

## Static and Dynamic Analysis of Contrast Agents – Parameter Estimates and the Effect of Constitutive Law

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Boundary element simulations of pulsating contrast agents in response to an acoustic disturbance are performed in order to ascertain the range of stable pulsations vs. transient break-up depending on the constitutive law of the coating considered as a shell of very small thickness. Shell viscosity provides the main dissipation mechanism while potential flow is assumed in the surrounding fluid. The normal and tangential force balance on the interface involves coupling of the dynamic overpressure with the stretching and bending elastic stresses along with viscous dissipation on the shell.

Static analysis is also performed pertaining to AFM measurements of contrast agents and capsules<sup>1</sup>. Following earlier studies on the response of a thin shell to a point load<sup>2</sup> the linear and nonlinear regime of the force–displacement curve of a coated microbubble can be employed to provide independent estimates of the shell area dilatation modulus and bending resistance. As it turns out they are of the same order of magnitude as those provided by acoustic measurements, but they can be more reliable as they are free of dynamic effects.

In the context of acoustic disturbances and in agreement with linear theory<sup>3</sup>, beyond a certain threshold sound amplitude shape modes emerge as a result of resonance. When the microbubble is at harmonic resonance with the forcing, especially for strain softening shells, exchange of elastic energy between the emerging bending mode and the radial stretching mode stabilizes growth of the former leading to steady axisymmetric pulsations with the radial mode exhibiting a small amount of excessive compression with respect to its dynamics without shape deformation. Most of the unstable mode growth occurs during compression in a fashion similar to available experimental observations<sup>4</sup>. When subharmonic resonance occurs, for both strain softening and strain hardening shells, energy exchange cannot stabilize shape pulsations and transient break-up eventually prevails.

As the sound amplitude is further increased dynamic buckling is observed, in agreement with linear theory<sup>3</sup>, followed by transient break-up. However, when an initial amount of prestress is present the threshold for parametric mode excitation and dynamic buckling to occur is significantly reduced. In this case switching from strain softening to strain hardening behaviour stabilizes the microbubble due to reduction of its radius and the resulting excessive viscous damping. This process may explain the onset of “compression only behaviour” at relatively small sound amplitudes<sup>4</sup> as a result of a folding instability that generates lipid bi-layer structures<sup>5</sup>.

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<sup>1</sup> Glynos et al. , *Mater. Scien. & Engin. B.* **165**, 231 (2009).

<sup>2</sup> Pogorelov, *Providence, R. I.: American Mathematical Society*, **viii**, 77 (1988).

<sup>3</sup> Tsiglifis & Pelekasis, *Phys. Fluids* **23** 012102 (2011)

<sup>4</sup> Overvelde *Ph.D. Thesis* University of Twente, (2009)

<sup>5</sup> Lee *Ann. Rev. Phys. Chem.* **59**, 771–791 (2008)