Effect of Dynamic Behaviors of Microtubules in Cytosol

C. Y. Wang,* C. F. Li ** and S. Adhikari ***

School of Engineering, Swansea University

Singleton Park, Swansea, Wales SA2 8PP, UK

* chengyuan.wang@swansea.ac.uk
** c.f.li@swansea.ac.uk
*** s.adhikari@swansea.ac.uk

ABSTRACT

An orthotropic shell-Stokes flow model has been developed to explore the distinctive vibration behaviors of microtubules (MTs) in the cytosol of eukaryotic cells. The slip boundary condition has been considered for the MTs due to the existence of an ionic slip layer formed on the MT-cytosol interface. The dispersion relations have been derived and the viscous effect of cytosol has been examined quantitatively. The results show that an MT-cytosol system only supports the torsional and longitudinal vibrations of MTs where negligible or small damping occurs for the axisymmetric torsional and long-wavelength longitudinal vibrations whereas the non-axisymmetric torsional or longitudinal vibration of MTs decays exponentially in cytosol.

Keywords: microtubules, cytosol, vibration

1 INTRODUCTION

Microtubules (MTs) (Fig.1) with hollow cylindrical structure are rigid polymers composed of tubulin heterodimers. As a principle component of the cytoskeleton in eukaryotic cells MTs play an essential role in providing mechanical rigidity, maintaining the shape of cells and facilitating other physiological processes, e.g., cell division, cell motility and intracellular transport [1-6].

The fulfillment of the functions of MTs depends crucially on their mechanical properties. The mechanics of MTs thus become a major topic of numerous recent researches [7-11], where the vibration of MTs [12-18] is of primary interest. Particularly, since MTs are immersed in cytosol the vibration of MTs in a fluid has attracted considerable attention in last decade [12, 14-15]. In studying the longitudinal vibration Pokorny [14-15] pointed out that an ionic charge layer formed around the surfaces of MTs minimizes the viscous effect of the cytosol, which allows slide between MT and the surrounding fluid. So far, the most comprehensive investigation on the relevant issues has been carried out by Sirenko et.al [12]. The authors showed that an MT-fluid system supports a spectrum of non-radiative vibrations including three axisymmetric acoustic modes, and an infinite set of non-axisymmetric modes obeying a parabolic dispersion law. In this study, an isotropic shell model is used for MTs, where the bending stiffness of MTs is implicitly ignored [18] and the cytosol around MTs is tacitly assumed to be an ideal fluid and the viscous force of cytosol is completely neglected [19]. Such an isotropic shell model is oversimplified for highly anisotropic MTs with significant bending resistance [20]. In addition, the viscous force of cytosol could be predominant over the inertial force and thus, should be taken into consideration in the vibration analysis. Form these discussions it follows that to give a reliable description of the MT vibration in cytosol it is imperative to develop a more realistic model for an MT-cytosol system and reexamine the issues by using the new model that reflects the unique features of such a solid -fluid system.

2 SHELL-STOKES FLOW MODEL

In this study we consider an MT submerged in cytosol as shown in Fig 1.

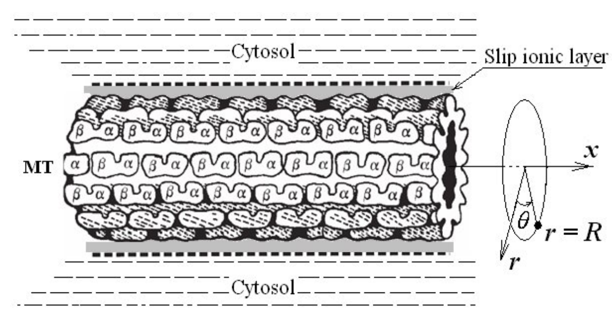


Fig. 1 A schematic picture of an MT immerged in cytosol.

