BME2 – Biomedical Ultrasonics

Lecture 6: An Introduction to Non-Linear Effects

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Acknowledgments: Prof. Ronald A. Roy, George Eastman Visiting Professor 2006-07

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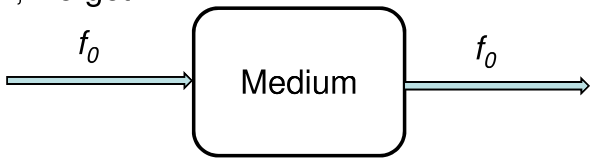
6.1 Non-linear sound propagation

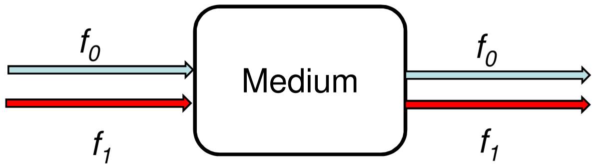
- Recall that for *linear* sound propagation, we must have

$$p(\mathbf{r},t) = p_o + p'(\mathbf{r},t) \quad p' << p_o$$
$$\rho(\mathbf{r},t) = \rho_o + \rho'(\mathbf{r},t) \quad \rho' << \rho_o$$
$$\mathrm{u}(\mathbf{r},t) = \mathrm{u}'(\mathbf{r},t) \quad |\mathrm{u}'| \ \mathrm{small}$$

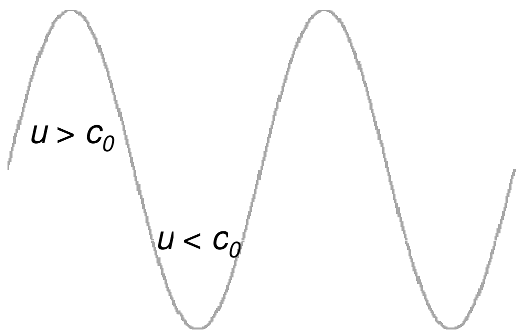
- In practice, this means that if we feed a wave at a single frequency f_0 through a medium, we get



- Similarly, if the input consists of two or more signals of different frequencies:



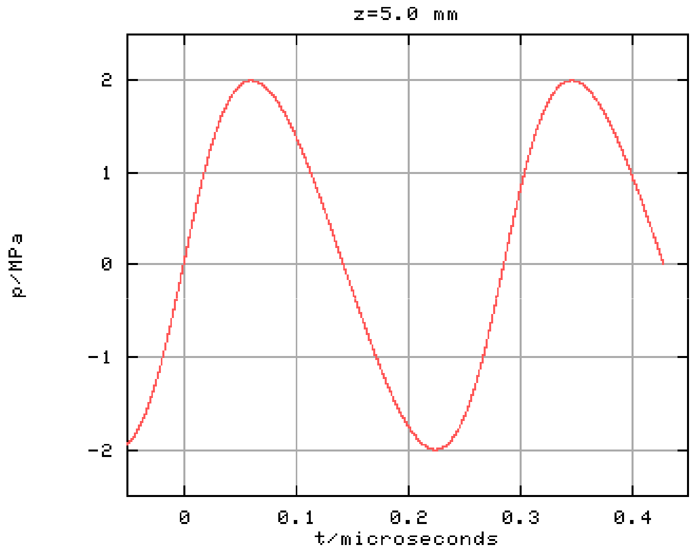
- What happens if the excitation amplitude is not small?
- The local fluid velocity is no longer small *compared to the speed of wave propagation*



- Hence, sound in regions of positive u travels faster, whilst sound in regions of negative u travels slower.

