Bifurcations and Instabilities in Fluid Dynamics
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Session T7 Micro- and nano-systems

«Static response and stability of coated microbubbles as a means of parameter estimation»

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Outline

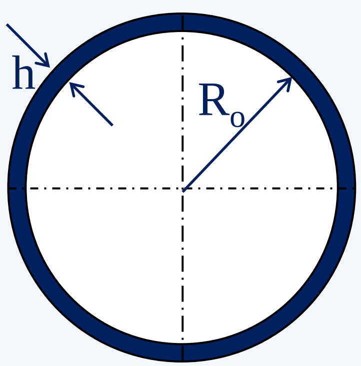
- Introduction
- Theoretical Background
- Numerical Analysis
- Results
- Conclusions and Discussion

Geometry

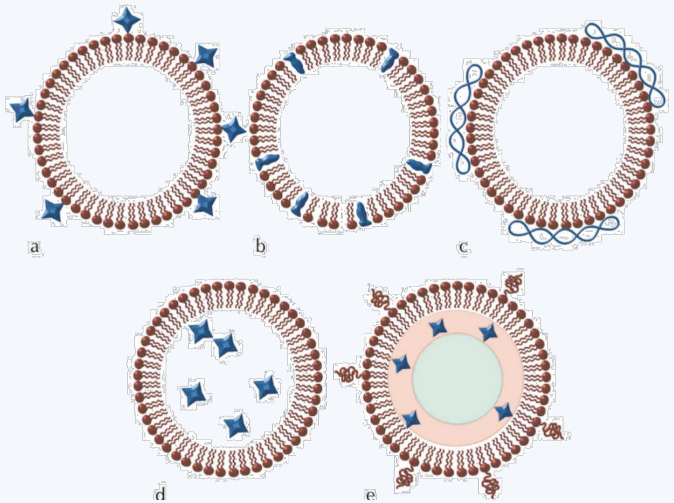
- Initial Radius ~ 1.5-2.5 μm
- Thickness ~ 5-40 nm

Material

- Polymer : Stiff Shell → BiSphere
- Lipid : Soft Shell → BR14



- ❖ Drug Delivery
- ❖ Medical Imaging



Elastic Properties

- ✓ Stability issues
- ✓ Adhesion to various surfaces
- ✓ Transport behavior through biological channels

