An Ultrasound Modeling Tool for Contrast Agent Imaging

-- Introduction to BubbleSim

Kangqiao Zhao, 2010, May

Outline

- Introduction to Contrast Agent Imaging
  - Applications
  - Detection techniques
  - Mechanical Index
- Bubble and Shell models
- BubbleSim simulation program
  - Compromised model
  - Simulation examples

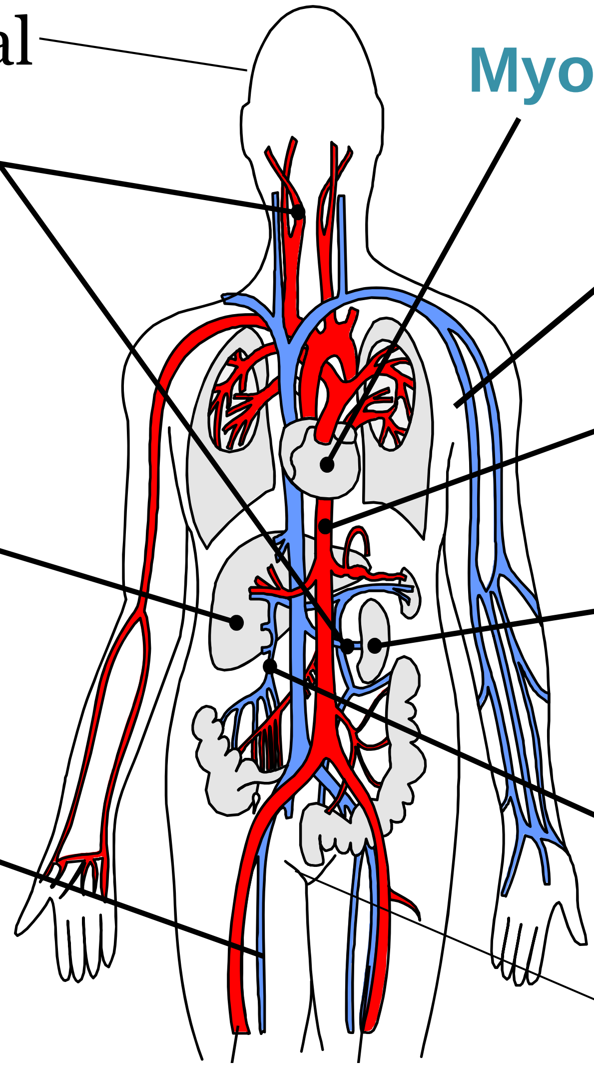
WHAT IS ULTRASOUND CONTRAST AGENTS ?

- Gas bubbles in fluid gives strong echoes due to the large difference in acoustic impedance between the fluid and the gas. The bubble's ability to oscillate at resonant frequency further increase the signal
- Example: Shake saline and inject into blood. Gives a nice opacification of the right side of the heart.
- Problem: Free air bubbles does not pass the lungs, and the contrast effect is very short. Gas bubbles dissolve in blood.

Improvement

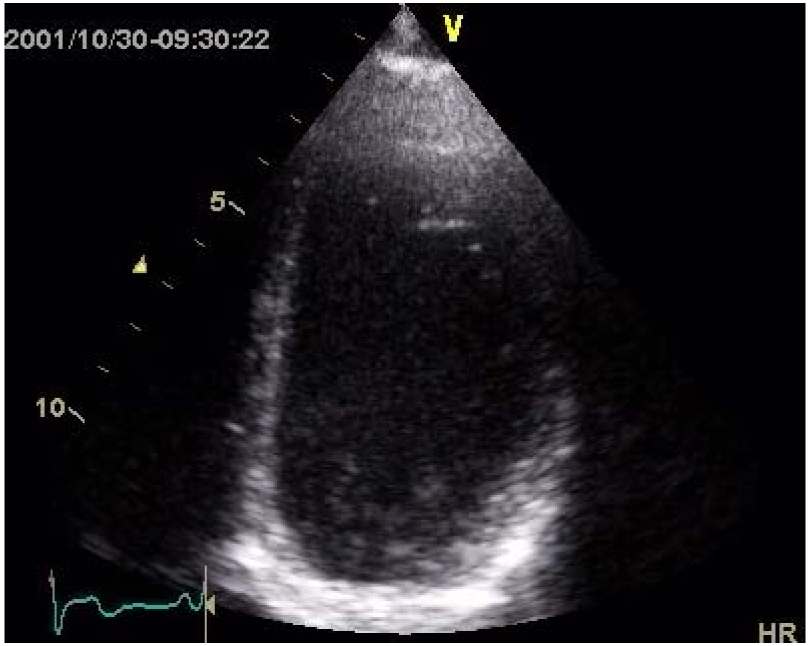
- Stabilize the gas bubble by encapsulating it in thin shell to give a lasting gas bubble effect
- Size must be small enough to pass capillary vessels. Typical diameter 2-5um. (Red blood cells ~7 um)
- The shell must be strong enough to get the particle through the lungs
- Must of course be non toxic.

