A Continuum Theory for the Natural Vibrations of Spherical Virus Capsids

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Master's Thesis in Mathematical Engineering

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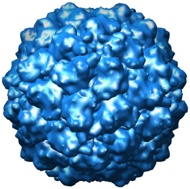
Outline

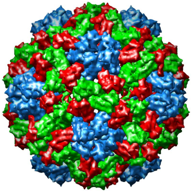
Viral Capsids

Viral capsids: nanometre-sized protein shells that enclose and protect the genetic materials (RNA or DNA) of viruses in a host cell, transport and release those materials inside another host cell.

In most cases, their shape is either helical (nearly cylindrical) or icosahedral (nearly spherical).

Typical examples of spherical capsids: STMV and CCMV capsids.

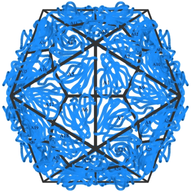


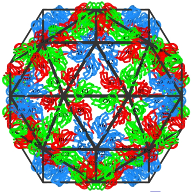


Viral Capsids

They consists of several structural subunits, the *capsomers*, made up by one or more individual proteins. In spherical capsids, the capsomers are classified as *pentamers* and *hexamers*.

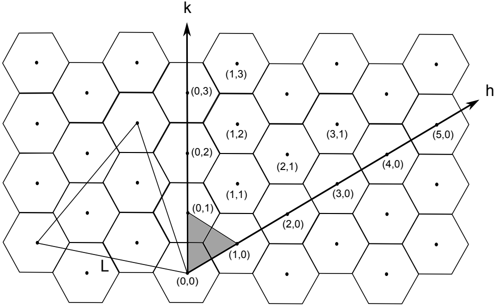
- STMV capsid: 60 copies of a single protein, clustered into 12 pentamers.
- CCMV capsid: 180 copies of a single protein, clustered into 12 pentamers and 20 hexamers.





Triangulation Number

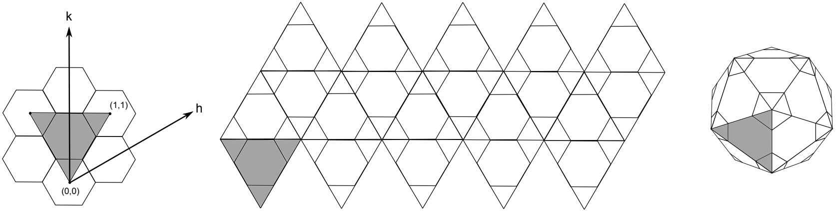
There are 12 pentamers in any spherical capsid. The number of hexamers depends on the *T-number* of the capsid (Caspar and Klug, 1962).



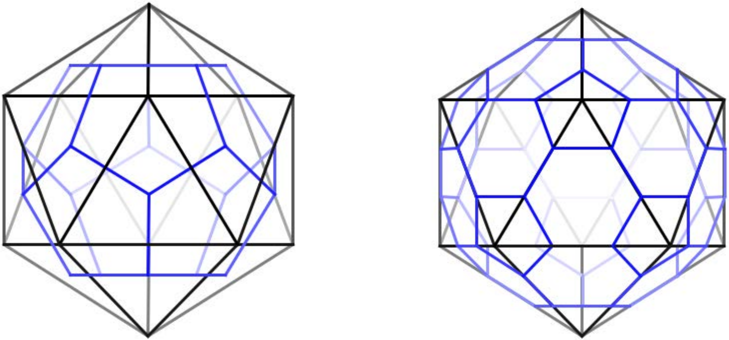
$$T = \frac{\frac{\sqrt{3}}{4}L^2}{\frac{\sqrt{3}}{4}} = L^2 = h^2 + hk + k^2$$

Triangulation Number

- $T = 1 \implies$ only pentamers (STMV capsid)
- $T > 1 \implies$ pentamers + hexamers
  Example: $T = 3$ (CCMV capsid)



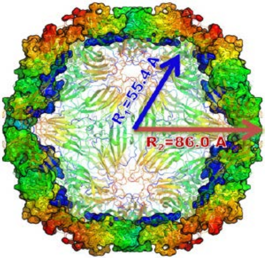
Triangulation Number



$T = 1$ capsid (left) and $T = 3$ capsid (right) surfaces

Geometry

The thickness of a spherical capsid is actually non-uniform. Ideal values of the inner and outer radii of the STMV capsid are $R_1 = 55.4\,\text{Å}$ and $R_2 = 86\,\text{Å}$ (Yang et al., 2009). The thickness of the spherical shell is then $t_{\mathcal{S}} = 30.6\,\text{Å}$ and its middle surface has radius $\rho_o = 70.7\,\text{Å}$.



