The effect of fluid compressibility on multi-bubble cavitation for high-intensity focused ultrasound

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Clinical Practice

- High-Intensity Focused Ultrasound (HIFU) offers an effective and non-invasive way of treating cancerous tumours through ablation via mechanical and thermal effects
- Cavitation may occur during treatment and, like in diagnostic applications, be used for monitoring
- However, it is believed that cavitation activity is more than just an indicator of the pressure and temperature fields: cavitation can enhance or inhibit heat deposition.
- The stability of the bubbles will determine how long cavitation may last, affecting thermal contributions
- Although classically well-understood, the mechanisms for cavitation inception in tissue remain unclear - work on pressure and frequency dependence is ongoing . . .

Some predictive models of HIFU use effective medium models to measure effects of cavitation. These incorporate the oscillations of many bubbles which are typically assumed to be equally sized and independent into propagation equations[1] to predict changes in:

- Attenuation
- Dispersion
- Pressure
- Temperature

Motivation:

The validity and consequences of these assumptions are investigated, and the effects of delayed interactions studied.

[1] R. E. Caflisch *et. al* Effective equations for wave propagation in bubbly liquids. *J. Fluid Mech.* **185** (1985) pg. 259–274. P. Smereka A Vlasov equation for pressure wave propagation in bubbly fluids *J. Fluid Mech.* **454** (2002) pg. 287–325.

Types of cavitation

For a single bubble the physical characteristics are well defined mathematically

pressure

1 Weakly oscillating bubbles

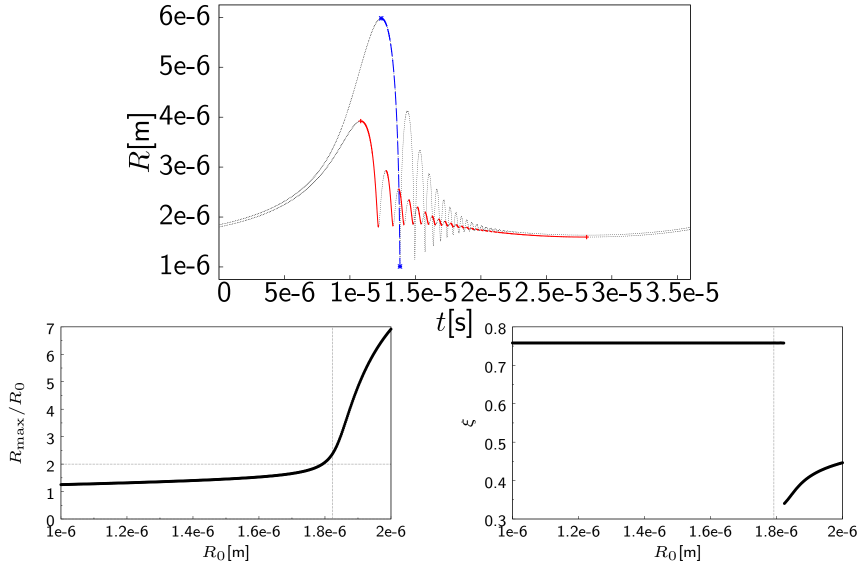
Transition radius

Flynn criteria

2i 'Violent collapse' : rapid expansion
2ii Inertial collapse : shock waves

Lyapunov exponents...

3 Chaos : broadband noise


6e-6
5e-6
4e-6
3e-6
2e-6
1e-6
R[m]
0
5e-6
1e-5
1.5e-5
2e-5
2.5e-5
3e-5
3.5e-5
t[s]
7
6
5
4
3
2
1
0
$R_{\max}/R_0$
1e-6
1.2e-6
1.4e-6
1.6e-6
1.8e-6
2e-6
R_0[m]
0.8
0.7
0.6
0.5
0.4
0.3
ξ
1e-6
1.2e-6
1.4e-6
1.6e-6
1.8e-6
2e-6
R_0[m]