ULTRASOUND CONTRAST APPLICATIONS

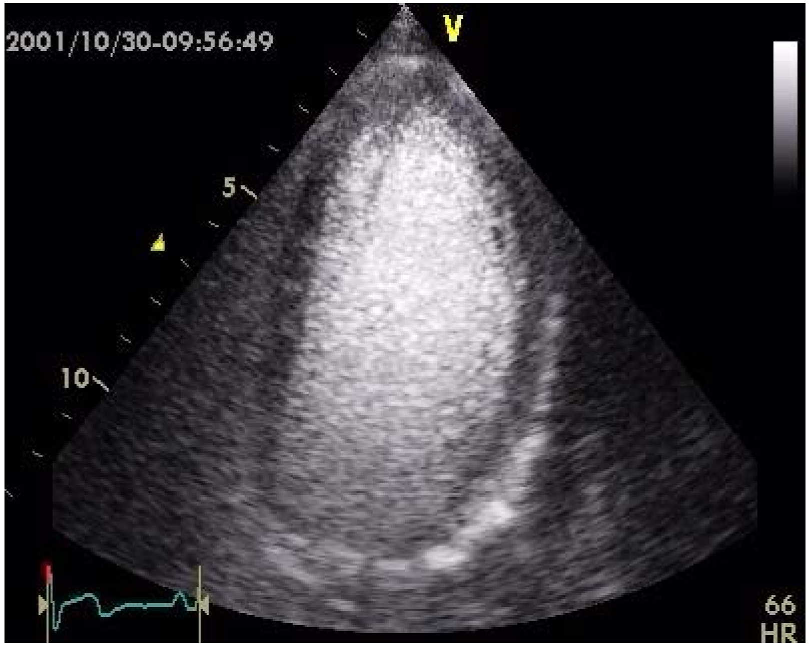


EXAMPLE ON LEFT VENTRICULAR OPACIFICATION (LVO)

2nd Harmonic Imaging



Contrast Imaging – LVO



Myocardial wall motion is difficult to assess in
~ 30% of the patients – despite 2.harmonic imaging !

CONTRAST AGENT IMAGING

- Is based on exciting small gas-filled microbubbles by an ultrasonic pulse, and receiving the sound radiated from these microbubbles.
- Is highly nonlinear
  - Harmonics
  - Differences between positive and negative pressure half-cycles
  - Sub-harmonics
  - etc.
- Enlighten the Tissue Harmonic Imaging

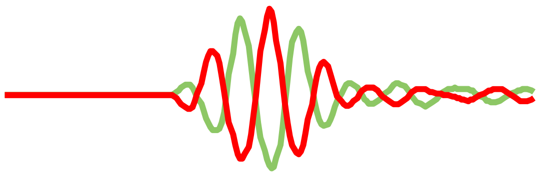
Detection techniques

- Harmonic imaging (second, third, subharmonic)
- Power Doppler
- Harmonic Power Doppler
- Pulse Inversion
- Pulse Inversion Angio
- Power Modulation (Amplitude Modulation)

PULSE INVERSION (PHASE INVERSION)

- **Tx:** transmitting two pulses p_1 and p_2 , where: $p_2 = -p_1$
- **Rx:** summing the two echoes: $e_{pi} = e_1 + e_2$

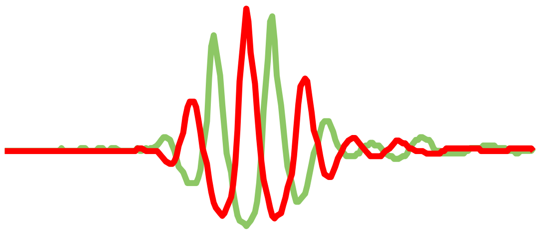
Linear:



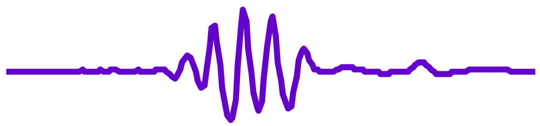
$e_2 = -e_1$

$e_{pi} = 0$

Non-Linear:



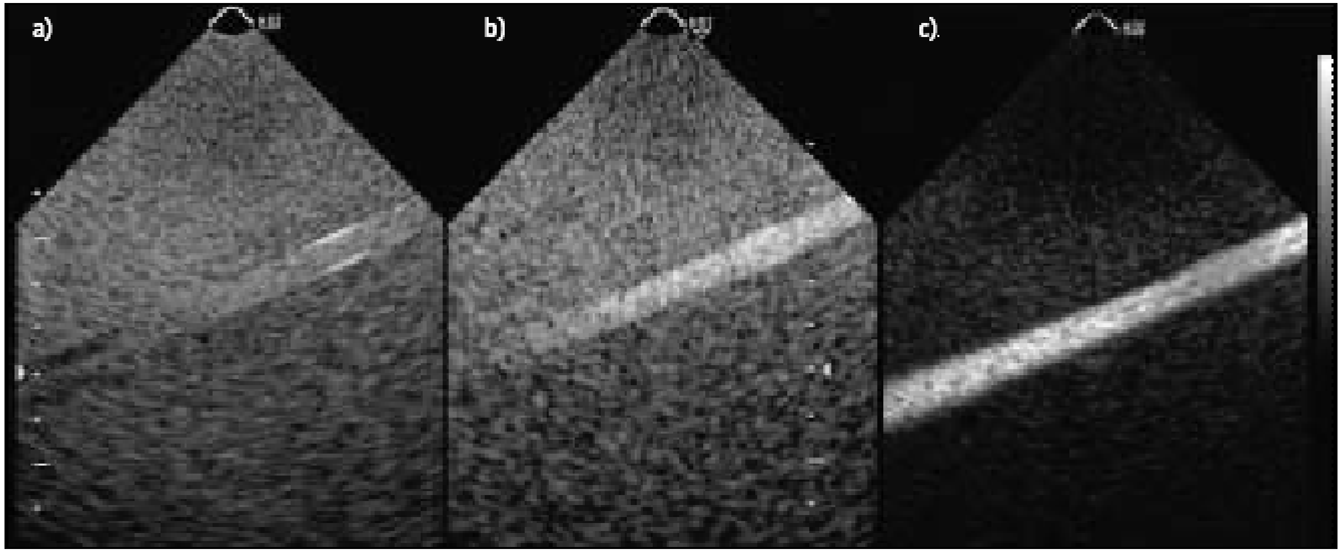
$e_2 \neq -e_1$



$e_{pi} \neq 0$

EXAMPLE ON PULSE INVERSION IMAGING

Fundamental | Second Harmonic | Pulse Inversion



Pulse Inversion Imaging

- Advantages:
  - Better Contrast/Tissue
  - Wide-band -> Better resolution
  - Also picking up contrast in motion

- Disadvantages:
  - Two pulses -> reduced frame rate
  - Tissue motion artifacts

MECHANICAL INDEX

- Mechanical Index is a standard measure of the acoustic output in a diagnostic ultrasound system, defined as:

$$MI = \frac{\hat{P}_{neg}\,(MPa)}{\sqrt{Freq(MHz)}}$$

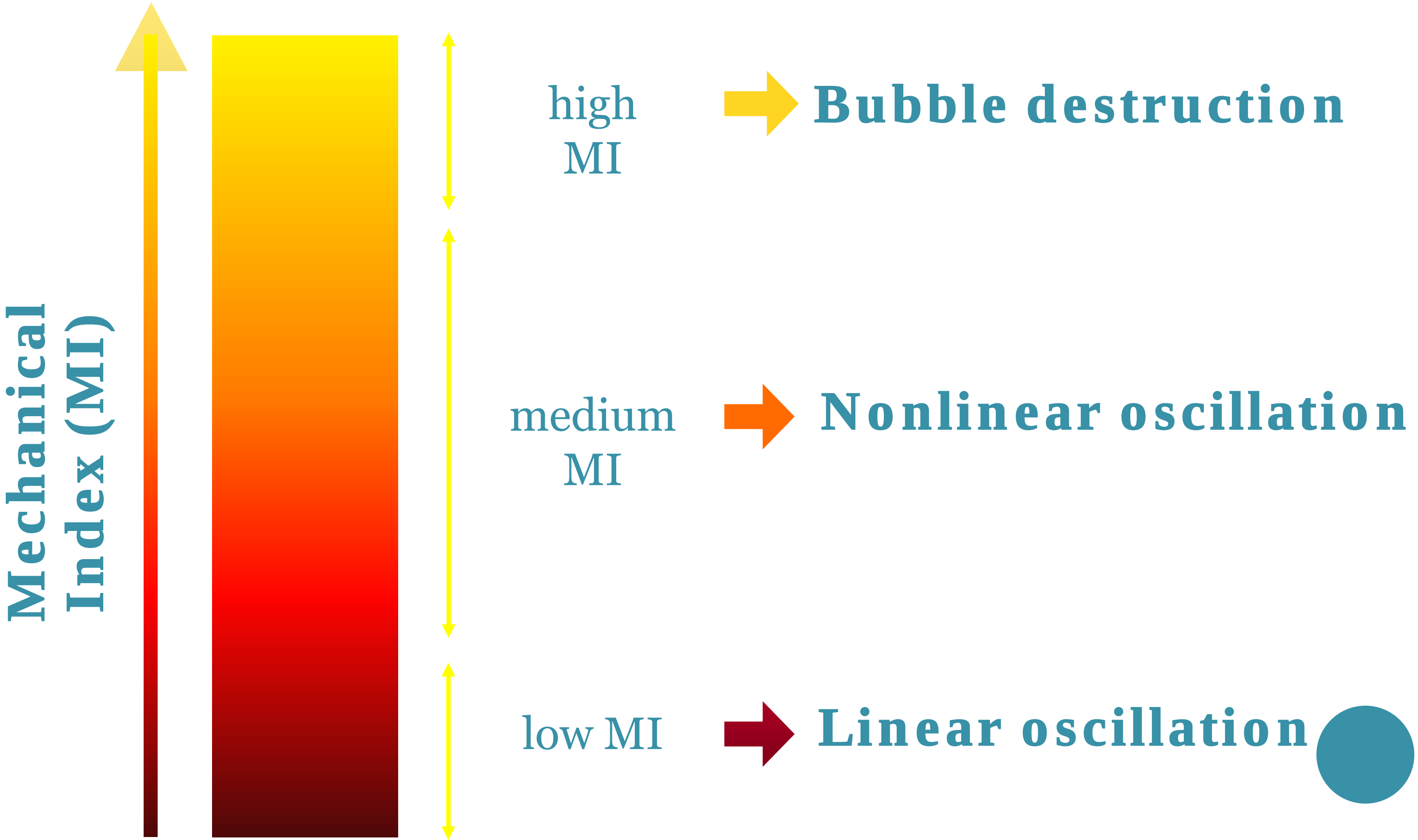
- Ex:

$$\hat{P}_{neg} = 1.0\ MPa$$

$$F = 1.0\ MHz$$

$$\Rightarrow \quad MI = 1.0$$

RESPONSE OF BUBBLES TO ULTRASOUND



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- Bubble and Shell models
- BubbleSim simulation program
  - Compromised model
  - Simulation examples

