Non-Destructive Characterization of Ultrasound Contrast Agent

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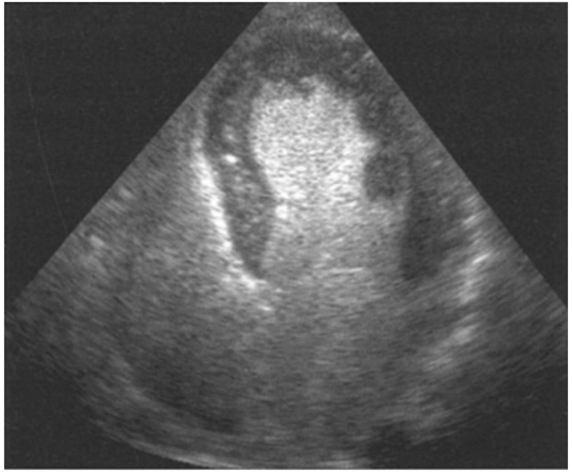
Supervisor: Dmitry Grishenkov

Motivation



Contrast enhanced harmonic image of the left ventricle *

- Ultrasound contrast agents used for image enhancement e.g. in echocardiography
- PVA shelled microbubbles: advantages over commercially available UCA
- Resonance frequency:

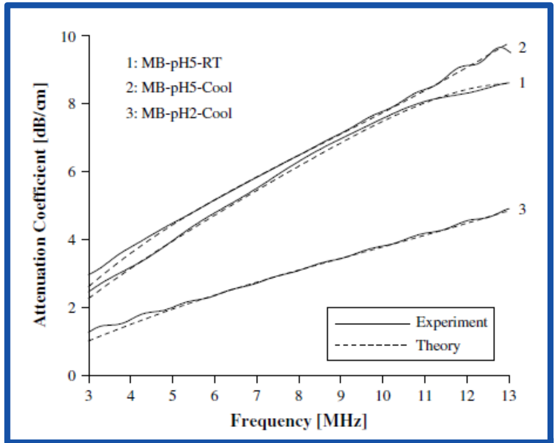
  Maximum oscillation => maximum scattering

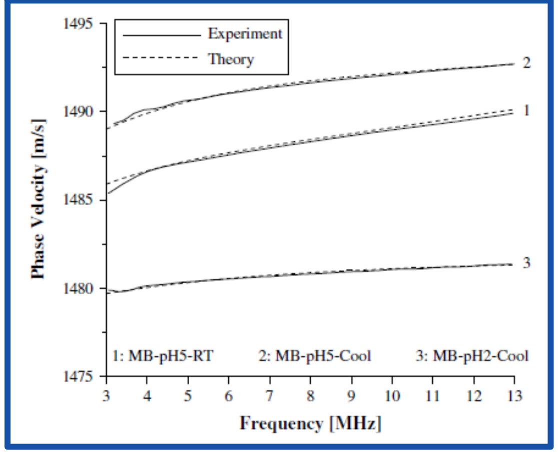
*Becher, Harald, and Peter N. Burns. Handbook of contrast echocardiography: Left ventricular function and myocardial perfusion. Springer Science & Business Media, 2012.

Motivation

- Grishenkov:*
  - One broadband transducer f =10 MHz
- Hoff:**
  - Model thin shelled MB

Aim: Create procedure to determine shell parameters and resonance frequency of different MB suspensions reproducible, easy and fast





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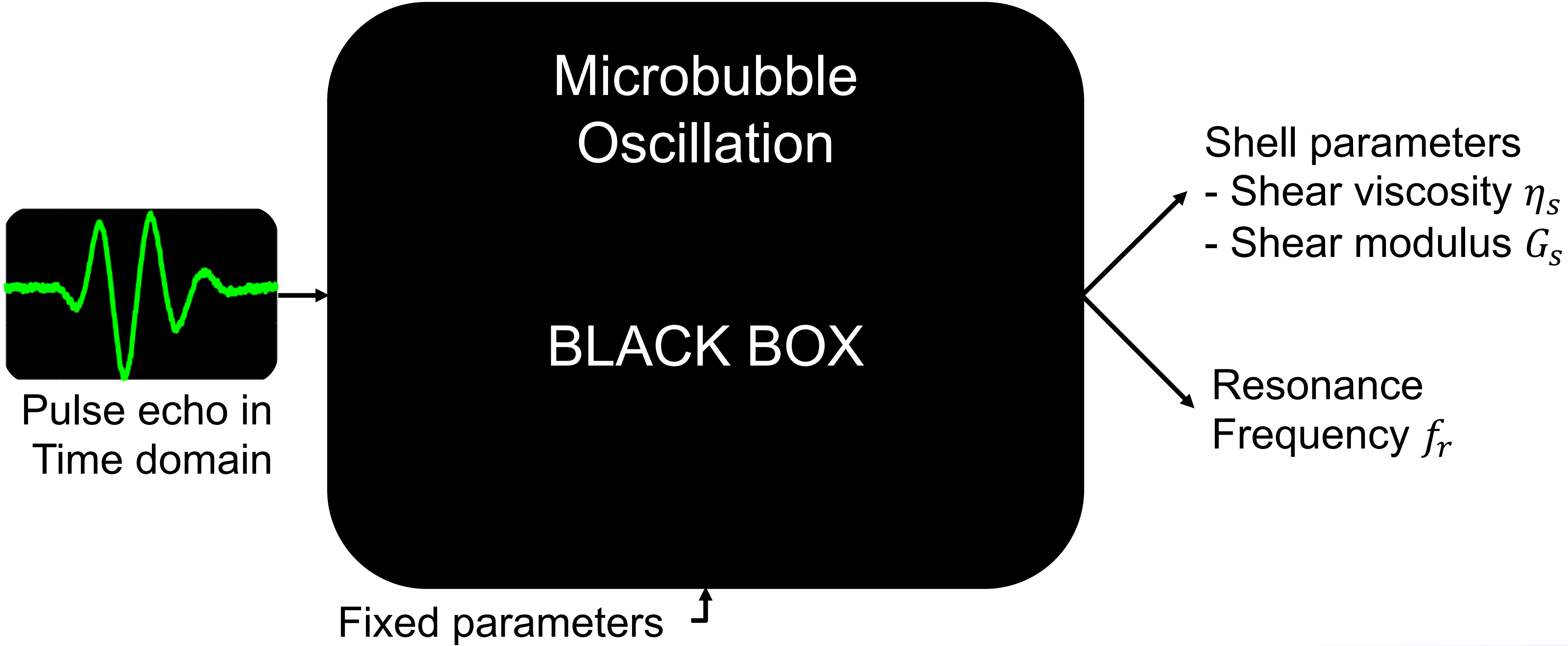
* Dmitry Grishenkov et al. “Characterization of acoustic properties of PVA-shelled ultrasound contrast agents: linear properties (part I)”. In: Ultrasound in medicine&biology 35.7 (2009), pp. 1127–1138.