It is noted in Refs. 21 and 22 MTs can be modeled as orthotropic shells, whose dynamic equations are shown in [21]. The dimensional analysis shows that the motion of a fluid induced by the vibration of nanoscale tubules is characterized by a low Reynolds number much smaller than unit. The flow of cytosol fluid thus can be modeled as Stokes flow whose governing equation is

$$\nabla v_f = 0 \text{ and } \nabla p_f = \mu_f \nabla^2 v_f \tag{1}$$

where v_f denotes the velocity, p_f the pressure and μ_f the dynamical viscosity of cytosol. The solutions of equation (1) consisting of three potential functions that satisfy the Laplace's equation can be found in Ref. 19. The continuity condition requires that cytosol moves with the same radial velocity with MTs at the boundary *r* = *R* (radius of the MT). In addition, due to the existence of the slip layer on the surface of MTs [14-15] (Fig.1) the free slip boundary condition is enforced at the MT-cytosol interface, i.e., the friction between MTs and cytosol is assumed to be zero. Furthermore, such a slip layer is so thin that its momentum and angular momentum of inertial can be safely neglected. As a result the tangential velocities of cytosol should vanish at the boundary *r* = *R*. In view of these analyses the boundary conditions of cytosol at *r* = *R* are as follows

$$(v_f)_x = 0, \quad (v_f)_\theta = 0 \text{ and } (v_f)_r = \frac{\partial w}{\partial t} \tag{2}$$

where x and θ are axial and angular circumferential coordinates. *t* is time and *w* is the radial displacement of the MT. Substituting the suitable form of displacement functions of MTs into their vibration equations (Ref. 21) and the above obtained solution to equation (1) with proper form of the potential functions (Ref.19) into equation (2) leads to the following algebraic equations:

$$H(n,k,\Omega)_{3\times3} \cdot \begin{bmatrix} U \\ V \\ W \end{bmatrix} = 0 \tag{3}$$

where *n* and *k* are circumferential wave number and wave vector in axial direction, Ω is frequency quantity and (*U*, *V*, W) are vibration amplitudes in axial, circumferential and radial directions, respectively. The existence condition of a nonzero solution of (*U*, *V*, W) is:

$$\det H(n,k,\Omega)_{3\times3} = 0 \tag{4}$$

Solving equation (4) one can obtain Ω as a function of n and k for a coupled MT-cytosol system. Subsequently, substituting the value of Ω into equation (3) yields the amplitude ratio ($\frac{U}{W}$, $\frac{V}{W}$, 1) which defines the vibration modes associated with the specific frequency quantity Ω.

3 Results and discussions

Following the way shown above we shall explore the vibration behavior of MTs in cytosol. Since cytosol has about 70% (weight) of water a coupled MT-water system will be considered as a typical example. The values of material constants used in the present analysis are $\rho = 1.47 g/cm^3$, $\nu_x = 0.3$, $E_x = 1GPa$ and $\alpha = \beta = 10^{-3}$ [18,21-23] for MTs, and $\rho_f = 1g/cm^3$ and $\mu_f = 1.002 \times 10^{-3} N \cdot s/m^2$ for water.

3.1 Axisymmetric vibration

In this section we study the axisymmetric vibration of MTs where the circumferential wave number $n = 0$. The phonon-dispersion curves are shown in Fig.2 for an MT in cytosol and compared with those of free MTs.

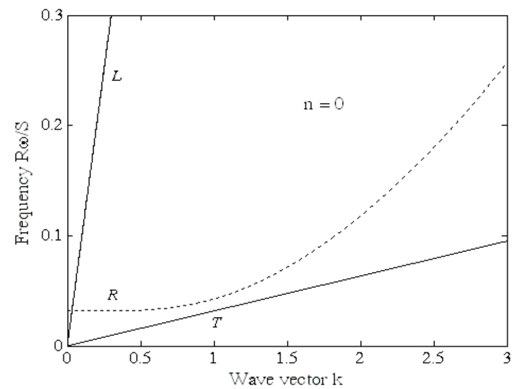


Fig. 2 The phonon dispersion curves of axisymmetric modes of free MTs (dotted lines) and MTs immersed in cytosol (solid lines).

