

Acoustic Interaction Between a Coated Microbubble and a Rigid Boundary

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Motivation

- Contrast perfusion imaging \Rightarrow check the circulatory system by means of contrast enhancers in the presence of ultrasound (Sboros et al. 2002, Frinking & de Jong, Postema et al., Ultrasound Med. Bio. 1998, 2004)
- Sonoporation \Rightarrow reinforcement of drug delivery to nearby cells that stretch open by oscillating contrast agents (Marmottant & Hilgenfeldt, Nature 2003)
- Micro-bubbles act as vectors for drug or gene delivery to targeted cells (Klibanov et al., adv. Drug Delivery Rev., 1999, Ferrara et al. Annu. Rev. Biomed., 2007)

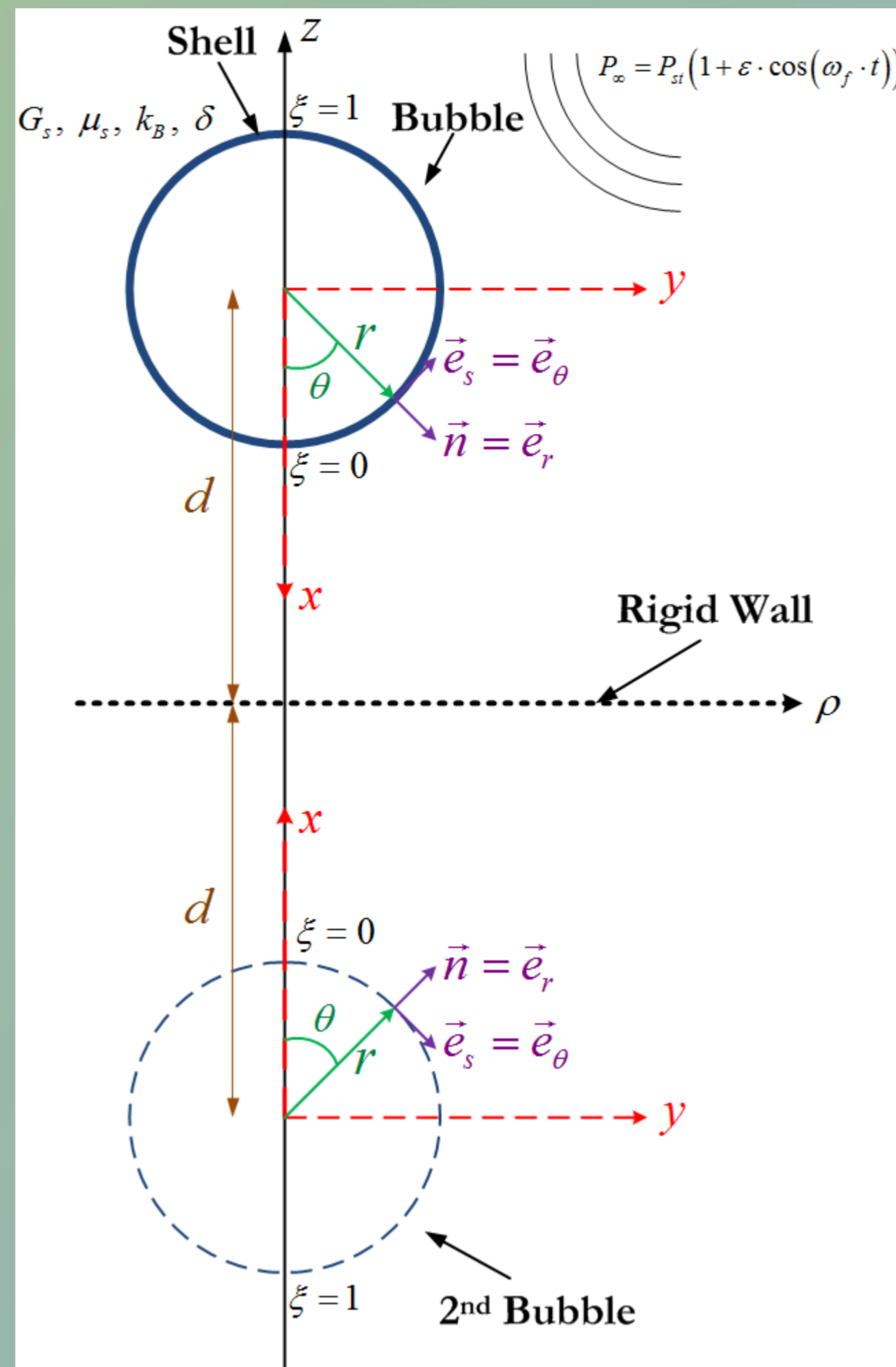
- Need for specially designed contrast agents:
 - Controlled pulsation and break-up for imaging and perfusion measurements
 - Chemical shell treatment for controlled wall adhesion for targeted drug delivery
- Need for models covering a wider range of CA behavior (nonlinear material behavior, shape deformation, buckling, interfacial mass transport etc., compression vs. expansion only behavior, nonlinear resonance frequency-thresholding)
- Need to understand experimental observations and standardize measurements in order to characterize CA's

Parameters for coated microbubble (phospholipid-type shell):

$$R_0 = 3.6 \mu\text{m}, \mu_s = 20 \text{ Pa}\cdot\text{s}, G_{3D} = 80 \text{ MPa}, \sigma = 0.051 \text{ N/m}, k_B = 3 \cdot 10^{-14} \text{ N}\cdot\text{m}, b = 0 \text{ (neo-Hookean)}, v_f = 1.7 \text{ MHz}, \gamma = 1.07, P_{st} = 101325 \text{ Pa}, \mu_l = 0, \delta = 1 \text{ nm}$$

Parameters for air (uncoated) microbubble in water:

$$R_0 = 3.6 \mu\text{m}, \sigma = 0.075 \text{ N/m}, v_0 = 1.7 \text{ MHz}, v_f = 1.7 \text{ MHz}, \gamma = 1.4, P_{st} = 101325 \text{ Pa}, \mu_l = 0$$



Schematic representation of a coated microbubble near a rigid boundary depicting the global coordinate system (q, z) , the local coordinate system (r, θ) , the initial distance (d) between bubble and wall, the disturbance of the pressure field, where ϵ is the amplitude of the latter and ξ is the Lagrangian marker on the interface

Asymmetric oscillations of a microbubble near a wall

- Experiments have shown that the presence of a nearby wall affects the bubble's oscillations. In particular its maximum expansion
- Asymmetric oscillations, toroidal bubble shapes during jet inception have been observed
- The bubble oscillates asymmetrically in the plane normal to the wall, while it oscillates symmetrically in the plane parallel to the wall (i.e. deformation has an orientation perpendicular to the wall) (H. J. Vos et al., Ultrasound in Med. & Biol., 2008) (S. Zhao et al., Applied Physics, 2005)