** Lars Hoff. Acoustic characterization of contrast agents for medical ultrasound imaging. Springer Science & Business Media, 2001.

Agenda

- Project overview
- Experimental Methods
    - Experimental setup
    - Data evaluation
- Theoretical Approach
    - Modeling of a single MB
    - Model of suspension
- Results
- Conclusion and Future work

Project overview



Microbubble Oscillation

BLACK BOX

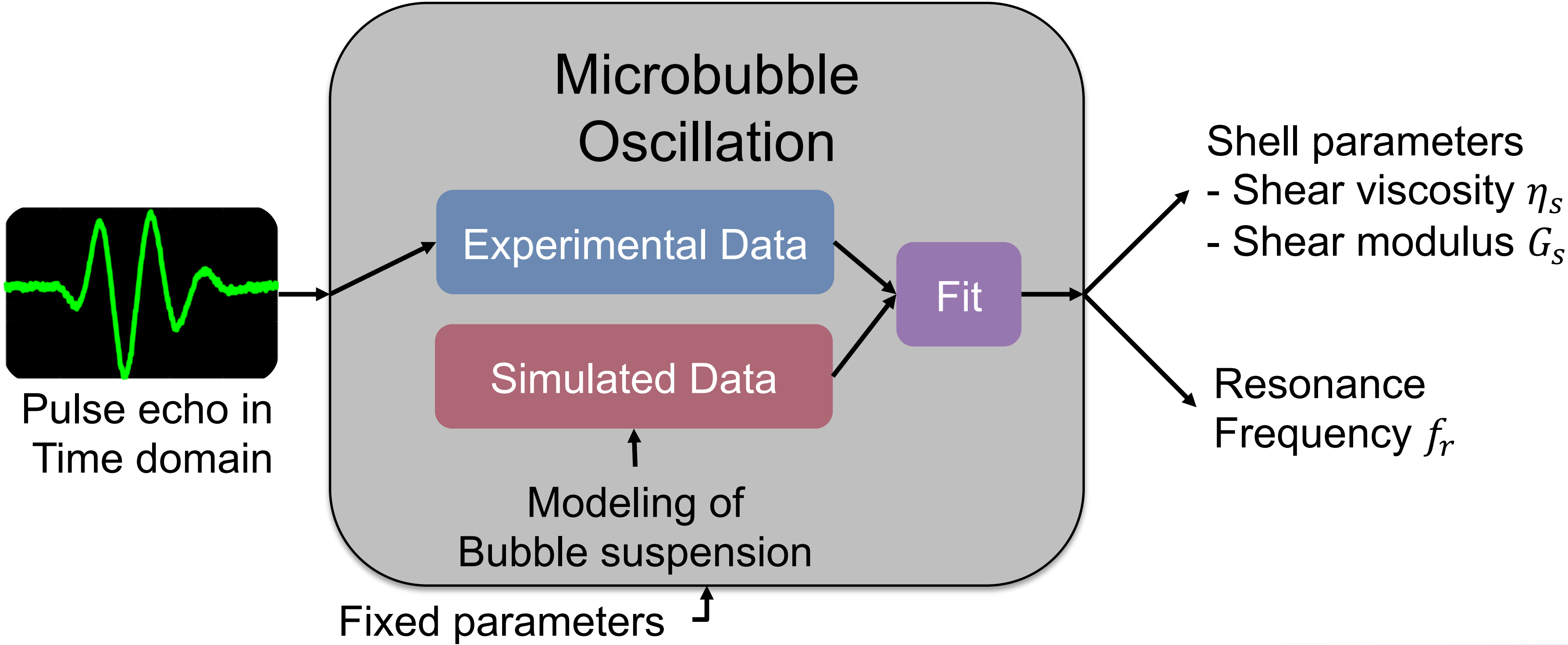
Pulse echo in Time domain

Shell parameters
- Shear viscosity η_s
- Shear modulus G_s

Resonance Frequency f_r

Fixed parameters

Project overview



Microbubble Oscillation

Experimental Data

Simulated Data

Fit

Modeling of Bubble suspension

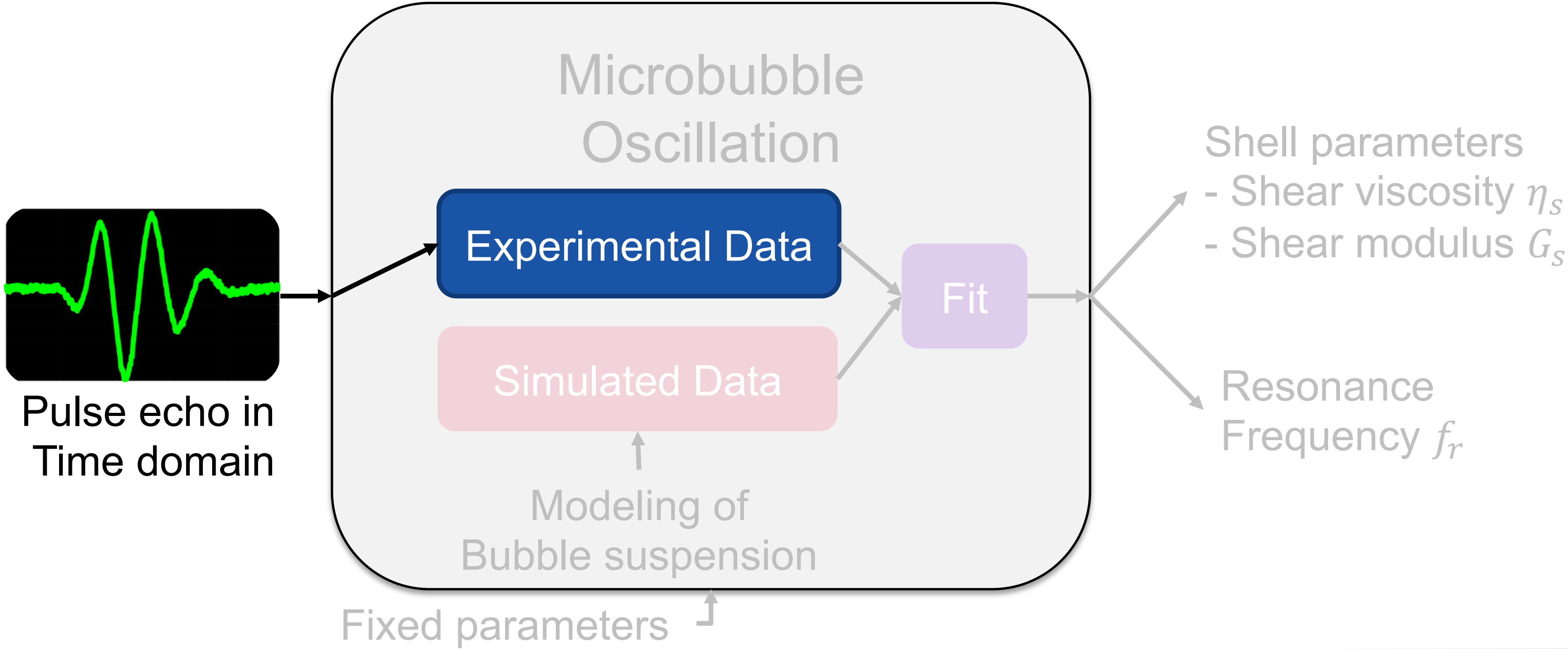
Fixed parameters

Pulse echo in Time domain

Shell parameters
- Shear viscosity η_s
- Shear modulus G_s