BUBBLE MODELS

- Rayleigh-Plesset equation
  - Describe a bubble in an incompressible liquid
  - No damping from sound radiation
- Rayleigh-Plesset with radiation damping: Trilling and Keller models
  - Includes liquid compressibility in the acoustic Mach-number M
  - Computational unstable for high Mach-numbers (negative inertia term)
- Gilmore's model
  - For large amplitude bubble oscillations

Shell Models

- For most contrast agents, the shell has major influence on the acoustic properties of the microbubbles and in general, it
  - Makes the bubble stiffer than a free gas bubble
    - Higher resonance frequency
    - Limited oscillation amplitude
  - Makes the bubble more viscous
    - More absorption
    - Low scatter to attenuation ratio
- **Church** presented a non-linear *theoretical* model for shell-encapsulated bubbles in 1995 which is the basis of BubbleSim.
  - Does not give information about the nonlinear stress-strain relationship of the shell
- Nonlinear *ad hoc* model added exponential stress-strain relationship for the shell

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Compromised Model

- Bubble model
  - Start from R-P model with damping term from Trilling and Keller models
  - Omit the correction terms of first-order in the Mach-number
  - Avoid the unphysical negative inertia and associated numerical instability problem
  - Is easy to implement using standard numerical software packages
- Shell model
  - Modeled by using Church's visco-elastic model, with the exponential stress-strain relationship proposed by Angelsen et al.

Bubble response

- The particle radius *a(t)* is

$$a(t)=a_e(1+x(t)), \quad |x(t)|\ll 1.$$

  and radial oscillation

$$\hat{x}(\omega)=\frac{1}{\Omega^2-1-i\Omega\delta}\frac{\hat{p}_i(\omega)}{\rho_L\omega_0^2a_e^2}, \quad \Omega=\frac{\omega}{\omega_0}.$$

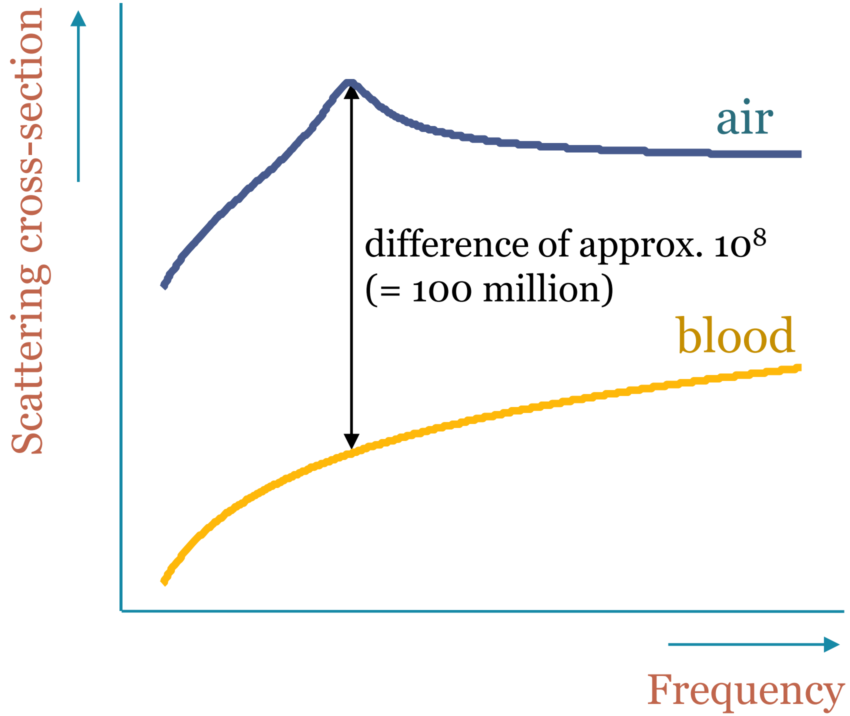
  is the Fourier Transform of *x(t)*
- At certain frequency, $x(\omega)$ is proportional to $p_i(\omega)$
- At fixed $p_i(\omega)$, $x(\omega)$ is a bandpass function with resonant frequency of $(\omega_0/2\pi)$.
- δ is the damping constant, represent the attenuation of the sound

Scattering Cross Section (SCS)

- SCS in the model

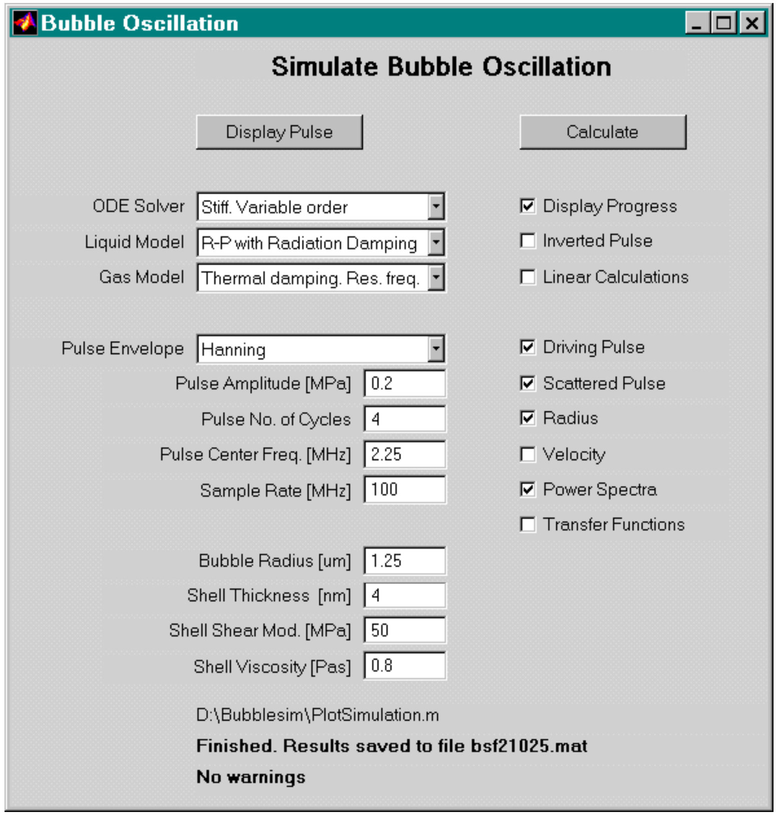
$$\sigma_S(a_e,\omega) = 4\pi a_e^2 \frac{\Omega^4}{(\Omega^2-1)^2+\Omega^2\delta^2}.$$

