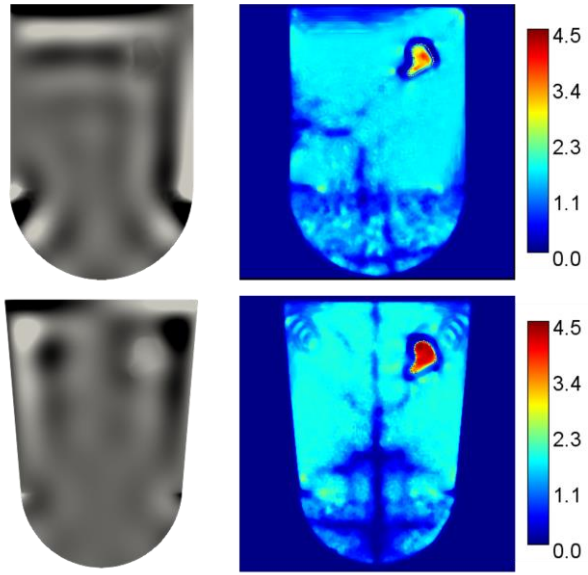

Simulation of shear wave propagation in soft tissue for elastography purposes

Aline Bel-Brunon[1], Simon A. Lambert[2]

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Introduction on biological tissues

Mechanical stimulus triggers cells reaction

Mechanotransduction

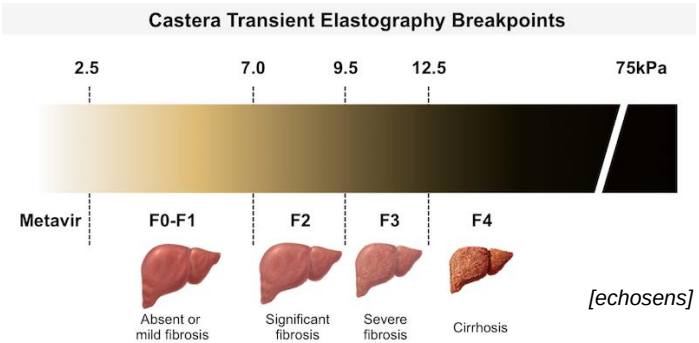
mechanics ⟶ biology

Growth, remodeling

Cells synthetize tissue to recover a mechanically stable state (homeostatic stress)

Material properties are modified by biological action

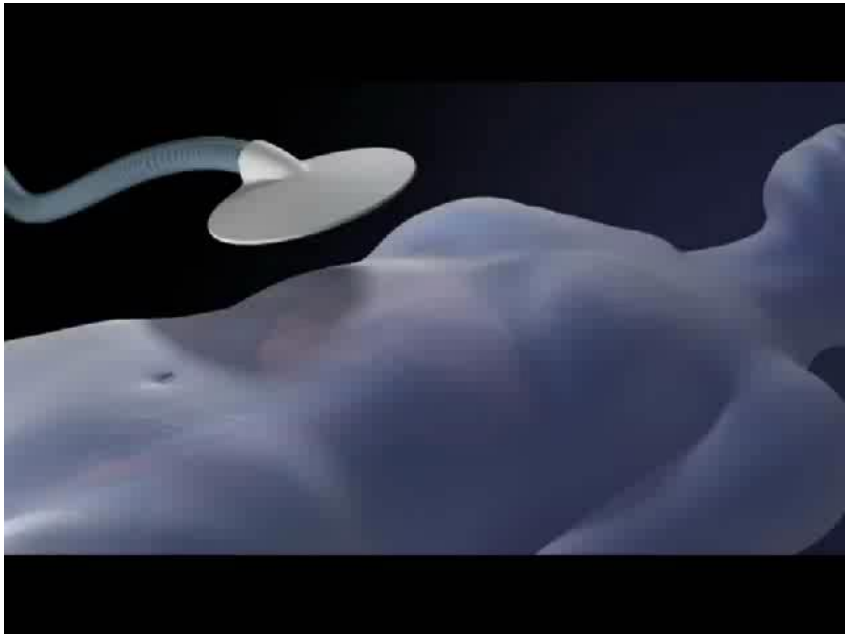
PATHOLOGY



[echosens]

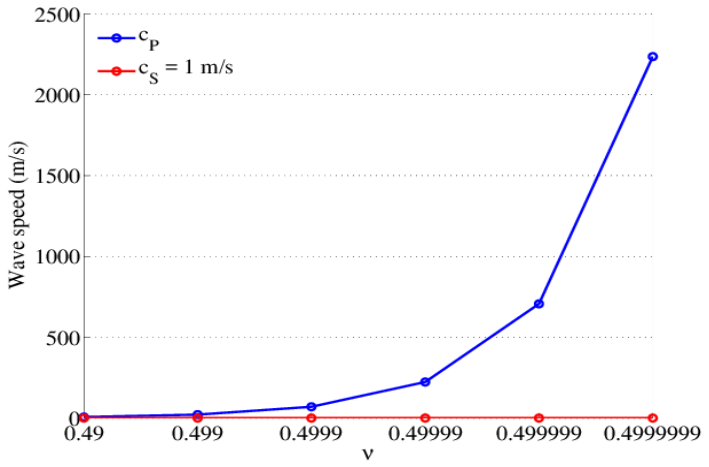
Elastography

- **In-vivo** characterization of soft tissue elasticity
- General principle: imaging shear wave propagation into a tissue to reconstruct a stiffness map
- Steps:
  1. Generating a mechanical wave
  2. Imaging wave propagation: US or MRI
  3. Reconstructing the stiffness field