Experiments

Ultrasound Measurements

Static Measurements

AFM : Atomic Force Microscopy

Elastic Properties

Polymeric Bubbles

Lipid Shells

Geometry

Initial Radius: R_o

Shell Thickness :h

Initial Radius: R_o

Elastic Properties

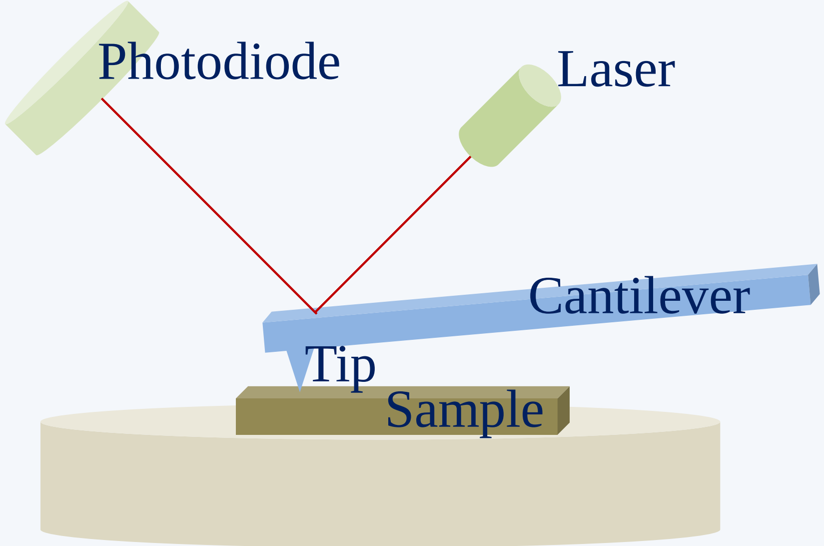
Shear Modulus: G_s

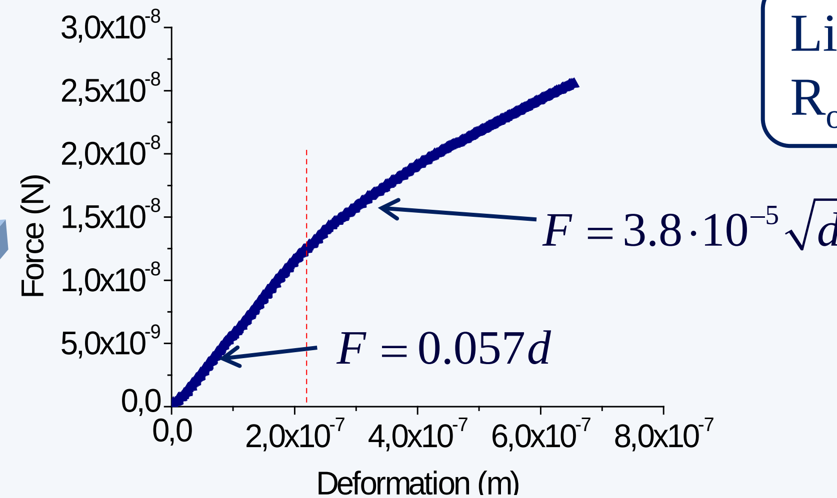
Bending Modulus: $k_b=k_b(G_s, h)$

Area Dilatation: $\chi=3G_sh$

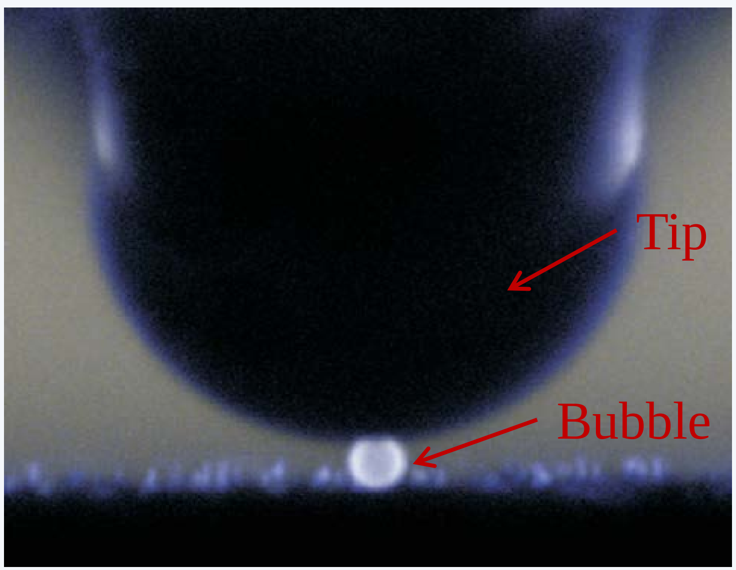
Bending Modulus: k_b

Atomic Force Microscopy Experiment

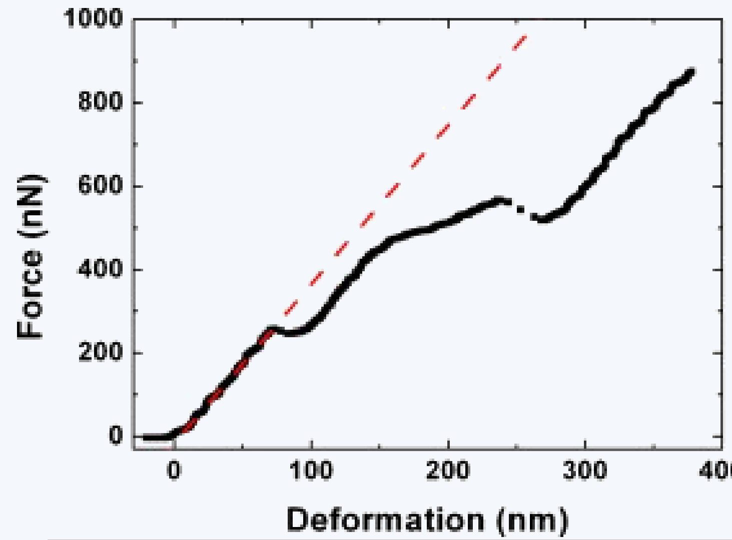




Lipid
R_o=2.6 μm



O. I. Vinogradova, J. Phys. Condens. Matter 2004, 16, R1105–R1134



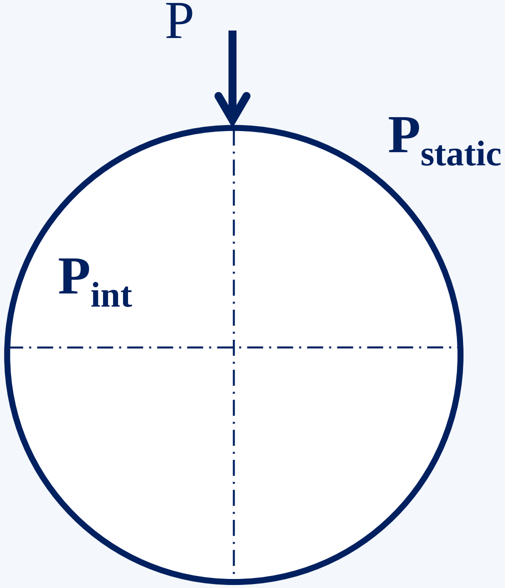
Polymer
R_o=2.6 μm
h=39 nm

Glynos, Sboros, Koutsos, *Polymeric thin shells: Measurement of elastic properties at the nanometer scale using atomic force microscopy.* Materials Science and Engineering

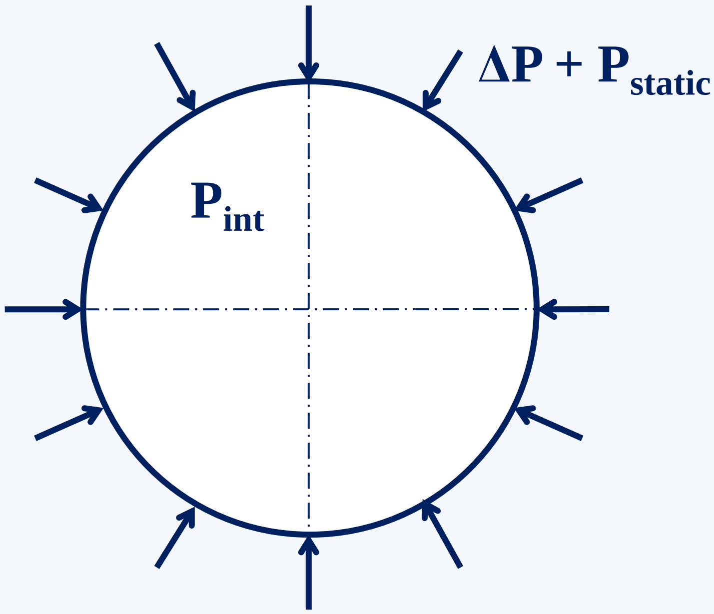
Aim of this work

Effect of gas compressibility on force-displacement curves for different static loads

Point Load

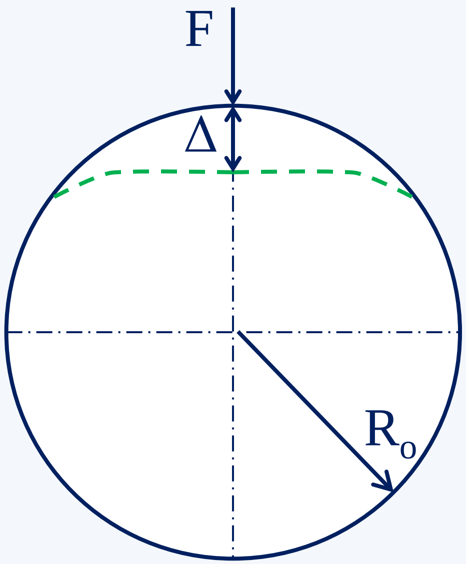
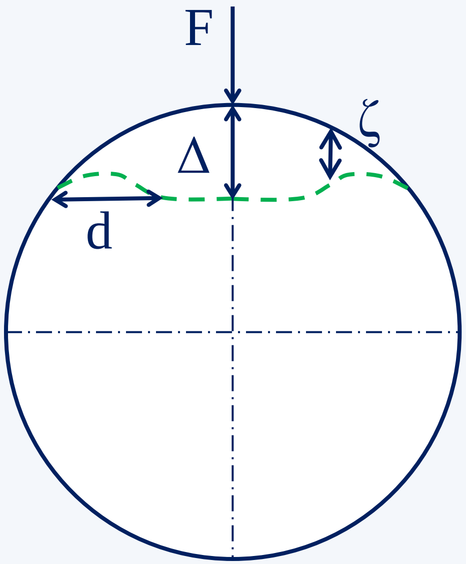