Resonance Frequency f_r

Project overview



Pulse echo in
Time domain

Microbubble
Oscillation

Experimental Data

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Bubble suspension

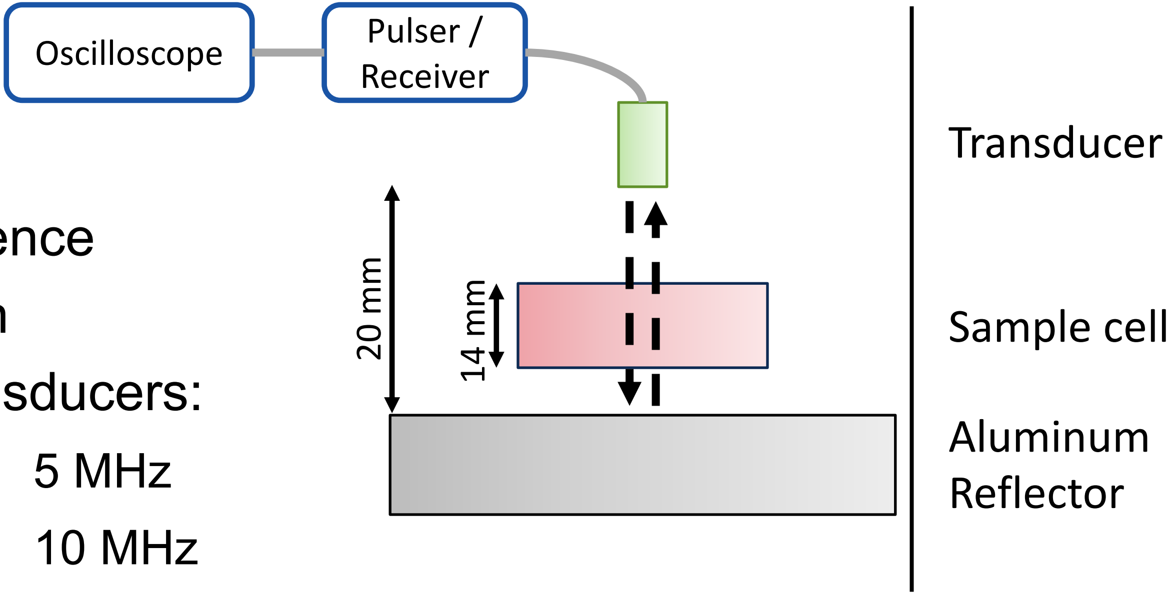
Fixed parameters

Shell parameters
- Shear viscosity η_s
- Shear modulus G_s

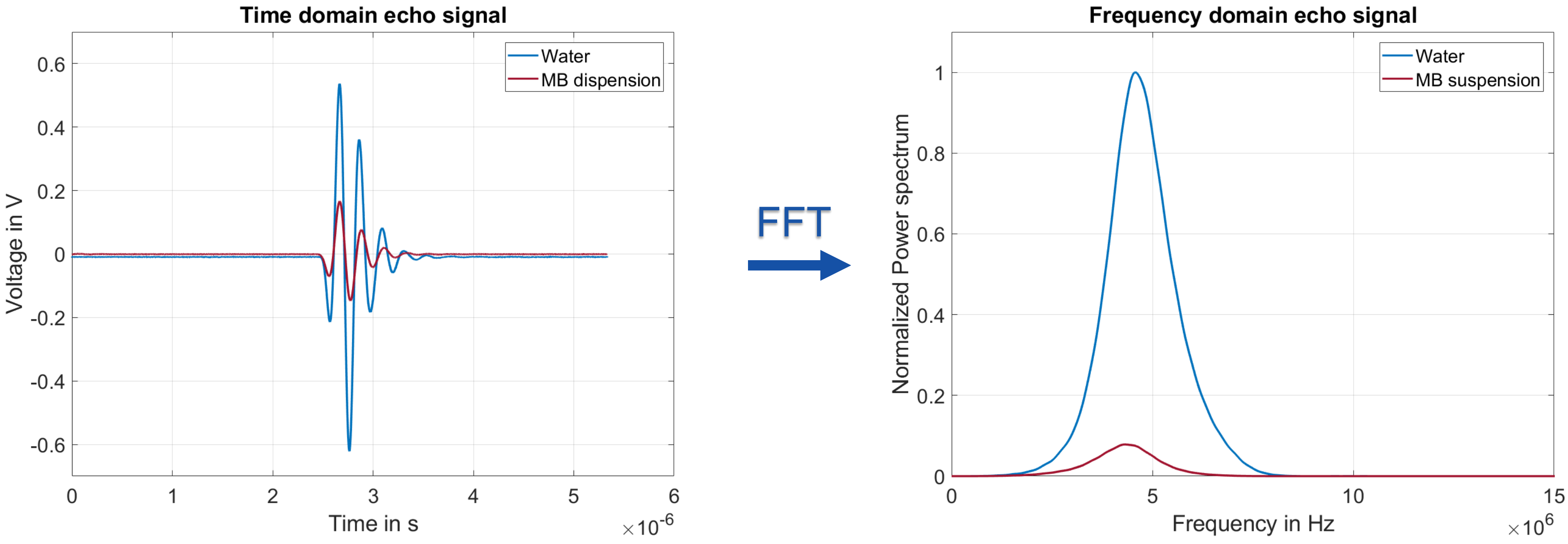
Resonance
Frequency f_r

Experimental Setup

- Two sample cells:
  - Water as reference
  - MB suspension
- Repeat with 6 transducers:
  - f_c: 1 MHz 5 MHz
    2.25 MHz 10 MHz
    3.5 MHz 15 MHz



Experimental Data



Time domain echo signal

FFT

Frequency domain echo signal

Characteristics

Attenuation

From Magnitude

Decline in magnitude of reflected signal

$$\alpha(\omega) = -\frac{20}{2L} \cdot \log\left(\frac{|F_{MB}(\omega, L)|}{|F_{ref}(\omega)|}\right)$$