Assumptions

- Axisymmetry,
- Ideal, irrotational flow of high Reynolds number,
- Incompressible surrounding fluid with a sinusoidal pressure change in the far field,
- Ideal gas in the microbubble undergoing adiabatic pulsations,
- Very thin viscoelastic shell whose behavior is characterized by the constitutive law (e.g. Hooke, Mooney-Rivlin or Skalak),
- The shell exhibits bending modulus that determines bending stresses along with curvature variations,
- Shell parameters: area dilatation modulus $\chi = 3G_s\delta$, dilatational viscosity μ_s , degree of softness b for strain softening shells or area compressibility C for strain hardening ones and the bending modulus k_B

Methodology

- Define a global cylindrical coordinate system (q, z) with its origin at the cross-section of rigid wall with the axis of symmetry along with a local spherical coordinate system (r, θ) with its origin at the centre of mass of the microbubble
- The coordinates of the interface are computed via FEM using the kinematic condition in r -direction and the tangential force balance on the interface
- The velocity potential is computed via FEM using the dynamic condition on the interface and the normal velocity of the interface is calculated via BEM using the boundary integral equation
- Integration in time of the kinematic and dynamic interfacial conditions is performed via the 4th order explicit Runge – Kutta method

Results

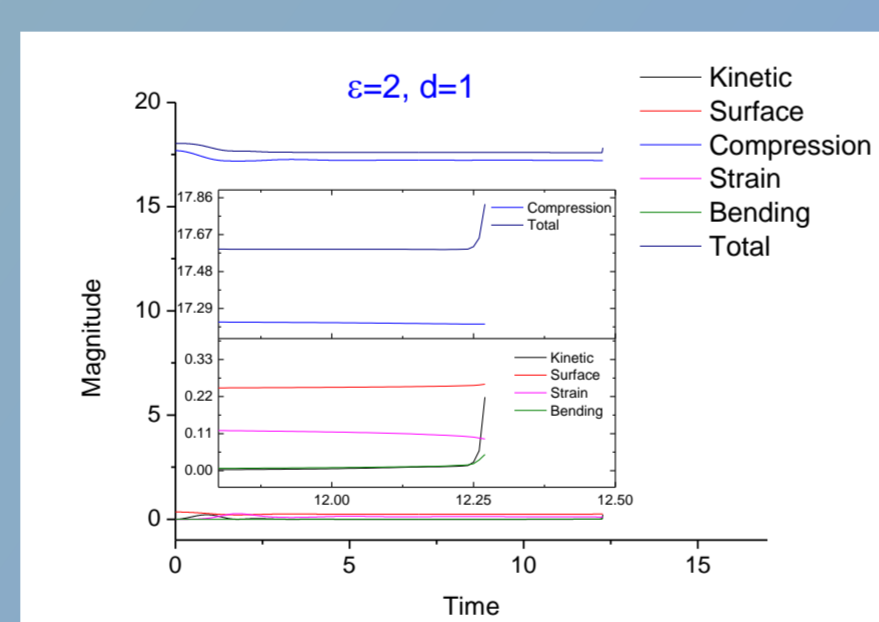
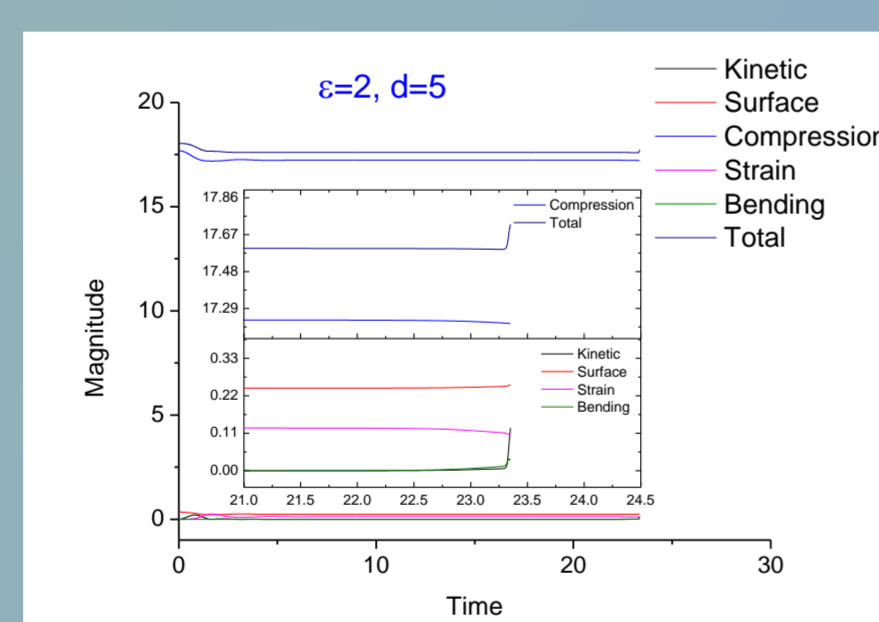
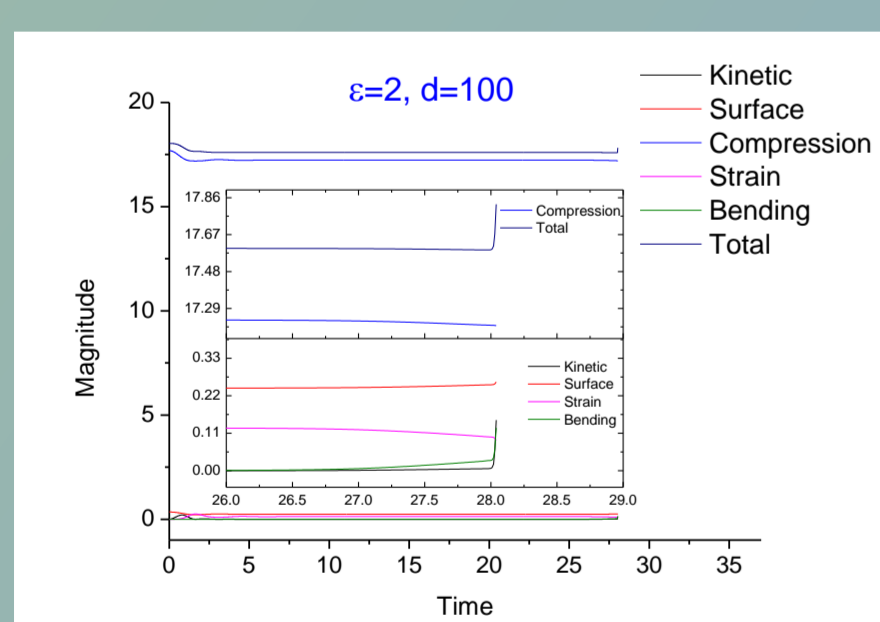
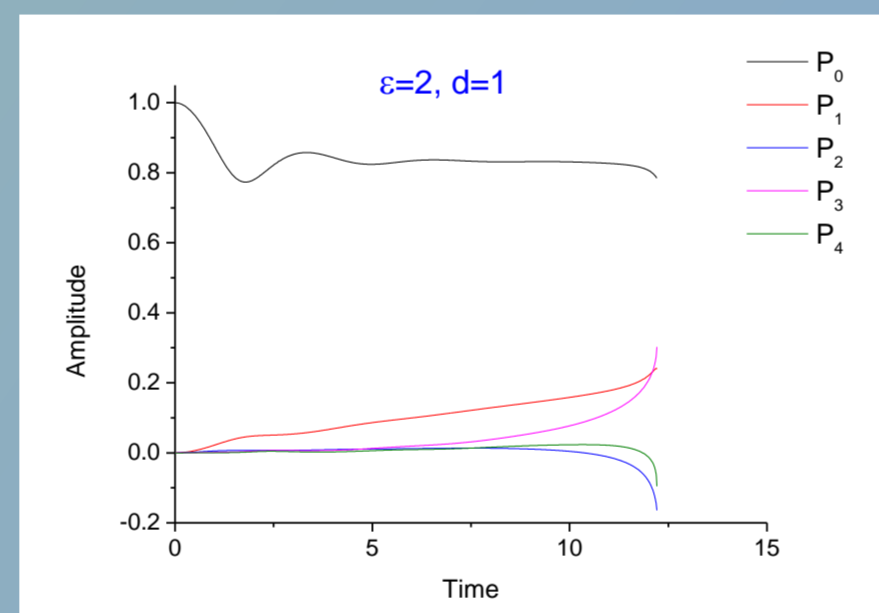
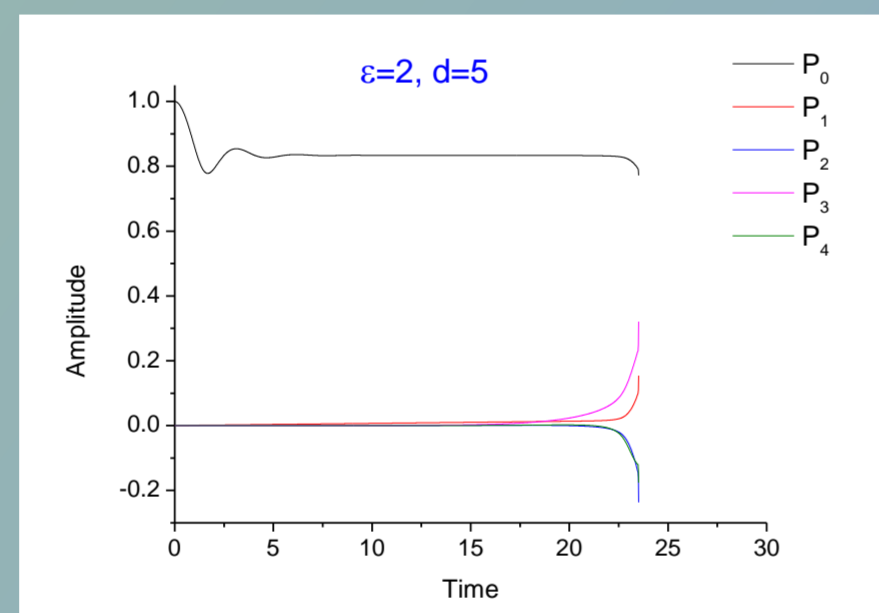
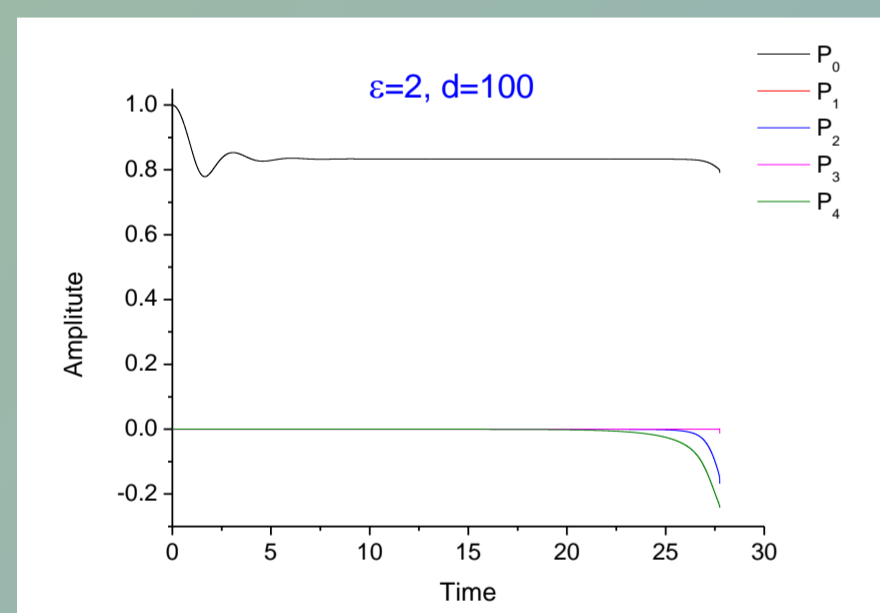
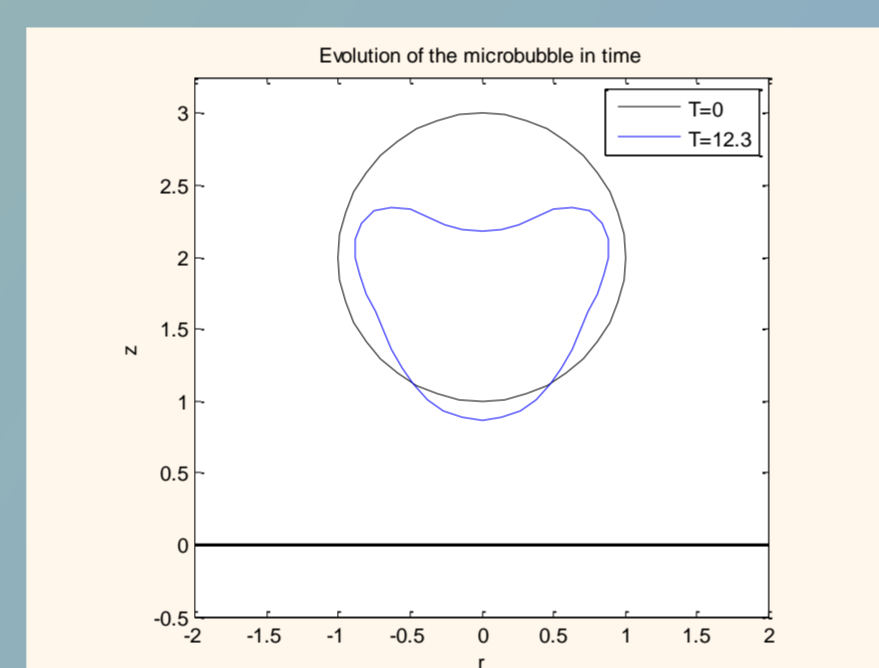
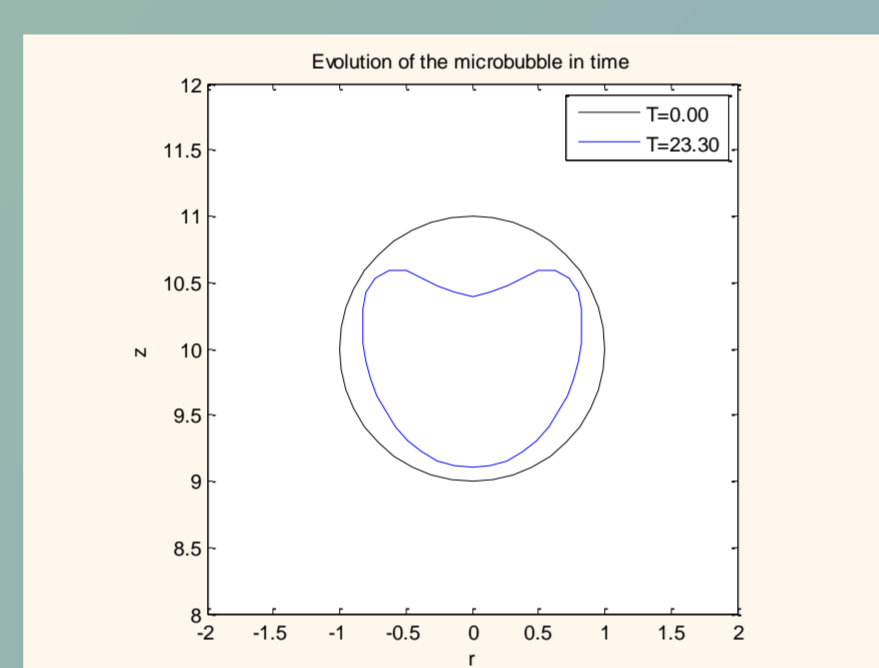
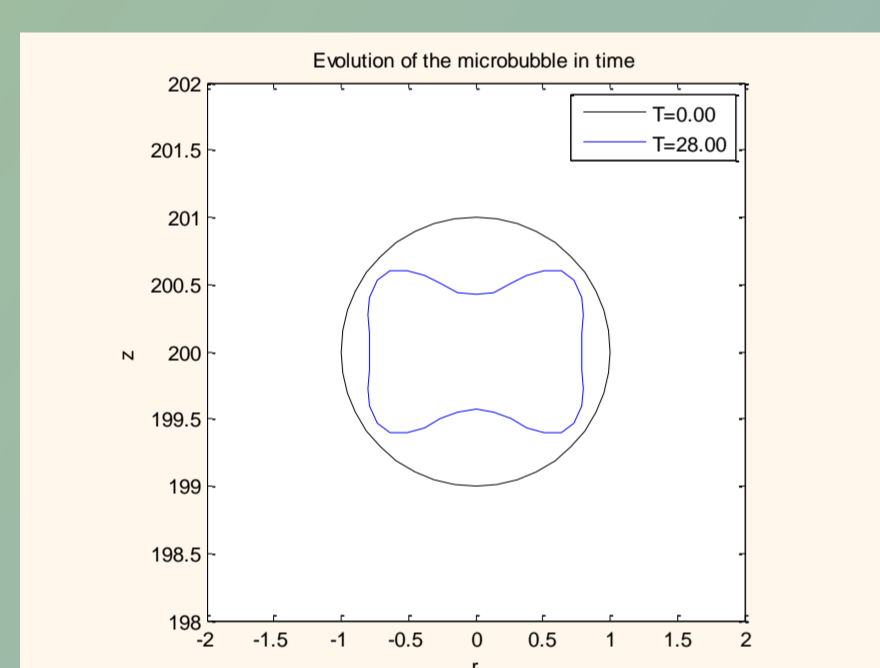
Coated Microbubble – Rigid Boundary