Uniform External Overpressure



Approximation for AFM Measurements

Mechanical Properties of Microbubbles – Point Load

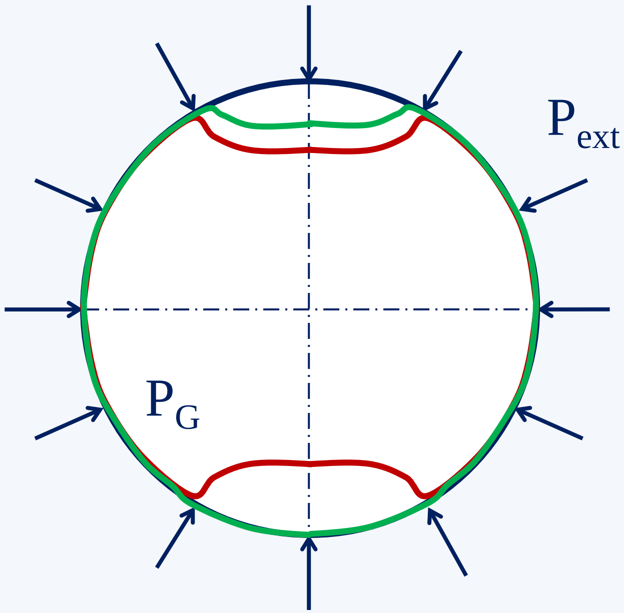
Small Deformations	Large Deformations
	

Stretching Energy: $E_s \sim Eh\left(\frac{\Delta}{R_o}\right)^2$ $E_s \sim Eh\left(\frac{\zeta}{R_o^2}\right)^2$

Bending Energy: $E_b \sim Eh^3\left(\frac{\Delta}{a^2}\right)^2$ $E_b \sim Eh^3\left(\frac{\zeta}{d^2}\right)^2$

Force-Displacement: $\boxed{F = \frac{4}{\sqrt{3\left(1-\nu^2\right)}}\frac{Eh^2}{R_o}\Delta}$ Reissner's Equation $\boxed{F = \sqrt{\frac{E^2h^5}{R_o^2}}\sqrt{\Delta}}$ Pogorelov's Equation

Uniform External Overpressure



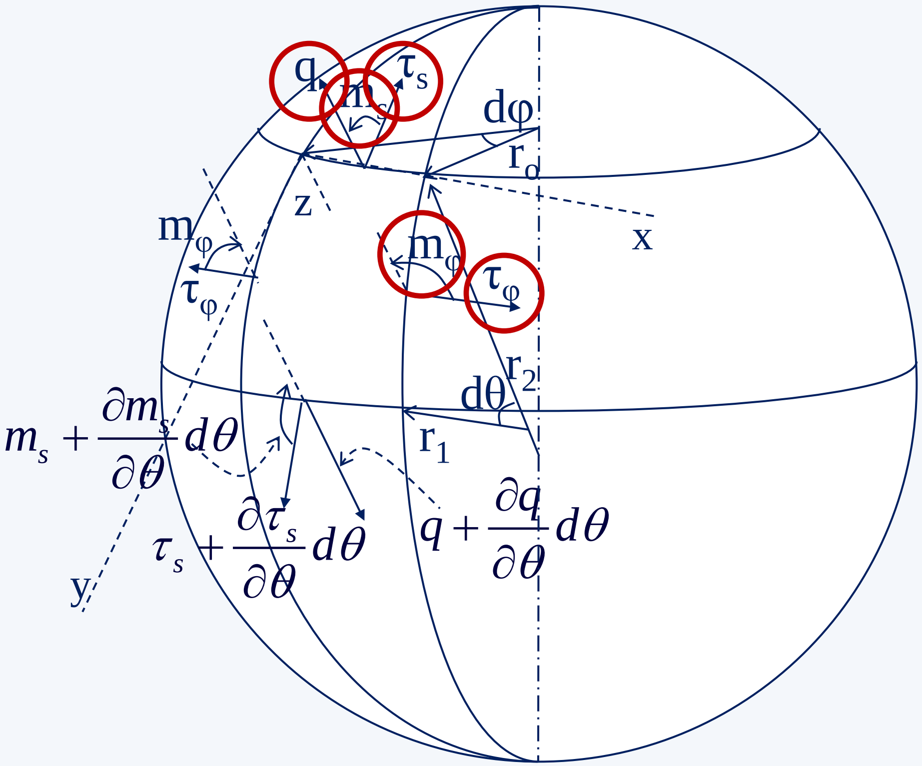
Critical Buckling Load

$$\Delta P_{cb} = \frac{6G_s}{\sqrt{3\left(1-\nu^2\right)}}\left(\frac{h}{R_o}\right)^2$$

Two Dominant Eigenmodes

- Symmetrically buckled
- Simply buckled (asymmetric)

Force Balance



Normal Force Balance

$$\Delta F_N = \Delta P = P_{Ext} - P_G = \left(\vec{\nabla}_s \cdot \left(\underline{\underline{\tau}} + \vec{q}\vec{n} \right) \right) \Big|_{Elastic} \cdot \vec{n}$$

Tangential Force Balance

$$\Delta F_t = 0$$

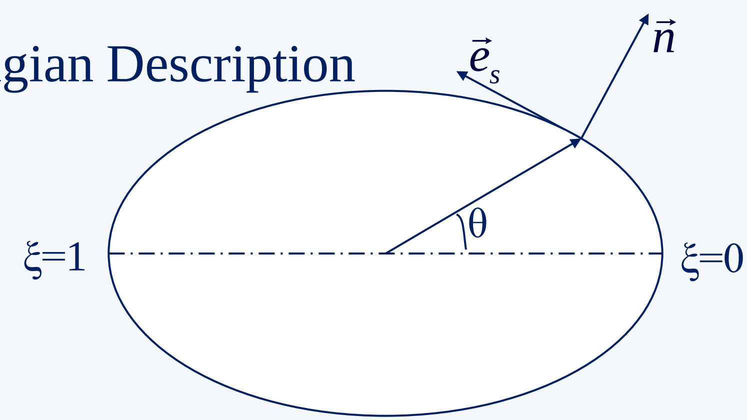
Isothermal Gas Compression

$$P_{G0} V_0 = P_G V$$

Axisymmetric Approximation

$$\frac{\partial r}{\partial \xi} = \frac{\partial^2 \theta}{\partial \xi^2} = 0 \quad \text{when} \quad \xi = 0,1$$

Lagrangian Description



$$\vec{n} = \frac{r\theta_\xi}{\sqrt{r_\xi^{\,2} + r^2\theta_\xi^{\,2}}} \vec{e}_r - \frac{r_\xi}{\sqrt{r_\xi^{\,2} + r^2\theta_\xi^{\,2}}} \vec{e}_\theta$$

$$\vec{e}_s = \frac{r_\xi}{\sqrt{r_\xi^{\,2} + r^2\theta_\xi^{\,2}}} \vec{e}_r - \frac{r\theta_\xi}{\sqrt{r_\xi^{\,2} + r^2\theta_\xi^{\,2}}} \vec{e}_\theta$$

