Probing of micro and nanocapsules properties with instrumented indentation

A.E. Giannakopoulos[1*], V.I. Zafiropoulou[1], Th. Zisis[2], A.D. Lytra[3] and N.A. Pelekasis[3]

[1]Department of Civil Engineering, University of Thessaly, Volos 38334, Greece
[2]School of Applied Mathematical and Physical Sciences, National Technical University of Athens, Athens 15773 Greece
[3]Department of Mechanical Engineering, University of Thessaly, Volos 38334, Greece
*Corresponding Author: agiannak@uth.gr

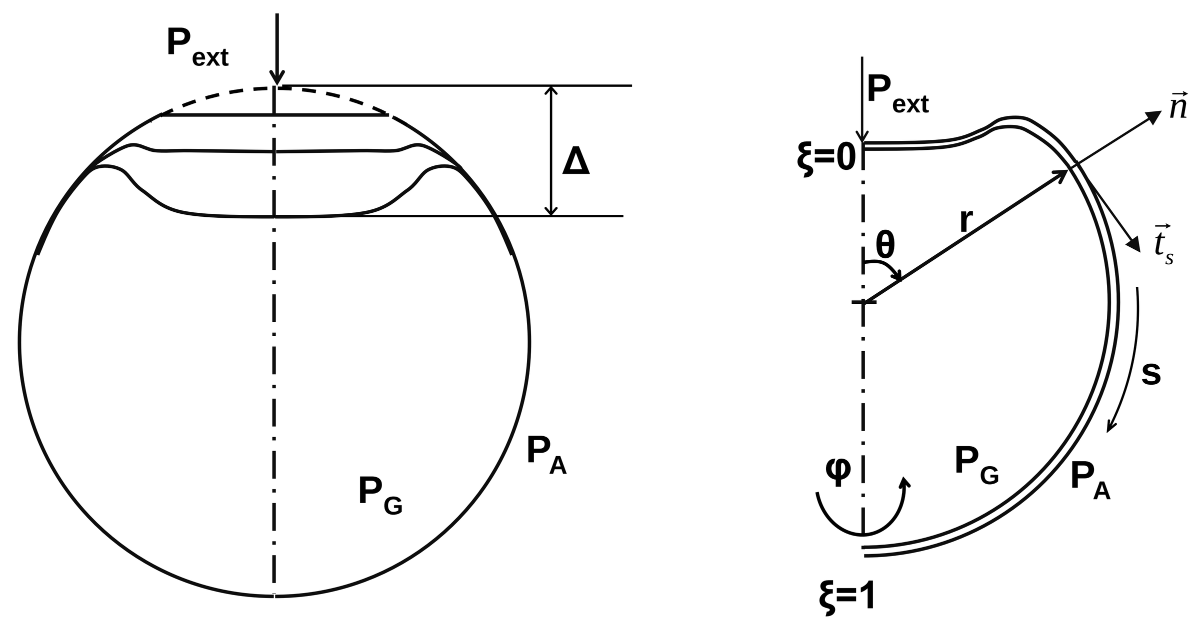
4th INTERNATIONALCONFERENCE ON BIO-SENSING TECHNOLOGY, 10-13 MAY 2015, Lisbon, Portugal

Introduction

Contrast agents (CA) are microbubbles covered with an elastic shell, usually made of polymeric or lipid biomaterials providing mechanical strength and decelerating the gas dissolution in vivo. Their initial diameter ranges from 3 to 5 μm and their thickness from 10 to 40 nm[1-2] . CA microbubbles have been successfully used the last decades for imaging of human organs and they are considered as drug/gene carriers for therapeutic application of diseases. In both cases the elastic properties of the shell are the key parameters that control their behavior in ultrasound environment through arteries and tissues. The present work aims at:

- The estimation of Young's and bending modulus
- The numerical investigation of their static response (FEM & Abaqus)

