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Dynamic behaviors of microtubules in cytosol

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ABSTRACT

Highly anisotropic microtubules (MTs) immersed in cytosol are a central part of the cytoskeleton in eukaryotic cells. The dynamic behaviors of an MT–cytosol system are of major interest in biomechanics community. Such a solid–fluid system is characterized by a Reynolds number of the order 10^{-3} and a slip ionic layer formed at the MT–cytosol interface. In view of these unique features, an orthotropic shell-Stokes flow model with a slip boundary condition has been developed to explore the distinctive dynamic behaviors of MTs in cytosol. Three types of motions have been identified, i.e., (a) undamped and damped torsional vibration, (b) damped longitudinal vibration, and (c) overdamped bending and radial motions. The exponentially decaying bending motion given by the present model is found to be in qualitative agreement with the existing experimental observation [Felgner et al., 1996. Flexural rigidity of microtubules measured with the use of optical tweezers, Journal of Cell Science 109, 509–516].

1. Introduction

Microtubules (MTs) (Fig. 1) are principle components of the cytoskeleton in eukaryotic cells, which play an essential role in providing mechanical rigidity, maintaining the shape of cells and facilitating many important physiological processes (Ingber et al., 1995; Nogales, 2000; Cotterill, 2002; Boal, 2002; Howard and Hyman, 2003; Stamenovic, 2005; Watanabe et al., 2005). The mechanics of MTs is a topic of numerous researches (Gittes et al., 1993; Venier et al., 1994; Kurachi et al., 1995; Felgner et al., 1996; dePablo et al., 2003), where MT vibration is of major interest (Sirenko et al., 1996; Pokorny, 2003, 2004; Kasas et al., 2004; Portet et al., 2005; Wang and Zhang, 2008). In particular, since MTs are immersed in cytosol, the vibration of MTs in a fluid has attracted attention in the last decade (Sirenko et al., 1996; Pokorny, 2003 2004). In studying the longitudinal vibration, Pokorny (2003, 2004) revealed that an ionic charge layer on the surfaces of MTs minimizes the viscous effect of the cytosol and allows slide between MTs and cytosol. The more comprehensive investigation has been carried out by Sirenko et al. (1996), where three axisymmetric acoustic modes and an infinite set of non-axisymmetric modes have been obtained. In this study, an isotropic membrane shell model is used for MTs and the fluid around MTs is tacitly assumed to be an ideal fluid with an infinitely large Reynolds number. However, such a model is oversimplified for anisotropic MTs with bending resistance. Furthermore, as will be shown later, the nanoscale radius of MTs gives a Reynolds number of the surrounding fluid three orders of magnitude smaller than unity. The ideal fluid model is thus not valid for an MT–fluid system. It follows that a more realistic model for an MT–cytosol system is needed to give a reliable description of the dynamic behaviors of MTs immerged in cytosol.

Recently, an orthotropic shell model (Wang et al., 2006a,b; Wang and Zhang, 2008) has been developed to study the mechanical behaviors of MTs. A good agreement has been achieved between this shell model, available discrete models and experiments. Motivated by its valid applications, the present paper will further extend the model to the vibration analysis of an MT–cytosol system. The motion of the cytosol will be modeled as Stokes flow characterized by a small Reynolds number and the free slip boundary condition will be specified on the MT surface.

Based on this orthotropic shell-Stokes flow model, the governing equations for the vibration of MTs in cytosol are derived in Section 2. In Section 3, the phonon-dispersion relations are predicted for MTs immersed in cytosol and compared with those of free MTs. Here the major attention is focused on the damping effect of cytosol on various MT motions. The major conclusions are summarized in Section 4.

2. The orthotropic shell-Stokes flow model

In this section, we shall develop an orthotropic shell-Stokes flow model for the dynamic behaviors of MTs in cytosol.