Wave propagation in soft tissues

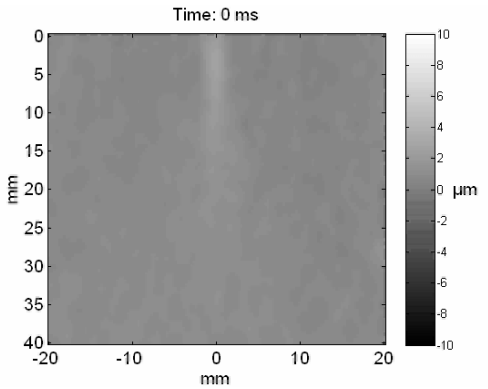
- In soft tissues, pressure waves propagate much faster than shear waves due to high incompressibility
  - $c_S \approx$ a few m/s
  - $c_P \approx 1500\ m/s$
- Shear waves are much more attenuated than pressure waves due to viscosity, especially at high frequency.
- Across interfaces, waves are transmitted, reflected and converted → experimentally, shear and pressure waves coexist.



Elastography - impactor

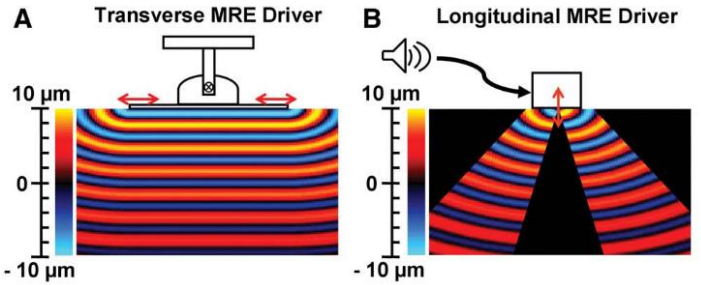
Acoustic radiation force

- Shock or harmonic excitation depending on the imaging modality



- Impactor shape and excitation direction impact the wave field

  → only the shear wave is imaged



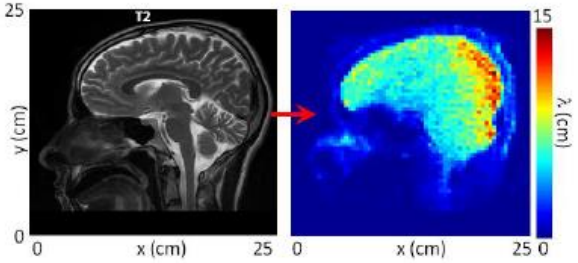
Yin et al., *Magnetic Resonance Imaging*, 2008

- Compromise between spatial resolution and wave penetration into the tissue:

High frequency ↔ High spatial resolution ↔ high attenuation

- Reconstruction often based on plane waves assumption

- More recently: passive elastography

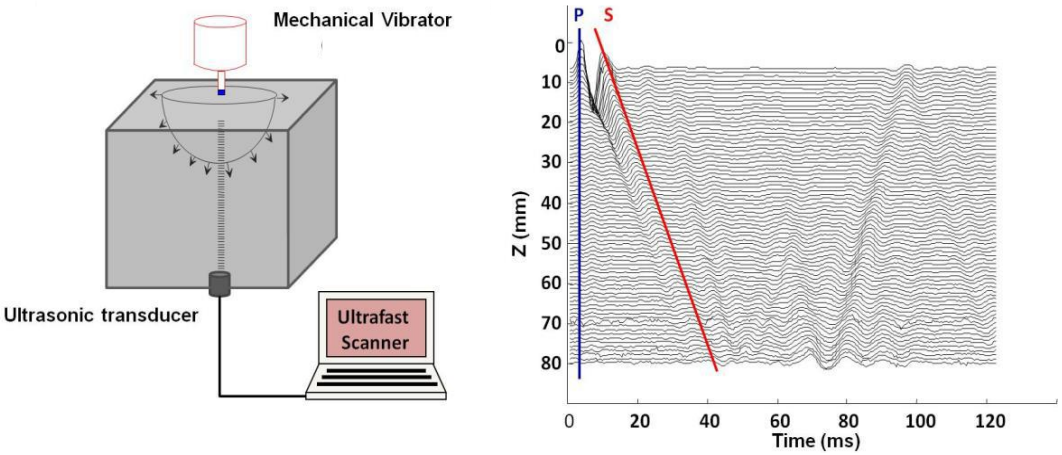


Passive brain MR elastography [Zorgani et al., PNAS, 2016]