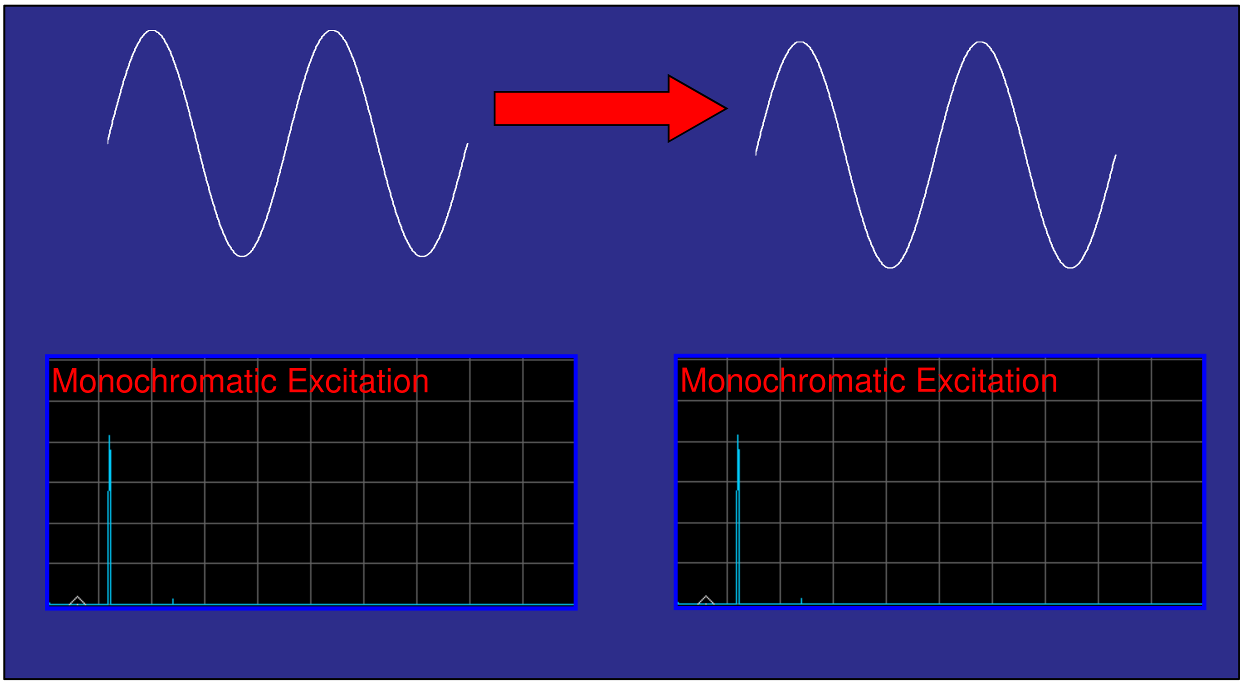
- However, sound in regions of zero u still travels at speed c_0, meaning that the period is unchanged!

- This results in steepening of the wave and gradual shock formation:

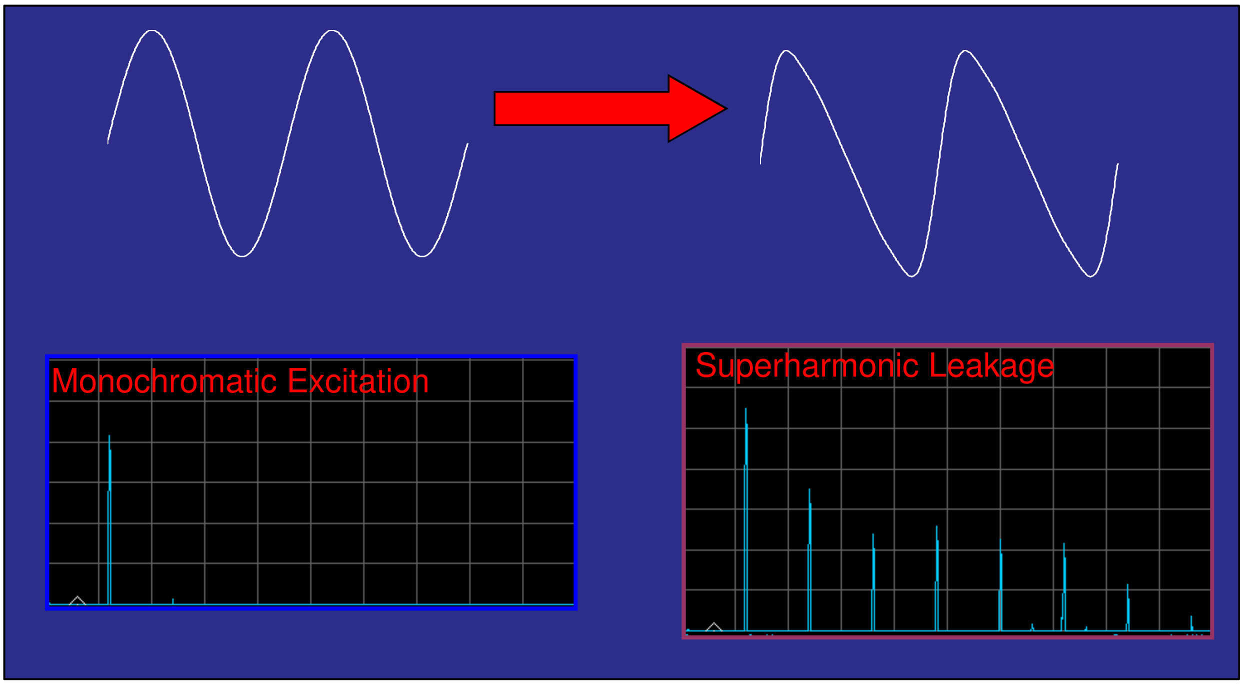


(recall that in most media attenuation is a power law of frequency).

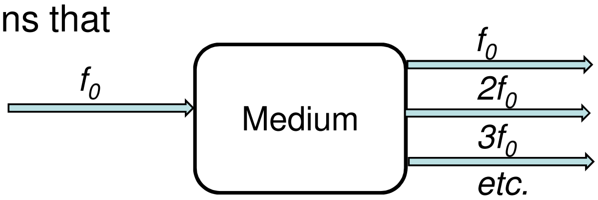
Frequency response of a linear medium



Frequency response of a non-linear medium



- This now means that



- The degree of wave steepening / harmonic generation is primarily a property of the medium, described by the parameter *B/A* or the coefficient of non-linearity $\beta = 1 + B/2A$
- For comparison, note that
  - Liver: *B/A = 7.6*
  - *Water: B/A = 5.2*

- The propagation distance required for an initially-sinusoidal plane wave to form a shock wave is termed the shock formation distance

$$\bar{x} = \frac{\lambda}{2\pi\beta M}$$

This means that shocks form sooner at higher frequencies, in more non-linear media and at higher amplitudes *M*.

- The Westervelt equation* includes diffraction, absorption, nonlinearity and inhomogeneity

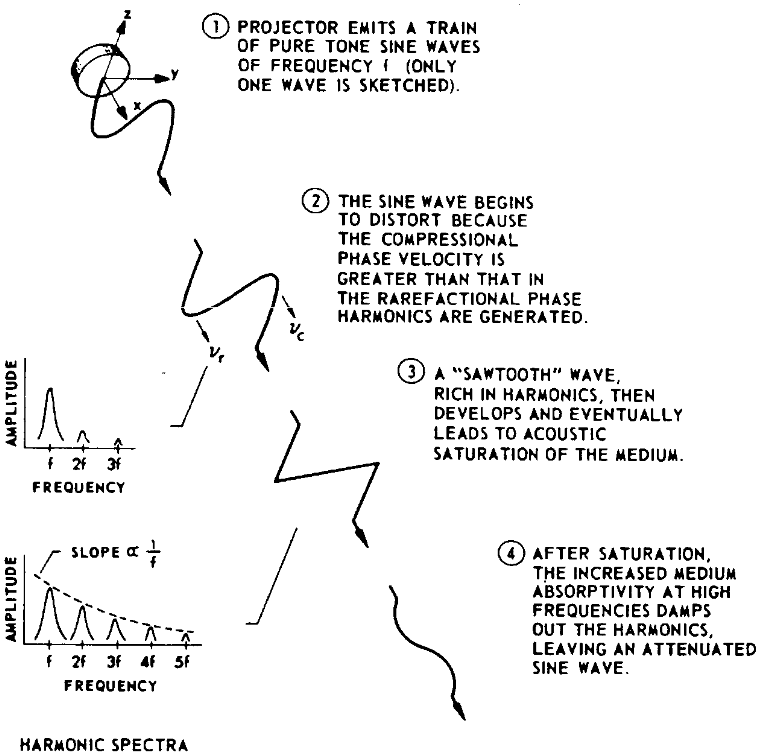
$$\boxed{\left(\nabla^2 - \frac{1}{c^2}\frac{\partial^2}{\partial t^2}\right)p - \frac{1}{\rho}\nabla p \cdot \nabla \rho + \frac{\delta}{c^4}\frac{\partial^3 p}{\partial t^3} + \frac{\beta}{\rho c^4}\frac{\partial^2 p^2}{\partial t^2} = 0}$$

where p is the propagating acoustic pressure perturbation, c is the local sound speed, ρ is the local density for the medium, δ the local acoustic diffusivity, and β is a local coefficient of nonlinearity. [4.2]

- Note that a major limitation of this equation is that it does not accurately account for the frequency dependence of attenuation.