Theoretical Formulation



Normal and Tangential Force Balance[3]

$$\Delta F_n = k_s \tau_s + k_\varphi \tau_\varphi - \frac{1}{\sigma}\frac{\partial(\sigma q)}{\partial s} = \Delta P, \qquad \Delta F_s = -\left(\frac{\partial \tau_s}{\partial s} + \frac{1}{\sigma}\frac{\partial \sigma}{\partial s}\left(\tau_s - \tau_\varphi\right) + k_s q\right) = 0$$

$$q = \frac{1}{\sigma}\frac{\partial \sigma}{\partial s}\left(\frac{\partial(\sigma m_s)}{\partial \sigma} - m_\varphi\right), \qquad \sigma = r\sin\theta$$

Isothermal Gas Compression

$$P_G V_f = P_A V_i$$

Position of Mass Center

$$z_{cm} = \frac{1}{V}\oiiint_V \vec{r}\cdot\vec{e}_z dV = 0$$

Kinematic Condition

$$r(\xi = 0) = r\cos\theta \quad \text{for} \quad \xi \in [0, \xi_c]$$

Constitutive Law[6]

$$\tau_i = G_s \frac{1+\nu}{1-\nu}\left(\lambda_i^2 - 1\right), \qquad m_i = \frac{k_b\left(K_i + \nu K_j\right)}{\lambda_j}$$

$$K_i \equiv \lambda_i k_i - k_i^R, \qquad k_b = \frac{Eh^3}{12\left(1-\nu^2\right)}, \qquad \lambda_i = \frac{ds_i}{dS_i} \quad i,j = s \text{ or } \varphi$$

Boundary Conditions

$$r_\xi = 0 \quad \text{and} \quad \theta_{\xi\xi} = 0 \quad \text{at} \quad \xi = 0 \quad \text{and} \quad \xi = 1$$
$$P_{ext,\xi} = 0 \quad \text{and} \quad P_{ext,\xi\xi} = L_{\xi\xi} \quad \text{at} \quad \xi = 0$$
$$P_{ext,\xi} = L_\xi \quad \text{at} \quad \xi = \xi_c$$

Numerical Implementation

Finite Elements with B-Cubic Splines as Basis Functions[4]

$$r(\xi) = \sum_{i=0}^{N+1} a_i B_i, \qquad \theta(\xi) = \sum_{i=0}^{N+1} b_i B_i \quad \text{and} \quad P_{ext}(\xi) = \sum_{i=0}^{M+1} c_i B_i$$

Newton-Raphson Iterations

$$J_{ij}\left(x_i^k\right)\Delta x_j^k = R_i^k\left(x_i^k\right), \qquad J_{ij} = \frac{\partial R_{ij}}{\partial x_j} \approx \frac{R_i\left(x_j + \Delta x_j\right)}{\Delta x_j}, \qquad \Delta x_j^k = x_j^k - x_j^{k+1}$$

Asymptotic Analysis

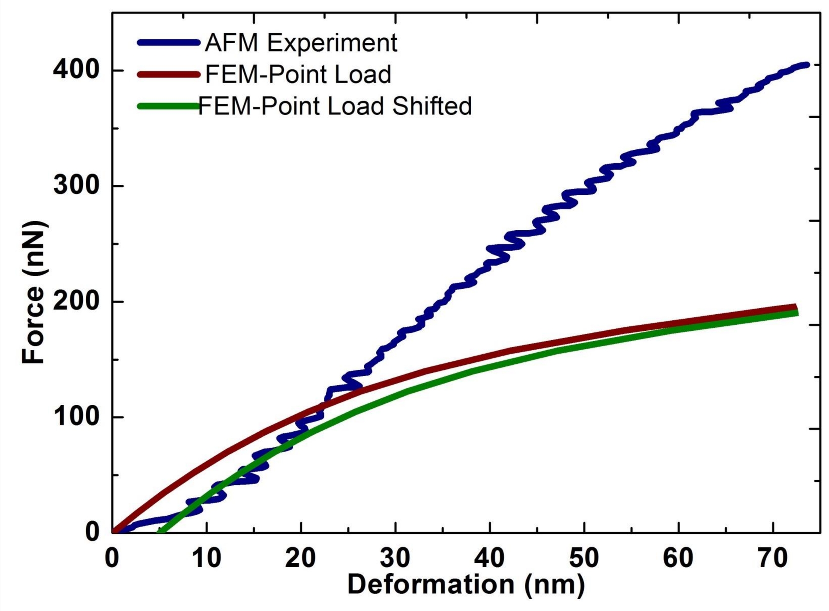
Point Load[5-6]

$$\text{Reissner} \quad F = \frac{4}{\left[3\left(1-\nu^2\right)\right]^{0.5}}\frac{Eh^2}{R_o}\Delta; \qquad \text{Pogorelov} \quad F = \left[\frac{3.56E^2h^5}{\left(1-\nu^2\right)^2 R_o^2}\Delta\right]^{0.5}$$