Elastography – acquisition by US

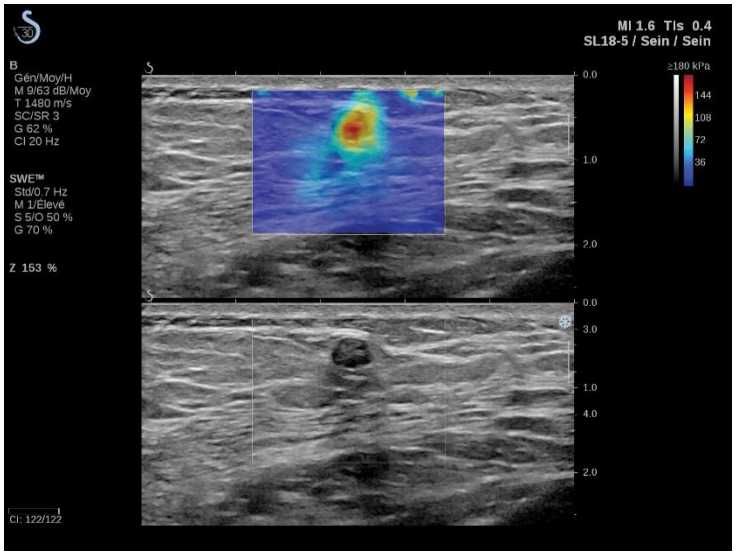
- Shear wave propagation measured using ultra-sound
- High temporal resolution (30 kHz for ultrafast probes)

  → possibility to image propagation itself!
- Imaging on a single line or in a slice, in one direction



[Catheline et al., IEEE, 1999]

Breast elastography

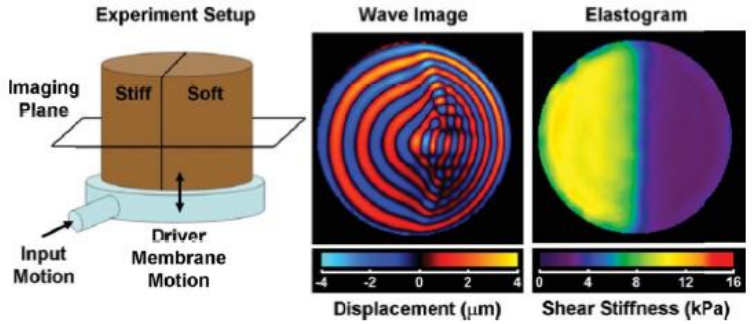


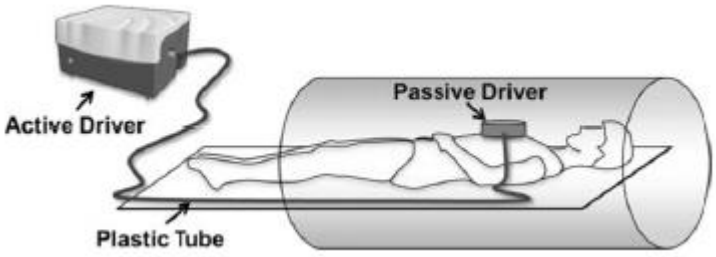
[Aixplorer website]

Elastography – acquisition by MRI

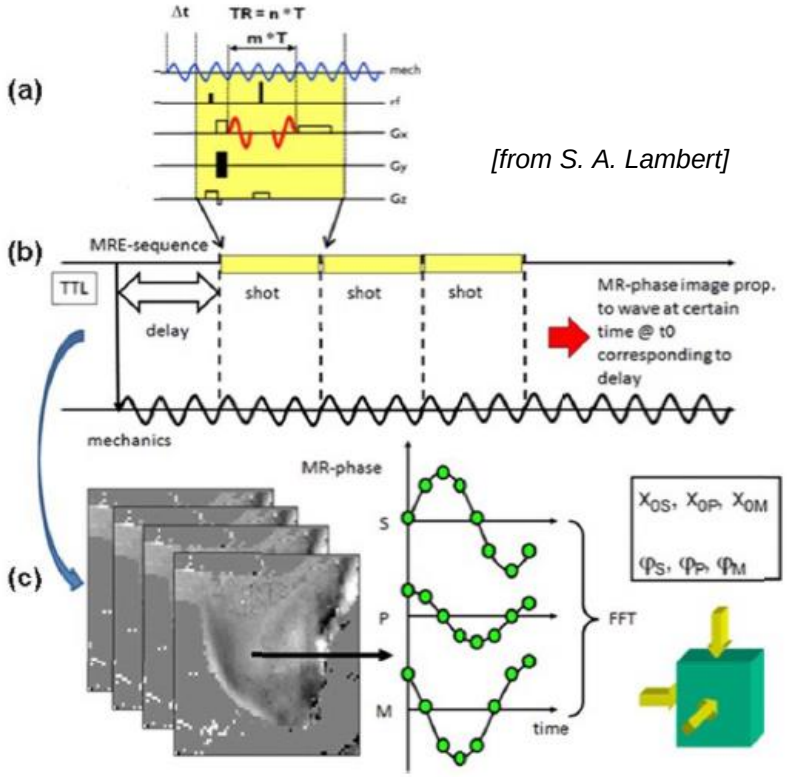
- Wave propagation imaged by MRI
- Much more complex process:
  1. Harmonic waves generation
  2. Snapshots acquisition
  3. Snapshots preprocessing (remove pressure from displacement signal)
- Data in the 3 directions of space