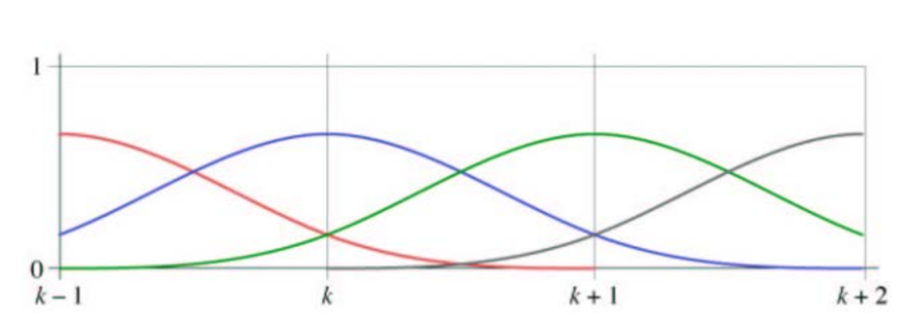
Solution Procedure

Numerical Solution with FEM

Galerkin method for discretization of normal and tangential force balance.

$$u(t)=\sum_{j=1}^{N+3} u_{c,j} B_j(t)$$

$$\left[K^{(e)}\right]\left\{u^{(e)}\right\}=\left\{F^{(e)}\right\}$$



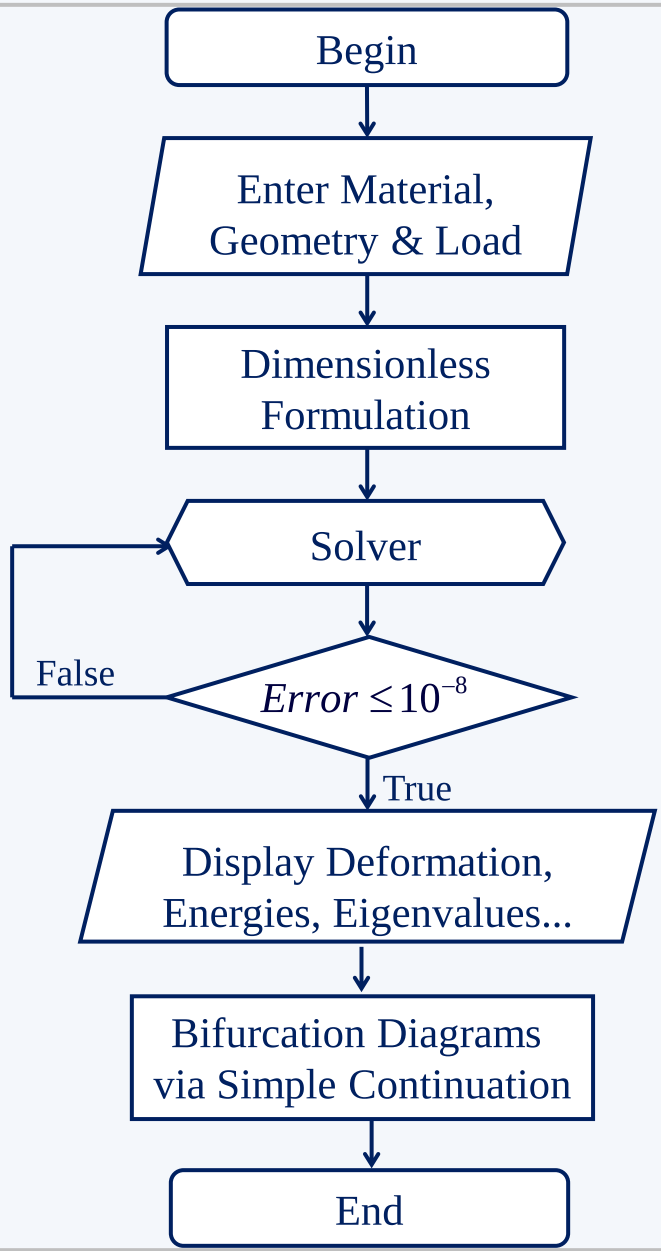
Basis Functions

$$B_i\left(t_j\right)=\begin{cases} 4, & j=1 \\ 1, & j=i\pm 1 \\ 0, & j=i\pm 2 \end{cases}$$

Tsiglifis, K., *Numerical simulation of bubble dynamics in response to acoustic disturbances*, Doctoral Thesis, in *Department of Mechanical Engineering*. 2007, University of Thessaly: Volos.

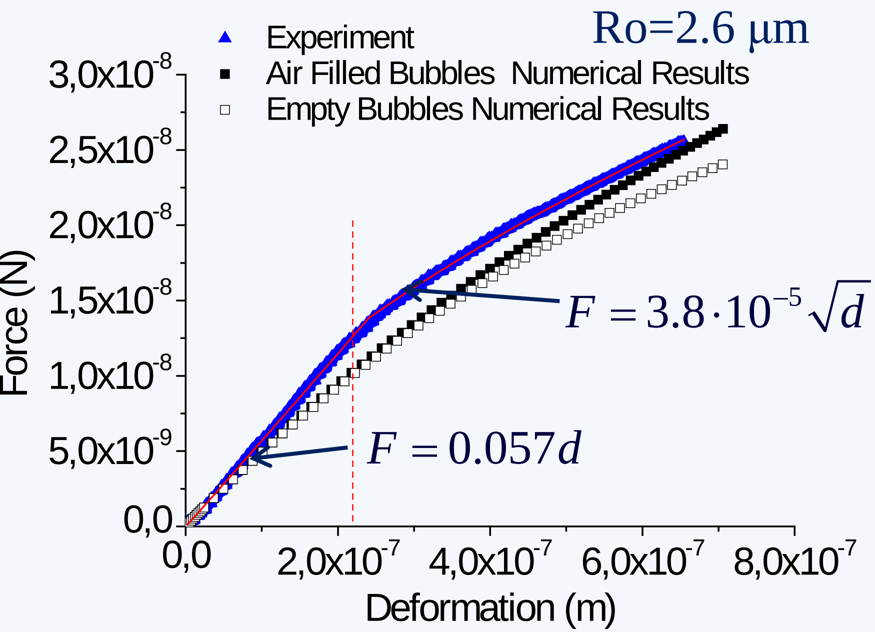
Serpetsi, S., *Numerical study of mechanical properties of microbubbles with elastic shell-application in Atomic Force Microscopy*, Master Thesis, in *Department of Mechanical Engineering*. 2011, University of Thessaly: Volos.