Fig.2 shows that, in the absence of cytosol MTs show longitudinal (*L*) and torsional (*T*) modes characterized by a linear dispersion law and a radial (*R*) mode with nonzero asymptotic frequency at $k = 0$. An MT-cytosol system however only supports two acoustic modes, i.e., *L* and *T* modes, whose phonon-dispersion curves coincide with their counterparts of free MTs. In contrast, the *R* mode vanishes due to the viscous damping of cytosol. Three dispersion relations for axisymmetric modes can be derived based on Eq. 4 with $n = 0$. The first is the linear one for axisymmetric torsional vibration as shown in Fig.2,

$$\Omega = 0.032 k \tag{2}$$

Such a torsional mode is decoupled with axial and radial displacements and thus, will not be affected by surrounding cytosol flow when the friction between MTs and cytosol is neglected in the presence of the slip layer. The second linear dispersion relation obtained at $\gamma < 0.1$ and $k < 0.1$ is

$$\Omega = k \tag{3}$$

which corresponds to the *L* mode of MTs in Fig.2. In the limit of small *k*, i.e., large axial wavelength λ ($= 2\pi R/k$), MTs originally modeled as thin shells behave like elastic columns where the longitudinal deformation is almost decoupled with the radial one. In this special case, the effect of cytosol on the *L* mode is negligibly small. In general case however *L* mode is coupled with radial displacement due to the effect of Poisson ratio and bending stiffness. Thus, *L* mode is generally damped by cytosol via the MT-cytosol interaction in radial direction. The vibration amplitude of the axial mode is obtained as

$$A = A_0 e^{\frac{-DS}{R}t} \tag{4}$$

Here A_0 and D are positive real numbers and S is the propagation speed of the wave. Eq. 4 shows that the L mode generally decays exponentially with time. The relaxation time, i.e., the time for the vibration amplitude to reduce to the tenth of its initial value is calculated in Table 1 for the L mode of different k.

k	10^{-4}	10^{-3}	10^{-2}	10^{-1}	1
τ (s)	3×10^5	304	30.4	0.3	3.2×10^{-6}
τ / T_f	3×10^{11}	4×10^9	4×10^8	3.8×10^7	4.2×10^6

Table 1 The relaxation time τ (s) and the relaxation time (τ)-to-vibration period (T_f) ratio calculated for the axisymmetric L mode of MTs in cytosol.

In addition, for R mode the following relation can be derived based on Eq. 4 with n = 0 and k << 1.

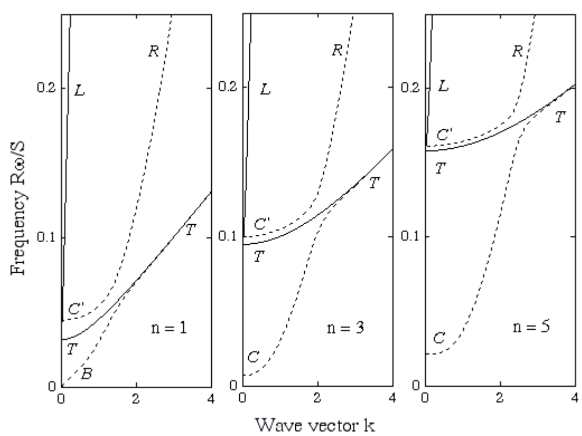
$$\Omega = \frac{M_{nk} \pm \sqrt{M_{nk}^2 + 4\alpha}}{2} \tag{5}$$

where M_{nk} is usually an negative imaginary number. This gives two negative imaginary numbers. Our numerical results indicate that such negative imaginary solutions actually can be obtained for the axisymmetric R mode throughout the full length of k considered here. Therefore, as shown in Fig.2, the R mode of MTs evaporates in an MT-cytosol system. On the other hand, in the absence of cytosol M_{nk} = 0. The above equation then reduces to $\Omega = \sqrt{\alpha}$ at small k, which is the dispersion relation for the axisymmetric R vibration of free MTs shown in Fig. 2 (the dotted line).