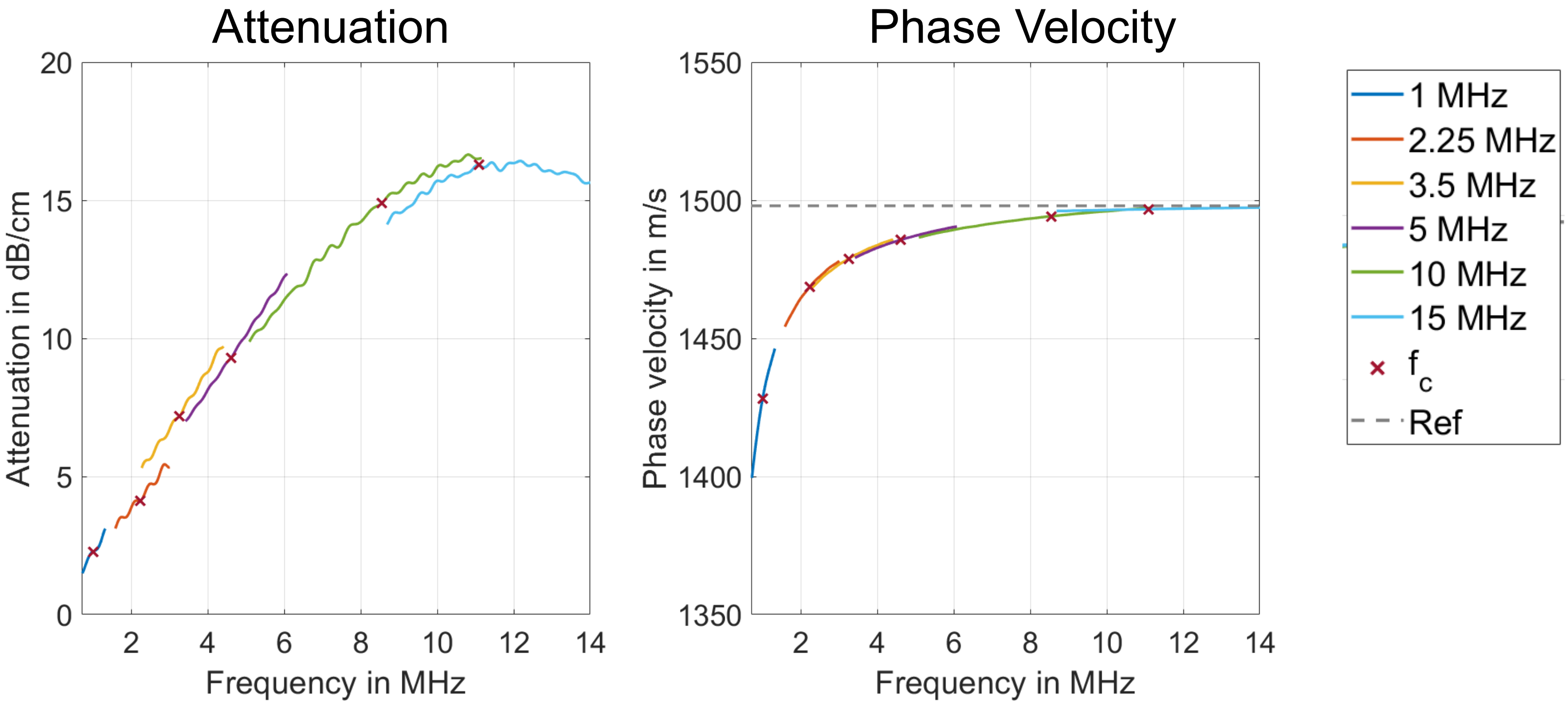
Phase Velocity

From Phase

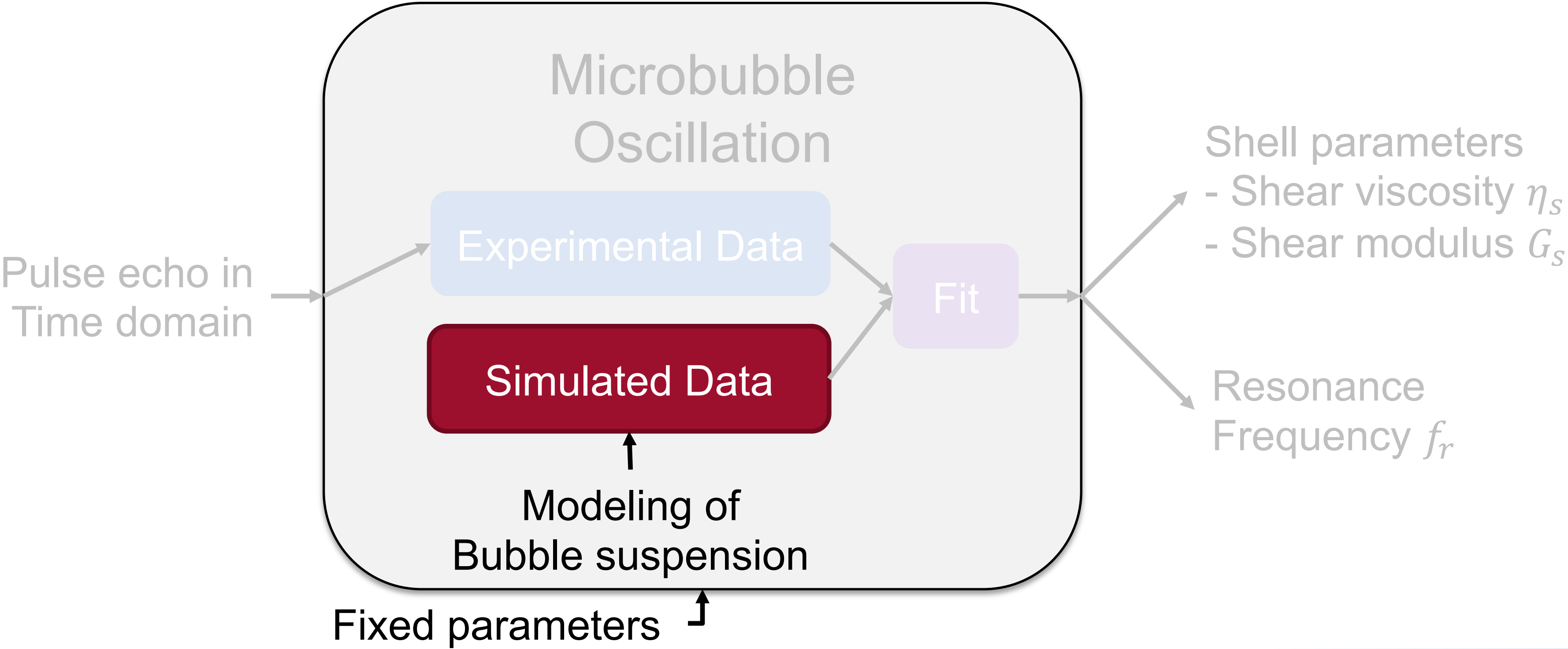
Rate at which the phase of a signal propagates in space

$$\frac{1}{c(\omega)} = \frac{1}{c_{ref}} - \frac{\varphi_{MB} - \varphi_{ref}}{2L\omega}$$

