

Circumferential vibration of microtubules with long axial wavelength

C.Y. Wang, L.C. Zhang*

The School of Aerospace, Mechanical and Mechatronic Engineering, University of Sydney, Sydney 2006, Australia

Accepted 31 March 2008

Abstract

This paper uses an orthotropic shell model to investigate in detail the long axial wavelength circumferential vibration of microtubules (MTs). The deformation patterns in the vibrations were explored and their phonon dispersion relations were presented for MTs with increasing radius. It was shown that with the growth of the axial wavelength, the associated frequency of MTs would finally approach a nonzero asymptotic value, rising considerably with the increase of circumferential wave number but dropping linearly with the growing radius. This study corrects the previous misunderstanding drawn by an oversimplified model, and points out that a parabolic dispersion law does not apply to the circumferential modes when the MT bending stiffness is properly considered.

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Keywords: Microtubules; Orthotropic elastic shells; Circumferential vibration

1. Introduction

Hollow cylindrical microtubules (MTs) composed of tubulin heterodimers are one of the principal components of eukaryotic cytoskeleton, and play an essential role in providing mechanical rigidity, maintaining the shape of cells and facilitating many physiological processes (Ingber et al., 1995; Volokh et al., 2000; Nogales, 2000; Howard, 2001; Howard and Hyman, 2003; Stamenovic, 2005; Watanabe et al., 2005). The functions of MTs depend crucially on their mechanical properties. Thus the mechanics of MTs has become a subject of primary interest in recent research (Gittes et al., 1993; Venier et al., 1994; Kurachi et al., 1995; Felgner et al., 1996; Wang et al., 2001). Specifically, the vibration of MTs has attracted considerable attention in the last decade (Sirenko et al., 1996; Pokorný et al., 1997; Pokorný, 2003, 2004; Kasas et al., 2004a,b; Portet et al., 2005).

Since 1997 Pokorný et al. (1997) and Pokorný (2003, 2004) have conducted a series of studies on the longitudinal vibration of MTs. It was shown that the excitation of the vibration of MTs would not be extinguished by the viscous damping of the surrounding cytosol due to the slip

boundary condition on MT surfaces (Pokorný, 2003, 2004). In 2004 Kasas et al. (2004a,b), using the finite element method, investigated the free vibration of MTs with radial deformation, where MTs were treated as hollow cylinders consisting of parallel beams with weak lateral interaction. A year later, a two-dimensional lattice model was developed by Portet et al. (2005) for longitudinal and transverse modes. So far, the most comprehensive study on MT vibration has been carried out by Sirenko et al. (1996) based on an isotropic continuum model. Possible vibration modes, e.g., longitudinal, torsional, radial and transverse bending vibrations, were predicted for MTs. Particularly, an infinite set of helical waves with a parabolic dispersion law were reported to be corresponding to the circumferential vibrations of MTs with large radial deformation. As revealed in Kasas et al. (2004a,b), such vibrations are of major interest because they could play a role in the polymerization/depolymerization process of MTs, which is essential for MT positioning, cell shape maintaining, cell migration and division (Watanabe et al., 2005). Furthermore, as will be shown in this work the excitation of the vibrations will lead to predominant bending of MTs along circumferential direction, where the constituent protofilaments are bonded with lateral interaction that is orders of magnitude weaker than axial interaction within protofilaments (Kis et al., 2002; Kasas et al., 2004a,b; Tuszyński

*Corresponding author.

E-mail address: L.Zhang@usyd.edu.au (L.C. Zhang).

et al., 2005). As a result, large deformation will occur for MT cross-sections, which could exert significant influence on the mechanical performance and structural integrity of MTs. On account of these it is essential to characterize the unique behavior of MTs in circumferential vibrations more precisely in detail.