3.2 Non-axisymmetric vibration

In this section let us study the non-axisymmetric vibration of MTs in cytosol, which is characterized by $n \geq 1$. It is noted that in non-axisymmetric case coupling always occurs among the displacements of MTs in longitudinal, circumferential and radial directions. Although longitudinal or circumferential displacement could be orders of magnitude larger than the radial one the latter never vanishes during the vibration. Naturally, the energy dissipation of the vibrations will take place as a result of the MT-cytosol interaction in radial direction and the strong viscous force in cytosol. Thus, the solution of Eq. 4 with $n \geq 1$ is always given in the form of A - Di, where A gives the frequency quantity RA/S and D (D > 0) measures vibration damping. The phonon-dispersion relations of the non-axisymmetric vibrations of an MT-cytosol system have been derived and the dispersion curves with n = 1, 3 and 5 are shown (solid lines) in Fig. 3 in comparison with those obtained for free MTs (dotted lines).

Analogous to the axisymmetric case, for each combination of (n, k) three non-axisymmetrical vibration modes are shown in Fig. 3 for free MTs. For n = 1 and k <1 the lowest frequency (Fig.3a) corresponds to the beam-like bending (B) mode where MTs deform in transverse direction with rigid body motion of their circular cross-sections. For n > 2 and k < 1 the lowest frequency (Fig.3b and c) corresponds to the circumferential (C) modes where predominant local bending of MT wall distorts their cross-sections [18]. These vibration modes exhibit a radial displacement which is comparable to the circumferential displacement but much larger than the longitudinal one. Thus, as shown in Fig. 3 they have been eliminated in an MT-cytosol system owing to the strong damping effect of cytosol. For similar reasons, C' (circumferential) mode at $k < 2$ and R mode at $k \geq 2$ associated with the intermediate frequency of free MTs also disappear in an MT-cytosol system (Fig.3). In fact, due to the presence of cytosol these modes become over damped non-oscillation motions whose displacements decay exponentially with time. In particular, such exponential decaying of transverse motion predicated based on the present model has already been observed for MTs in a fluid in experiment [10].



(a) (b) (c)

Fig. 3 The phonon dispersion curves of non-axisymmetric modes of free MTs (dotted lines) and MTs immersed in cytosol (solid lines) with (a) n = 1, (b) n = 3 and (c) n =5.

It is noted in Fig.3 that the vibration supported by an MT-cytosol system is limited to L and T modes where longitudinal and circumferential displacements are at least two orders of magnitude greater than the radial one. Specifically, as far as the T mode at $k > 2$ and L mode are concerned no visible discrepancy can be found in Fig. 3 between free MTs and those immersed in cytosol. As mentioned before, similar phenomenon has been observed in Fig.2 for axisymmetric T and L modes. It follows that cytosol cannot significantly alter the *L* and *T* mode frequency of MTs. Thus the most prominent influence of cytosol on the MT vibration is to demolish their amplitudes. More detailed study show that the relaxation time of the *L* mode is of the order of 10^{-6} to 10^{-4}s and that of the *T* mode varies from the order of $10^{-8}$to 10^{-6}s, which is extremely short. However this relaxation time is still four to six orders of magnitude greater than the period of the *L* mode and one to three orders of magnitude larger than that of *T* mode.

4 CONCLUSIONS

Based on a orthotropic shell-Stokes flow model the vibration of MTs immerged in cytosol has been studied. The friction on the surface of MTs is neglected due to the existence of a slip layer at the MT-cytosol interface. The coupling between the MT vibration and the flow of cytosol is achieved merely via their motions in radial direction. It is found that

In axisymmetric case ($n=0$), torsional and longitudinal vibration are two acoustic modes obeying a linear dispersion law. The torsional mode is decoupled with radial displacement and thus free from the damping effect. For the longitudinal modes with large wavelength, the MT-cytosol coupling is very small giving the relaxation time greater than 3×10^5 s (3.5 days) and the relaxation time-to-period ratio of the order of 10^{11}.

