TRANSIENT BREAK-UP, SATURATED PULSATIONS AND STATIC/DYNAMIC BUCKLING OF INSONATED CONTRAST AGENTS - EFFECT OF THE CONSTITUTIVE LAW AND CHARACTERIZATION

Nikos Pelekasis[*a)] & Kostas Tsiglifis[*]
[*]*Department of Mechanical Engineering, School of Engineering, University of Thessaly, Pedion Areos, Volos, 38334, Greece*

Summary Axisymmetric boundary element simulations are performed in order to investigate nonlinear evolution of contrast agent pulsations. Preferential mode excitation during compression is obtained, leading to saturated pulsations or transient break-up of strain softening shells under conditions of harmonic or subharmonic resonance. Switching from strain softening to strain hardening shell behavior stabilizes contrast agent pulsations leading to saturated mode oscillations exhibiting "compression only behavior".

INTRODUCTION

Under insonation contrast agents, i.e. microbubbles that are coated by a lipid monolayer or a polymer shell, are known to perform nonlinear pulsations and deform dynamically via parametric or explosive mode excitation, while exhibiting a wealth of dynamic phenomena like jetting and transient break-up in a fashion similar to bubbles that are not coated [1]. Experimental observations also reveal dynamic phenomena, such as the enrichment of the harmonic content and the abrupt vibration onset as the sound amplitude increases and the compression only behavior for not so large sound amplitudes, [2], [1], [3], that cannot be explained by a simple linear constitutive law pertaining to the viscoelastic behavior of the coating. Strain softening shells produce the rich harmonic content [2] exhibited by contrast agents coated by a lipid monolayer, and recover the abrupt vibration onset via the reduction of the resonance frequency with increasing sound amplitude [4]. On the other hand, invoking a strain hardening behavior at compression, coupled with an almost linear behavior at expansion, can account for the compression only behavior of lipid shells [3] which is almost invariably associated with some sort of shell buckling at compression while the shell regains its sphericity at expansion [1], [3]. Shell buckling/deformation has been dynamically observed for lipid monolayer shells leading to steady shape oscillations or transient break-up [5]. It occurs for lower overpressures that static buckling and it is not necessarily associated with compression only behavior. Linear stability analysis predicts shape mode excitation via harmonic or subharmonic resonance as well as explosive growth via dynamic buckling [6]. An extensive numerical study is presented herein, that aims at identifying conditions for saturated shape mode pulsation and transient break-up depending on the constitutive law and the amount of pre-stress present on the shell. It can also be viewed as a tool for characterizing shell behavior if it is properly coupled with acoustic measurements.

PROBLEM FORMULATION & NUMERICAL SOLUTION

The response of a single coated microbubble is studied that is pulsating subject to an acoustic disturbance, relatively far from nearby boundaries. The microbubble may initially be at the spherical stress-free state or possess a certain amount of prestress while remaining spherical or even be at a buckled state. The surrounding fluid is taken to be inviscid and incompressible with shell viscosity, μ_s, providing the dominant damping mechanism. Consequently, the Laplacian governs the surrounding fluid motion with the normal and tangential force balances incorporating the balance between pressure, inertia and viscoelastic forces on the shell/liquid interface; bending, k_B, and stretching elasticities, $3G\delta$, are accounted for on the shell. Due to negligible liquid viscosity, continuity of only the normal component of shell velocity need be satisfied.

Due to linearity the Laplacian can be substituted by an integral equation defined on the shell/liquid interface. Subsequently, axisymmetry allows for discretization of the generating curve of the microbubble interface which minimizes numerical cost. Upon application of an acoustic disturbance, $P_\infty = P_{St}[1+\varepsilon\cos(2\pi f)]$, and with known shell deformation, the Laplacian provides the normal shell velocity, the adiabatic law updates internal bubble pressure, while the tangential and normal force balances, the latter incorporates dynamic pressure variations in the surrounding liquid, provide the azimuthal and radial displacements of interfacial particles. Then the process is repeated into the next time step. The finite element method is employed for the spatial discretization of the above two force balances coupled with the Runge Kutta time integrator for updating the position of interfacial particles.

Code Validation

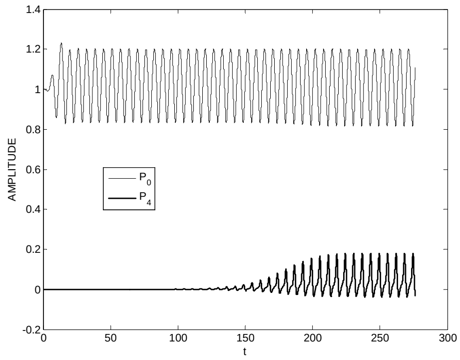
The above methodology was first employed in order to recover eigenfrequencies of free oscillating shape modes as well as amplitude thresholds for the onset of harmonic or subharmonic shape mode excitation of insonated contrast agents, as predicted by stability analysis [6]. Indeed agreement with the results of axisymmetric stability and Floquet analysis is obtained and the stability limits for parametric mode excitation are recovered with accuracy.

[a)] Corresponding author. Email: pel@uth.gr.