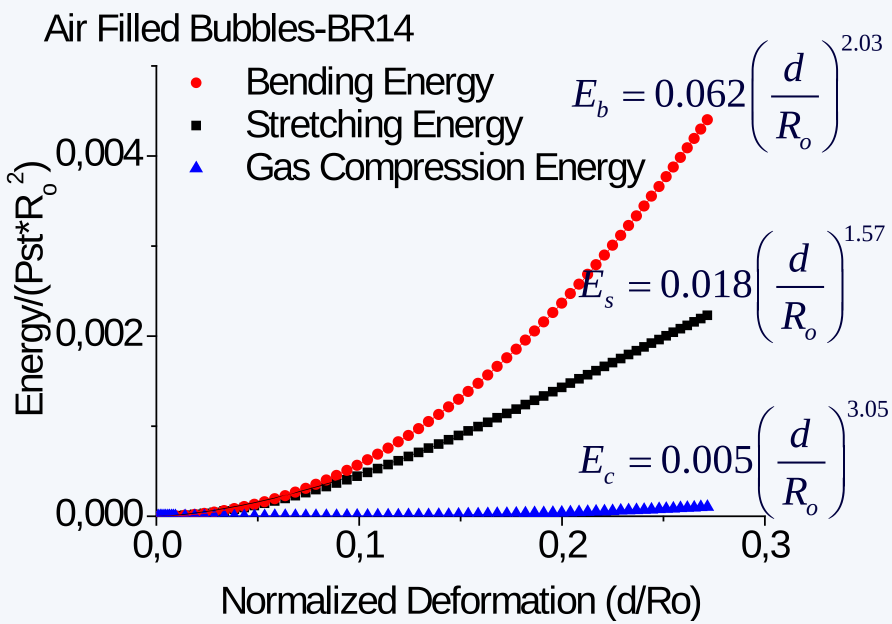
Flow Chart - Fortran Source Code



Results Outline

- 1. Simulations for Point Load
  - Lipids & Polymers
  - Parametric Analysis
- 2. Simulations for Uniform External Overpressure
  - Polymers





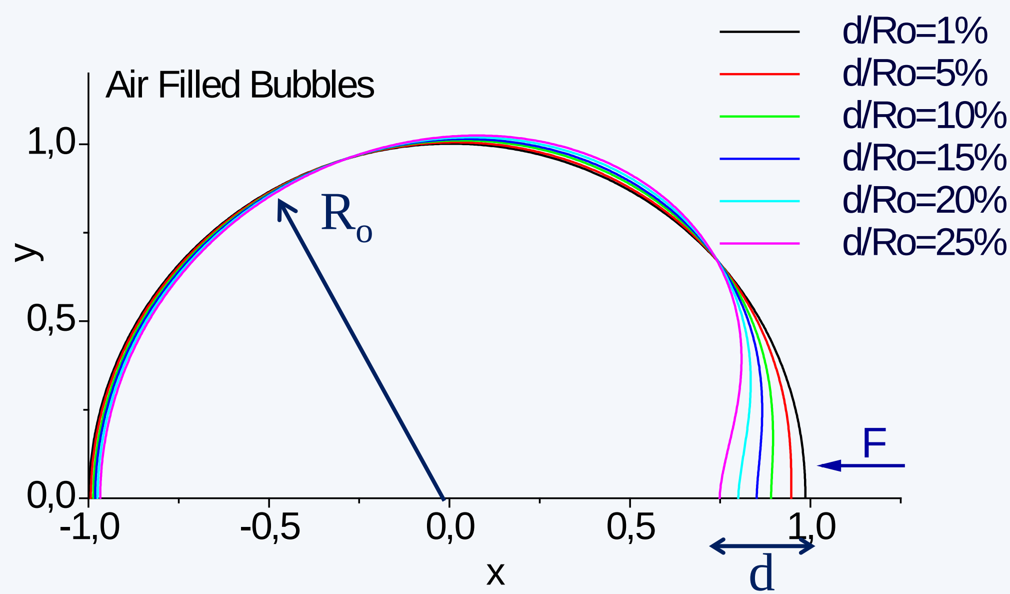
$$F = \frac{4\chi\sqrt{\gamma}}{3\sqrt{3\left(1-\nu^2\right)}}\Delta$$

$$F = \sqrt{\frac{36\left(1-\nu^2\right)\chi k_b}{\sqrt{\gamma}R_o}}\sqrt{\Delta}$$

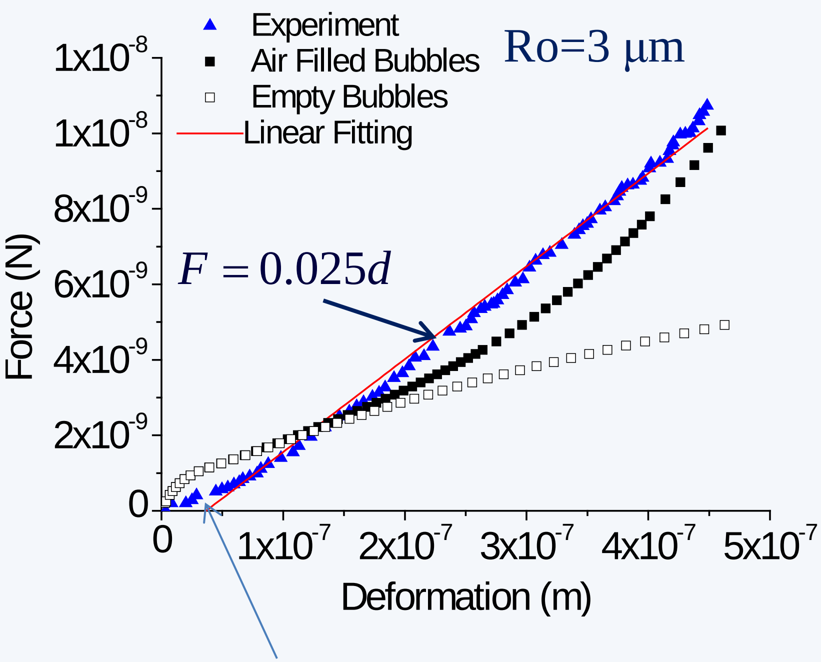
$$\gamma = \left(\frac{3R_o}{h}\right)^2$$