Multi-Bubble Cavitation Models

The (secondary Bjerknes) interaction leads to an

Enhanced **Multi**-Bubble Spherical Rayleigh-Plesset Equation

$$\rho\left(\ddot{R}_i R_i + \frac{3}{2}\dot{R}_i^2 + \sum_{\substack{j=1,\\ j\neq i}}^{N} \frac{R_j}{D_{ij}}\left(R_j\ddot{R}_j + 2\dot{R}_j^2\right)\right) = p_g\left(R_i\right) + p_\infty - p\left(t\right) - \frac{2\sigma}{R_i} - \frac{4\mu\dot{R}_i}{R_i} + \frac{R_i}{c}\frac{\mathrm{d}}{\mathrm{d}t}\left(p_g - p\right) \tag{1}$$

- Now an $2n$-dimensional system but does the system possess more complicated dynamics?
- How do the spatial and size distributions affect stability?

- Analytical measures of stability for single bubbles do not easily carry over for multi-bubble systems.
- In a single highly degenerate case for bubbles of equal size arranged in a certain configuration analytical estimates can be performed giving an estimate in terms of number and distance
- From bifurcation diagrams numerical evidence strongly suggest
  - Transition radius demarcates change in expansion ratio[1]
  - Inertial cavitation exactly demarcates instance of collapse.
- Numerical and analytical results suggest both measures are independent of number of bubbles
  - Interaction only manifests itself when bubbles collapse inertially

[1] Hilgenfeldt et al. *Analysis of Rayleigh–Plesset dynamics for sonoluminescing bubbles*, J. Fluid Mech **365**, (1998), pp. 171–204

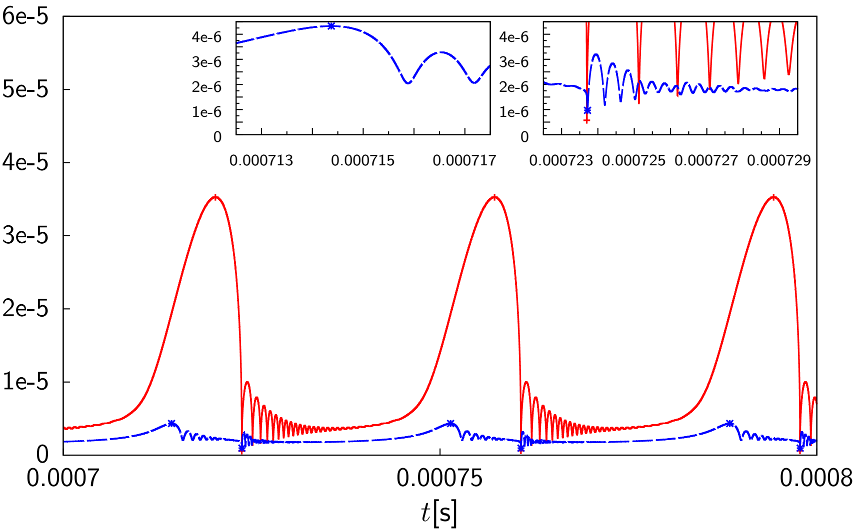


Figure: Coupled bubble dynamics : the larger bubble initiates the collapse of the smaller bubble through a shock-like reradiated pressure field

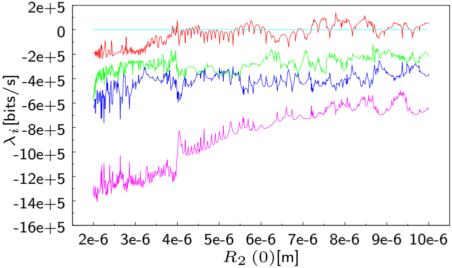


Figure: Lyapunov exponents of polydisperse few bubble system gives stability and KS-entropy of the multi-bubble system

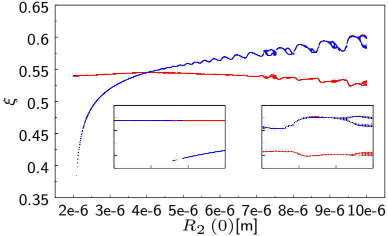


Figure: Bifurcation diagram of collapse phase shows when synchronisation occurs for a two-bubble system as the initial size of one bubble is increased