Experimental Results



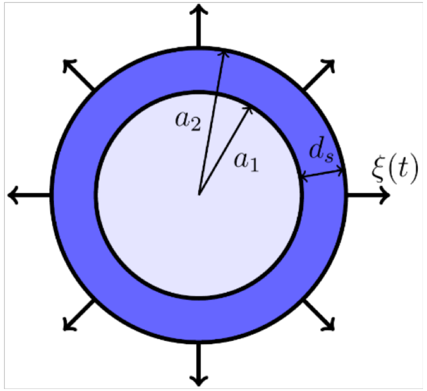
Project overview



Model of single Microbubble

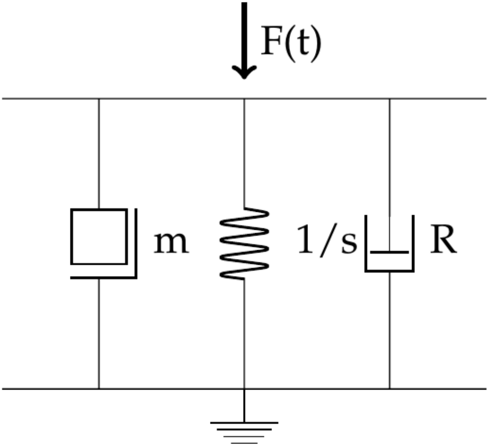
Linear oscillation:

$$a(t) = a_2 + \xi(t)$$



Equation of motion:

$$m\ddot{\xi} + R\dot{\xi} + s\xi = F(t)$$



Characteristics of
The oscillator

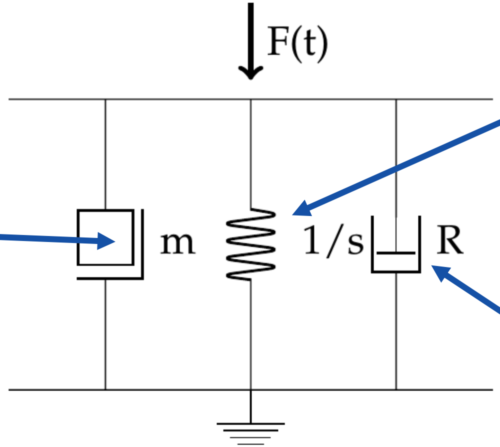
$$f_0 = \frac{1}{2\pi} \cdot \sqrt{\frac{s}{m}}$$

$$\delta = \frac{R}{2\pi f_0 \cdot m}$$

Components of the oscillator

Equation of motion:

$$m\ddot{\xi} + R\dot{\xi} + s\xi = F(t)$$



Mass of the PVA shell

Dynamic mass:

$$m = 4\pi a_2^3 \rho_L + \pi(a_2^2 - a_1^2)\rho_S$$

Mass of liquid set in motion
through bubble oscillation

Gas pressure
Inside bubble

Shell stiffness

Stiffness:

$$s = 12\pi a_2 \kappa p_0 + 48\pi G_s d_{se}$$

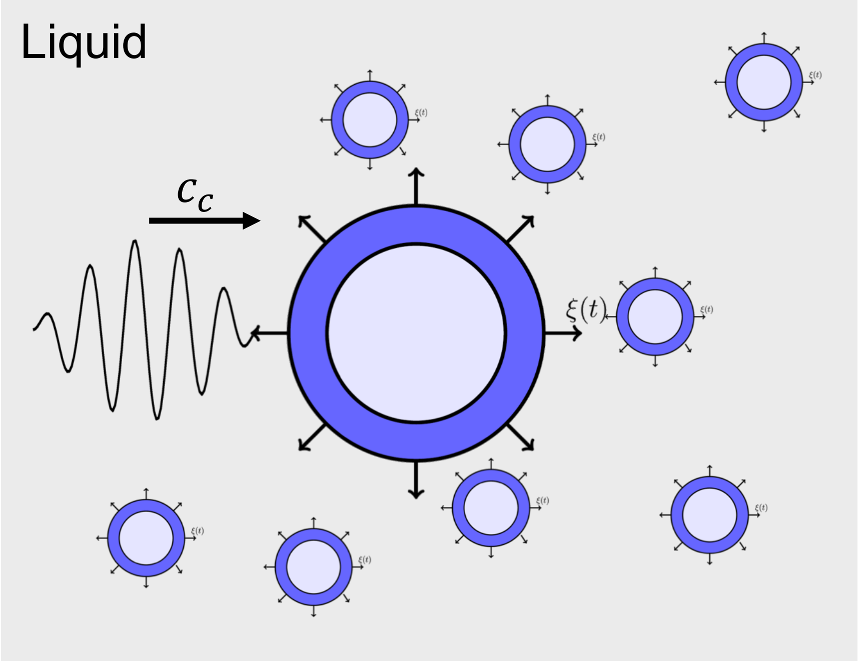
Damping:

$$R = \frac{\beta(a_1, a_2)}{\omega_0} \cdot (\mu_L a_1^3 + \mu_s(a_2^3 - a_1^3))$$

Viscous damping
Of liquid

Viscous damping of shell

Model for MB suspension



HOFF*: Radial strain function:

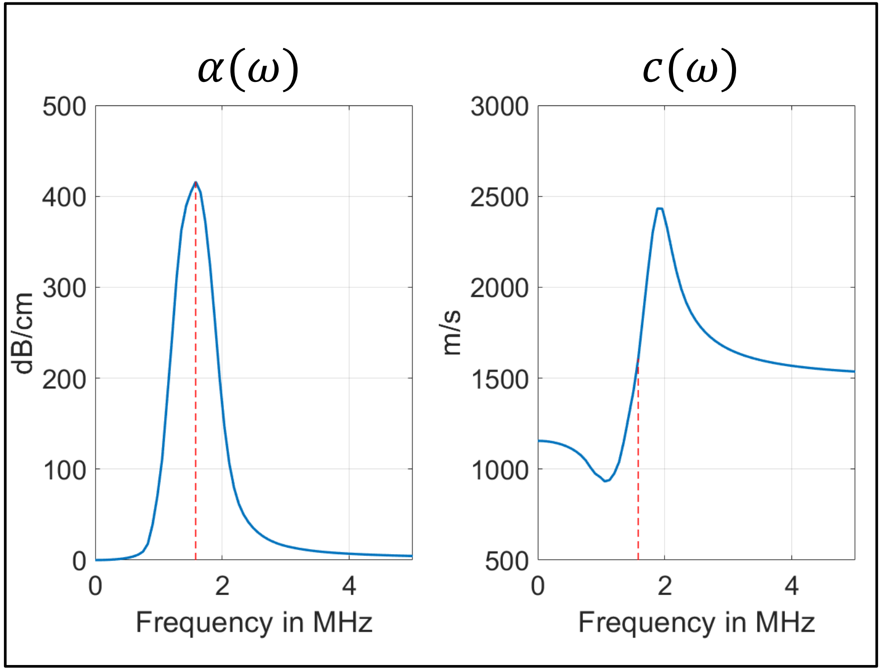
$$H\left(\frac{\omega}{\omega_0}\right) = \frac{1}{\frac{\omega}{\omega_0}^2 - 1 - j\frac{\omega}{\omega_0}\delta}$$