Muir & Carstensen (1980)

Imaging Ultrasound is not Necessarily Linear



Imaging Ultrasound is not Necessarily Linear

Harmonic Imaging

- Finite amplitude sound waves propagate nonlinearly through real media
- This results in the transfer of energy from the fundamental frequency to higher harmonics
- This conversion occurs further away from the source, this near field abberating layers do not impact the formation of these harmonics.
  - Nearfield aberration not as important at the 2nd harmonic
- Since the conversion to harmonics is second order in the pressure amplitude, this higher frequency energy is generated along a narrower beam
  - Better lateral resolution at the 2nd harmonic

Tranquart et al. (1999)

2nd Harmonic Imaging Mode

B-Mode Image of
Chronic Cholecystitis

2nd Harmonic Image

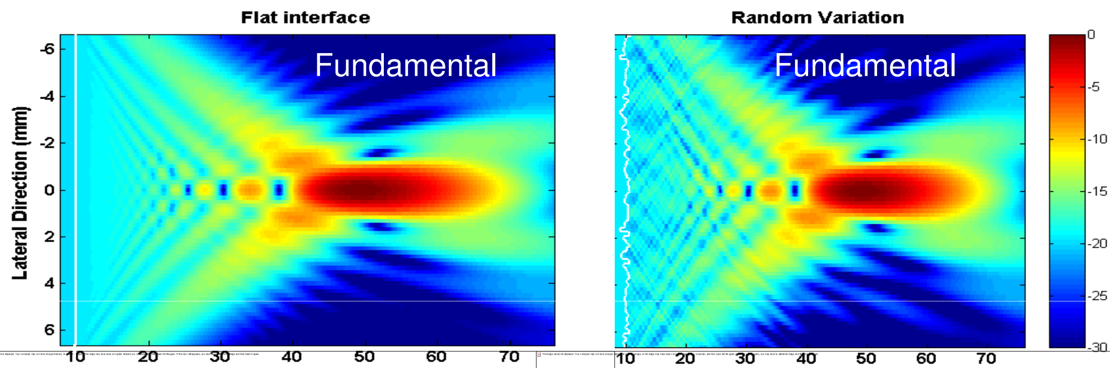
Improved Detail and Contrast

Can Resolve Contents and Wall of the Gall Bladder

Computed Nonlinear Pressure Fields

FDTD Simulations

2.5 MHz



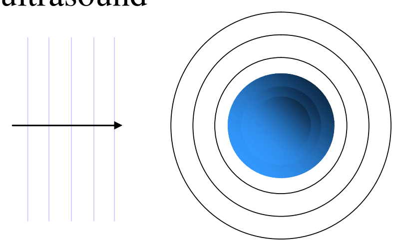
5.0 MHz

6.3 Acoustic cavitation

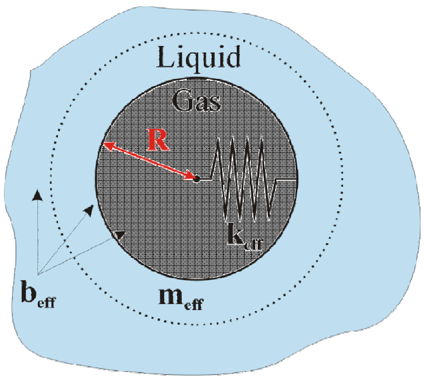
- Linear Bubble Behaviour

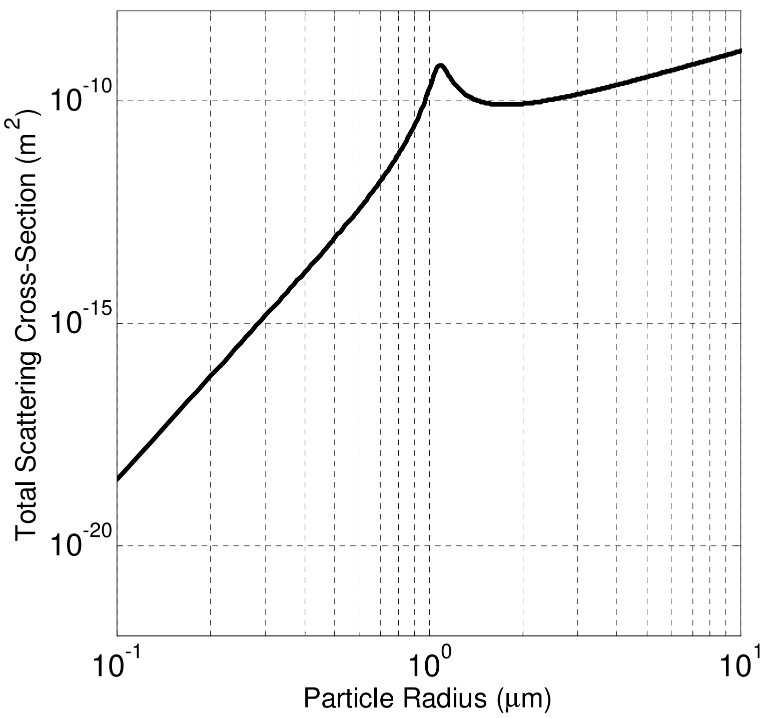
Incident

ultrasound

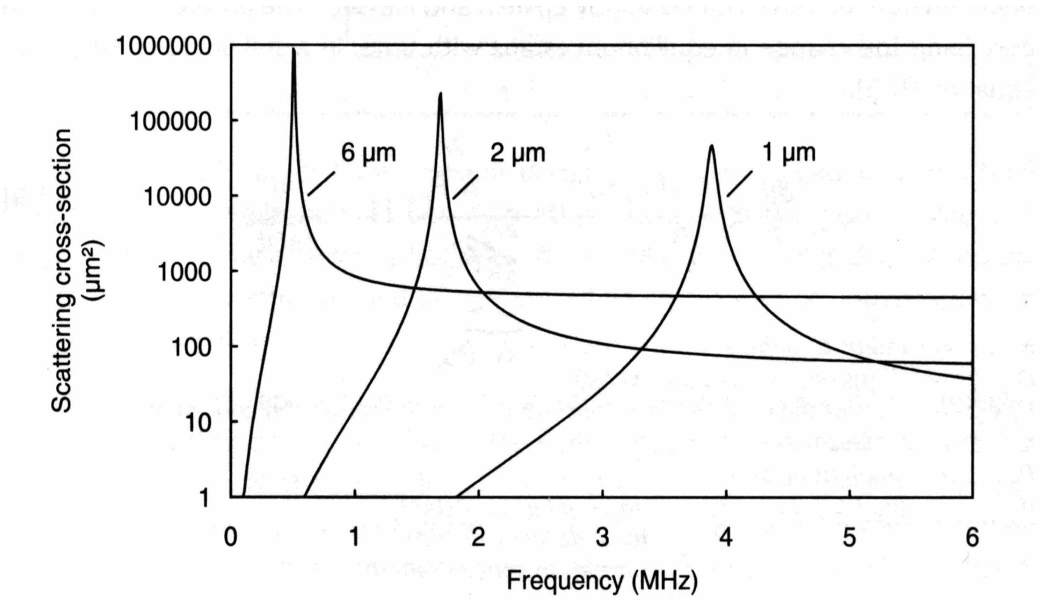


$$\boxed{m_{eff}\ddot{r} + b_{eff}\dot{r} + k_{eff}r = F(t)}$$



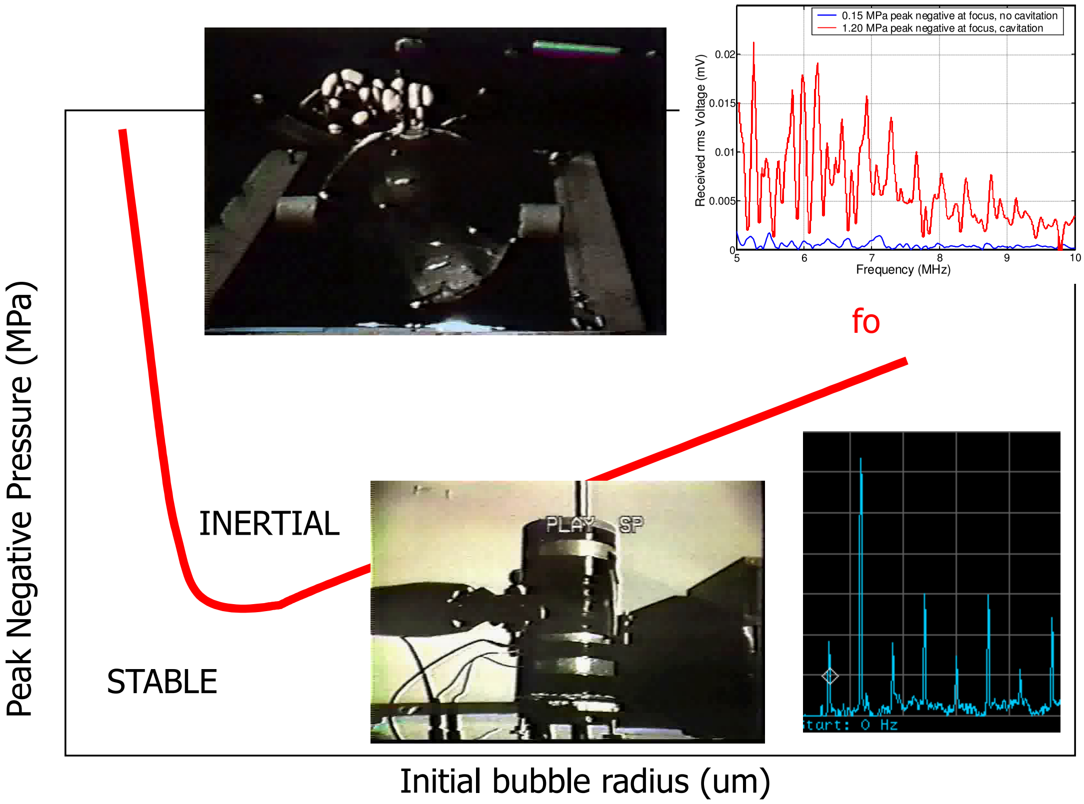


Linear bubble resonance



$$f_o R_o = \frac{1}{2\pi}\sqrt{\frac{3\gamma P_o}{\rho}} \approx 3.25\ Hz-m \qquad \left\{ \begin{array}{l} 1\text{mm} \Rightarrow 3.25\,\text{kHz} \\ \hline 1\mu\text{m} \Rightarrow 3.25\,\text{MHz} \end{array} \right.$$