Parameter Estimation

χ=0.1 N/m
$k_b = 3.6 \cdot 10^{-15}$ Nm

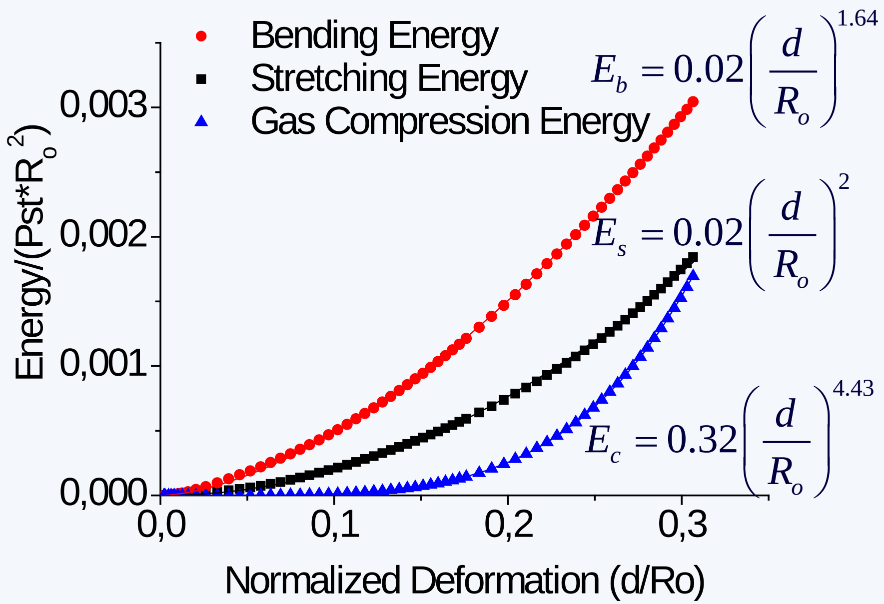


Point Load · Lipid Shell · Force · Energy



Adhesion Forces

The experimental results gave linear response ~ Reissner Theory



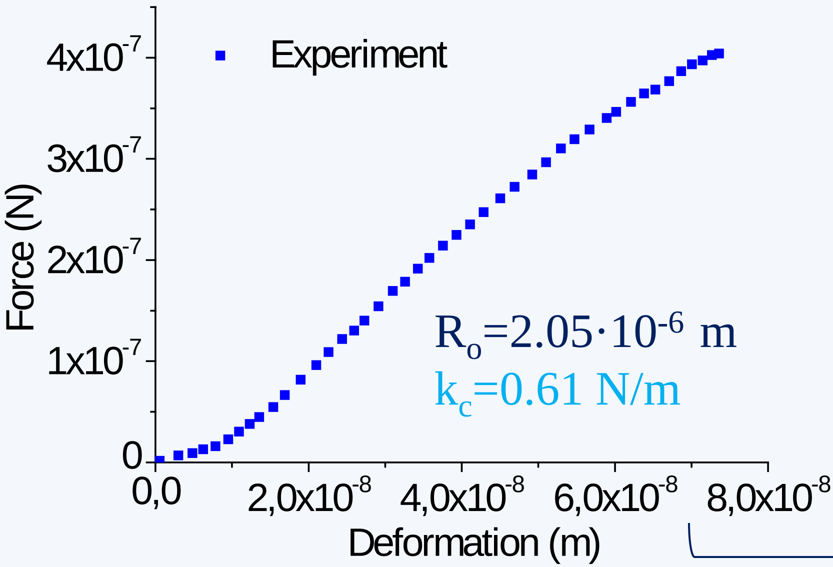
Parameter Estimation

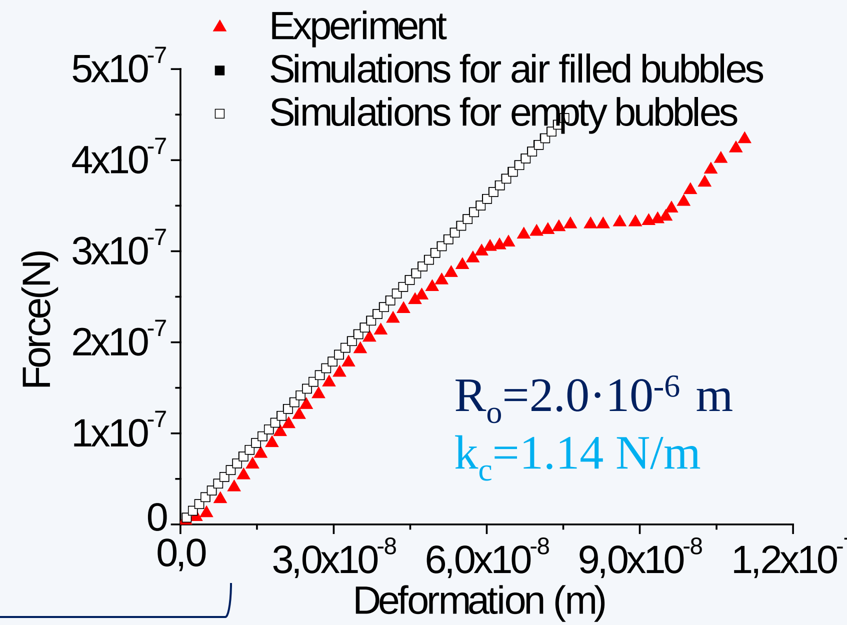
χ=2.43 N/m

$k_b = 8\cdot 10^{-17}$ N·m

Sboros et al., *Nanomechanical Properties of Phospholipid Microbubbles*. Langmuir,2012.

Point Load · Polymeric Bubble · Force Curves





- Same material and geometry
- Different response

Parameter Estimation

$G_s=1\cdot10^9$ Pa

$h=35\cdot10^{-9}$ m

Parameter Estimation

$G_s=1.8\cdot10^6$ Pa

$h=920\cdot10^{-9}$ m

Glynos et al., *Nanomechanics of Biocompatible Hollow Thin-Shell Polymer Microspheres*. Langmuir, 2009

Dimensionless Parameters

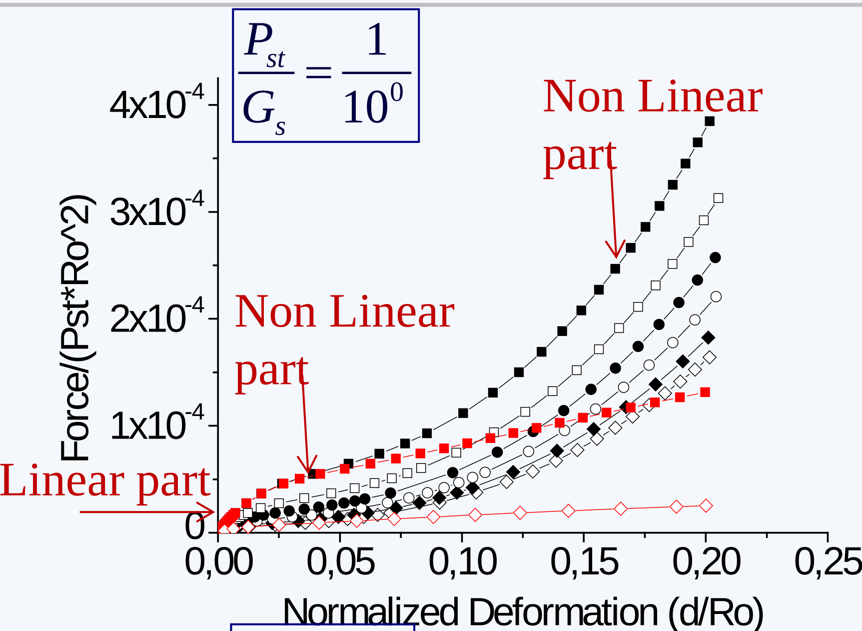
$$N_1 = \frac{\chi R_o^{\;2}}{k_b} = \frac{\text{Stretching Resistance}}{\text{Bending Resistance}}$$