Sound velocity c_c in bubbly liquid:

$$\left(\frac{c_w}{c_c}\right)^2 = 1 - 4\pi c_w \cdot \int_0^\infty \frac{a_2}{\omega_0} H\left(\frac{\omega}{\omega_0}\right) n(a_2) da_2$$

* Lars Hoff. Acoustic characterization of contrast agents for medical ultrasound imaging. Springer Science & Business Media, 2001

Model for MB suspension



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Attenuation α and phase velocity c

$$\alpha(\omega) = -20\,\lg(e)\,Im(k_c)$$

$$c(\omega) = \frac{\omega}{Re(k_c)}$$

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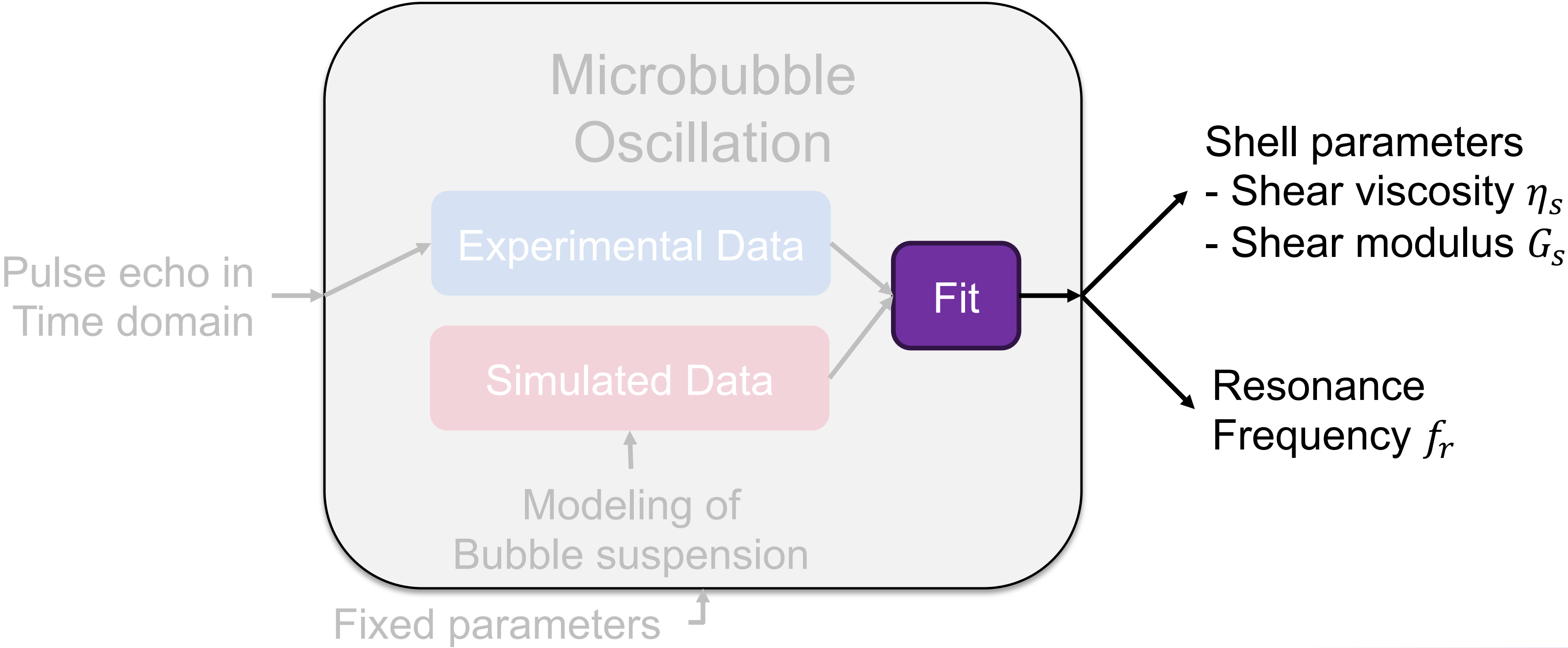
Project overview


Microbubble
Oscillation

Experimental Data

Simulated Data

Fit

Pulse echo in
Time domain

Modeling of
Bubble suspension

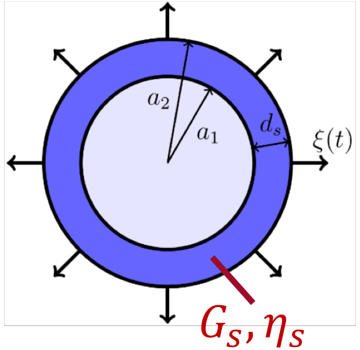
Fixed parameters

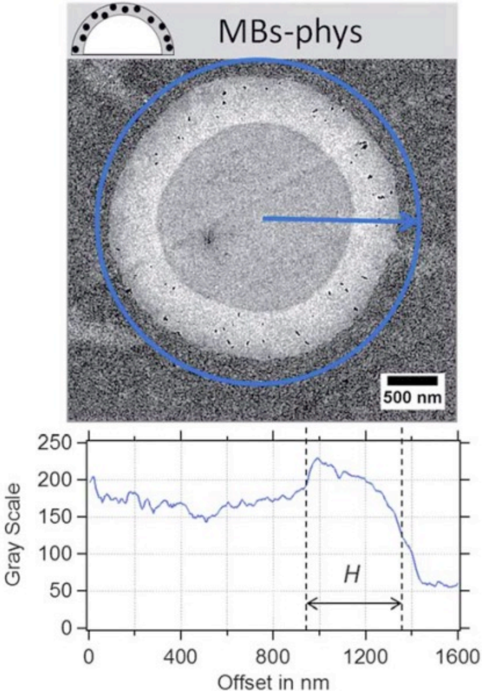
Shell parameters
- Shear viscosity η_s
- Shear modulus G_s

Resonance
Frequency f_r

Fit Model to Experimental Data

- Parameters to change:
  - Shear modulus of the shell G_s
  - Shear viscosity of the shell η_s
  - Shell thickness d_s