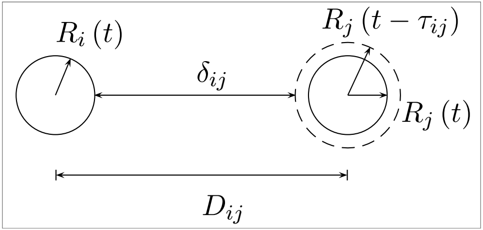
Delay Differential Equations

- Due to fluid compressibility bubble interactions are no longer considered to be instantaneous. The interaction, given in equation (1), is now modelled as a

Delayed Multi-Bubble Spherical Rayleigh-Plesset Equation

$$\begin{aligned} &\frac{R_j\left(t\right)}{D_{ij}}\left(R_j\left(t\right)\ddot{R}_j\left(t\right)+2\dot{R}_j^2\left(t\right)\right)\mapsto \\ &\qquad \frac{R_j\left(t-\tau_{ij}\right)}{\delta_{ij}}\left(R_j\left(t-\tau_{ij}\right)\ddot{R}_j\left(t-\tau_{ij}\right)+2\dot{R}_j^2\left(t-\tau_{ij}\right)\right) \end{aligned} \tag{2}$$

Exact delay is $\tau_{ij} = \delta_{ij}/c$ where $\delta_{ij} = D_{ij} - (R_i(t) + R_j(t - \tau_{ij}))$



May be approximated[1]

$$\delta_{ij} \approx D_{ij} - \left(R_i(t) + R_j(t) - \tau_{ij}\dot{R}_j(t)\right)$$

$$\Rightarrow \tau_{ij} \approx \left(D_{ij} - (R_i(t) + R_j(t))\right) / \left(c + \dot{R}_j(t)\right)$$

System is a state-dependent neutral delay differential equation

[1] C. Chicone, Inertial and slow manifolds for delay equations with small delays, *J Diff. Eqns.* (2003) **190**, pg. 364–406

- Neutral: delay appears in $\ddot{R}$ terms
- State-dependent: delay depends on radius

The delay can be calculated exactly using many standard solvers capable of solving neutral delay equations

$$M\dot{\boldsymbol{x}} = f\left(\boldsymbol{x}, \boldsymbol{z}\right)$$

with f given by equation (1) where $f_3 = \ddot{R} - f_2 = 0$ and

$$M = \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}, \quad \boldsymbol{x} = \begin{pmatrix} R\left(t\right) \\ \dot{R}\left(t\right) \\ \ddot{R}\left(t\right) \\ \bar{\tau} \end{pmatrix}, \quad \boldsymbol{z} = \begin{pmatrix} R\left(t-\tau\right) \\ \dot{R}\left(t-\tau\right) \\ \ddot{R}\left(t-\tau\right) \\ 0 \end{pmatrix}$$