RESULTS AND DISCUSSION

Based on optical [5] and acoustic [7] measurements of phospholipid coated contrast agents, we obtain estimates for the viscoelastic properties of the shell by recovering the resonance frequency and the threshold for shape pulsations [6] recorded in the experiments, upon selecting a particular constitutive law. Figure 1a illustrates the onset of saturated pulsations of P4 in the parameter range for which Floquet analysis predicts parametric P4 excitation via harmonic resonance for a shell obeying a strain softening constitutive law. Growth of P4 preferentially occurs during compression while the microbubble almost regains its sphericity during expansion. Saturation of the shape mode is achieved via periodic energy exchange with the radial mode, manifested by a small amount of excess contraction of the microbubble radius during compression. When parametric mode excitation arises as a result of subharmonic resonance it again primarily takes place during the compression phase. However it cannot be equilibrated via energy transfer to the radial mode thus leading to transient break-up. As the amplitude of sound increases explosive growth of shape modes is observed, identified as dynamic buckling [6], that also eventually leads to transient break-up of the microbubble. Parametric shape mode excitation of strain hardening shells typically leads to transient break-up for both harmonic and subharmonic resonance, whereas dynamic buckling occurs for much higher sound amplitudes compared with strain softening ones, mainly as a result of viscous damping during the very small radii achieved during compression of such shells [6].

When pre-stress is present, $R_{Eq} \neq R_0$, the amplitude threshold for parametric mode excitation as well as dynamic buckling decreases. In the latter case transient break-up is observed for relatively smaller sound amplitudes and at an earlier time. If, however, we allow for a switch in the constitutive law from strain softening (Mooney Rivlin or MR) to strain hardening (SHkalak or SK) beyond a certain level of growth of the unstable shape mode, or equivalently as the radius of curvature decreases below a certain level, then compression only behavior is recovered while pulsations are stabilized and saturation is achieved. Figure 1b illustrates this pattern in the evolution of the different modes. This behavior is in accord with recent studies pertaining to folding instabilities of phospholipid monolayers [8] where formation of bilayer and multilayered structures is reported. As is well known lipid bilayers are strain hardening. Consequently, as growth of unstable shape modes proceeds during compression, in the parameter range corresponding to parametric excitation or dynamic buckling for prestressed shells, lipid bilayers form that exhibit strain hardening behavior which facilitates further compression as a means to stabilize pulsations. The latter mechanism may explain compression only behavior reported at low sound amplitudes [1], [3], as a combined result of shell mechanics and the dynamic response of the microbuble subject to insonation.



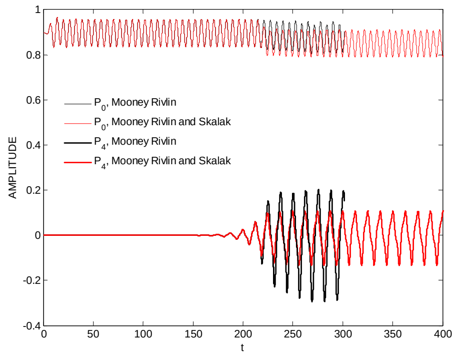


Figure 1: (a) Saturated shape mode pulsations subject to harmonic resonance (MR shell with R_{Eq}=3.6 μm, ε=2 and f=1.7 MHz) and (b) saturated shape mode pulsations for a mode that grows as a result of subharmonic excitation (MR and MR switching to SK shell with R_{Eq}=4 μm, ε=3.5 and f=3.4 MHz); R_0=3.6 μm, μ_s=20 Pa*s, G=80 MPa, k_B=3.0d-14 N*m, γ=1.07, v=0.5, Pst=101325Pa, δ=1 nm.

References

[1] Overvelde M.: Ultrasound Contrast Agents-Dynamics of Coated Microbubbles. *Ph.D. Thesis* University of Twente, 2009.

[2] Paul S., Katiyar A.., Sarkar K., Chatterjee D., Shi W.T., Forsberg F.: Material characterization of the encapsulation of an ultrasound contrast microbubble and its subharmonic response: Strain-softening interfacial elasticity model, *J. Acoust. Soc. Am*. **127:**3846-3857, 2010.

[3] Marmottant P., van der Meer S., Emmer M., Versluis M., de Jong N., Hilgenfeldt S., Lohse, D.: A model for large amplitude oscillations of coated bubbles accounting for buckling and rupture *J. Acoust. Soc. Am*. **118**: 3499-3505, 2005.

[4] Tsiglifis K., Pelekasis N.: Radial oscillations of insonated contrast agents – Effect of the membrane constitutive. *J. Acoust. Soc. Am*. **123**:4059-4070, 2008.

[5] Dollet B., van der Meer S. M., Garbin V., De Jong N., Lohse D. Versluis M.: Nonspherical oscillations of ultrasound contrast agent microbubbles. *Ultrasound in Med. & Biol.* **34**, 1465-1473, 2008.

[6] Tsiglifis K., Pelekasis N.: Parametric Stability and Dynamic Buckling of an Encapsulated Micro-Bubble subject to Acoustic Disturbances. *Phys Fluids*, [**23**] 012102, 2011.

[7] van der Meer S.M., Dollet B., Voormolen M.M., Chin C.T., Bouakaz A., De Jong N., Versluis M., Lohse, D.: Microbubble spectroscopy of ultrasound contrast agents, *JASA*, **121**, 648-656, 2007.

[8] Lee K.Y.C.: Collapse mechanisms of langmuir monolayers. *Ann. Rev. Phys. Chem*. **59**:771–791, 2008.