[Glaser et al. J Magn Reson Imaging 2012]





[Wassenaar et al., Magn Reson Med 2015]



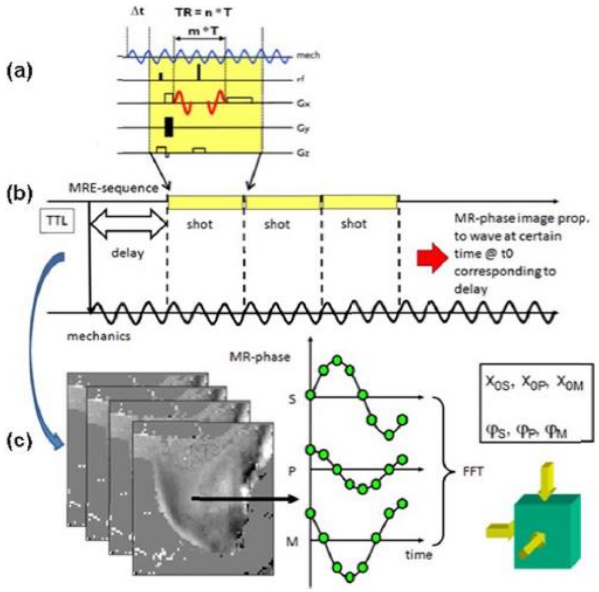
[from S. A. Lambert]

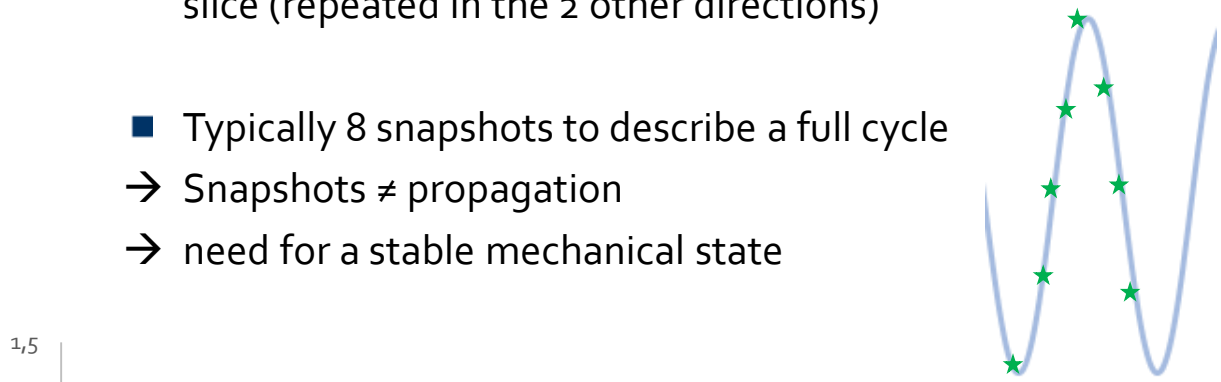
Elastography – acquisition by MRI

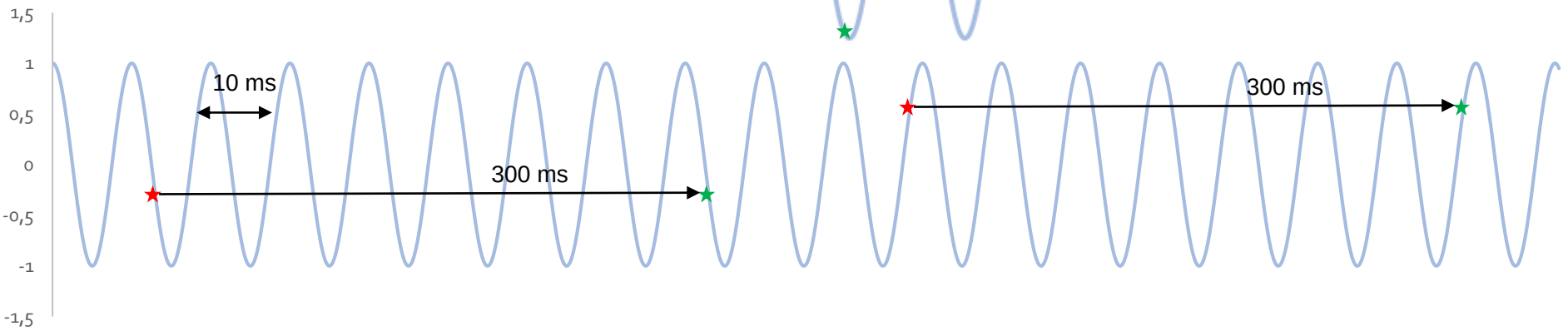
- A focus on MRI acquisition in MRE:
  - Typical mechanical frequency: 100 Hz
  - MRI acquisition: image generation in 300 ms / direction / slice (repeated in the 2 other directions)
  - Typically 8 snapshots to describe a full cycle