In previous studies of such vibrations the finite element method (Kasas et al., 2004a,b) is unable to give the detailed phonon dispersion relations while the isotropic continuum model (Sirenko et al., 1996) is obviously not adequate for highly anisotropic MTs (Kis et al., 2002; Kasas et al., 2004a,b; Tuszyński et al., 2005). To account for the anisotropy of MTs, an orthotropic shell model (Wang et al., 2006a,b; Qian, et al., 2007) has been developed with good agreement with discrete models and experiments, but substantially different from isotropic models. Particularly, even under the isotropic assumption, discrepancy can be identified between the two continuum models used in Sirenko et al. (1996) and Wang et al. (2006a) for circumferential modes (see Fig. 2 of Wang et al. (2006a) with $n = 2$ and small k). Thus, in the present work the more realistic orthotropic shell model (Wang et al., 2006a,b) will be employed to obtain a deeper understanding on the circumferential modes of MTs. The corresponding phonon dispersion relations will be derived and the associated deformation patterns will be depicted for MTs. In addition, the radius dependence of the MT vibrations will also be examined in detail.

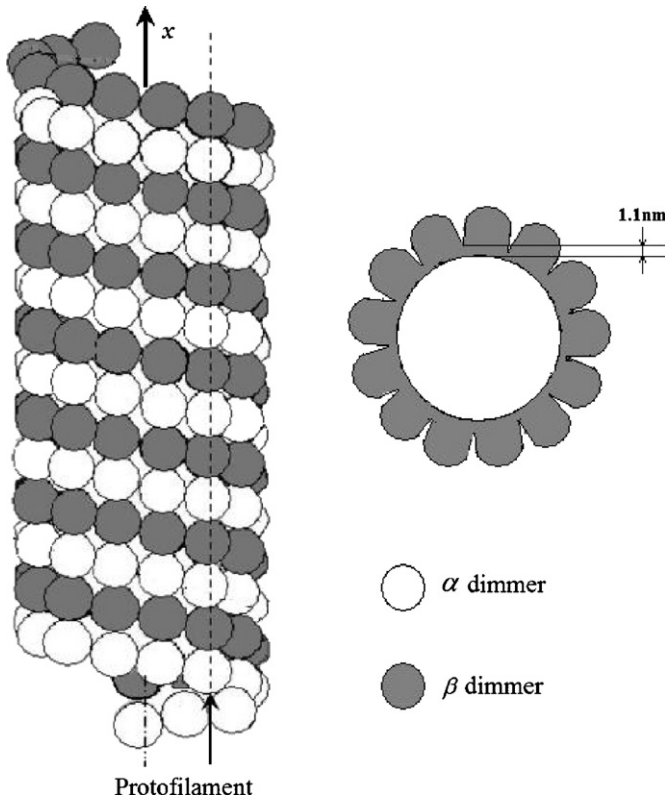


Fig. 1. The illustration of the structure of a 13-protofilament MT with the 'bridge thickness' of 1.1 nm (dePablo et al., 2003).

2. Analysis method

MTs are composed of parallel protofilaments built by the self-association of α , β -tubulin dimmers (Nogales, 2000; Howard, 2001). Head-to-tail binding of these dimmers leads to protofilaments that run along the length of the MTs, and lateral interaction between adjacent protofilaments complete the MT wall (Fig. 1). Typically, MTs are constructed with 13 protofilaments. Other MTs with 8–17 protofilaments and thus, increasing radius, are also reported (Chrétien et al., 1998; Janosi et al., 1998).

As shown in Wang et al. (2006a,b), Qian et al. (2007), an MT can be modeled as an orthotropic elastic shell with longitudinal Young's modulus E_x , circumferential Young's modulus E_θ , shear modulus $G_{x\theta}$ and longitudinal Poisson ratio ν_x . The governing equations for free vibration of an MT are as follows (Wang et al., 2006a; Qian et al., 2007):