by appending a singular equation for the delay into the function f

$$f_4 = \tau - \delta/c = 0.$$

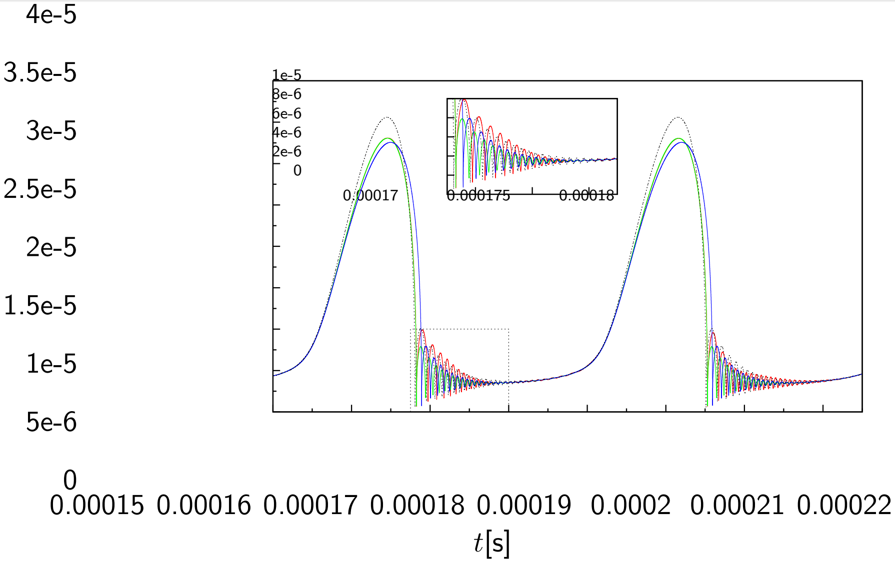


Figure: Single bubble (dotted), instant (red), constant (blue), exact (green).

- First examine the stability of the (fully) nondimensional linearised system[1] of equally sized bubbles

$$\ddot{x}(t) + 2\zeta\dot{x}(t) + x(t) = p\sin(\Omega t) + h\ddot{x}(t-\tau)$$

with constant delay $\tau = D/c$.

- Now there are essentially two fields acting on the bubble
  - (i) The applied acoustic pressure
  - (ii) The reradiated pressure — dependent on the bubble oscillations

[1] Y. Kyrychko *et al.* Real-time dynamic substructuring in a coupled oscillator–pendulum system. *Proc. Roy. Soc.* **462** (2006) pg. 1271–1294

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In the absence of the applied field, the equation has a trivial steady state. The corresponding characteristic equation is

$$\lambda^2 + 2\zeta\lambda + 1 + h\lambda^2 e^{-\lambda\tau} = 0$$

which is transcendental: infinite number of natural frequencies, resonances, subharmonics etc. Let $\lambda = \pm i\mu$, then

$$\mu_{\pm}^2 = \frac{1}{1-h^2}\left(\left(1-2\zeta^2\right) \pm \sqrt{\left(1-2\zeta^2\right)^2 - \left(1-h^2\right)} \right)$$

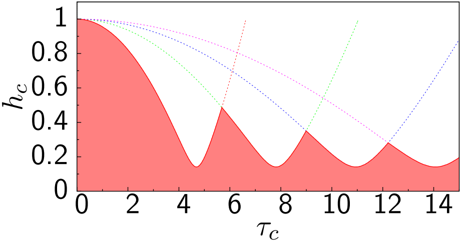
Thus explicit expressions for the stability boundaries for the delay

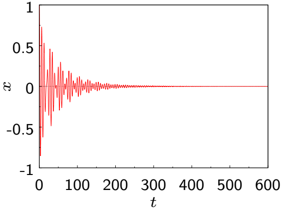
$$\tau_c = \frac{1}{\mu_{\pm}}\left(\tan^{-1}\left(\frac{2\zeta\mu_{\pm}}{\mu_{\pm}-1} \right) \pm n\pi \right)$$

Analysis states that $\zeta = \dfrac{2\mu}{\rho R_0^2 \omega_0} = \dfrac{1}{\sqrt{2}}$ is the critical value

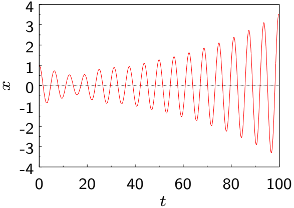
- If below this value the bubble is always stable regardless of the separation distance.
- If above this value the bubbles may grow unboundedly if the separation distances are within domains of instability.
  - If the bubbles drift apart then the delay changes, the trivial equilibrium undergoes successive switches in stability before eventually becoming unstable.
  - Arbitrary bubble configurations may have bubbles which undergo unbounded growth, thus undergo inertial collapse

$\Rightarrow$ Linearised equations of motion may yield **unphysical** results!

