A STUDY ON NATURAL FREQUENCIES OF SPHERICAL VIRAL SHELLS

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Abstract - A refined elastic shell model is used to study the effect of high structural heterogeneity on natural frequencies of spherical viral shells. With this model, the structural heterogeneity of a spherical viral shell is characterized by an effective bending thickness (which can be quite different from the average thickness) and the transverse shear modulus (which can be much lower than the in-plane shear modulus). The results show that actual natural frequencies of spheroidal modes of a spherical viral shell can be much lower than those predicted by the classical homogeneous shell model, although natural frequencies of torsional modes are close to those predicted by the classical model. For example, with physically realistic parameters for virus capsid STMV, the natural frequencies of spheroidal modes predicted by the present model are about 30-50% lower than those predicted by the classical model, in better agreement with known simulation results. These results suggest that the refined shell model could offer a relatively simple model to calculate natural frequencies of spherical viral shells of high structural heterogeneity.

Keywords - Natural Frequency, Spherical Viral Shells, Structural Heterogeneity, Thickness Non-uniformity

I. INTRODUCTION

A spherical viral shell (viral capsid) protects viral genome from hostile environment of the host cell, and excitation of capsid vibration could find application in either diagnosis or treatment of viral diseases [1], [2]. A number of approaches have been developed to investigate natural frequencies of spherical viral shells. For example, Babincová et al. [1] suggested that viruses can be inactivated by ultrasound resonance in the GHz region. Ford [2] has reported theoretical estimates of vibrational frequencies of spherical virus particles using the liquid drop model and an elastic sphere model. Widom et al.

[3] identified and classified vibration modes of a virus capsid based on a simple mass-and-spring model. It is of great significance to study natural frequencies of spherical viral shells and the influence on their biological functions and life cycle. A common key feature of spherical viral shells is their high structural heterogeneity and thickness non-uniformity. The present work aims to investigate the role of high structural heterogeneity and thickness nonuniformity on natural frequencies of viral capsids.

For this purpose, a refined shell model originally proposed in [4] for pressured buckling of viral capsids is employed, in which two additional parameters (called "effective bending thickness" and "transverse shear modulus") are added to the classical elastic homogeneous shell model to define the high structural heterogeneity and thickness nonuniformity. An analysis procedure similar to that developed in Wilkinson's [5], [6] on natural frequencies of a classical homogeneous spherical shell is employed to investigate natural frequencies of viral capsids (the detailed analysis is omitted in the present work).

II. TWO FREQUENCY EQUATIONS OF VIRAL CAPSIDS

In view of the fact that spherical viral shells are characterized by high geometrical heterogeneity and thickness non-uniformity, the effect of structural heterogeneity and thickness non-uniformity on the natural frequencies of spheroidal vibration modes is given by

$$\Omega^6\left[\frac{2k_1}{k_s(1-\mu)}(k_1k_r-k_2c_r)\frac{G}{G^*}\left(\frac{h}{h_0}\right)^3\right]-\Omega^4\left\{(k_1k_r-k_2c_r)\right.$$
$$\left[r\left(\frac{h}{h_0}\right)^3+\frac{4(1+\mu)}{k_s(1-\mu)}\frac{G}{G^*}\left(\frac{h}{h_0}\right)^3\right]+k_1\left[\xi(k_1+k_2)+(c_r+k_r)\left(\frac{h}{h_0}\right)^3\right.$$
$$\left.+\frac{2}{k_s}\left(k_1+k_r\left(\frac{h}{h_0}\right)^3\right)\frac{G}{G^*}\left(\frac{r}{1-\mu}-1\right)\right]\Bigg\}+\Omega^2\left\{(1+\mu)(2-r)\left(\xi k_2+\left(\frac{h}{h_0}\right)^3c_r\right)\right.$$
$$+k_r\left[r(r-3-\mu)\left(\frac{h}{h_0}\right)^3+2(1+\mu)\left(\frac{(r-2)}{k_s}\frac{G}{G^*}+1\right)\left(\frac{h}{h_0}\right)^3\right]$$
$$\left.+k_1\left[\frac{2}{k_s(1-\mu)}r(r+4\mu)\frac{G}{G^*}+r(r+\xi+\mu)+(1+3\mu)\left(\xi-\frac{2}{k_s}\frac{G}{G^*}\right)-(1-\mu)\right]\right\}$$
$$-(r-2)\left[r(r-2)+\frac{2(1+\mu)}{k_s}(r-1+\mu)\frac{G}{G^*}+(1-\mu^2)(\xi+1)\right]=0, \tag{1}$$