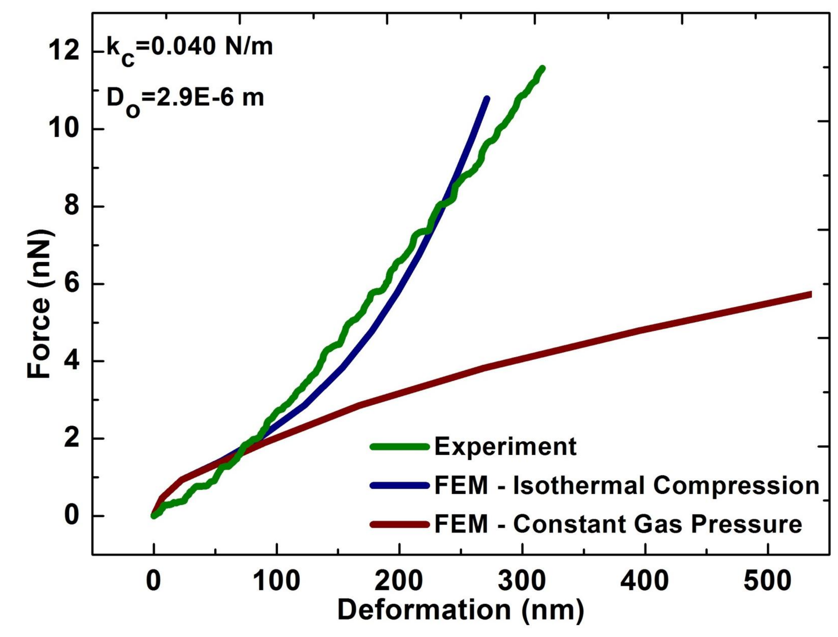
Plane Contact

$$\text{Stage I} \quad F = \frac{4}{\sqrt{3\left(1-\nu^2\right)}}\frac{Eh^2\Delta}{R_o} + 0.06543\frac{Eh\Delta^2}{R_o}; \qquad \text{Stage II} \quad F = 3.807\frac{Eh^3}{\left(1-\nu^2\right)R_o}\left(\frac{\Delta\sqrt{1-\nu^2}}{h}\right)^{1/2}$$