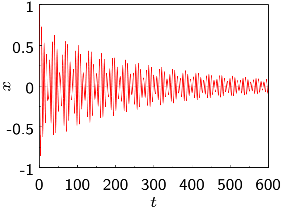




(a) τ =14



(b) τ=17

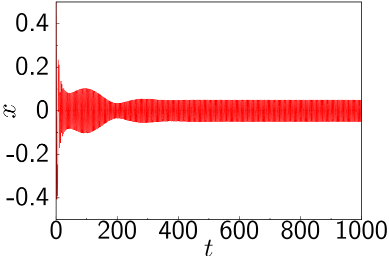


(c) τ =20

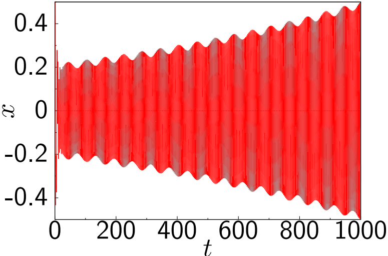
The secondary Bjerknes force estimates the translational force on a weakly oscillating pair of bubbles due to interactions

$$\begin{aligned}\langle \boldsymbol{f}_{ij} \rangle &= \int_T \dot{V}_i\left(t\right) \dot{V}_j\left(t - \tau_{ij}\right) \mathrm{d}t \\ &= \frac{2\pi\rho R_i\left(0\right) R_j\left(0\right) \omega^2}{D^2} \left|A_i A_j\right| \cos\left(\theta_i - \theta_j - \omega\left(\tau_i - \tau_j\right)\right)\end{aligned}$$

Stable periodic motion occurs after a Hopf bifurcation - two scale perturbation analysis yields A_i and θ_i



(a) $\tau =$1.55



(b) $\tau =$1.61

There are two pathways to shape instability

Rayleigh-Taylor instability is the formation of shape instability during the bubble collapse. Bubble modelled using small perturbation with Legendre polynomials

$$R\left(t\right) \mapsto R\left(t\right) + \sum_{i=2}^{\infty} a_i\left(t\right) Y_i\left(\theta, \varphi\right)$$

with $a_n \sim \mathcal{O}\left(\varepsilon^n\right)$. Unstable when a_2/R is $\mathcal{O}\left(1\right)$

Parametric instability is a shape deformation which occurs during the afterbounce regime and grows slowly and leads to shape instability after a large number of cycles. This is ongoing work : computation of Floquet multipliers for a driven delayed system requires analysis ...

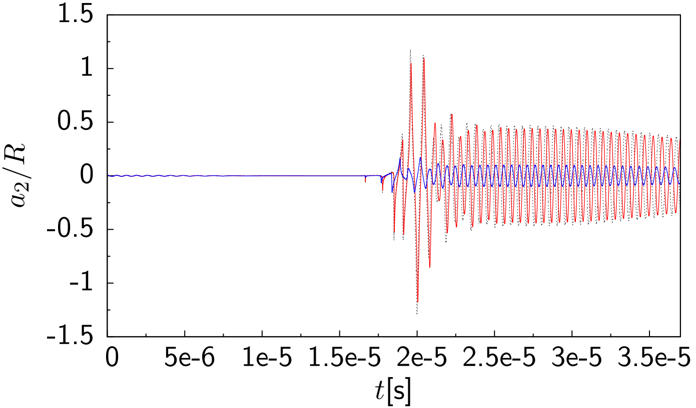
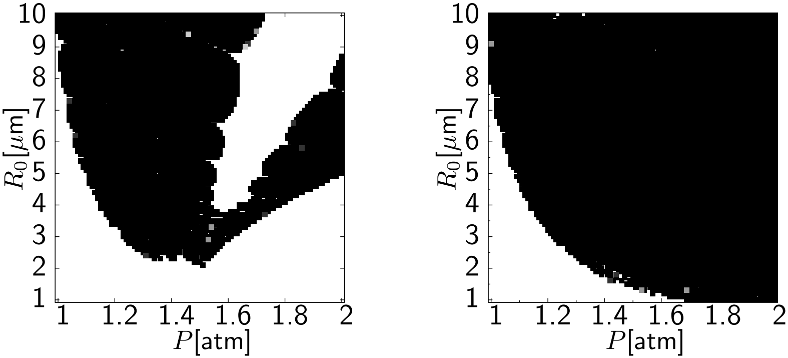
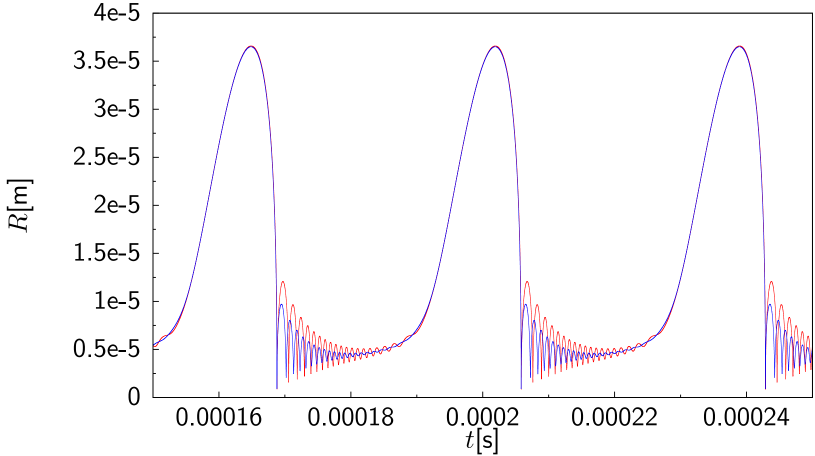