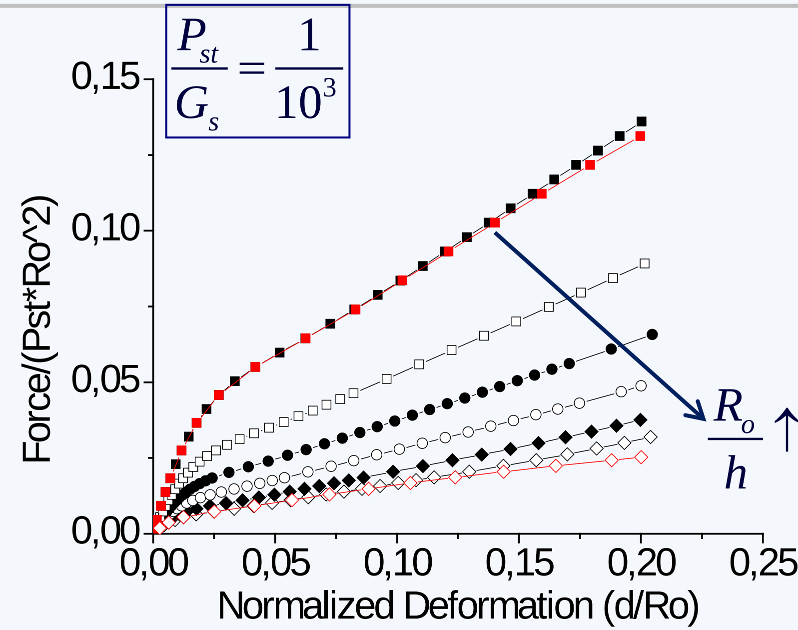
$$N_2 = \frac{P_{st} R_o}{\chi} = \frac{\text{Gas Compressibility Resistance}}{\text{Stretching Resistance}}$$

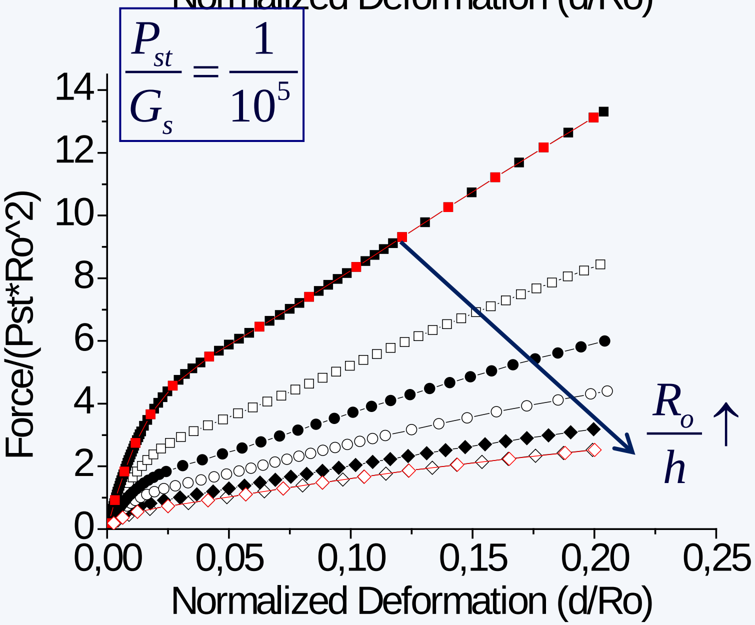
$$\boxed{\text{Polymeric Bubbles}}$$

$$N_1 = \frac{\chi R_o^{\;2}}{k_b} = \ldots = \left(\frac{3R_o}{h}\right)^2$$

$$N_2 = \frac{P_{st} R_o}{\chi} = \ldots = \frac{P_{st}}{3G_s}\frac{R_o}{h}$$

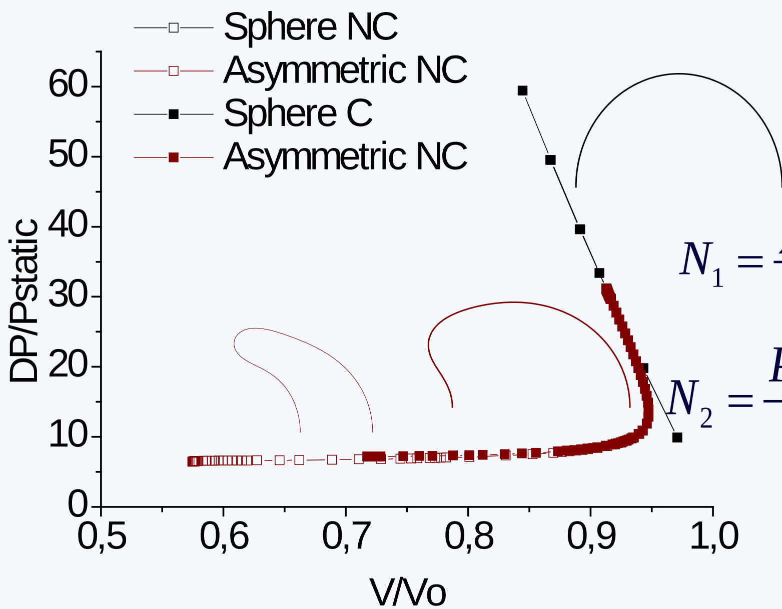






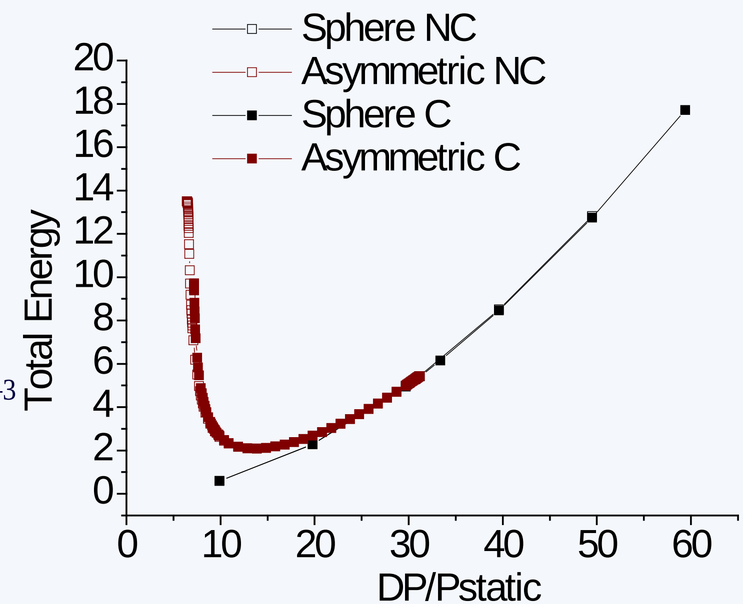
- Ro/h=50 Air Filled Bubbles
- Ro/h=60 Air Filled Bubbles
- Ro/h=70 Air Filled Bubbles
- Ro/h=80 Air Filled Bubbles
- Ro/h=90 Air Filled Bubbles
- Ro/h=100 Air Filled Bubbles
- Ro/h=50 Empty Bubbles
- Ro/h=100 Empty Bubbles