Density, material moduli

- Mass density of the STMV capsid: $\delta_o = 823.82\ \mathrm{kg/m^3}$.
- From the measured value of the longitudinal sound speed c_l in STMV crystals, Yang et al. determined the value of the Young's modulus of the STMV capsid. The Poisson ratio is thought to be close to that of soft condensed matter, i.e., $\nu = 0.3$. In a generic three-dimensional isotropic elastic continuous body,

$$c_l = \sqrt{\frac{E(1-\nu)}{\delta_o(1+\nu)(1-2\nu)}}.$$

Remark

This formula does not account for the shell-like geometry of the STMV capsid: it involves only its density, but none of its geometrical features, such as the thickness and the radius of the middle surface.

Part I

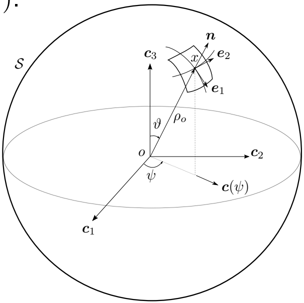
Linearly Elastic Spherical Shells

Features

- The shell is capable of both transverse shear deformation and thickness distension.
- The shell is transversely isotropic with respect to the radial direction, with fiber-wise constant elastic moduli, in order to account for the rotational symmetries of the capsomers.
- The thickness may vary over the middle surface.

Middle Surface

Curvilinear coordinates $z^1 = \vartheta$, $z^2 = \psi$.
Let $\mathsf{S} \coloneqq (0,\pi) \times (0,2\pi)$.



$$\mathsf{S} \ni (\vartheta,\psi) \leftrightarrow x = x(\vartheta,\psi) = o + \boldsymbol{x}(\vartheta,\psi) \in \mathcal{S},$$
$$\boldsymbol{x}(\vartheta,\psi) = \rho_o(\sin\vartheta\, \boldsymbol{c}(\psi) + \cos\vartheta\, \boldsymbol{c}_3),$$
$$\boldsymbol{c}(\psi) = \cos\psi\, \boldsymbol{c}_1 + \sin\psi\, \boldsymbol{c}_2.$$

Local Bases

- Covariant basis

$$
\begin{aligned}
\boldsymbol{e}_1 &= \frac{\partial \boldsymbol{x}}{\partial \vartheta} = \rho_o(\cos\vartheta\, \boldsymbol{c} - \sin\vartheta\, \boldsymbol{c}_3) \\
\boldsymbol{e}_2 &= \frac{\partial \boldsymbol{x}}{\partial \psi} = \rho_o \sin\vartheta\, \boldsymbol{c}' \\
\boldsymbol{e}_3 &= \boldsymbol{n} = \rho_o^{-1}\boldsymbol{x} = \sin\vartheta\, \boldsymbol{c} + \cos\vartheta\, \boldsymbol{c}_3
\end{aligned}
$$

- Contravariant basis

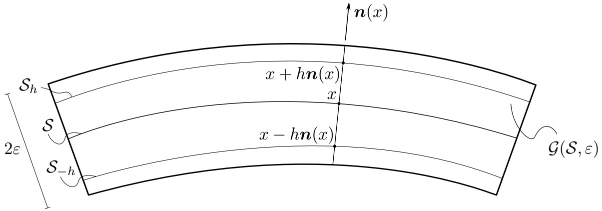
$$
\begin{aligned}
\boldsymbol{e}^1 &= {}^{\mathrm{s}}\nabla\vartheta = \rho_o^{-2}\boldsymbol{e}_1 \\
\boldsymbol{e}^2 &= {}^{\mathrm{s}}\nabla\psi = (\rho_o \sin\vartheta)^{-2}\, \boldsymbol{e}_2 \\
\boldsymbol{e}^3 &= \boldsymbol{n}
\end{aligned}
$$

- Physical basis

$$
\begin{aligned}
\boldsymbol{e}_{<1>} &= \frac{\boldsymbol{e}_1}{|\boldsymbol{e}_1|} \\
\boldsymbol{e}_{<2>} &= \frac{\boldsymbol{e}_2}{|\boldsymbol{e}_2|} \\
\boldsymbol{e}_{<3>} &= \boldsymbol{n}
\end{aligned}
$$