Non-axisymmetric ($n\geq1$) torsional and longitudinal vibrations are strongly coupled with the motion of cytosol via a small but none zero radial displacement. Thus these vibrations will decay exponentially with time. The relaxation time however is still up to six orders of magnitude greater than the corresponding vibration period. This indicates that the excitation of non-axisymmetric torsional and longitudinal vibrations may have significant impact on the mechanical integrity and normal functioning of MTs.

5 REFERENCES

[1] E. Nogales, Annual Review Biochemistry 69, 277, 2000.

[2] R. Cotterill Biophysics –an introduction , John Wiley. New York, 2002.

[3] D. Boal 2002 Mechanics of the cell Cambridge University Press. Cambridge.

[4] J. Howard and A. A. Hyman , Nature **422,** 753, 2003.

[5] T. Watanabe, J. Noritake and K. Kaibuchi, Trends in Cell Biology **15,** 76 , 2005

[6] G. Y. Huang, Y-W. Mai1 and C. Q. Ru, Nanotechnology **19,** 125101, 2008.

[7] P. Venier, A. C. Maggs, M. F. Carlier and D. Pantaloni , Journal of Biological Chemistry 269, 13353, 1994.

[8] M. Kurachi, M. Hoshi and H. Tashiro, 1995 Cell Motility and the Cytoskeleton 30, 221, 1995.

[9] F. Gittes, B. Mickey, J. Nettleton and J. Howard, The Journal of Cell Biology 120, 923, 1993

[10] H. Felgner, R. Frank and M. Schiwa, Journal of Cell Science 109, 509, 1996.

[11] N. Wang, K. Naruse, D. Stamenovic et al., Proceedings of the National Academy of Sciences 98, 7765 , 2001.

[12] Y. M. Sirenko, M. A. Stroscio and K. W. Kim, Physical Review E **53,** 1003, 1996

[13] J. Pokorny, F. Jelinek et al., Astrophysical and Space Science 23, 171, 1997.

[14] J. Pokorny, Electromagnetic Biology and Medicine 22, 15, 2003

[15] J. Pokorny, Bioelectrochemistry 63, 321, 2004.

[16] S. Kasas, C. Cibert, A. Kis et al., Biology of the Cell 96, 697, 2004.

[17] S. Portet, J. A. Tuszynski, C. W. V. Hogue and J. M. Dixon, European Biophysics Journal 34 , 912, 2005

[18] C. Y. Wang and L. C. Zhang, Journal of Biomechnaics 41, 1892, 2008.

[19] J. Happel and H. Brenner, ‘‘Low Reynolds Number Hydrodynamics’’ the Netherlands: Noordhoff International Publishing, 1973

[20] P. J. dePablo, I. A. T. Schaap, F. C. Mackintosh, C. F. Schmidt, Physical Review Letters 91, 098101, 2003.

[21] C. Y. Wang, C. Q. Ru and A. Mioduchowski, Physica E 35, 48, 2006.

[22] C. Y. Wang, C. Q. Ru and A. Mioduchowski, Physical Review E 74, 52901, 2006

[23] X. S. Qian, J. Q. Zhang and C. Q. Ru, Journal of Applied Physics 101, 084702, 2007.

[24] W. Flugge, ‘‘Stresses in shells’’ (2nd edn), Berlin: Springer, 1973.

[25] J. Schwaighofer and H. F. Microys, Journal of Applied Mechanics (ASME) 46, 356, 1979

[26] R. D. Zou and C. G. Foster, Thin-walled Structures 22, 143, 1995.

[27] X. Li and Y. Chen, Journal of Sound and Vibration 257, 967, 2002.

[28] S. Karl, G. S. Bobby, E. T. Robert and W. N. Donald Nanotechnology 9, 30, 1998.