule frequencies. The torsional frequencies for a typical microtubule with $E_x = 1$ GPa, $E_\theta = 1$ MPa, $\xi = 0$ and $\mu = 0$ are plotted in Fig. 6 for $n = 1$ and four different non-dimensional shear modulus values ($\beta = G_{x\theta}/E_x$) $\beta = 0.001, 0.0001, 0.00001$ and 0.000001 . The viscosity is neglected in this section where the effect of the shear modulus is investigated in order to compare to results in the literature for beam models. It is seen that predicted frequencies are very close to each other for small values of β ($\beta \leq 0.00001$). Moreover, for a specific wave vector, the frequencies decrease as the shear modulus decreases. As shown in Fig. 6, the results presented in this figure are in good agreement with those reported by Shi et al. [13] in which a Timoshenko-beam model has been used to examine the effects of transverse shearing on flexural rigidity of microtubules for β varying between 0.000001 and 0.001 . They used exactly our dimensions for the microtubule, with average radius = 12.8 nm, equivalent thickness = 2.7 nm, and effective thickness = 1.6 nm, and compared their results to those obtained by the classical isotropic Euler–Bernoulli beam model and the 2D orthotropic elastic shell model. They confirmed that the length dependence of flexural rigidity of an isolated microtubule is attributed to transverse shearing due to extremely low shear modulus of microtubules. Finally, it should be noted that the choice of the value of $G_{x\theta}$ has no significant effect on the radial mode of the microtubule. Moreover, and as can be seen from Fig. 6, the result obtained by first-order shear deformation theory shows almost a linear behavior, which is different from the behavior observed using the classical shell theory.

4 Summary and conclusions

This work was possible owing to a recently obtained experimental and numerical body of data coming from several groups and describing a number of physical and structural properties of the microtubule and the cytoplasm [18, 19, 25, 30, 33]. A first-order shear deformation shell theory for orthotropic materials was developed for microtubules to predict the coupled frequencies of the microtubule–cytoplasm system. The results were also compared to those obtained using Sanders–Koiter shell theory. The cytoplasm was modeled as a medium including a viscous cytosol and an elastic filament network. The motion of the cytosol was modeled as Stokes flow. The dynamic equations of the cytosol were solved analytically and three-dimensional coupled microtubule–cytoplasm equations of motion were obtained. An approximate solution was obtained in an explicit form that can easily be implemented in a computer code.

The variations of longitudinal, radial, and torsional frequencies of a microtubule with the dynamic viscosity of the cytosol, filament network elasticity, microtubule shear modulus, and circumferential wave-number were examined. The results showed that the torsional mode of the microtubule is more sensitive to variation of different parameters than the longitudinal modes. The results also revealed that the lateral constraint has a significant effect on the microtubule vibration. Moreover, it was shown that the low elastic modulus along the microtubule helix and small equivalent thickness for bending lead to low bending stiffness. This physically means that the torsional (circumferential) motions have the smallest frequencies and large deformations occur for cross sections of microtubules, which could exert a significant influence on the mechanical performance and structural integrity of microtubules. Longitudinal axial modes are most electromagnetically active in comparison to twisting or bending modes and will be damped much more weakly since they do not cause any displacement of the surrounding water. It should also be noted that the water

surrounding a microtubule is strongly organized and therefore the in vivo damping of microtubule elastic vibrations will be lower than that measured in vitro [40].

Finally, it is believed that the results proposed in this investigation would be helpful to understand the vibration characteristics of microtubule immersed in cytoplasm.

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