Shell-like Region

Curvilinear coordinates $z^1 = \vartheta$, $z^2 = \psi$, $z^3 = \zeta$.
Let $I := (-\varepsilon, +\varepsilon)$.



$$\mathsf{S} \times I \ni (\vartheta, \psi, \zeta) \leftrightarrow p = p(\vartheta, \psi, \zeta) = o + \boldsymbol{p}(\vartheta, \psi, \zeta) \in \mathcal{G}(\mathcal{S}, \varepsilon),$$
$$\boldsymbol{p}(\vartheta, \psi, \zeta) = \boldsymbol{x}(\vartheta, \psi) + \zeta \boldsymbol{n}(\vartheta, \psi).$$

We can define analogous local bases for any $p \in \mathcal{G}(\mathcal{S}, \varepsilon)$.

Kinematics

Displacement field

$$\boldsymbol{u}(x,\zeta;t) = \overset{(0)}{\boldsymbol{u}}(x,t) + \zeta\overset{(1)}{\boldsymbol{u}}(x,t),$$

$$\overset{(0)}{\boldsymbol{u}}(x,t) = \boldsymbol{a}(x,t) + w(x,t)\boldsymbol{n}(x), \quad \overset{(1)}{\boldsymbol{u}}(x,t) = \boldsymbol{\varphi}(x,t) + \gamma(x,t)\boldsymbol{n}(x),$$

$$\boldsymbol{a}(x,t)\cdot\boldsymbol{n}(x) = 0, \ \boldsymbol{\varphi}(x,t)\cdot\boldsymbol{n}(x) = 0, \quad \forall x \in \mathcal{S}, \ \forall t \in (0,+\infty)$$

$$\boldsymbol{a} = a_{<1>}\,\boldsymbol{e}_{<1>} + a_{<2>}\,\boldsymbol{e}_{<2>}$$

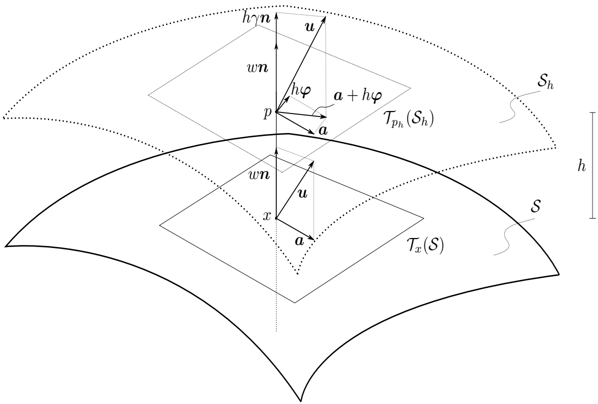
$$\boldsymbol{\varphi} = \varphi_{<1>}\,\boldsymbol{e}_{<1>} + \varphi_{<2>}\,\boldsymbol{e}_{<2>}$$

Six scalar parameters: $a_{<1>}, a_{<2>}, \varphi_{<1>}, \varphi_{<2>}, w, \gamma$

Strain tensor

$$\boldsymbol{E} = \mathrm{sym}\,\nabla\boldsymbol{u} = \frac{1}{2}\left(\nabla\boldsymbol{u} + \nabla\boldsymbol{u}^T\right)$$

Kinematics


$h\gamma\boldsymbol{n}$
$\boldsymbol{u}$
$w\boldsymbol{n}$
$h\boldsymbol{\varphi}$
$\boldsymbol{a}+h\boldsymbol{\varphi}$
p
$\boldsymbol{a}$
$\mathcal{T}_{p_h}(\mathcal{S}_h)$
$\mathcal{S}_h$
h
$w\boldsymbol{n}$
$\boldsymbol{u}$
x
$\boldsymbol{a}$
$\mathcal{T}_x(\mathcal{S})$
$\mathcal{S}$

Weak Formulation

Let $\boldsymbol{S}$ be the Piola stress tensor, $\boldsymbol{d}_o$ the distance force per unit volume and $\boldsymbol{c}_o$ the contact force per unit area. Define the *internal virtual work*

$$\mathcal{W}^{int}(\mathcal{G})\,[\delta\boldsymbol{u}] := \int_{\mathcal{G}} \boldsymbol{S}\cdot\nabla\delta\boldsymbol{u}$$

and the *external virtual work*

$$\mathcal{W}^{ext}(\mathcal{G})\,[\delta\boldsymbol{u}] := \int_{\mathcal{G}} \boldsymbol{d}_o\cdot\delta\boldsymbol{u} + \int_{\partial\mathcal{G}} \boldsymbol{c}_o\cdot\delta\boldsymbol{u}.$$