→ Snapshots ≠ propagation

→ need for a stable mechanical state







Elastography: reconstruction

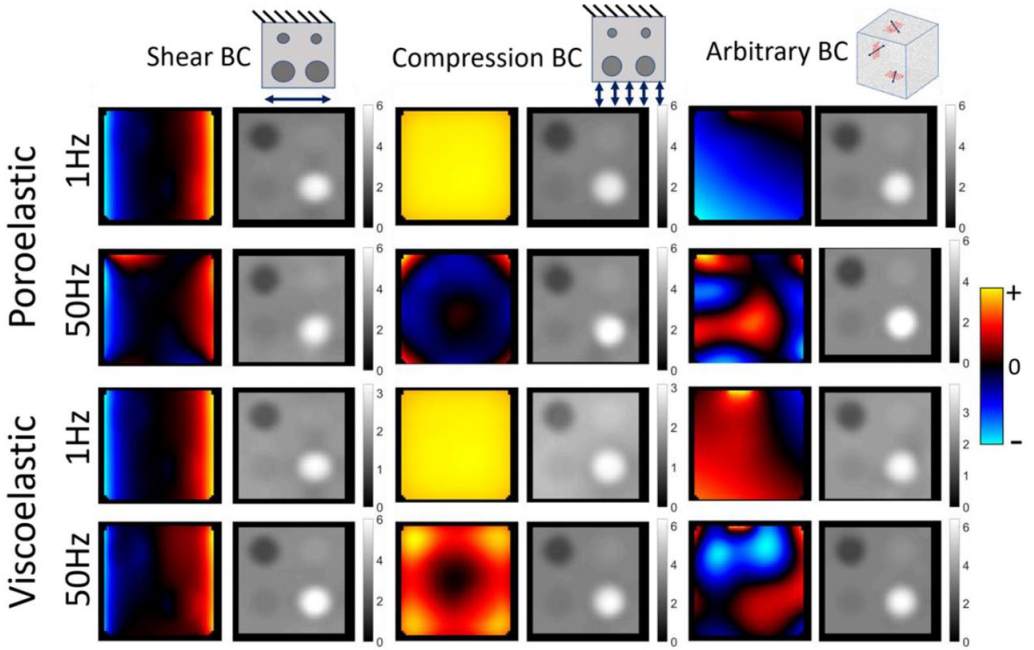
- Direct method applied under simplifying assumptions:
  - Linear elasticity
  - Local homogeneity
  - Isotropy
  - Plane wave

$$\mu = \rho . c_S^2$$

+ incompressibility → $E = 3\mu$

- Inverse methods based on wave equation resolution

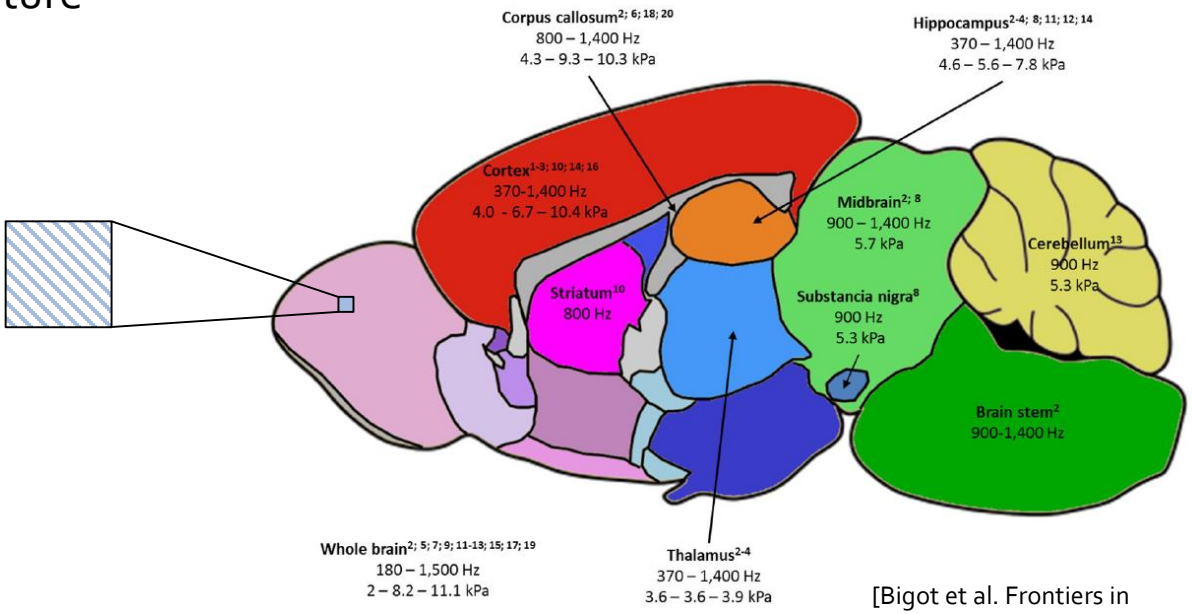
- Inverse methods based on FEM:
  - More complex behaviour
  - Account for boundary conditions
  - Computationaly heavy