$$\begin{aligned} & \left\{ r^2 \frac{\partial^2}{\partial x^2} + \frac{K_{x\theta} r^2 + D_{x\theta}}{K_x r^2} \frac{\partial^2}{\partial \theta^2} \right\} u + \left\{ \frac{(\nu_x K_\theta + K_{x\theta} r)}{K_x} \frac{\partial^2}{\partial x \partial \theta} \right\} v \\ & + \left\{ \begin{aligned} & -\frac{\nu_x K_\theta r}{K_x} \frac{\partial}{\partial x} \\ & + \frac{D_{x\theta} r}{K_x} \frac{\partial^3}{\partial x^3} \\ & - \frac{D_{\theta\theta}}{K_{x\theta} r} \frac{\partial^3}{\partial x \partial \theta^2} \end{aligned} \right\} w = \frac{\rho h}{K_x} r^2 \frac{\partial^2 u}{\partial t^2}, \\ & \left\{ \left(v_\theta + \frac{K_{x\theta} \theta}{K_x} \right) r \frac{\partial^2}{\partial x \partial \theta} \right\} u + \left\{ \begin{aligned} & \frac{K_\theta \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} \end{aligned} \right\} v \\ & + \left\{ \begin{aligned} & -\frac{K_\theta}{K_x} \frac{\partial}{\partial \theta} \\ & + \frac{v_\theta D_{x\theta} + 3D_{x\theta}}{K_x} \frac{\partial^3}{\partial x \partial \theta^2} \end{aligned} \right\} w = \frac{\rho h}{K_x} r^2 \frac{\partial^2 v}{\partial t^2}, \\ & \left\{ \begin{aligned} & -v_\theta r \frac{\partial}{\partial x} \\ & - \frac{D_{x\theta}}{K_x} r \frac{\partial^3}{\partial x^3} \\ & + \frac{D_{\theta\theta}}{K_{x\theta} r} \frac{\partial^3}{\partial x \partial \theta^2} \end{aligned} \right\} u + \left\{ \begin{aligned} & \frac{K_\theta}{K_x} \frac{\partial}{\partial \theta} \\ & - \frac{v_\theta D_{x\theta} + 3D_{x\theta}}{K_x} \frac{\partial^3}{\partial x \partial \theta^2} \end{aligned} \right\} v \\ & + \left\{ \begin{aligned} & -\frac{D_{x\theta}}{K_x} r^2 \frac{\partial^4}{\partial x^4} \\ & - \frac{v_x D_{\theta\theta} + v_\theta D_{x\theta} + 4D_{x\theta}}{K_x} \frac{\partial^4}{\partial x^2 \partial \theta^2} \\ & - \frac{D_{\theta\theta}}{K_{x\theta} r^2} \left(\frac{\partial^2}{\partial \theta^2} + 1 \right)^2 - \frac{K_\theta}{K_x} \end{aligned} \right\} w \\ & = \frac{\rho h}{K_x} r^2 \frac{\partial^2 w}{\partial t^2} \end{aligned} \quad (1)$$

Here x and θ are axial and circumferential angular coordinates, respectively, u , v and w are axial, circumferential and (inward) radial displacements, ρ ($\approx 1.47 \text{ g/cm}^3$) (Sirenko et al., 1996) is the mass density, and r is the average radius of MTs. In addition, $\nu_\theta (= \nu_x E_\theta / E_x)$ is the circumferential Poisson ratios, $K_x (= E_x h / (1 - \nu_x \nu_\theta))$, $K_\theta (= E_\theta h / (1 - \nu_x \nu_\theta))$ and $K_{x\theta} (= G_{x\theta} h)$ represent the in-plane stiffnesses in longitudinal and circumferential directions, and in-plane stiffness in shear, and $D_x (= E_x h_0^3 / 12(1 - \nu_x \nu_\theta))$, $D_\theta (= E_\theta h_0^3 / 12(1 - \nu_x \nu_\theta))$ and $D_{x\theta} (= G_{x\theta} h_0^3 / 12)$ denote the bending stiffnesses in longitudinal and circumferential directions, and bending stiffness in shear (Flügge, 1960; Zou and Foster, 1995; Li and Chen, 2002). Here, h ($= 2.7 \text{ nm}$) (Sirenko et al., 1996; dePablo et al., 2003) is the equivalent thickness of MTs for the in-plane deformation while h_0 ($= 1.6 \text{ nm}$) (dePablo et al., 2003) is the effective thickness for bending. For simply supported ends the solution to (1) reads

$$\begin{aligned} u(x, \theta, t) &= U \cos k_x x \cos n\theta e^{i\omega t} \\ v(x, \theta, t) &= V \sin k_x x \sin n\theta e^{i\omega t} \\ w(x, \theta, t) &= W \sin k_x x \cos n\theta e^{i\omega t} \end{aligned} \quad (2)$$

where U , V and W represent the vibration amplitudes in longitudinal, circumferential and radial directions, respectively, k_x ($k_x = m\pi/L$, m is the half-axial wave number and L is the length of an MT) is the wave vector (nm^{-1}) along the longitudinal direction, n is the circumferential wave number and ω is the angular frequency related to frequency f by $\omega = 2\pi f$.