- Non-linear bubble behaviour: stable and inertial cavitation

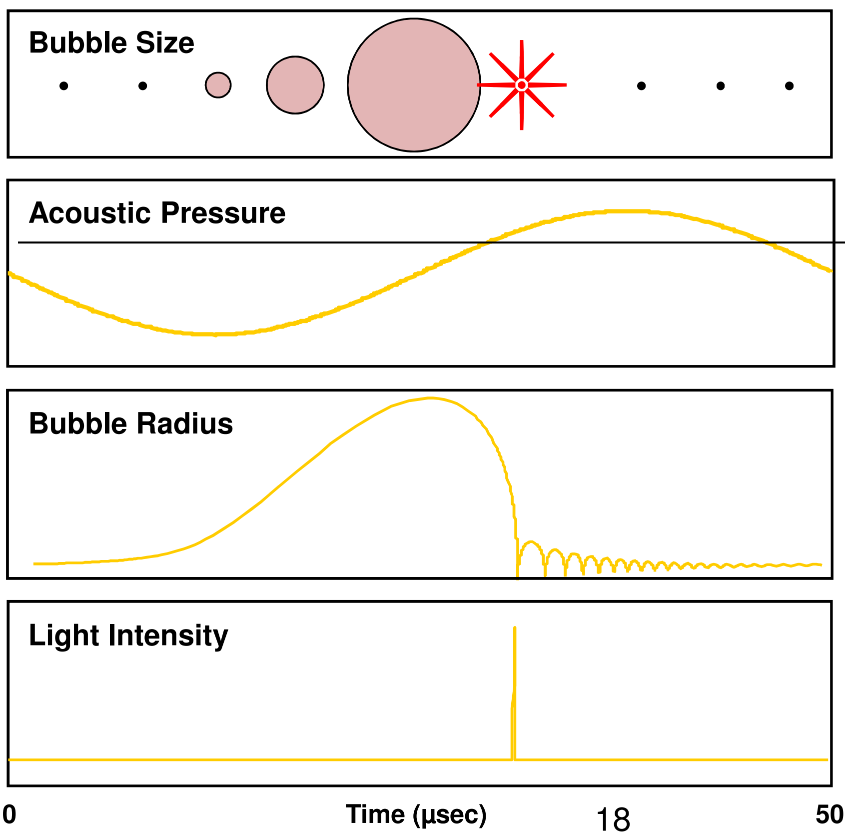


Physical Effects: *Inertial Cavitation*

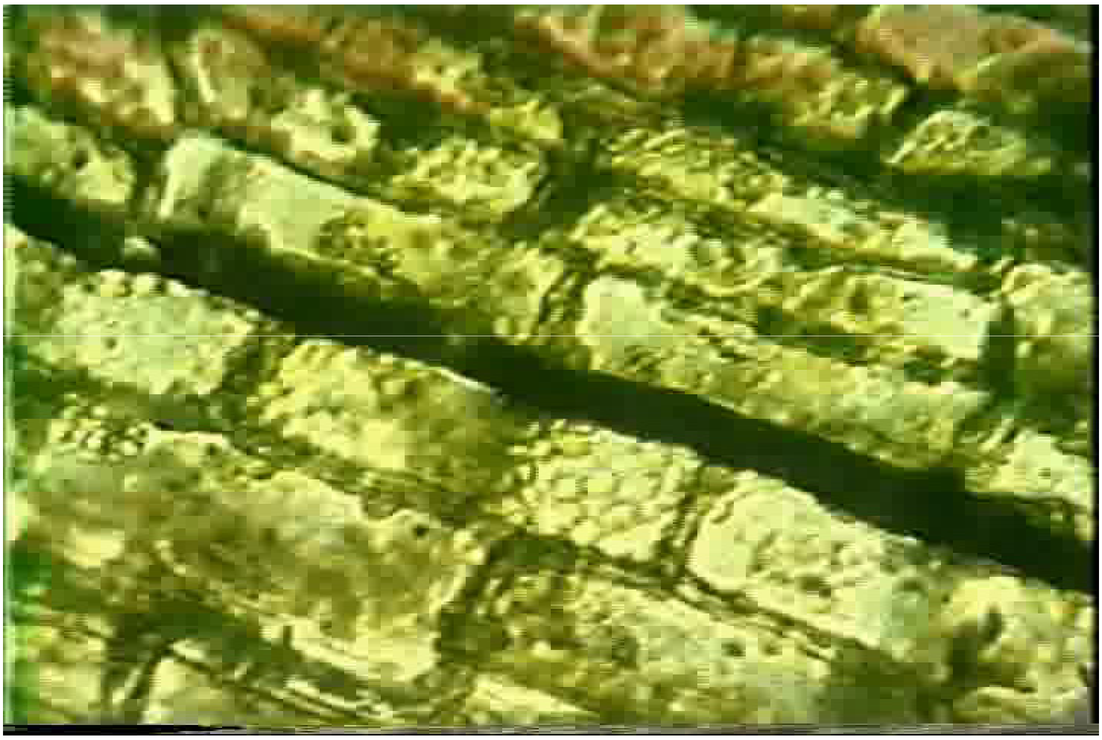
Inertial collapse of an acoustically forced bubble in a liquid

- Isothermal expansion
- Rapid adiabatic collapse
- Chemical dissociation
- Light production