[McGarry et al. Physics in Medecine & Biology, 2019]

Some scientific et technical challenges in elastography

- Reaching the targeted area with sufficient amplitude (attenuation, SNR) – trade-off with spatial resolution
- Enriching reconstruction with more complex mechanical behaviours, heterogeneities and boundaries while controling computational cost
- Investigating the microstructure
- In MRE, quantify how much what we measure is close to the mechanical state of the tissue



[Bigot et al. Frontiers in Technology, 2018]

Outline

1. Introduction

2. **Identifying the non-linear properties of soft tissue using transient elastography**

[W. Ye PhD thesis]

3. Investigation of steady-state in MRE

[Q. Du PhD thesis]

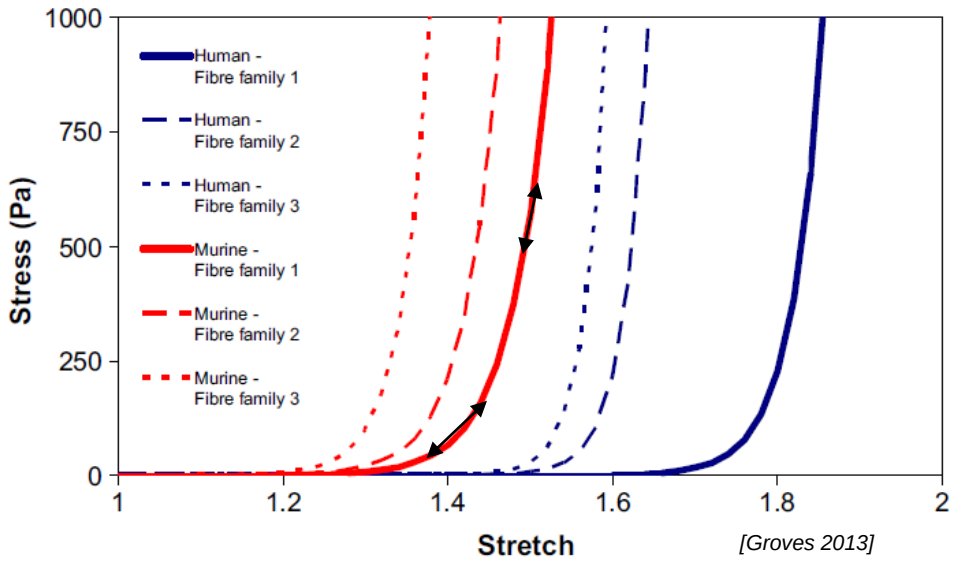
4. Conclusions

Tissue non-linearity – analytical identification

- Elastography = small amplitude waves, typically few dozens of µm
- Soft tissues are hyperelastic

  → elastography provides the tissue <u>tangent modulus</u>

- Need for a wider characterization (surgery simulation, improved diagnosis)



[Groves 2013]

Landau's law, typical in acoustic field:

$$W_{Landau} = \mu II + \frac{A}{3} III + D II^2 + \frac{1}{2} K (J-1)^2$$

With $II = tr(\boldsymbol{E}^2)$ and $III = tr(\boldsymbol{E}^3)$

Non-linear in shear

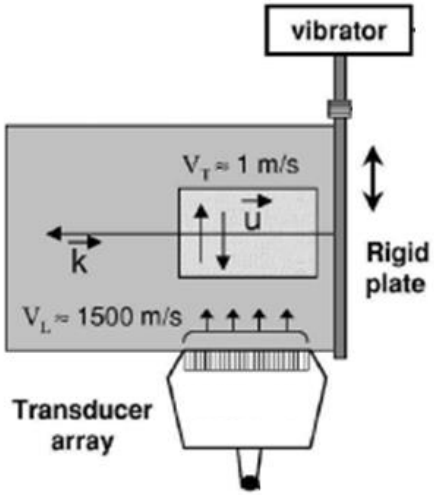
$\mu, A \text{ and } D$: shear moduli at orders 2, 3 and 4

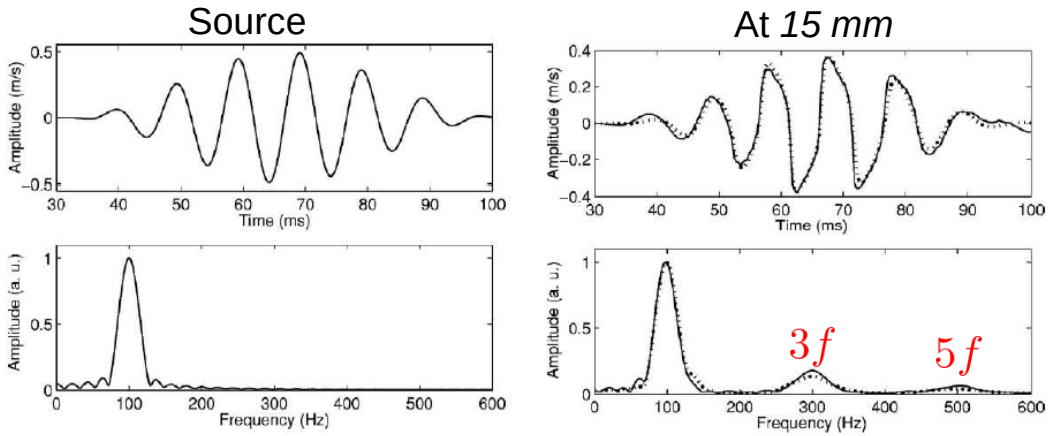
How to identify them ?