Step Change in Pressure Field

Far from boundary

At middle distance

Close to the boundary

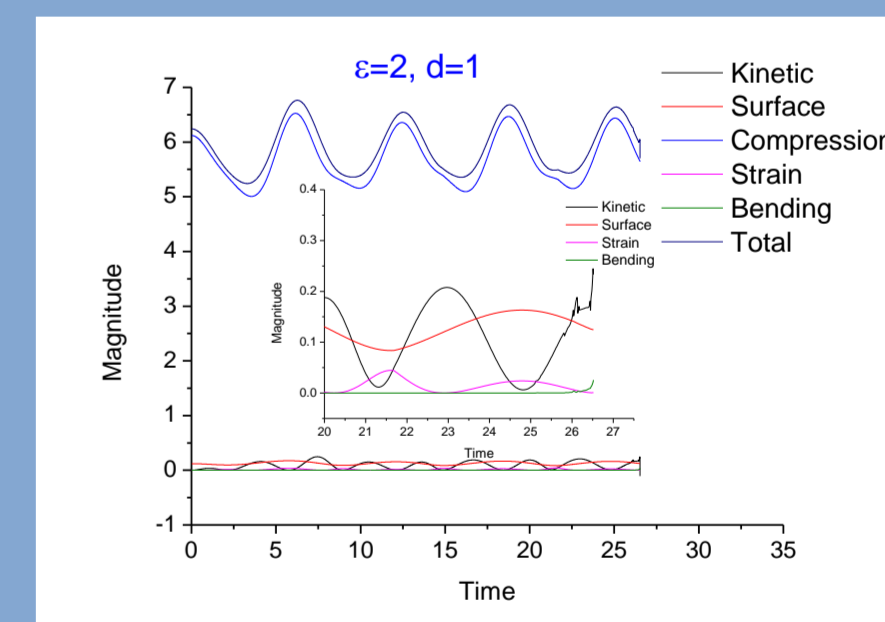
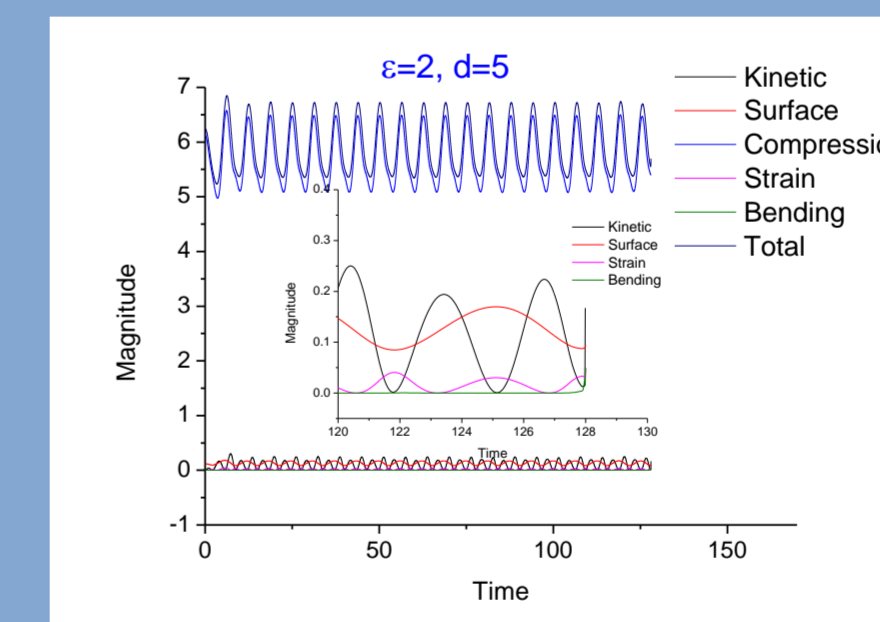
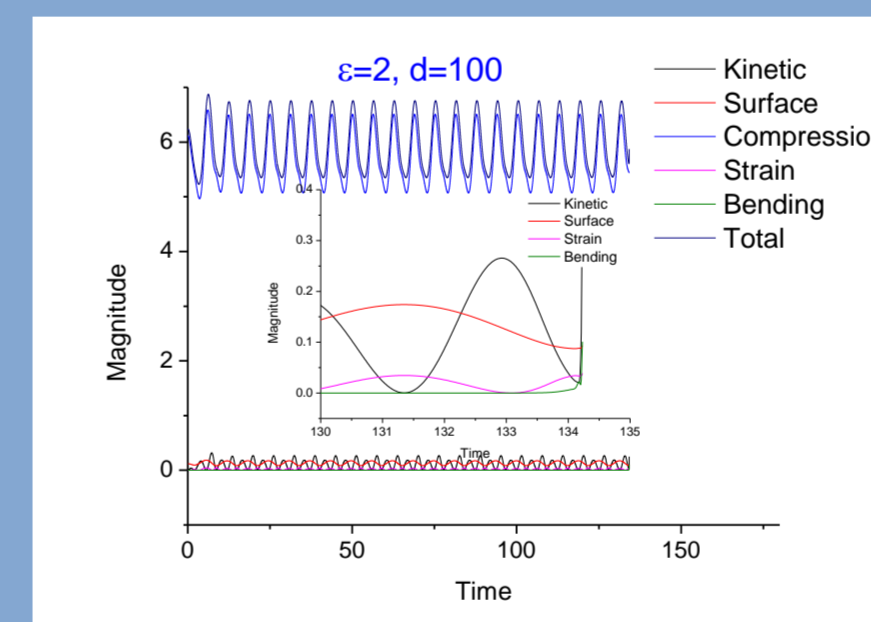