***F* = 20 kHz**
***R_{Res}* = 160 μm**
***R_0* = 0.1 μm**



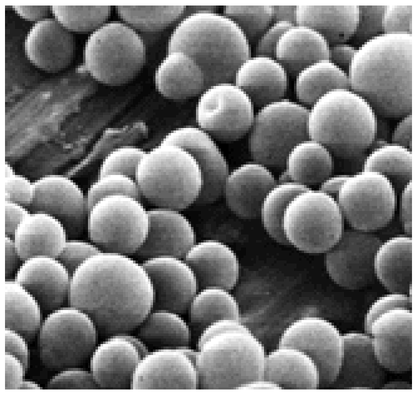
Bioeffects caused by cavitation

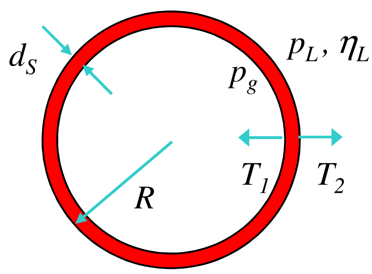


Bubbles are excellent scatters of sound

Ultrasound Contrast Agents (UCAs)
- **Micron-sized bubbles injected**
- **Sizes range from 0.2 - 3 μm**
- **Must be stabilized against dissolution**
  - **Insoluble gases**
  - **Surface skins**