2.1. Dynamic equations of MTs

An orthotropic shell model developed for the free vibration (Wang et al., 2006a; Wang and Zhang, 2008) and elastic buckling

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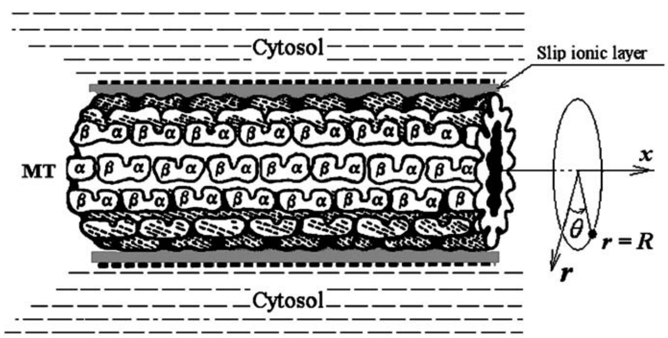

Fig. 1. A schematic picture of an MT immerged in cytosol with a slip ionic layer at the MT–cytosol interface. α and β are tubulin dimers that form MTs.

(Wang et al., 2006b) of MTs will be further used to study the dynamic behaviors of MTs in cytosol. Previous studies (Pokorny, 2003, 2004) indicated that the viscous force on MTs is minimized by a slip ionic layer formed at the MT–cytosol interface (Fig. 1). The friction acting on MT surface is thus neglected in the present study. On the other hand, the inner radial pressure ${P_{rr}}^i$ and the outer radial pressure ${P_{rr}}^o$ of MTs due to cytosol have to be considered. The dynamic equations of MTs in cytosol can then be written as follows (Wang et al., 2006a; Wang and Zhang, 2008):

$$\left\{R^2\frac{\partial^2}{\partial x^2}+\frac{K_{x\theta}R^2+D_{x\theta}}{K_xR^2}\frac{\partial^2}{\partial\theta^2}\right\}u+\left\{\frac{(v_xK_\theta+K_{x\theta})R}{K_x}\frac{\partial^2}{\partial x\partial\theta}\right\}\times v+\left\{-\frac{v_xK_\theta R}{K_x}\frac{\partial}{\partial x}+\frac{D_xR}{K_x}\frac{\partial^3}{\partial x^3}-\frac{D_{x\theta}}{K_xR}\frac{\partial^3}{\partial x\partial\theta^2}\right\}\times w=\frac{\rho h}{K_x}R^2\frac{\partial^2u}{\partial t^2}$$

$$\left\{\left(v_\theta+\frac{K_{x\theta}}{K_x}\right)R\frac{\partial^2}{\partial x\partial\theta}\right\}u+\left\{\frac{K_\theta}{K_x}\frac{\partial^2}{\partial\theta^2}+\frac{K_{x\theta}R^2+3D_{x\theta}}{K_x}\frac{\partial^2}{\partial x^2}\right\}\times v+\left\{-\frac{K_\theta}{K_x}\frac{\partial}{\partial\theta}+\frac{v_\theta D_x+3D_{x\theta}}{K_x}\frac{\partial^3}{\partial x^2\partial\theta}\right\}\times w=\frac{\rho h}{K_x}R^2\frac{\partial^2 v}{\partial t^2}$$

$$\left\{v_\theta R\frac{\partial}{\partial x}-\frac{D_x}{K_x}R\frac{\partial^3}{\partial x^3}+\frac{D_{x\theta}}{K_xR}\frac{\partial^3}{\partial x\partial\theta^2}\right\}\times u+\left\{\frac{K_\theta}{K_x}\frac{\partial}{\partial\theta}-\frac{v_xD_\theta+3D_{x\theta}}{K_x}\frac{\partial^3}{\partial x^2\partial\theta}\right\}\times v+\left\{-\frac{D_x}{K_x}R^2\frac{\partial^4}{\partial x^4}-\frac{v_xD_\theta+v_\theta D_x+4D_{x\theta}}{K_x}\frac{\partial^4}{\partial x^2\partial\theta^2}-\frac{D_\theta}{K_xR^2}\left(\frac{\partial^2}{\partial\theta^2}+1\right)^2-\frac{K_\theta}{K_x}\right\}\times w+\frac{R^2}{K_x}(P^i_{rr}-P^o_{rr})=\frac{\rho h}{K_x}R^2\frac{\partial^2 w}{\partial t^2} \quad (1)$$