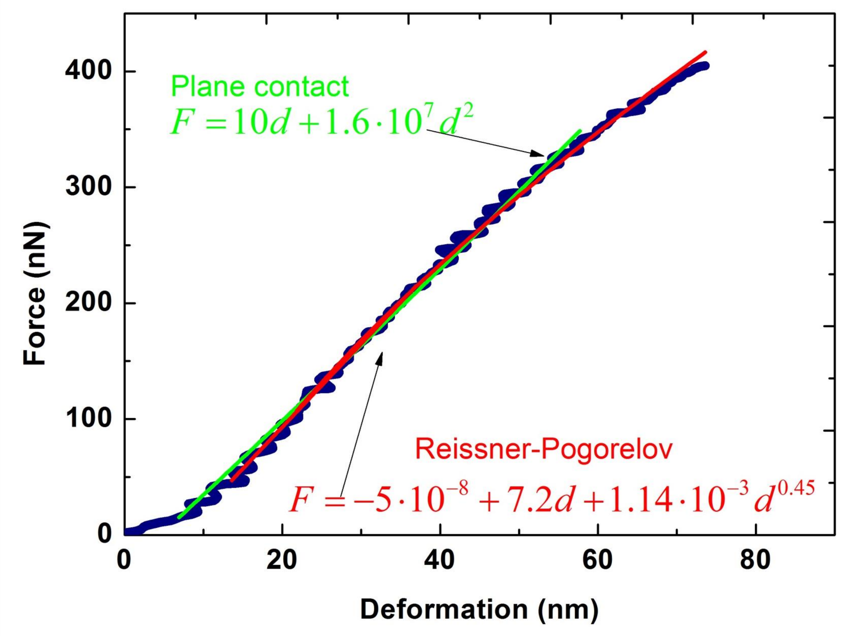
Results



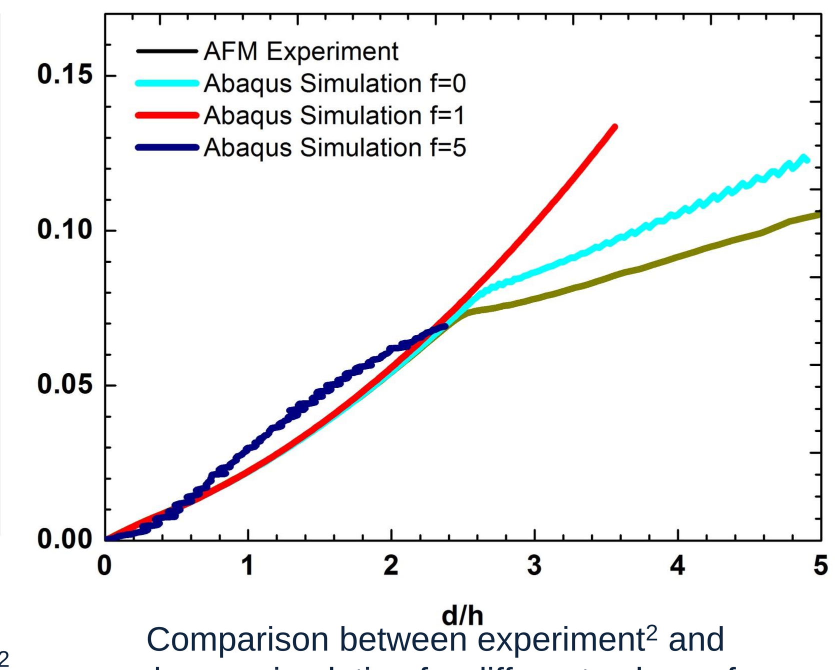
Comparison between experiment[2] and point-load (fem) simulation for polymeric microbubbles



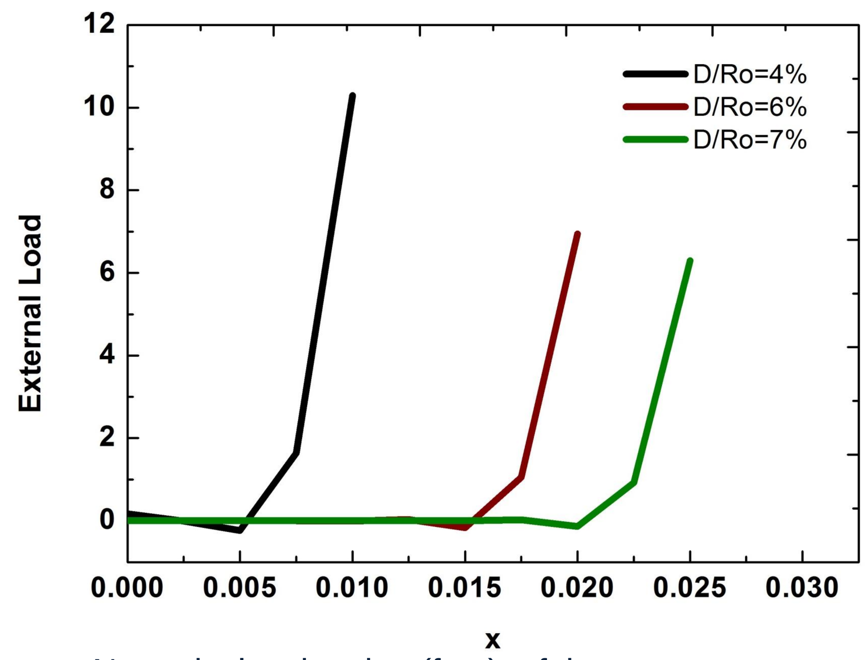
Comparison between experiment[1] and point-load (fem) simulation for phospholipid microbubbles