With solution (2) Eq. (1) can be rewritten as

$$H(n, k, f)_{3 \times 3} \begin{bmatrix} U \\ V \\ W \end{bmatrix} = 0 \quad (3)$$

where the magnitude of $k (= rk_x)$ is equal to the cross-section perimeter ($2\pi r$)-to-axial wavelength ($2L/m$) ratio. The existence condition of a nonzero solution of U , V and W is

$$\det H(n, k, f)_{3 \times 3} = 0 \quad (4)$$

Solving Eq. (4) yields three eigenfrequencies for each (n, k) , which gives three different vibration modes defined by the amplitude ratios (U/W , V/W , 1). Following Wang et al. (2006a, b), Qian et al. (2007) the values of the elastic constants of an MT used in the present work are $E_x = 1$ GPa, $E_\theta = G_{x\theta} = 1$ Mpa and $\nu_x = 0.3$.

3. Circumferential vibrations of microtubules

Following the procedures shown above let us study the vibration of MTs with circumferential wave number $n \geq 1$. In view of the fact that MTs usually have large length-to-diameter aspect ratio we shall focus on the vibration of MTs with $k \leq 0.1$, i.e., the axial wavelength ranges from 10 times as much as the perimeter of MT cross-section to infinitely long. Our results reveal that among the three eigenfrequencies associated with given n the lowest one corresponds to the vibration with the radial vibration amplitude W comparable to the circumferential amplitude V , but much larger than the axial amplitude U . Specifically, at $n = 1$, $W = V$. It can be shown by a simple mathematic analysis that the lowest frequency with $n = 1$ leads to the transverse bending mode with a rigid body motion of the circular cross-section, while those with $n \geq 2$ correspond to the circumferential modes where local bending along circumferential direction dominates (Fig. 2).

It can be seen from Figs. 1 and 2 that the deformation induced by the circumferential vibration is controlled by the lateral interaction between the parallel protofilaments that establish the MT wall. Experiments (Kis et al., 2002; Kasas et al., 2004a, b; Tuszyński et al., 2005) confirmed that this interaction is the weakest in the nanostructures of MTs, measured by $G_{x\theta}$ or E_θ that are two to three orders of magnitude lower than E_x reflecting the much stronger axial interaction within protofilaments. Furthermore, as shown in (dePablo et al., 2003), the circumferential bending of MTs is largely withstood by the inner ring (Figs. 1 and 2) of MTs with the ‘bridge thickness’ only of 1.1 nm, much thinner than the equivalent thickness 2.7 nm for in-plane deformation of MTs. The low elastic modulus E_θ and small equivalent thickness h_0 for bending leads to low bending stiffness $D_\theta (\propto E_\theta h_0^3)$ of MTs, suggesting that the circumferential vibration could result in large deformation on MT cross-sections and thus significantly affect the mechanical performance and structural integrity of MTs.

To quantify these vibrations, their phonon dispersion curves ($n = 2-5$) have been calculated in Fig. 3 for 8, 13 and 17 protofilament MTs with radius growing from 8.6, 12.8,