- At resonant, bubbles give even more scattering energy
- Both damping constant δ and normalized frequency Ω depend on the viscoelastic properties of the shell (G_s and μ_s)

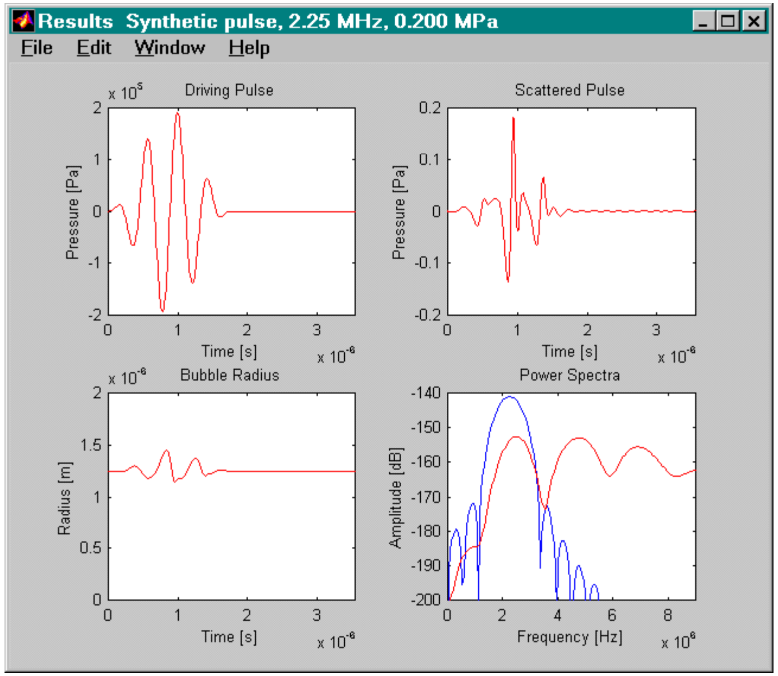


BUBBLESIM INTERFACE

Parameter setup panel



Result display



Demo …

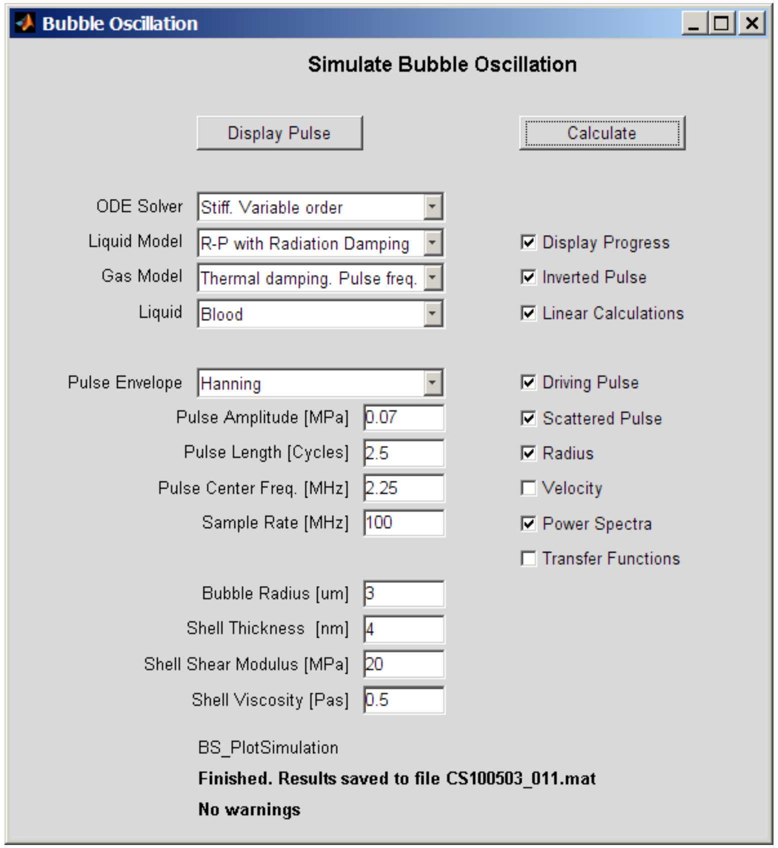
- Low MI

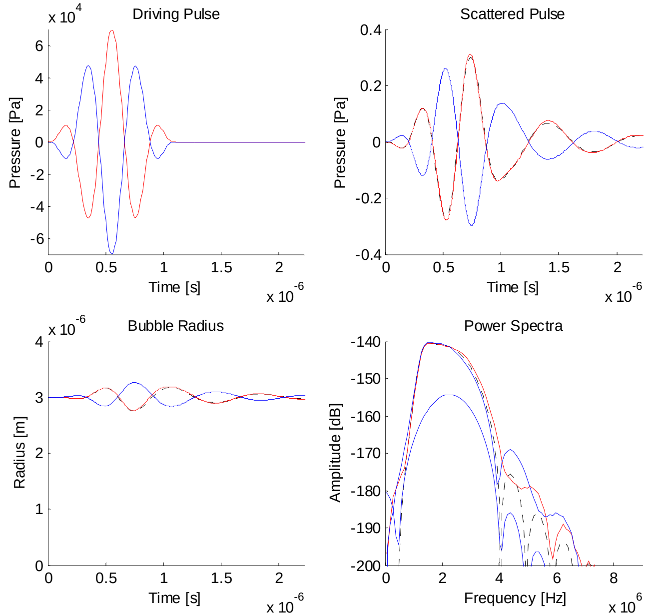
- Resonance
  - Linear resonate frequency:

$$f_0 = \frac{\omega_0}{2\pi} = \frac{1}{2\pi a_e}\sqrt{\frac{1}{\rho_L}\left(3\kappa p_0 + 12 G_S \frac{d_{Se}}{a_e}\right)}.$$

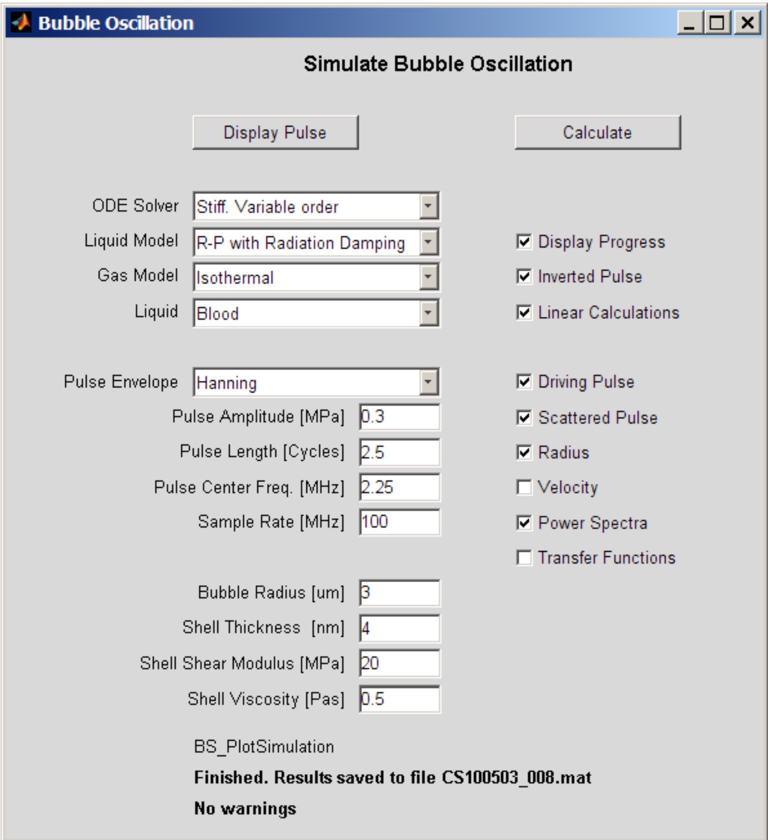
- High MI

Low MI

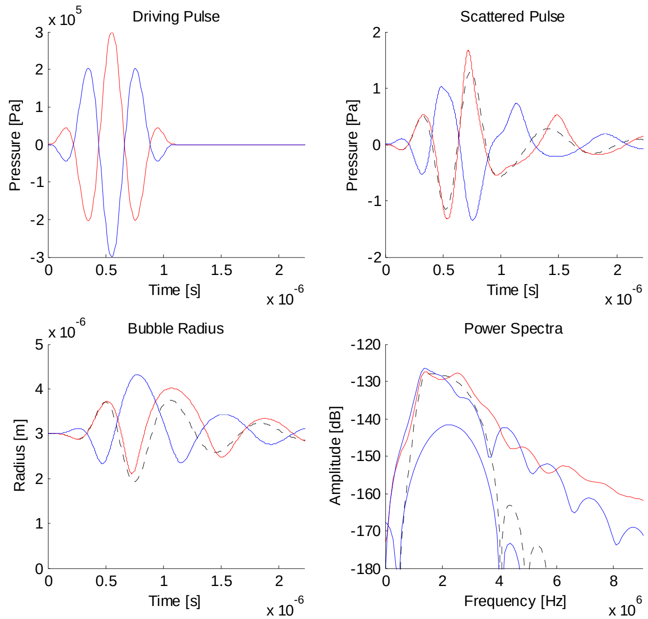

Bubble Oscillation
Simulate Bubble Oscillation
Display Pulse
Calculate
ODE Solver
Stiff. Variable order
Liquid Model
R-P with Radiation Damping
Gas Model
Thermal damping. Pulse freq.
Liquid
Blood
Display Progress
Inverted Pulse
Linear Calculations
Pulse Envelope
Hanning
Pulse Amplitude [MPa]
0.07
Pulse Length [Cycles]
2.5
Pulse Center Freq. [MHz]
2.25
Sample Rate [MHz]
100
Driving Pulse
Scattered Pulse
Radius
Velocity
Power Spectra
Transfer Functions
Bubble Radius [um]
3
Shell Thickness [nm]
4
Shell Shear Modulus [MPa]
20
Shell Viscosity [Pas]
0.5
BS_PlotSimulation
Finished. Results saved to file CS100503_011.mat
No warnings