Tissue non-linearity – analytical identification

- 2 options:
  1. Increasing wave amplitudes to reach a non-linear regime

Plane waves





[Jacob 2007]

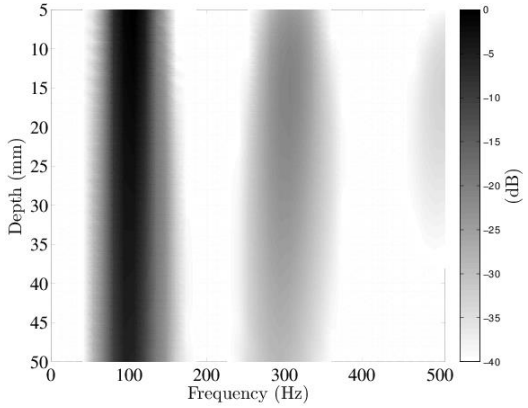
Distortion of wave shape ⟺ Nonlinearity

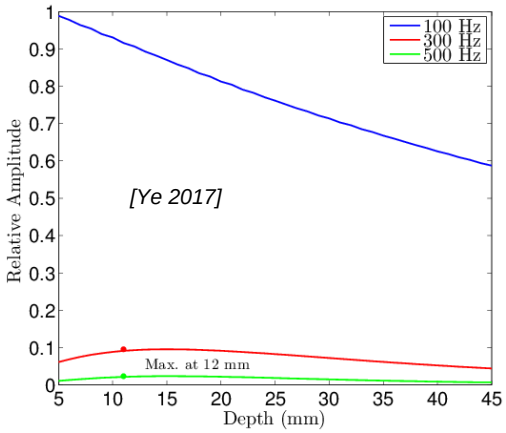
Investigating the wave spectrum theoretically provides a relationship between non-linear parameters, extended to a large range of application by Ye et al. [IJNMBE 2018]:

$$\mu, A, D = f(A_1, A_3, A_5)$$

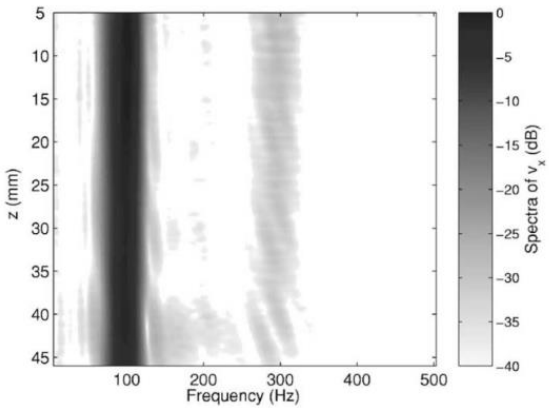
Tissue non-linearity – analytical identification