where x and θ are axial and circumferential angular coordinates (Fig. 1); u, v and w are axial, circumferential and radial displacements; t is the time; ρ is the mass density, h is the thickness and R is the average radius of MTs. In addition, v_x and v_θ are Poisson ratios in longitudinal and circumferential directions. (K_x, K_θ) and (D_x, D_θ) represent the in-plane and bending stiffnesses in longitudinal and circumferential directions, and ($K_{x\theta}$, $D_{x\theta}$) are stiffnesses in shear (Appendix A1). Here we consider MTs usually of a large length-to-diameter aspect ratio as infinitely long shells. The solution of Eq. (1) then reads (Sirenko et al., 1996)

$$\begin{bmatrix}u(x,\ \theta,\ t)\\ v(x,\ \theta,\ t)\\ w(x,\ \theta,\ t)\end{bmatrix}=\begin{bmatrix}U\\ V\\ -iW\end{bmatrix}\exp(in\theta+ik_xx-i\omega t) \quad (2)$$

where U, V and W represent the vibration amplitudes of MTs in longitudinal, circumferential and radial directions, k_x is the wave vector (nm^{-1}) along the longitudinal direction, n is the circumferential wave number and the real part of ω (Re ω) gives the angular frequency.

2.2. Dynamic equations of cytosol motion

The radius R of MTs is around 10 nm and their free vibration frequency f with $k<0.1$ ($k=Rk_x$) is of the order 0.1 GHz (Wang et al., 2006a). If the displacement amplitude Amp of MT vibration is 10 times smaller than MT radius, the velocity of the cytosol flow can be roughly estimated as $\tilde{v}=4\,\mathrm{Amp}\times f=0.4$ m/s. Since water is a major part (70%) of cytosol, its kinematic viscosity $\eta=1.004\times10^{-6}\,m^2/s$ (at 20 °C) should be close to that of cytosol. Thus, the Reynolds number of cytosol $Re=vR/\eta$ is of the order 4.0×10^{-3}. It follows that the motion of cytosol can be modeled as Stokes flow, i.e., an incompressible fluid with small Reynolds number (<1), whose governing equations are as follows (Happel and Brenner, 1973):

$$\nabla\bullet\tilde{v}_f=0 \quad \text{and} \quad \nabla p_f=\mu_f\nabla^2\tilde{v}_f \quad (3)$$

where $\tilde{v}_f$ denotes the velocity, p_f the pressure and μ_f the dynamical viscosity of cytosol.

The continuity condition requires that cytosol moves radially with the same velocity as that of MTs at $r=R$. However, due to the existence of a very thin slip ionic layer on MT surfaces, MTs and cytosol move independently along the longitudinal and circumferential directions. In fact, as there is no friction between the MTs and the thin slip layer with negligible momentum and angular momentum of inertia, the viscous force between the cytosol and the slip ionic layer must also be zero. It follows that the tangential velocities of cytosol should vanish at $r=R$. Thus, the boundary conditions of cytosol at $r=R$ are

$$(\tilde{v}_f)_x=0,\ (\tilde{v}_f)_\theta=0 \quad \text{and} \quad (\tilde{v}_f)_r=-\frac{\partial w}{\partial t} \quad (4)$$

By using the governing Equation (3) and boundary condition (4), the radial pressures ${P_{rr}}^i$ and ${P_{rr}}^o$ of cytosol at the inner and outer surfaces of MTs can be expressed as

$$\begin{bmatrix}P^i_{rr}\\ P^o_{rr}\end{bmatrix}=-\begin{bmatrix}A^i(n,\ k)\\ A^o(n,\ k)\end{bmatrix}\frac{\mu_f\,\omega\,W\exp(in\theta+ik_xx-i\omega t)}{R} \quad (5)$$

The derivation of Eq. (5) and the form of A^i and A^0 can be found in Appendix B.

2.3. Dynamic analysis of MTs in cytosol

By substituting Eqs. (2) and (5) into (1), the original partial differential can be transformed into the following three algebraic equations:

$$\{k^2+\beta(1+\gamma)n^2-\Omega^2\}U+\{-(\alpha v_x+\beta)kn\}\times V+\{\alpha v_xk+\gamma(k^2-\beta n^2)k\}W=0$$

$$\{(\alpha v_x+\beta)kn\}U+\{\alpha n^2+\beta(1+3\gamma)k^2-\Omega^2\}\times V+\left\{\alpha n+\gamma(\alpha v_x+3\beta)k^2n\right\}W=0$$