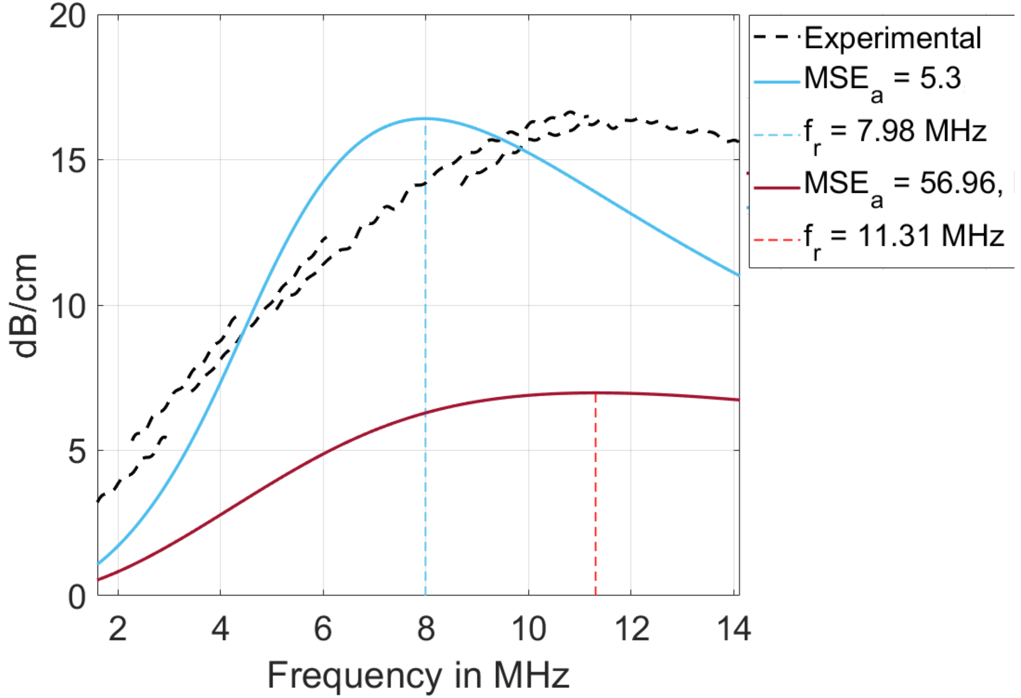
POEHLMANN *

* Melanie Poehlmann et al. “On the interplay of shell structure with low-and high-frequency mechanics of multifunctional magnetic microbubbles”. In: Soft Matter 10.1 (2014), pp. 214–226.

Fit to Model Experimental Data

- Optimize for:
  - Weighted MSE

$$MSE = \frac{1}{N}\sum_{i=1}^{N}(x_i - y_i)^2 \cdot sens_i$$



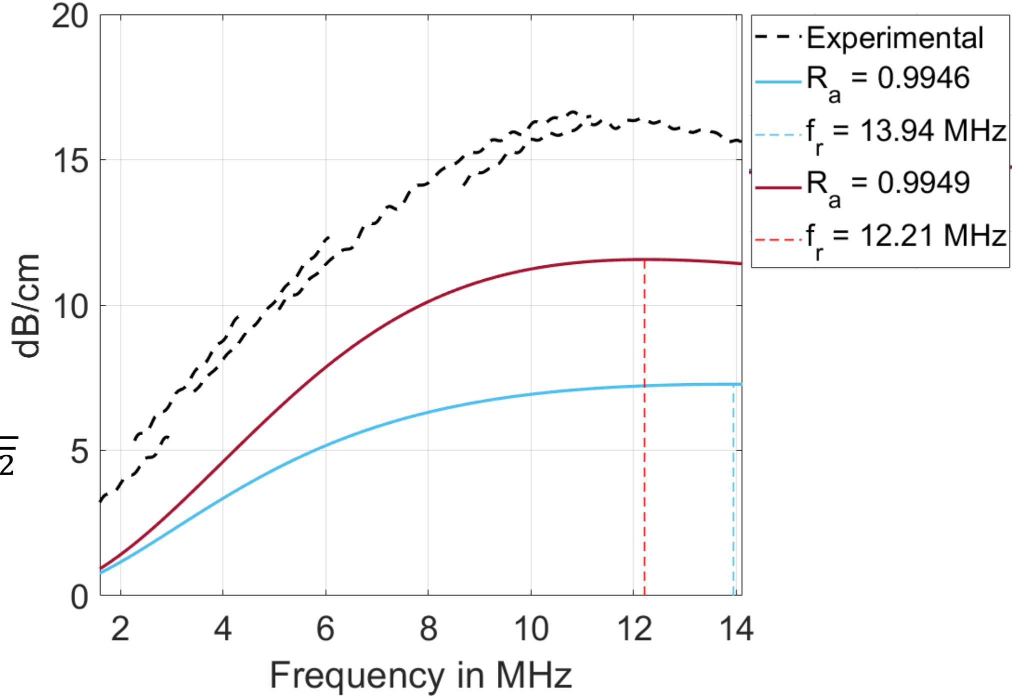
Fit to Model Experimental Data

- Optimize for:
  - Weighted MSE

$$MSE = \frac{1}{N}\sum_{i=1}^{N}(x_i - y_i)^2 \cdot sens_i$$

  - Cross correlation

$$R = \frac{N\sum xy - (\sum x)(\sum y)}{\sqrt{N(\sum x^2) - (\sum x)^2}\sqrt{N(\sum y^2) - (\sum y)^2}}$$



Fit to Model Experimental Data

- Optimize for:
  - Weighted MSE

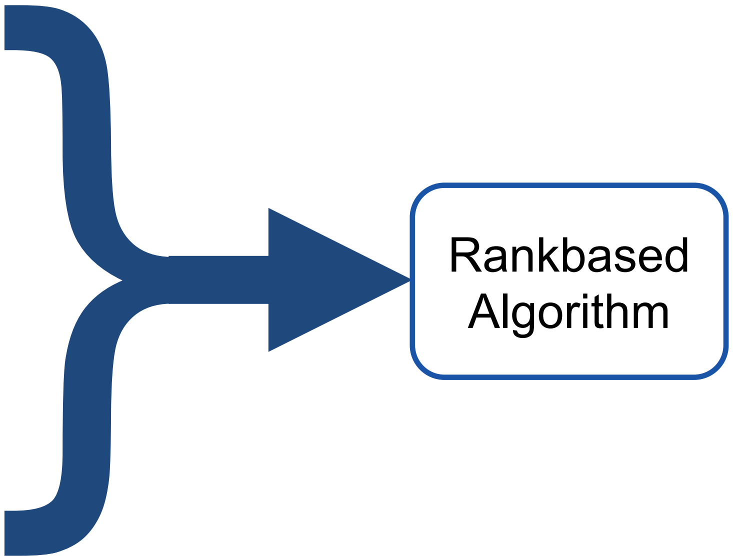
$$MSE = \frac{1}{N}\sum_{i=1}^{N}(x_i - y_i)^2 \cdot sens_i$$

  - Cross correlation

$$R = \frac{N\sum xy - (\sum x)(\sum y)}{\sqrt{N(\sum x^2) - (\sum x)^2}\sqrt{N(\sum y^2) - (\sum y)^2}}$$