Principle of Virtual Work:

$$\forall\delta\boldsymbol{u},\quad \mathcal{W}^{int}(\mathcal{G})\,[\delta\boldsymbol{u}] = \mathcal{W}^{ext}(\mathcal{G})\,[\delta\boldsymbol{u}]\,.$$

Weak Formulation

By integration over the thickness,

$$\mathcal{W}^{int}(\mathcal{G})\,[\delta \boldsymbol{u}] = \int_{\mathcal{S}} \left({}^{\mathrm{s}}\boldsymbol{F} \cdot {}^{\mathrm{s}}\nabla \delta \overset{(0)}{\boldsymbol{u}} + {}^{\mathrm{s}}\boldsymbol{M} \cdot {}^{\mathrm{s}}\nabla \delta \overset{(1)}{\boldsymbol{u}} + \boldsymbol{f}^{(3)} \cdot \delta \overset{(1)}{\boldsymbol{u}} \right),$$

where

$${}^{\mathrm{s}}\boldsymbol{F} := \left(\int_I \alpha \boldsymbol{S} \boldsymbol{g}^{\beta}\, d\zeta \right) \otimes \boldsymbol{e}_{\beta}, \quad {}^{\mathrm{s}}\boldsymbol{M} := \left(\int_I \alpha \zeta \boldsymbol{S} \boldsymbol{g}^{\beta}\, d\zeta \right) \otimes \boldsymbol{e}_{\beta},$$

$$\boldsymbol{f}^{(3)} := \int_I \alpha \boldsymbol{S} \boldsymbol{n}\, d\zeta\,.$$

Weak Formulation

By integration over the thickness,

$$\mathcal{W}^{ext}(\mathcal{G})\,[\delta \boldsymbol{u}] = \int_{\mathcal{S}} \left(\boldsymbol{q}_o \cdot \delta \overset{(0)}{\boldsymbol{u}} + \boldsymbol{r}_o \cdot \delta \overset{(1)}{\boldsymbol{u}} \right),$$

where

$$\boldsymbol{q}_o := \int_I \alpha\, \boldsymbol{d}_o\, d\zeta + \alpha^+ \boldsymbol{c}_o^+ + \alpha^- \boldsymbol{c}_o^-,$$

$$\boldsymbol{r}_o := \int_I \alpha\zeta \boldsymbol{d}_o\, d\zeta + \varepsilon \left(\alpha^+ \boldsymbol{c}_o^+ - \alpha^- \boldsymbol{c}_o^- \right).$$

Balance Equations

The Principle of Virtual Work reads

$$\int_{\mathcal{S}} \left({}^{\mathrm{s}}\boldsymbol{F} \cdot {}^{\mathrm{s}}\nabla \delta \overset{(0)}{\boldsymbol{u}} + {}^{\mathrm{s}}\boldsymbol{M} \cdot {}^{\mathrm{s}}\nabla \delta \overset{(1)}{\boldsymbol{u}} + \boldsymbol{f}^{(3)} \cdot \delta \overset{(1)}{\boldsymbol{u}} \right) = \int_{\mathcal{S}} \left(\boldsymbol{q}_o \cdot \delta \overset{(0)}{\boldsymbol{u}} + \boldsymbol{r}_o \cdot \delta \overset{(1)}{\boldsymbol{u}} \right).$$

By localization,

$$\begin{aligned} {}^{\mathrm{s}}\mathrm{Div}\, {}^{\mathrm{s}}\boldsymbol{F} + \boldsymbol{q}_o &= \boldsymbol{0}, \\ {}^{\mathrm{s}}\mathrm{Div}\, {}^{\mathrm{s}}\boldsymbol{M} - \boldsymbol{f}^{(3)} + \boldsymbol{r}_o &= \boldsymbol{0}. \end{aligned} \tag{1}$$

- $\partial \mathcal{S} = \varnothing \implies$ no boundary conditions

On inserting $\boldsymbol{S} = \mathbb{C}[\boldsymbol{E}]$, with $\boldsymbol{E} = \mathrm{sym}\, \nabla \boldsymbol{u}$, into the previous definitions, (1) yields a system of six scalar equations in terms of the six kinematical parameters.