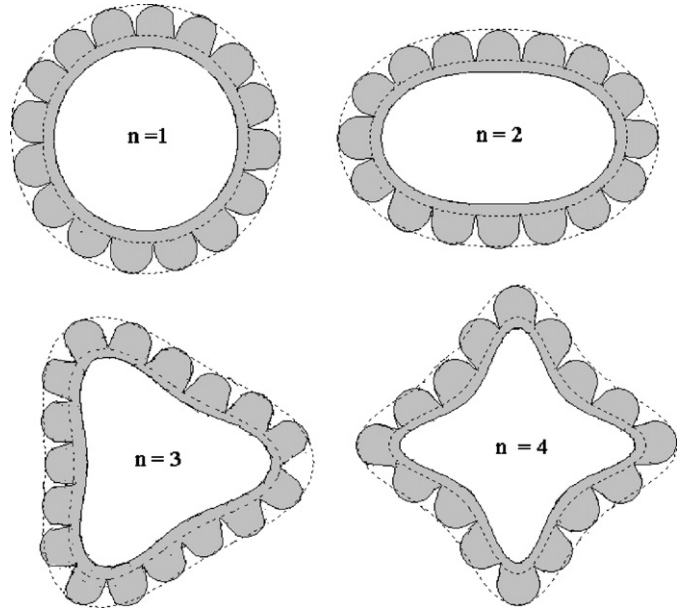


Fig. 2. The circular cross-section of MTs in transverse bending mode with $n = 1$ and the deformed cross-section of MTs in circumferential modes with $n = 2, 3$ and 4. The bending of the MT wall along circumferential direction is primarily withstood by the inner ring with the ‘bridge thickness’ of 1.1 nm (dePablo et al., 2003).

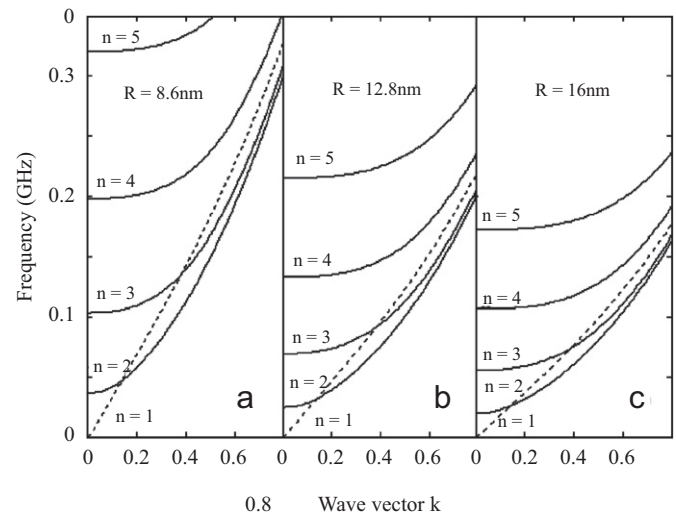


Fig. 3. The dispersion curves of beam-like bending mode with $n = 1$ and circumferential modes with $n = 2-5$ obtained for (a) 8-MTs ($r = 8.6$ nm), (b) 13-MTs ($r = 12.8$ nm) and (c) 17-MTs ($r = 16$ nm).

to 16 nm. For the sake of comparison, the dispersion curve of transverse bending mode ($n = 1$) is also presented in Fig. 3 (dotted lines). As seen from Fig. 3, at $k \geq 0.1$, all the frequencies decrease considerably with decreasing k , i.e., rising axial wavelength. Further increasing axial wavelength (i.e., decreasing k) at $k < 0.1$, while the frequency of transverse bending mode ($n = 1$) decreases and goes to zero at $k = 0$, those of circumferential modes ($n = 2$ to 5) become almost independent of axial wavelength and approaches a nonzero asymptotic value at infinite axial wavelength (i.e., $k \rightarrow 0$). Particularly, this asymptotic value

risers rapidly with growing circumferential wave number n and becomes more sensitive to the change of n for thinner MTs of smaller radius. For example, in Fig. 3, when n varies from 2 to 5 the associated frequency of 17-protofilament MTs ($r = 16$ nm) rises from 18.5 to 163 MHz while that of 8-protofilament MT ($r = 8.6$ nm) is raised from 36.7 to 322 MHz. On the other hand, for any given n the asymptotic value generally decreases with increasing MT radius. This effect of radius turns out to be more pronounced for the circumferential modes with larger n . As shown in Fig. 3, when the radius grows from 8.6 to 12.8 and to 16 nm, the frequency associated with $n = 2$ only changes slightly from 36.5 to 24.6 and to 19.6 MHz, much less than the decrease of the frequency associated with $n = 5$ which reduces substantially from 320 to 215 and to 172 MHz. Furthermore, detailed study shows (see Fig. 4) that at $k < 0.1$ the frequencies f of circumferential modes approximately satisfy $f \propto 1/r$, i.e., it increases almost linearly with the inverse of MT radius. In addition, the slope of the lines in Fig. 4 increases significantly with the rising circumferential wave number n , showing again the stronger radius dependence of the circumferential modes with larger n .