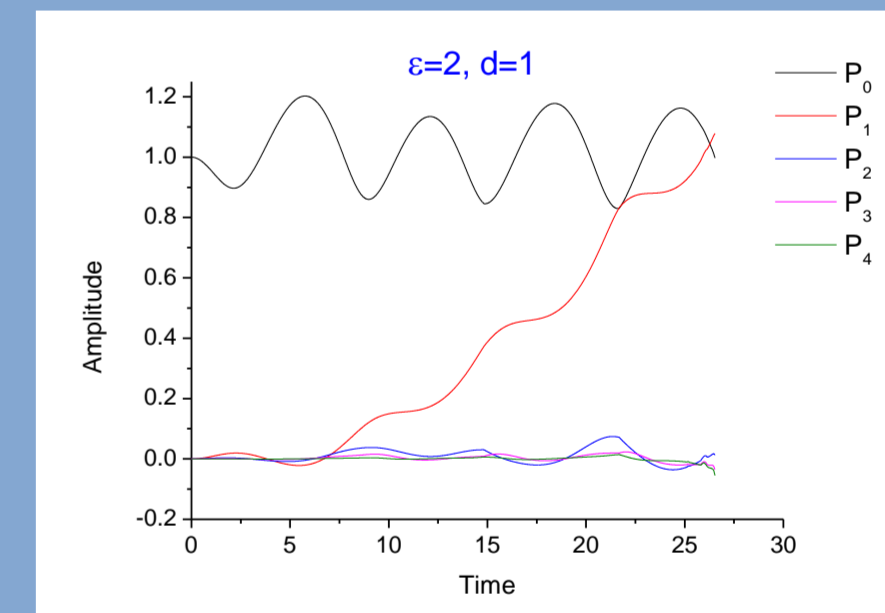
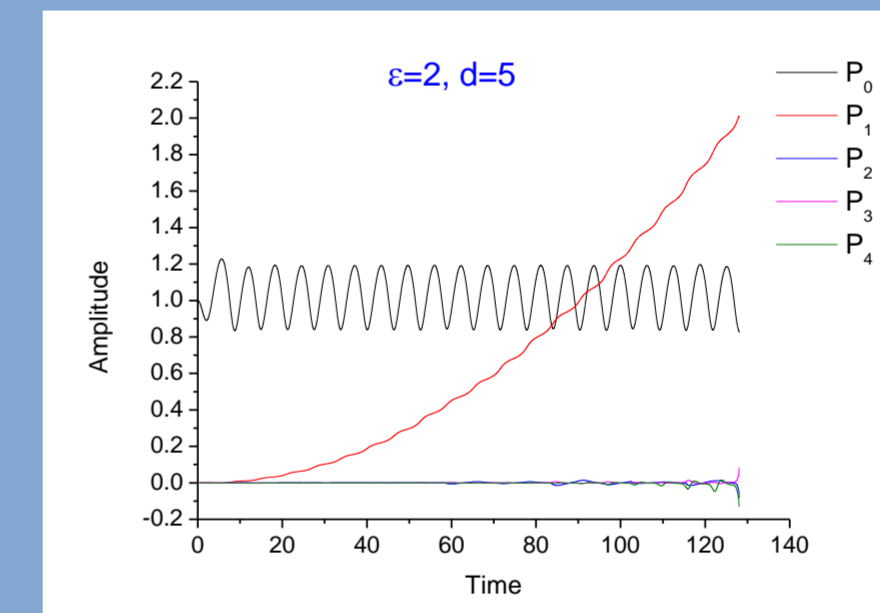
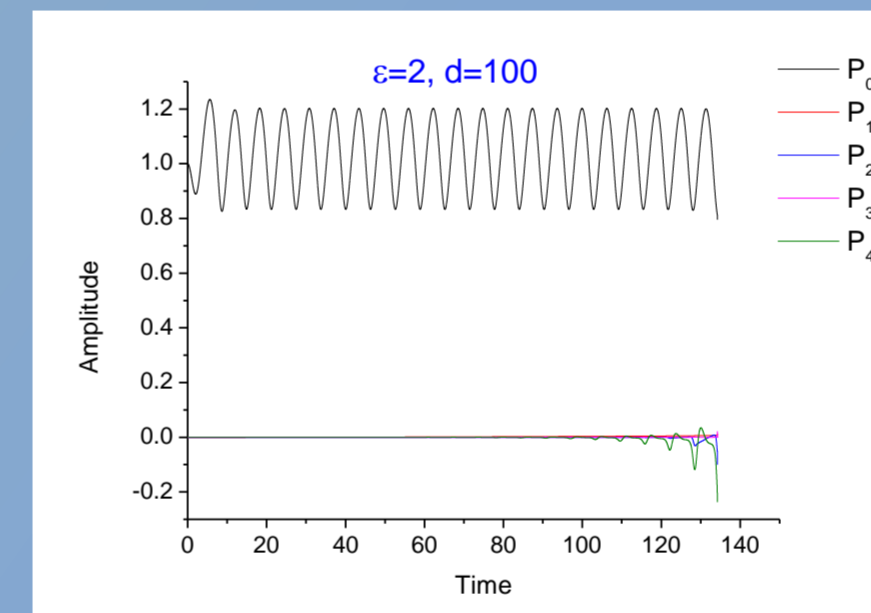
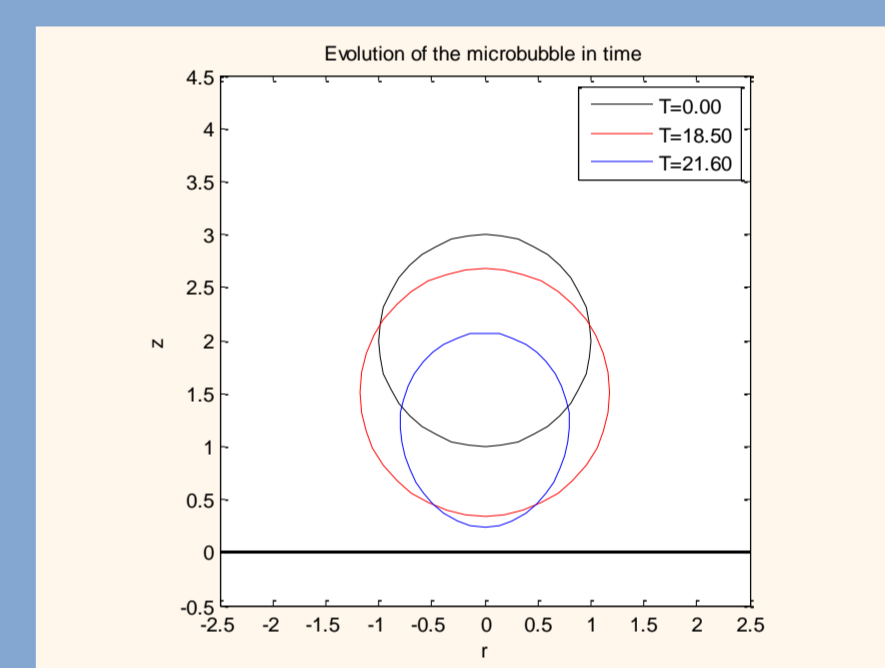
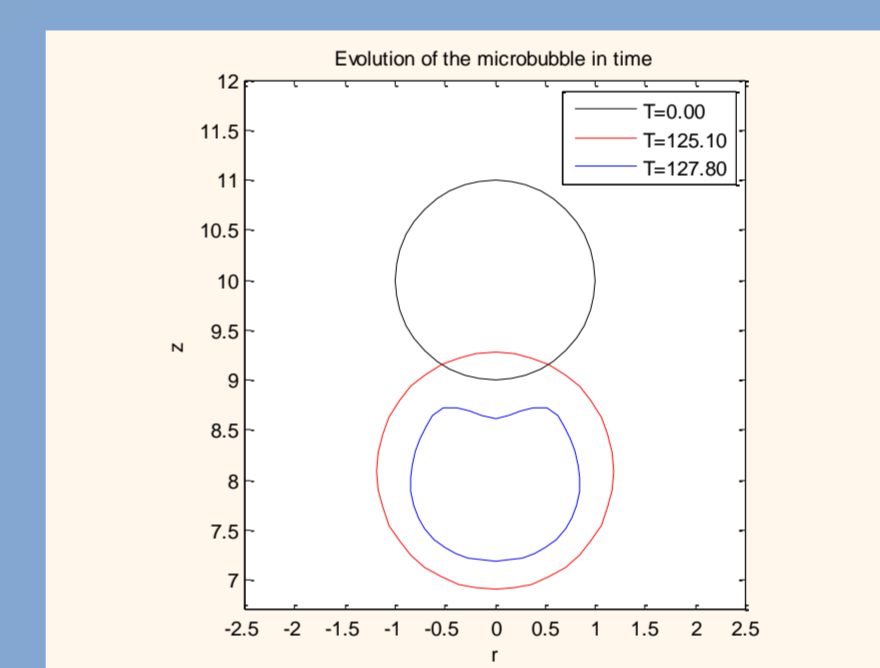
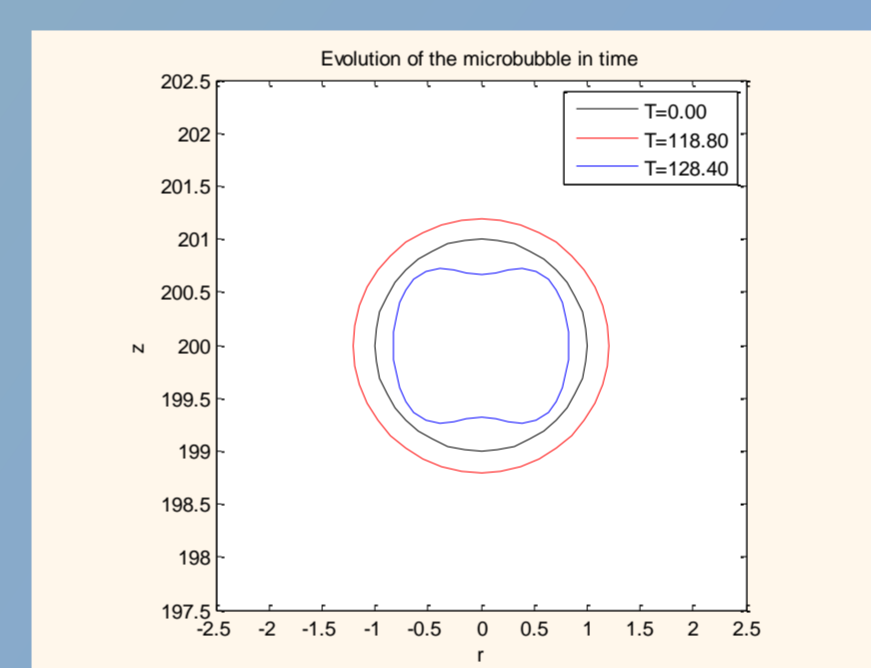