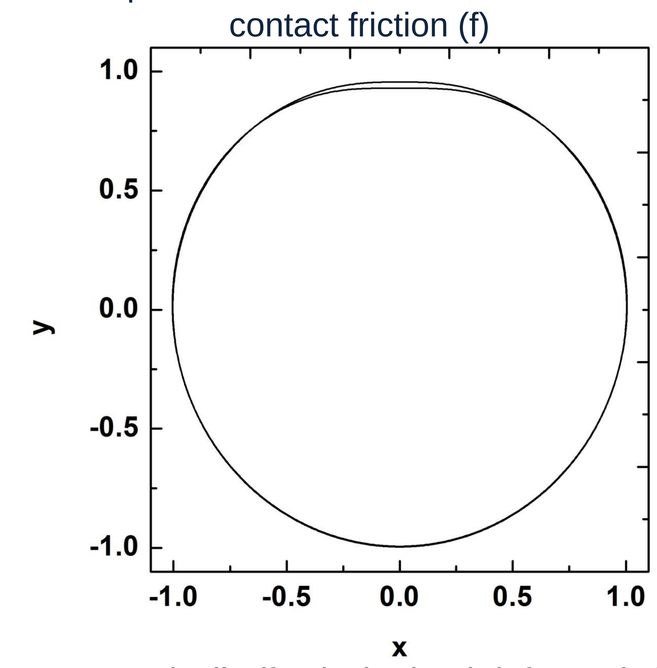
Asymptotic Fitting in the experimental curve[2]



Comparison between experiment[2] and abaqus simulation for different values of contact friction (f)



Numerical estimation (fem) of the contact pressure



Numerically (fem) obtained deformed shapes

k_c=0.61 N/m	Experimental Values		Asymptotic Estimation Point Load[7]		Asymptotic Estimation Plane Contact	
D_o [μm]	E [MPa]	h [nm]	E [Mpa]	h [nm]	E [MPa]	h [nm]
2.6	10-16	20	8.5	25	20	16
3.5	4-8	26	12	26	5	26
4.1	2.5-6	31	6.1	31	4.6	33
k_c=1.14 N/m						
3.1	6-10	23	3.4	35	10	19
3.2	6-10	24	14	20	6.7	27
4.0	2.5-6	30	4.7	30	4.7	28
4.9	1-3	37	4.5	31	4.9	28
5.5	1-3	41	1.7	47	2	40

Conclusions

1. It is possible to estimate both Young's modulus and shell thickness by a single force-deformation (f-d) curve.
2. The point load can qualitatively predict the f-d curve, while the abaqus calculation also predicts transition from a linear (Reissner) to a non linear (Pogorelov) regime.
3. Reliable estimates of the shell thickness and elasticity modulus of polymeric shells are obtained in this fashion
4. Relaxing the assumption of a point load provides reliable estimates for the pressure distribution, in accordance with previous investigations[12], and predicts reduced displacements when crater formation takes place, in comparison with the point load distribution.
5. Consideration of the surface tension delays the transition from Reissner to Pogorelov regime.
6. Proper accounting of adhesion forces is expected to capture the response of phospholipid shells by eliminating the Pogorelov regime in favor of the gas compressibility dominated regime in the f/d curve at large external loads.

Selected References

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Acknowledgments

This work is performed in the framework of the operational program: «Education and lifelong learning» - «Aristeia» and is cofounded by the European Union (European Social Fund) and national resources.
The authors wish also to thank Dr. Vasileios Koutsos, Dr. Vassilis Sboros and Dr. Emmanouil Glynos for fruitful discussions on the AFM and for kindly providing the experimental (AFM) data.

European Union European Social Fund
OPERATIONAL PROGRAMME EDUCATION AND LIFELONG LEARNING investing in knowledge society
MINISTRY OF EDUCATION & RELIGIOUS AFFAIRS MANAGING AUTHORITY
Co-financed by Greece and the European Union
NSRF 2007-2013 EUROPEAN SOCIAL FUND