where μ is Poisson's ratio of the viral shell, k_s is the shear coefficient (e.g. 5/6 in [7]), R is the average radius, G^* is the transverse shear modulus which is allowed to be much lower than the in-plane shear modulus G, h_0 is the effective bending thickness which can be different from the average thickness h, $k_1=1+(1/12)(h/R)^2$, $k_2=(1/6)(h/R)^2$, $k_r=1+(3/20)(h/R)^2$, $c_r=2$, $\xi=12(R/h)^2(h/h_0)^3$, $r=n(n+1)$ (spheroidal vibration mode number n is any non-negative integer ($n=0,1,2,3,\ldots$)), and Ω denotes the dimensionless natural frequency defined by

$$\Omega^2 = \frac{\rho R^2 \omega^2 (1-\mu^2)}{E}. \qquad (2)$$

where E is Young's modulus, ω is the angular frequency, ρ denotes the mass density of the viral shell.

It is noted that the frequency equation (1) given by the present refined model reduces to the classical formula (see Eq. (3) in [6]) when $G^* = G$ and $h_0 = h$, as expected. It is confirmed by solving (1) with Mathematica that for the present refined model with physically realistic parameters of spherical viral shells, there are always three positive roots $\Omega_1, \Omega_2, \Omega_3$ ($\Omega_1 < \Omega_2 < \Omega_3$) for $n = 1, 2, 3, \ldots$ and two positive roots Ω_2, Ω_3 for $n = 0$.

The effect of structural heterogeneity and thickness non-uniformity on the natural frequencies of torsional vibration modes is given by

$$\Omega^4\left[\frac{4}{k_s(1-\mu)}(k_1k_r - k_2c_r)\frac{G}{G^*}\left(\frac{h}{h_0}\right)^3\right] - 2\Omega^2\left[\xi(k_1+k_2)+(c_r+k_r)\left(\frac{h}{h_0}\right)^3 + \frac{1}{k_s}\left(k_1+k_r\left(\frac{h}{h_0}\right)^3\right)\frac{G}{G^*}(p-2)\right] + (1-\mu)(p-2)\left[\frac{r-2}{k_s}\frac{G}{G^*}+(\xi+1)\right] = 0, \qquad (3)$$

where $p = k(k+1)$ (torsional vibration mode number k is any non-negative integer ($k = 0, 1, 2, 3, \ldots$)). It is noted that the frequency equation (3) given by the present refined model reduces to the classical formula (see Eq. (4) in [6]) when $G^* = G$ and $h_0 = h$, as expected. Similarly, it is confirmed by solving (3) with Mathematica that for the refined model with physically realistic parameters of spherical viral shells, there are always two positive roots Ω_4, Ω_5 ($\Omega_4 < \Omega_5$) for $k = 1, 2, 3, \ldots$ and one positive root Ω_5 for $k = 0$.

Therefore, for natural frequencies of a spherical viral shell, for given parameters ($\mu, k_s, R/h, G^*/G, h_0/h$), one can determine the dimensionless nature frequencies from (1) or (3) for each value of n or k, respectively. Thus, there are total five natural frequencies associated with each pair (n, k). Three of them, determined by (1) for each value of n, are associated with the spheroidal modes, and the other two, determined by (3) for each value of k, are associated with the torsional modes.

III. INFLUENCE OF HIGH STRUCTRUAL HETEROGENEITY ON NATURAL FREQUENCIES OF A SPHERICAL VIRAL SHELL

The major goal of this work is to examine how the high structural heterogeneity and thickness uniformity, defined by the key parameters ($R/h, G^*/G, h_0/h$), affects the natural frequencies of a viral capsid.