Sinusoidal Change in Pressure Field

Far from boundary

At middle distance

Close to the boundary



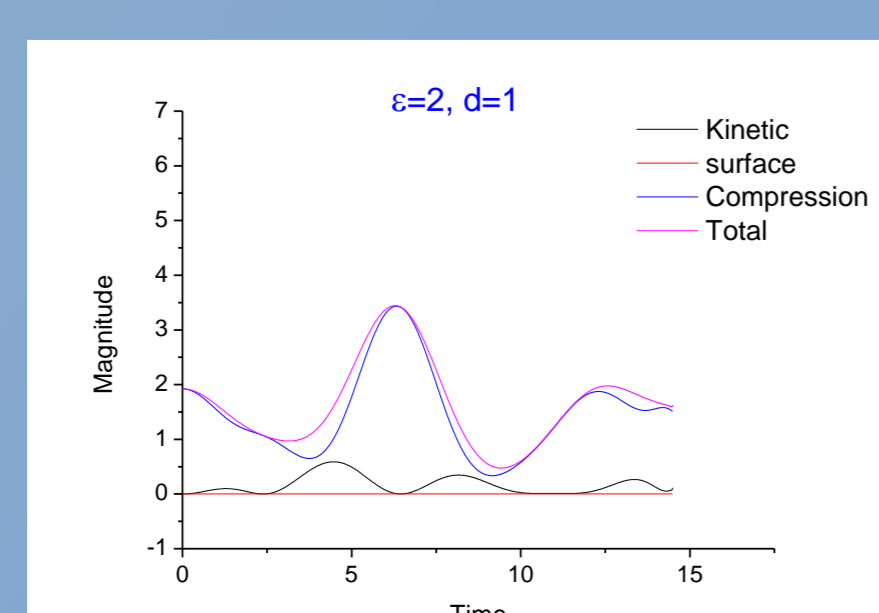
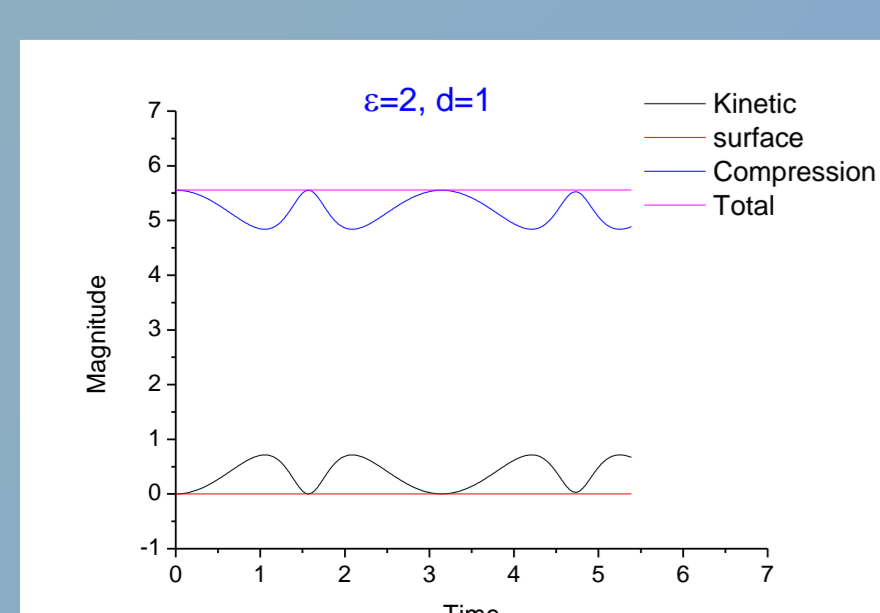
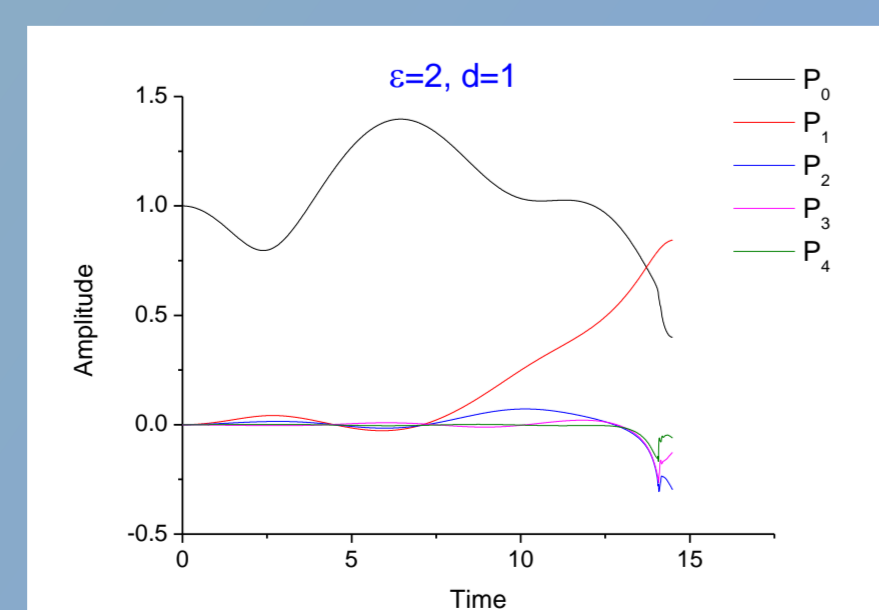
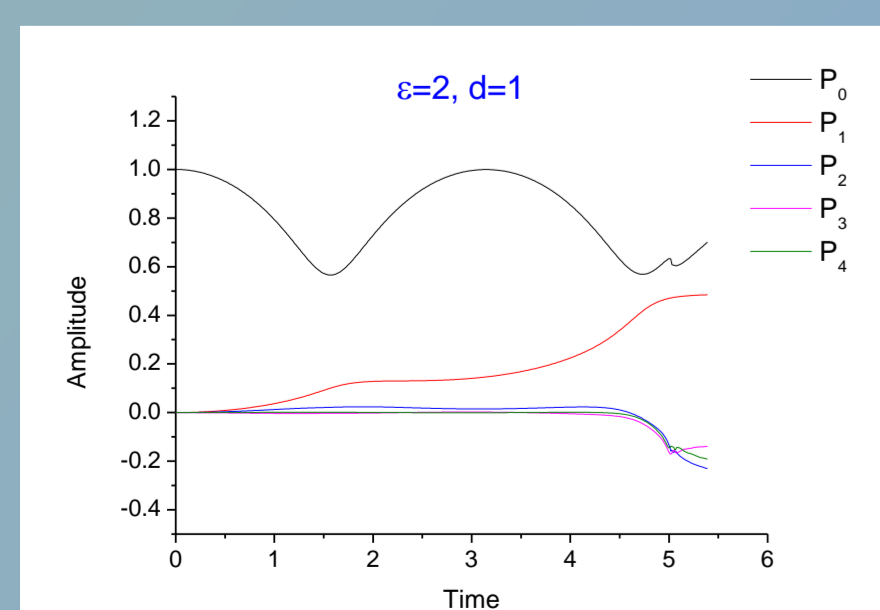
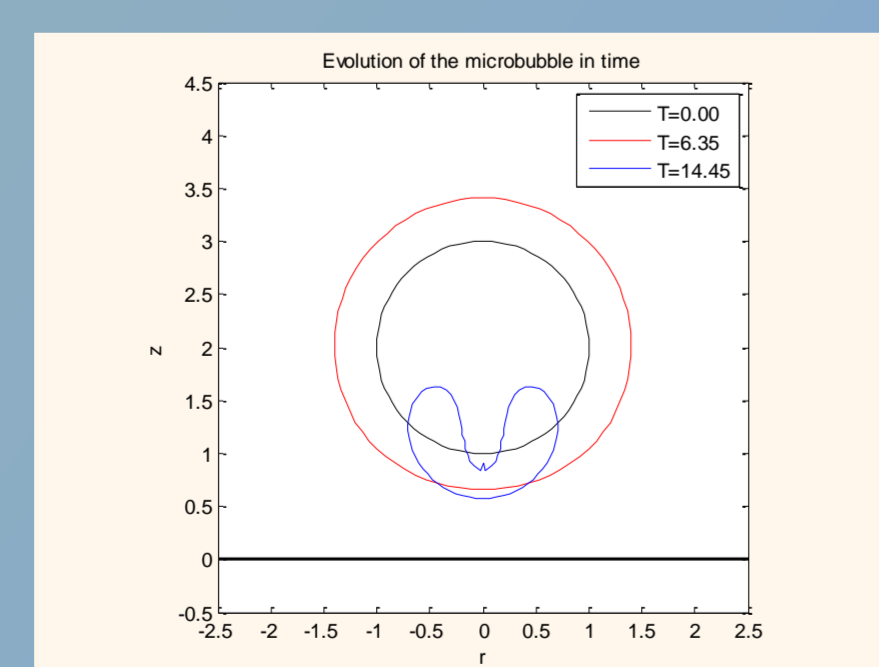
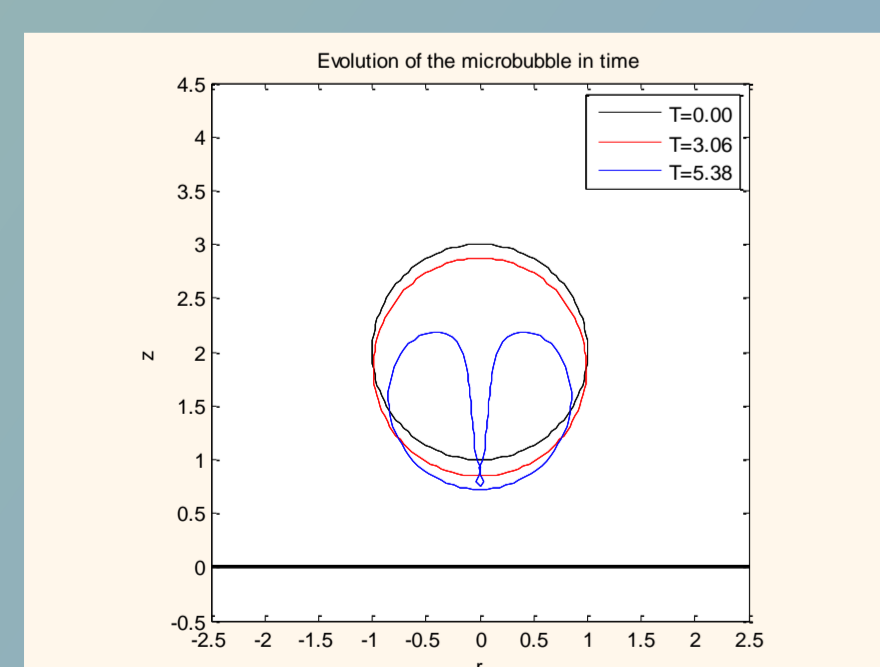
Uncoated Microbubble – Rigid Boundary