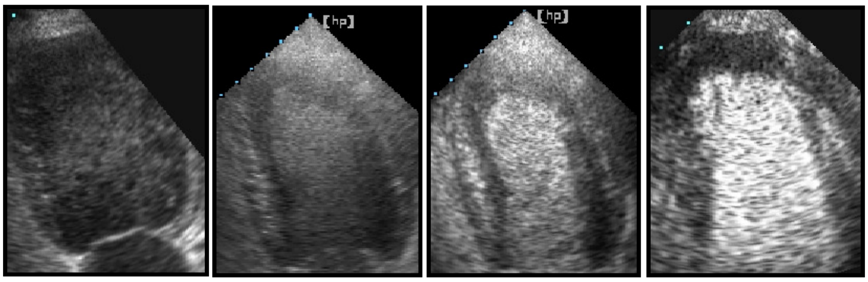
UCA's enhance backscatter from blood
- **Image remote regions**
- **Enhance Doppler flow imaging**
- **Highlight vascularized regions (tumors!)**
- **Measure perfusion into tissues**





The Role of Bubbles in Ultrasound Imaging

- **Bubble Contrast Imaging**
  - **Adding bubbles to blood enhances echogeneicity because everyone knows that bubbles are the most amazing scatterers of sound!**
  - **There are many different manifestations of bubble contrast agents -- all offer a measure of diffusional stability.**
  - **The stabilization mechanisms inhibit mechanical response -- regardless, they are still highly effective scattering sites.**
  - **The inherently nonlinear response of cavitation bubbles make them a natural for enhance harmonic imaging.**



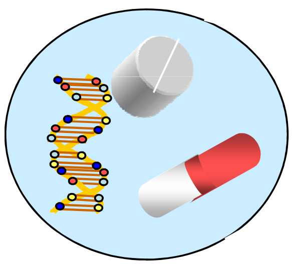
1st Generation @ f_o -- | 1st Generation @ $2f_o$- | 2nd Generation @ $2f_o$ - | Improved Xducer @ $2f_o$--

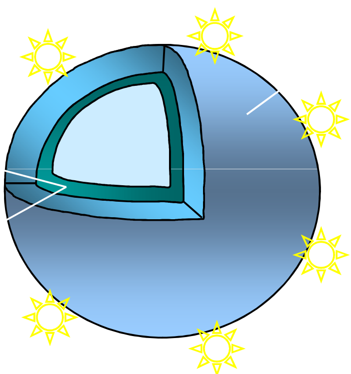
Applications

Targeted Drug Delivery

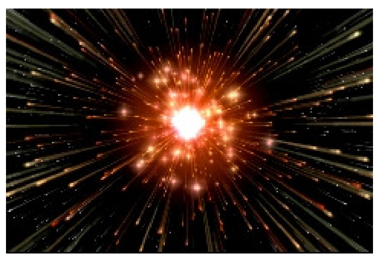
Gas core

Surfactant or polymer shell.





Targeting species may be attached to the shell surface.



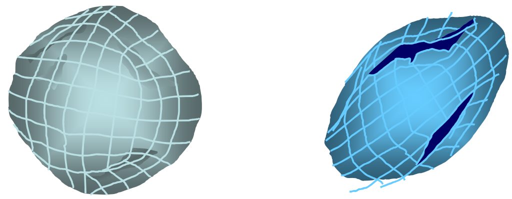
• Drugs or even DNA can be incorporated into the shell and released by destroying the bubble with high intensity ultrasound at the required location.

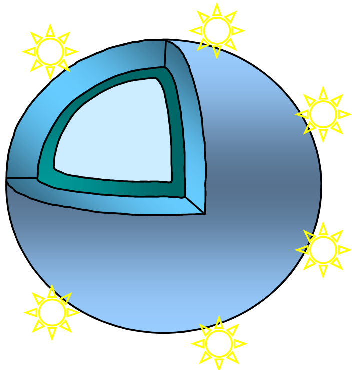
The Encapsulating Shell

Mechanisms of Destruction

Buckling

Rupture & fragmentation





Modification for Drug Delivery

(i) Asymmetric shell

(ii) Additional oil layer

(iii) Stiffened phospholipid coating