Driving Pulse
Pressure [Pa]
Time [s]
Scattered Pulse
Pressure [Pa]
Time [s]
Bubble Radius
Radius [m]
Time [s]
Power Spectra
Amplitude [dB]
Frequency [Hz]

MEDIUM MI

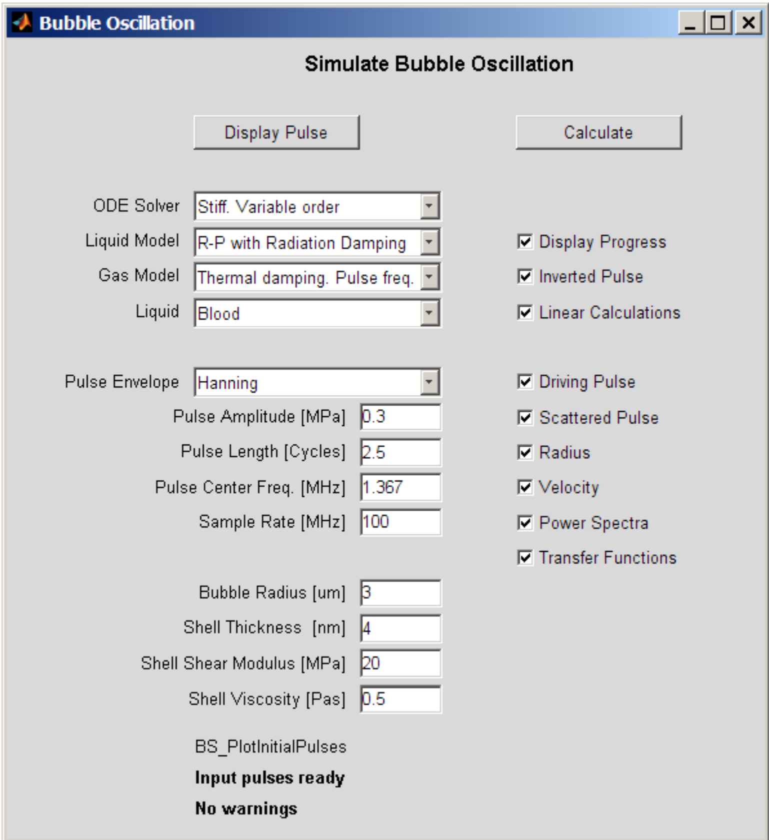


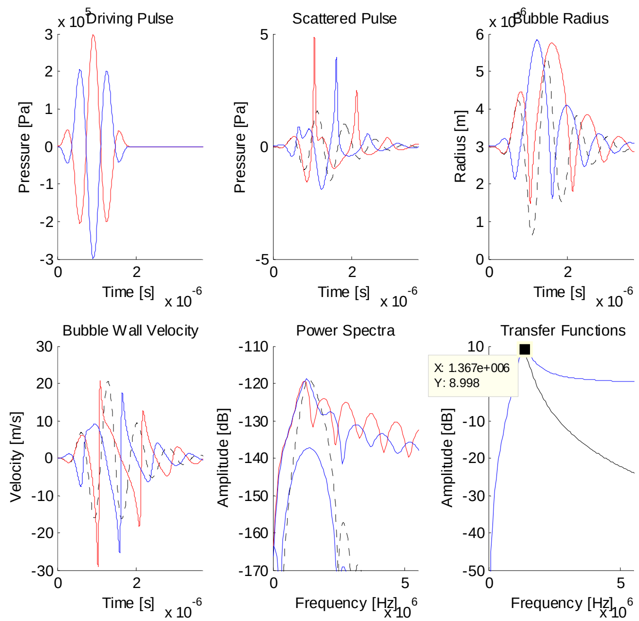
Bubble Oscillation
Simulate Bubble Oscillation
Display Pulse
Calculate
ODE Solver
Stiff. Variable order
Liquid Model
R-P with Radiation Damping
Gas Model
Isothermal
Liquid
Blood
Pulse Envelope
Hanning
Pulse Amplitude [MPa]
0.3
Pulse Length [Cycles]
2.5
Pulse Center Freq. [MHz]
2.25
Sample Rate [MHz]
100
Bubble Radius [um]
3
Shell Thickness [nm]
4
Shell Shear Modulus [MPa]
20
Shell Viscosity [Pas]
0.5
Display Progress
Inverted Pulse
Linear Calculations
Driving Pulse
Scattered Pulse
Radius
Velocity
Power Spectra
Transfer Functions
BS_PlotSimulation
Finished. Results saved to file CS100503_008.mat
No warnings