Step Change in Pressure Field

Sinusoidal Change in Pressure Field

Close to the boundary

Close to the boundary



- In all cases the microbubble approaches the rigid boundary. For smaller initial distance between the microbubble and the rigid boundary, the attraction among them is greater
- In the case of step change in pressure field the oscillations of the coated microbubble are damped due to dilatational viscosity of the shell – For the uncoated one the total energy is conserved whereas for sinusoidal change it oscillates in time with the period of the acoustic pressure field
- The amplitude of the volume pulsations is not significantly affected as the microbubble approaches the wall (the backscatter cross-section is also not affected)
- The translational velocity of the coated microbubble is constant for step change in pressure field while it is increasing for sinusoidal change due to the interaction with the boundary (secondary Bjerknes force)
- Once the volume pulsation stops the microbubble keeps propagating due to the absence of viscosity in the surrounding fluid
- The initial distance between the coated microbubble and the wall affects the shape modes growth (e.g. in this particular case far from the boundary shape mode 4 is emerging faster via harmonic resonance (four-lobed microbubble), while close to the boundary shape mode 3 is emerging (three-lobed microbubble))
- In the case of the uncoated microbubble at the late stages of the motion, the greater mobility of the fluid away from the boundary causes the surface of the bubble there to collapse faster than elsewhere, leading to the formation of a liquid jet that traverses the bubble and ultimately impacts upon the far side of the bubble
- In the case of the coated microbubble, at the late stages of the motion, formation of jet is suppressed due to the presence of the viscoelastic shell. Instead, in all cases, the microbubble exhibits a deformed shape without permitting extreme elongations
- As time evolves bending energy arrests growth of the kinetic energy – During the final stages areas of very small radius of curvature emerge during the compressive phase of the pulsation – Elastic energy is preferentially channeled towards bending until a conical angle is expected to locally form at a finite time in which case the computations have to stop
- Ongoing simulations with varying element size with local curvature are performed in order to accurately capture the above pattern of break-up