In Fig. 3, the almost constant frequency obtained for the circumferential modes with given n and $k < 0.1$ suggests that the local bending along the circumferential direction largely determines the associated frequency of MTs when the axial wavelength is more than an order of magnitude larger than the perimeter of MT cross-section. This in turn offers a physical interpretation for the insensitivity of the vibration modes to the axial wavelength, and their strong dependence on n and r that determine the circumferential wavelength. Specifically, this behavior (Fig. 3 with $n \geq 2$) is qualitatively different from that of the transverse bending mode ($n = 1$) where bending deformation occurs along the axial direction without circumferential deformation. It can

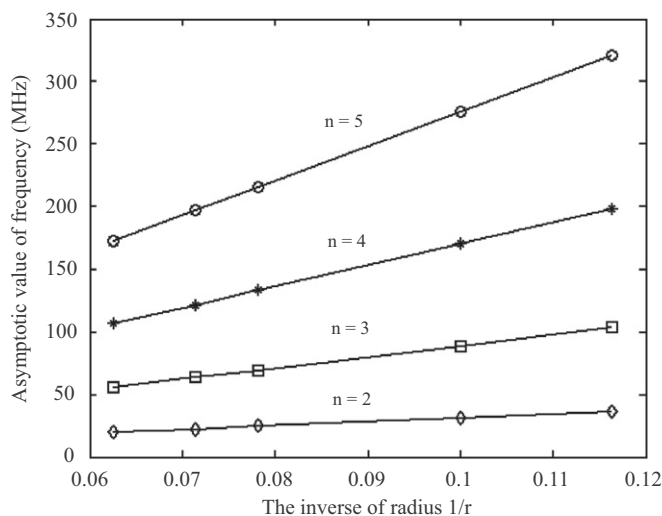


Fig. 4. The radius dependence of the frequency obtained for MTs vibrating in circumferential modes with long axial wavelength (i.e., $k < 0.1$).

be shown with simple analysis that under the condition $n = 1$ and $k \rightarrow 0$ we have $f \propto k^2$, and thus zero frequency at infinite axial wavelength ($k \rightarrow 0$).

In contrast to the present result, Sirenko et al. (1996) claimed that similar to the transverse bending modes the circumferential modes also abides by the parabolic law $f \propto k^2$. Evidently, this is in contradiction with the physical understanding explained above. Here we noticed that in (Sirenko et al., 1996) MTs are assumed to be so thin that the square of the thickness-to-radius ratio $(h/r)^2$ is ignored. As shown in Markus (1988), this in fact leads to the membrane shell model which is unable to account for the bending stiffness of MTs. The implicit negligence of the bending stiffness gives $f \propto k^2$ for the circumferential modes with zero f at $k \rightarrow 0$.

4. Conclusions

An orthotropic elastic shell model is employed to study the circumferential vibrations of MTs with large axial wavelength (i.e., $k < 0.1$). It is found that

- (1) In circumferential vibration the circumferential bending is predominant and controlled by the circumferential bending stiffness that is dependent on the weak lateral interaction between adjacent protofilaments and the small ‘bridge thickness’ of MTs. Thus, the excitation of the vibrations could lead to large deformation on MT cross-sections and thus significantly influence their mechanical performance and structural integrity.
- (2) With increasing axial wavelength, the frequency of the circumferential modes approaches a nonzero asymptotic value that increases significantly with the growing circumferential wave number n and decreasing radius of MTs. Specifically, the dependence of the frequency on the inverse of MT radius is almost linear and becomes much stronger for the circumferential modes with a larger n .
- (3) The unique features of the circumferential modes, captured by the present shell model, corrected the previous misunderstanding due to an oversimplified continuum model (Sirenko et al., 1996). Our study points out that a parabolic dispersion law does not apply to the circumferential modes.

It is worthwhile mentioning that the understanding achieved above is qualitative because the mechanical behavior of the microtubules has been assumed to be linearly elastic in the modeling. To obtain a quantitative prediction, the nonlinearity of the microtubule materials should be taken into account in further studies.

Conflict of interest statement

This is to confirm that all of the present authors do not have any financial and personal relationships with other

people or organizations that could inappropriately influence (bias) the research work presented in the submitted manuscript entitled ‘Circumferential vibration of microtubules with long axial wavelength’.

Acknowledgment

This work was supported by an ARC Discovery Grant.

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