Part II

Analysis of Natural Vibrations

Assumptions

1. The only distance actions per unit area involved are the inertial parts of $\boldsymbol{q}_o$ and $\boldsymbol{r}_o$ ($\boldsymbol{d}_o \equiv \boldsymbol{d}_o^{in} = -\delta_o \ddot{\boldsymbol{u}}$). No contact forces per unit area: $\boldsymbol{c}_o \equiv \boldsymbol{0}$.
2. As in the majority of the literature about capsids
   - We consider the subcase of *homogeneous* and *isotropic* response
   - We assume the thickness uniform over the middle surface
3. We restrict attention on *axisymmetric vibrations*: kinematical parameters independent of ψ. Notation: $\frac{\partial}{\partial \vartheta}(\cdot) = (\cdot)'$

Radial Vibrations without Thickness Changes

$$\boldsymbol{u} = w\boldsymbol{n}$$

Governing equation

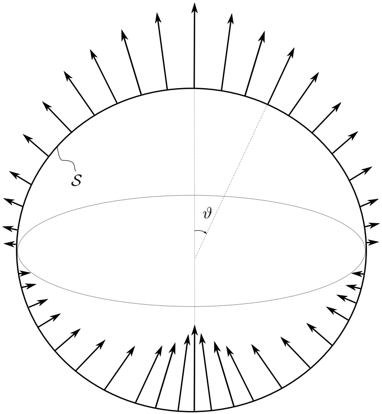
$$G(w'' + \cot\vartheta\ w') - \frac{2E}{(1+\nu)(1-2\nu)}w = \rho_o^2\delta_o\left(1 + \frac{\varepsilon^2}{3\rho_o^2}\right)\ddot{w}$$

- $w' = 0 \implies \ddot{w} + \omega_0^2 w = 0,\ \omega_0^2 = \dfrac{2E}{\rho_o^2\delta_o\left(1+\frac{\varepsilon^2}{3\rho_o^2}\right)(1+\nu)(1-2\nu)}$
- $w(\vartheta, t) = c\ \cos\vartheta\cos(\omega_1 t) \Rightarrow \omega_1^2 = \dfrac{E(3-2\nu)}{\rho_o^2\delta_o\left(1+\frac{\varepsilon^2}{3\rho_o^2}\right)(1+\nu)(1-2\nu)}$

$$\omega_1^2 > \omega_0^2$$

Radial Vibrations without Thickness Changes

$$w(\vartheta, t) = c \cos\vartheta \cos(\omega_1 t)$$



Uniform Radial Vibrations with Thickness Changes

$$\boldsymbol{u} = (w + \zeta\gamma)\boldsymbol{n}$$

$$w = \widehat{w}\cos(\omega t), \quad \gamma = \widehat{\gamma}\cos(\omega t)$$

Governing equations

$$-\omega^2\rho_o^2\delta_o\left(\left(1+\frac{\varepsilon^2}{3\rho_o^2}\right)\widehat{w}+\frac{2\varepsilon^2}{3\rho_o}\widehat{\gamma}\right)+\frac{2E}{(1+\nu)^2(1-2\nu)}\left((1+\nu)\widehat{w}+(1+\nu^2)\rho_o\widehat{\gamma}\right)=0, \tag{2}$$

$$-\omega^2\varepsilon^2\delta_o\left(\frac{2}{3}\widehat{w}+\rho_o\left(\frac{1}{3}+\frac{\varepsilon^2}{5\rho_o^2}\right)\widehat{\gamma}\right)+ \\ +\frac{E}{1-2\nu}\left\{\frac{2\varepsilon^2}{3\rho_o}\widehat{\gamma}+\frac{1}{1+\nu}\left[2\nu\widehat{w}+\left((1-\nu)\rho_o+(1+\nu)\frac{\varepsilon^2}{3\rho_o}\right)\widehat{\gamma}\right]\right\}=0 \tag{3}$$