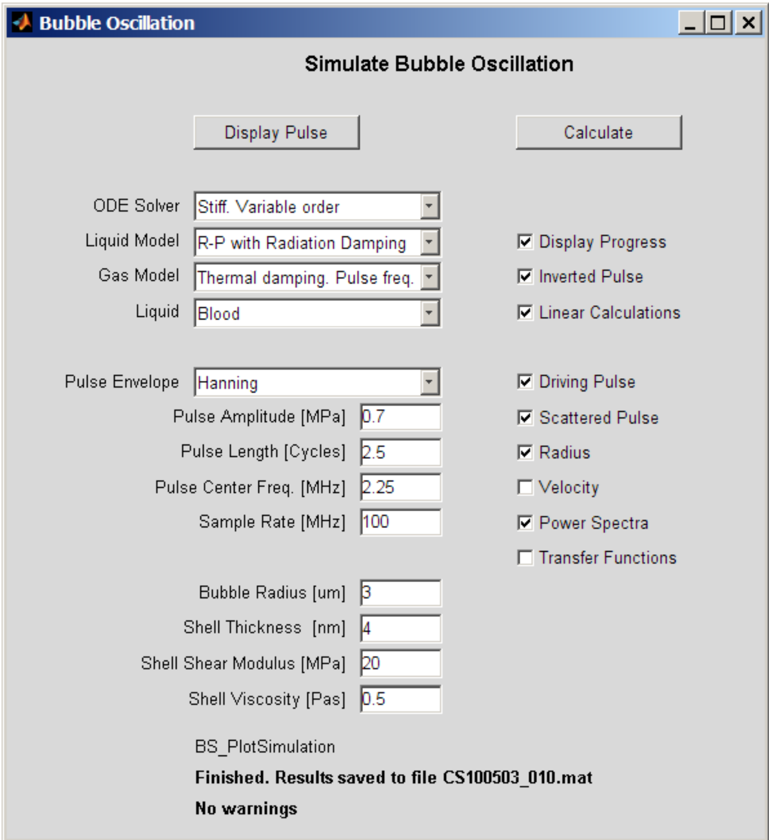
Driving Pulse
x 10^5
Pressure [Pa]
Time [s]
x 10^-6
Scattered Pulse
Pressure [Pa]
Time [s]
x 10^-6
Bubble Radius
x 10^-6
Radius [m]
Time [s]
x 10^-6
Power Spectra
Amplitude [dB]
Frequency [Hz]
x 10^6

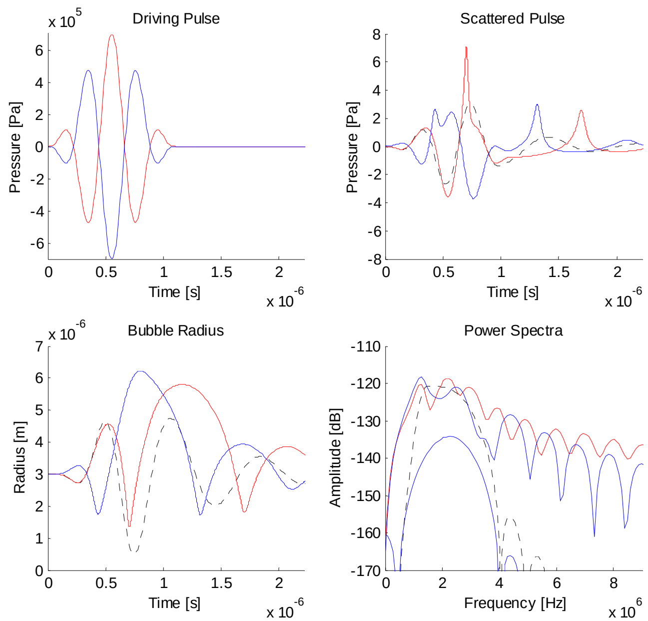
RESONATE


Bubble Oscillation
Simulate Bubble Oscillation
Display Pulse
Calculate
ODE Solver
Stiff. Variable order
Liquid Model
R-P with Radiation Damping
Gas Model
Thermal damping. Pulse freq.
Liquid
Blood
Display Progress
Inverted Pulse
Linear Calculations
Pulse Envelope
Hanning
Pulse Amplitude [MPa]
0.3
Pulse Length [Cycles]
2.5
Pulse Center Freq. [MHz]
1.367
Sample Rate [MHz]
100
Driving Pulse
Scattered Pulse
Radius
Velocity
Power Spectra
Transfer Functions
Bubble Radius [um]
3
Shell Thickness [nm]
4
Shell Shear Modulus [MPa]
20
Shell Viscosity [Pas]
0.5
BS_PlotInitialPulses
Input pulses ready
No warnings


Driving Pulse
Scattered Pulse
Bubble Radius
Pressure [Pa]
Radius [m]
Time [s]
Bubble Wall Velocity
Power Spectra
Transfer Functions
Velocity [m/s]
Amplitude [dB]
Frequency [Hz]
X: 1.367e+006
Y: 8.998

HIGH MI


Bubble Oscillation
Simulate Bubble Oscillation
Display Pulse
Calculate
ODE Solver
Stiff. Variable order
Liquid Model
R-P with Radiation Damping
Gas Model
Thermal damping. Pulse freq.
Liquid
Blood
Display Progress
Inverted Pulse
Linear Calculations
Pulse Envelope
Hanning
Pulse Amplitude [MPa]
0.7
Pulse Length [Cycles]
2.5
Pulse Center Freq. [MHz]
2.25
Sample Rate [MHz]
100
Driving Pulse
Scattered Pulse
Radius
Velocity
Power Spectra
Transfer Functions
Bubble Radius [um]
3
Shell Thickness [nm]
4
Shell Shear Modulus [MPa]
20
Shell Viscosity [Pas]
0.5
BS_PlotSimulation
Finished. Results saved to file CS100503_010.mat
No warnings


Driving Pulse
Pressure [Pa]
x 10^5
Time [s]
x 10^-6
Scattered Pulse
Pressure [Pa]
Time [s]
x 10^-6
Bubble Radius
Radius [m]
x 10^-6
Time [s]
x 10^-6
Power Spectra
Amplitude [dB]
Frequency [Hz]
x 10^6

Thanks

Reference

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