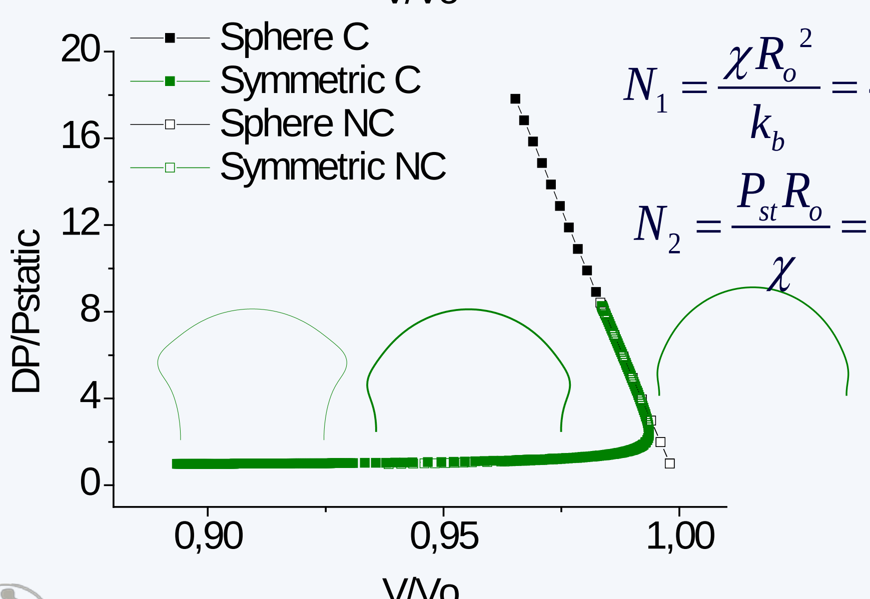
$$N_1 = \left(\frac{3R_o}{h}\right)^2 \qquad N_2 = \frac{P_{st}}{3G_s}\frac{R_o}{h}$$



$$N_1 = \frac{\chi R_o^{\,2}}{k_b} = 10^3$$

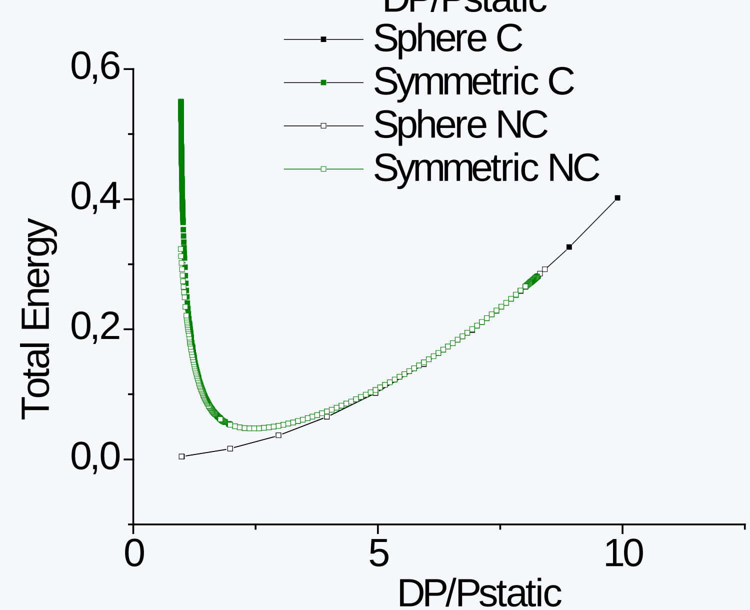
$$N_2 = \frac{P_{st} R_o}{\chi} = 4 \cdot 10^{-3}$$





$$N_1 = \frac{\chi R_o^{\,2}}{k_b} = 4 \cdot 10^4$$

$$N_2 = \frac{P_{st} R_o}{\chi} = 2 \cdot 10^{-3}$$



Point Load

- ✓ There is a gap in the literature of modeling AFM static response.
- ✓ Elastic forces (stretching and bending stiffness) determine the initial linear and nonlinear regimes in the force deformation curve (Reissner-Pogorelov).
- ✓ Gas compressibility controls microbubble and determines nonlinear regime at large deformations.
- ✓ Balance between above forces determines transition between linear and non linear behavior and can be used for estimating area dilatation χ and bending stiffness k_b (shell thickness is not always a-priori available for such small microbubbles and probably not a relevant parameter, especially for lipid monolayers).
- ✓ Both polymeric and lipid monolayer shells do not necessarily obey a Reissner-Pogorelov type transition.

Point Load

- ✓ In lipid monolayer shells adhesion forces may be of the same order as elastic forces thus stabilizing the shell by bypassing crater formation and transition to a Pogorelov type regime – Direct transition from Reissner type response to gas compressibility control is conjectured.

- ✓ Strain softening shell behavior is expected to increase shell elasticity at compression for large deformations.

- ✓ Cantilever elasticity may also affect the response of the microbubble and give rise to multiplicity of solutions

Uniform External Overpressure

- ✓ Two dominant unstable eigenmodes are detected corresponding to asymmetric and symmetric post-buckling shape
- ✓ They both correspond to a subcritical bifurcation and they require an initial imperfection in order to be captured
- ✓ The ratio between stretching and bending resistances determines which eigenmode is first observed.
- ✓ For small values of compressibility fraction, internal gas compressibility is not an important parameter.
- ✓ Combined use of critical overpressure and Overpressure-Relative volume change data may provide additional parameter estimate possibility for uniform external overpressure

Current & Future Work

- → Introduction of nonlinearity in shell constitutive law (strain softening vs strain hardening).
- → Account for cantilever deformability and consequently obtain proper external load distribution.
- → Account for adhesion forces and prediction of contact angle for small external forces (nN level) (normal and tensile components)
- → Three dimensional shell bending and parameter estimation based on wavelength along the azimuthal direction.
- → Modeling and parameter estimation based on static response is essential in complementing acoustic measurements, in verifying validity of available viscoelastic properties and ascertaining the nature of contrast agent shells as viscoelastic solids.

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Thank you for your attention!

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