  - Comparison of maxima

$$\Delta f_r = |f(x_{max}) - f(y_{max})|$$

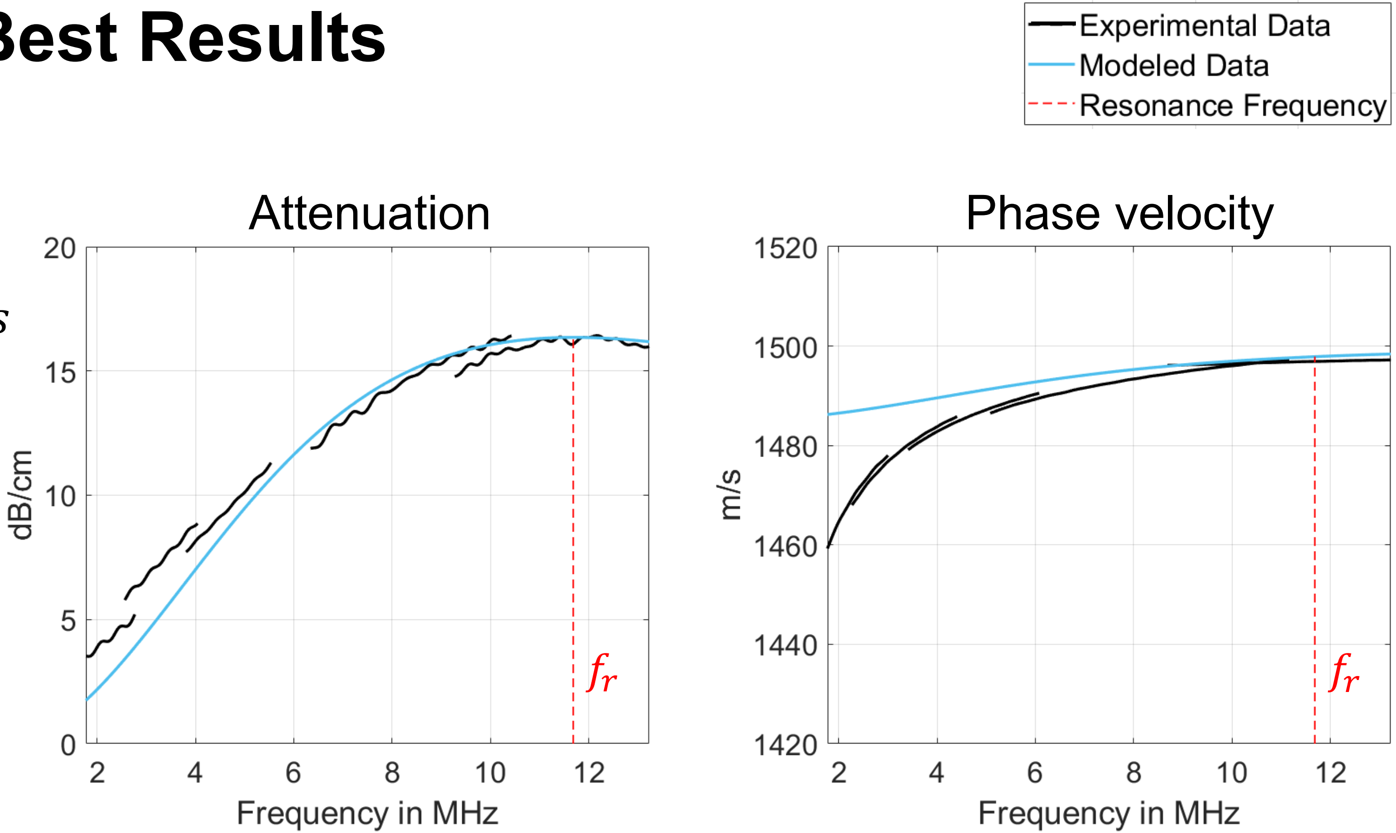


Rankbased Algorithm

Best Results

$G_s = 14.5\ MPa$
$\eta_s = 0.322\ Pa \cdot s$
$d_s = 0.16\ a_2$

$f_r = 11.68\ MHz$



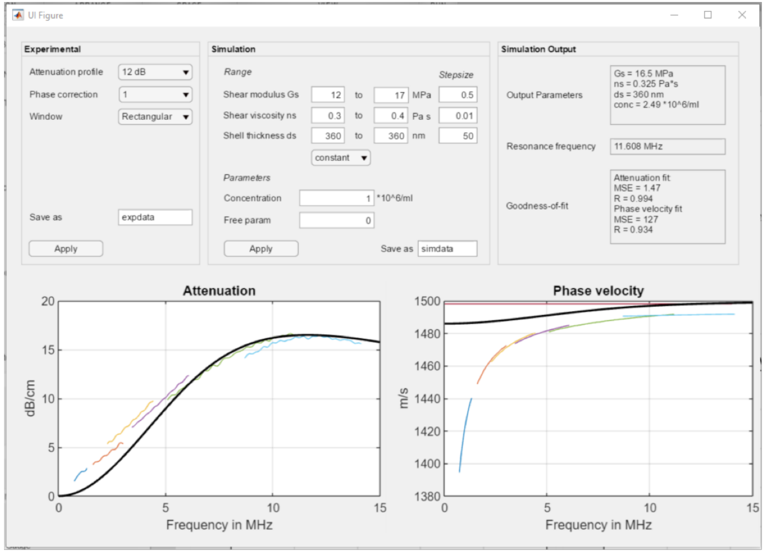
Summary

- Record and evaluate $\alpha(\omega)$ and $c(\omega)$ experimentally:
  - Higher accuracy for experimental data sets at broader frequency range
- Model $\alpha(\omega)$ and $c(\omega)$ profile:
  - Adjustment of HOFF‘s model for MB with thick shell
- Fit model to experimental data to estimate shell parameters and f_r of suspension
  - Consider both curves

Weaknesses / Future Work

- Refine assumption for shell thickness
- Adjust model for lower frequencies
- Integrate work into Matlab GUI

- Apply to new cellulose based MB
- Predict resonance frequency in different MB suspensions



UI Figure

Experimental

Attenuation profile: 12 dB
Phase correction: 1
Window: Rectangular
Save as: expdata

Simulation

Range / *Stepsize*
Shear modulus Gs: 12 to 17 MPa, 0.5
Shear viscosity ns: 0.3 to 0.4 Pa s, 0.01
Shell thickness ds: 360 to 360 nm, 50
constant

Parameters
Concentration: 1 *10^6/ml
Free param: 0
Save as: simdata

Simulation Output

Output Parameters:
Gs = 16.5 MPa
ns = 0.325 Pa*s
ds = 360 nm
conc = 2.49 *10^6/ml

Resonance frequency: 11.608 MHz

Goodness-of-fit:
Attenuation fit
MSE = 1.47
R = 0.994
Phase velocity fit
MSE = 127
R = 0.934

* Satya VVN Kothapalli et al. “Assessment of the viscoelastic and oscillation properties of a nano-engineered multimodality contrast agent”. In: Ultrasound in medicine & biology 40.10 (2014), pp. 2476–2487