Now, let us investigate how these parameters influence natural frequencies of a viral capsid with their physically realistic values. It is known that for spherical viral shells, the low-lying frequencies are usually involved in their biological functions, and one can gain insights into the collective motions relevant to biological function by examining the lowest frequency modes [1]-[3]. Therefore, we shall focus on the dimensionless natural frequency Ω_1 and Ω_2 for spheroidal modes and Ω_4 for the torsional modes.

Let us first investigate the influence of the parameter R/h, for fixed values $k_s = 5/6$, $\mu = 0.3$, $G^*/G = 1.0$ and $h_0/h = 1.0$. In this case, the present refined model reduces to the classical shell model (Eqs. (1) or (3) reduce to Eqs. (3) and (4) of [6]), and the effect of R/h on the natural frequencies of a classical spherical shell has been investigated (e.g. see [8], [9]). For the present study, the dependence of the dimensionless natural frequency Ω given by (1) for the spheroidal modes and (3) for the torsional modes on the non-negative integer n or k is shown in Fig. 1(a) and 1(b), respectively, for a range of R/h between 5 and 50. It is seen from Figs. 1(a) and 1(b) that the frequencies of the spheroidal modes decrease with increasing value of R/h, which is consistent with the known results (see e.g. table IV and figure 3 in [8], and figure 2 in [9]). On the other hand, the frequencies of the torsional modes remain fairly unchanged when R/h varies from $R/h = 5$ to $R/h = 50$, which is consistent with known results (e.g. Table V and figure 4 in [8]).

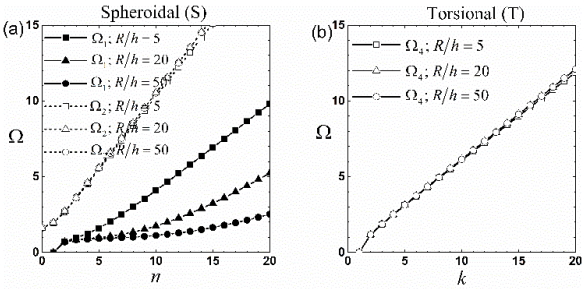


Fig. 1. The effect of R/h on natural frequencies

Next let us examine the effect of transverse shear modulus G^*/G and effective bending thickness h_0/h on natural frequencies for fixed values $k_s = 5/6$, $\mu = 0.3$ and $R/h = 5$. The influence of varying G^*/G within the range [0.01, 1] (with fixed value $h_0/h = 1.0$), and the influence of varying h_0/h within the range [0.2, 1] (with fixed value $G^*/G = 1.0$) on natural frequencies of a spherical shell are illustrated in Figs. 2 and 3, respectively. It is seen from Figs. 2 and 3 that when G^*/G decreases from 1.0 to 0.01, or when h_0/h decreases from 1.0 to 0.2, the frequencies of the spheroidal modes decrease substantially (especially for larger n). On the other hand, transverse shear modulus and effective bending thickness have almost no effect on the vibration frequencies of the torsional modes.

Therefore, for spherical viral shells characterized by relatively thicker and smaller in radius (defined by smaller radius-to-thickness ratio, e.g. see R/h ranging from 3 to 6 in table II of [10] for several viral capsids), and high structural heterogeneity and thickness non-uniformity (defined by transverse shear modulus much lower than the in-plane shear modulus and an effective bending thickness significantly smaller from the average shell thickness), the actual natural frequencies of spheroidal modes of a spherical viral shell could be much lower than those predicted by the classical homogeneous shell model (see Eqs. (3) and (4) in [6]), although natural frequencies of torsional modes can be quite close to those predicted by the classical homogeneous shell model.