Uniform Radial Vibrations with Thickness Changes

- $(2): \omega^2 = \dfrac{a\widehat{w} + b\widehat{\gamma}}{c\widehat{w} + d\widehat{\gamma}}$
- $(3): \omega^2 = \dfrac{e\widehat{w} + g\widehat{\gamma}}{h\widehat{w} + k\widehat{\gamma}}$

$$\Longrightarrow \quad \widehat{\gamma} = K_{\pm}\widehat{w}, \quad K_{\pm} = K_{\pm}(E, \nu, \delta_o, \rho_o, \varepsilon)$$

$$\omega_{\pm}^2 = \frac{2E\left((1+\nu) + (1+\nu^2)\rho_o K_{\pm}\right)}{\rho_o^2 \delta_o (1+\nu)^2 (1-2\nu)\left(\left(1 + \frac{\varepsilon^2}{3\rho_o^2}\right) + \frac{2\varepsilon^2}{3\rho_o} K_{\pm}\right)}$$

Parallel-Wise Twist Vibrations

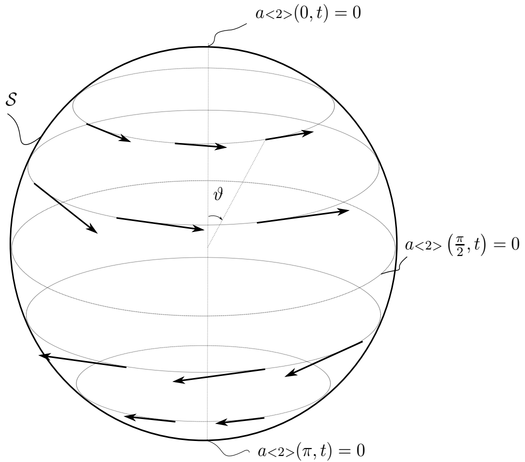
$$\boldsymbol{u} = a_{<2>} \boldsymbol{e}_{<2>}$$

Governing equation

$$a_{<2>}'' + \cot\vartheta \; a_{<2>}' - \cot^2\vartheta \; a_{<2>} = \frac{\rho_o^2 \delta_o}{G}\left(1 + \frac{\varepsilon^2}{3\rho_o^2}\right) \ddot{a}_{<2>}$$

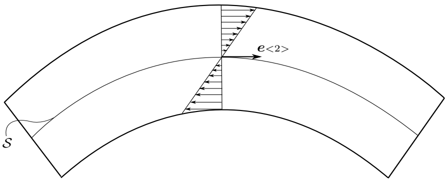
$$a_{<2>}(\vartheta, t) = c \, \sin\vartheta \cos\vartheta \cos(\omega t) \Longrightarrow \omega^2 = \frac{5G}{\rho_o^2 \delta_o \left(1 + \frac{\varepsilon^2}{3\rho_o^2}\right)}$$

Parallel-Wise Twist Vibrations



Parallel-Wise Shear Vibrations

$$\boldsymbol{u} = \zeta \varphi_{<2>} \boldsymbol{e}_{<2>}$$



Governing equation

$$\frac{\varepsilon^2}{\rho_o^2}\left(\varphi_{<2>}'' + \cot\vartheta\ \varphi_{<2>}' + (1-\cot^2\vartheta)\,\varphi_{<2>}\right) - 3\,\varphi_{<2>} = \frac{\varepsilon^2\delta_o}{G}\left(1+\frac{3}{5}\,\frac{\varepsilon^2}{\rho_o^2}\right)\ddot{\varphi}_{<2>}$$

Parallel-Wise Shear Vibrations

- $\varepsilon = 15.3\,\text{Å}$, $\rho_o = 70.7\,\text{Å}$ (Yang et al., 2009) $\Rightarrow \dfrac{3\varepsilon^2}{5\rho_o^2} \approx 0.024$

  $\Rightarrow$ approximate frequency $\widetilde{\omega}^2 = \dfrac{3G}{\varepsilon^2 \delta_o}$
- Without approximation,

  $$\varphi_{<2>}(\vartheta, t) = c \sin\vartheta \cos\omega t \Longrightarrow \omega^2 = \frac{G}{3\varepsilon^2\delta_o\left(1 + \frac{3}{5}\,\frac{\varepsilon^2}{\rho_o^2}\right)}$$

Remark

Both ω^2 and $\widetilde{\omega}^2$ diverge as $\varepsilon \to 0$.

Conclusions and Directions for Future Research

Conclusions

We have set forth some simple cases of natural vibrations that might be considered as a reference to infer a correct evaluation of Young's modulus and Poisson's ratio for a spherical capsid, when thought of as an isotropic body, by carrying out experiments that induce the relative vibrational modes.

Directions for Future Research

- Multiscale modeling of spherical capsids
- Full capsids in a hydrostatic environment