Figure: First mode of nonspherical deformation for single (dotted), instant (red) and delayed (blue) interactions

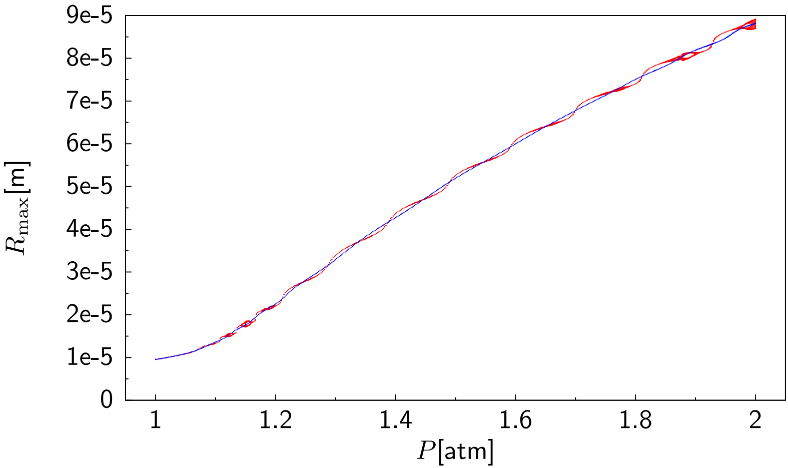


(a) Exact Delay (b) Instantaneous

Figure: Parameter plane for Rayleigh-Taylor shape instability for a pair of equally sized interacting bubbles. Unstable regimes shaded.



- Inclusion of time delays suggests a decreased likelihood of parametric instability
  - Reduced contributions from viscous heating



- Delays maybe a stabilizing factor when investigating bubble cloud densities and applied pressures

Summary & Conclusions

Cavitation in tissue may play a significant role in treatment

- Interactions only play a significant role for inertial collapse
  - → Implications for void fractions and bubble size distributions in propagation models

When compressibility is incorporated

- (Nondimensional) viscosity must be calculated in order to make assumption of linear oscillations
  - → Implications for driving pressure for propagation models : potentially unphysical results

However

- Threshold for shape instability is raised by interactions when delays are incorporated into the full nonlinear model
  - → Implications for treatment : greater thermal contributions

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Transcostal High-Intensity Focussed Ultrasound for the Treatment of Cancer

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Thank you for your attention

Any questions?

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The effect of delays on multibubble stability.
In preparation.

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