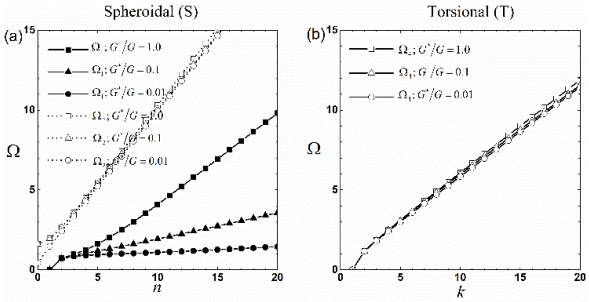


Fig. 2. The effect of G^*/G on natural frequencies

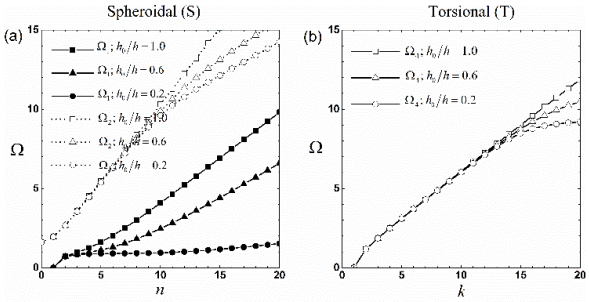


Fig. 3. The effect of h_0/h on natural frequencies

In order to justify the relevance of the present refined shell model for specific spherical viral shells, let us compare the results given by the present model (Eqs. (1) and (3)) for virus capsid STMV to those predicted by the classical shell model Eqs. (3) and (4) in [6] and simulation results of Yang et. al. (see table 3 in [11]). Yang et. al. [11] employed the coarse-grained elastic network to obtain discretized frequencies and associated vibration modes for virus capsid STMV, and then to estimate the Young's modulus (E) Poisson's ratio (μ) by fitting them to the continuum shell model (based on the assumptions of axisymmetric motion and the transverse shear modulus equal to the in-plane shear modulus). The parameters R and h are calculated based on the inner and outer radii shown in figure 3 in [11], which are given by $R = 7.0nm$ and $h = 3.1nm$. The parameters ρ, μ, E are obtained from table 4 in [11], which are given by $\rho = 823.82\, kg/m^3$, $\mu = 0.24$, $E = 3.7GPa$. To apply the present refined shell model to spherical viral shells of high structural heterogeneity, we have chosen $k_s = 5/6$, $G^*/G = 1.0$ (to be consistent with the assumption made in [8]) for virus capsid STMV with $h_0/h = 0.75$ determined by fitting the results shown in table 3 of [11]. The results of the classical shell model shown in Table I are obtained with $h_0/h = 1.0$ and otherwise identical parameters as the refined shell model. As shown in Table I, the results given by the present refined shell model, for both natural frequencies and associated vibration modes, agree well with the simulation results given in table 3 of [11], although the results given by the classical shell model show significant deviations from the simulation results (see table 3 of [11]). For example, it is seen from Table I that, compared to Yang et al's simulations in table 3 of [11], the classical shell model considerably overestimates the natural frequencies of spheroidal modes especially for larger n (see n=3,4,5 for virus capsids STMV, for which natural frequencies predicted by classical shell model are about 30-50% higher than the simulation results (see table 3 of [11]), while the latter are very close to those predicted by the present refined shell model with the maximum relative errors not more than 5%). This offers an evidence of the physical relevance and usefulness of the present refined shell model over the classical shell model for natural frequencies of spherical viral shells of high structural heterogeneity.

Table I. Comparisons for virus capsid STMV

The classical shell model		The refined shell model	
Frequency $\omega^2(ps^{-2})$	**Vibration Mode**	**Frequency** $\omega^2(ps^{-2})$	**Vibration Mode**
0.45131	$\Omega_1(n=2)$	0.40445	$\Omega_1(n=2)$
1.05	$\Omega_1(n=3)$	0.79236	$\Omega_1(n=3)$
0.94754	$\Omega_4(k=2)$	0.93702	$\Omega_4(k=2)$
2.05953	$\Omega_1(n=4)$	1.42567	$\Omega_1(n=4)$
1.64603	$\Omega_2(n=0)$	1.64603	$\Omega_2(n=0)$
3.56305	$\Omega_1(n=5)$	2.42355	$\Omega_1(n=5)$
2.23733	$\Omega_2(n=1)$	2.20857	$\Omega_2(n=1)$

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