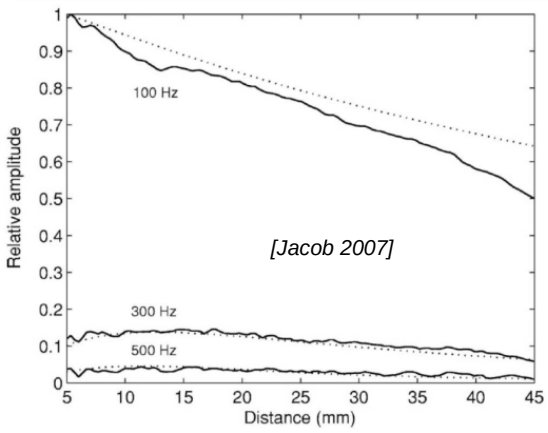
- Theoretical vs. experimental spectrum



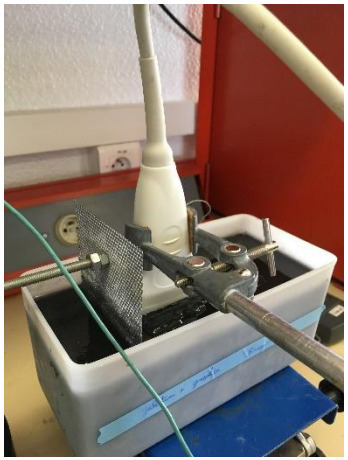


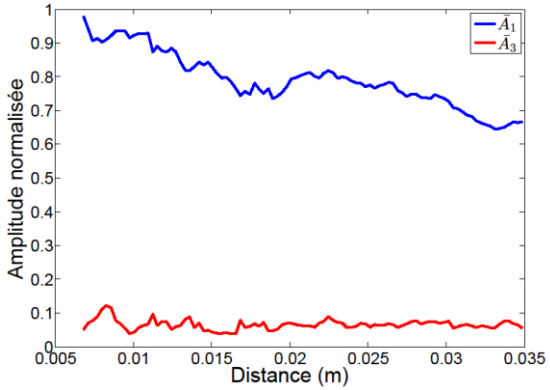
Numerical simulation





Experimental results

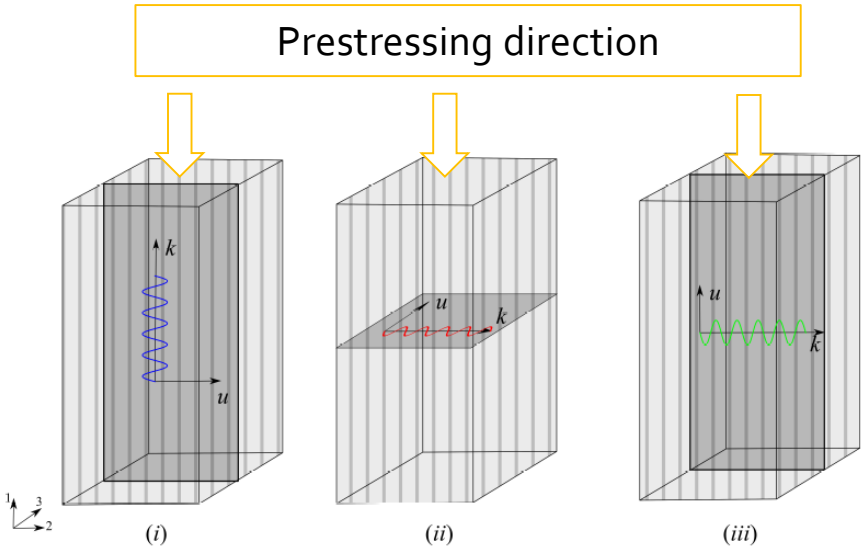


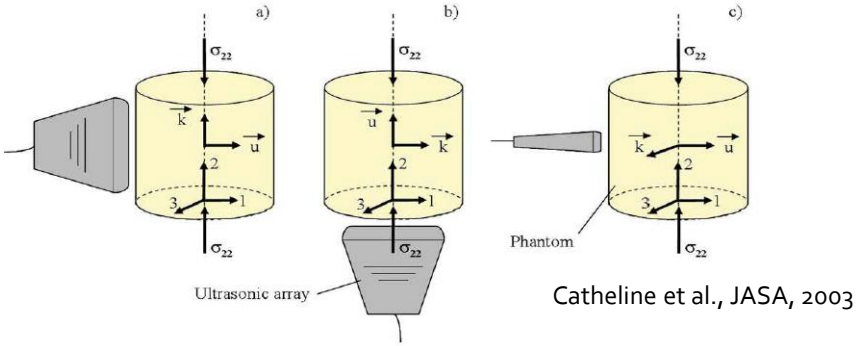


Non-linear wave method is very sensitive to noise!

Tissue non-linearity – analytical identification

- 2 options:
  1. Increasing wave amplitudes to reach a non-linear regime
  2. **Prestressing the tissue before performing elastography = acoustoelasticity**





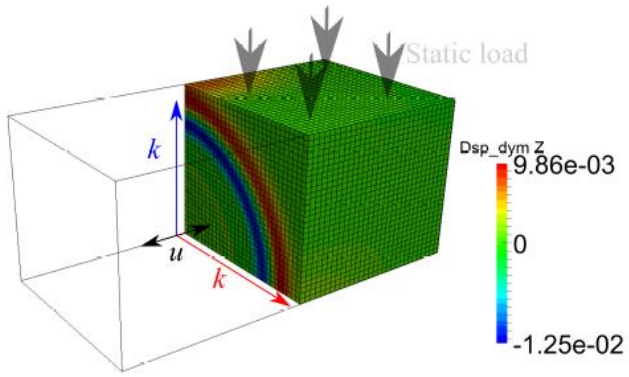
Catheline et al., JASA, 2003

Under a prestress, the tissue becomes extrinsiquely transverse isotropic
→ 3 wave types

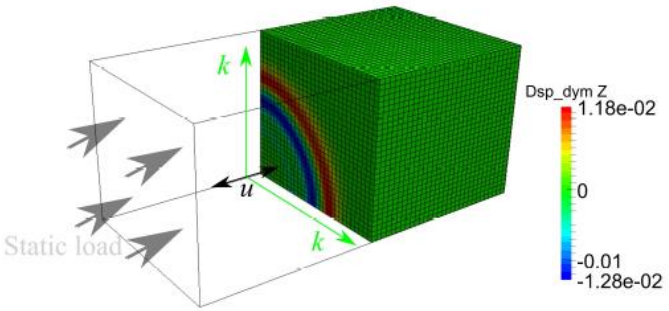
Acoustoelasticity provides additional relationships between material parameters.

Tissue non-linearity – analytical identification

- Analytical expressions of c_i, c_{ii} *and* c_{iii} proposed by Destrade at al. in 2010 and applied to various hyperelastic potentials



(a) In this configuration, wave types *i* (blue) and *ii* (red) can be measured

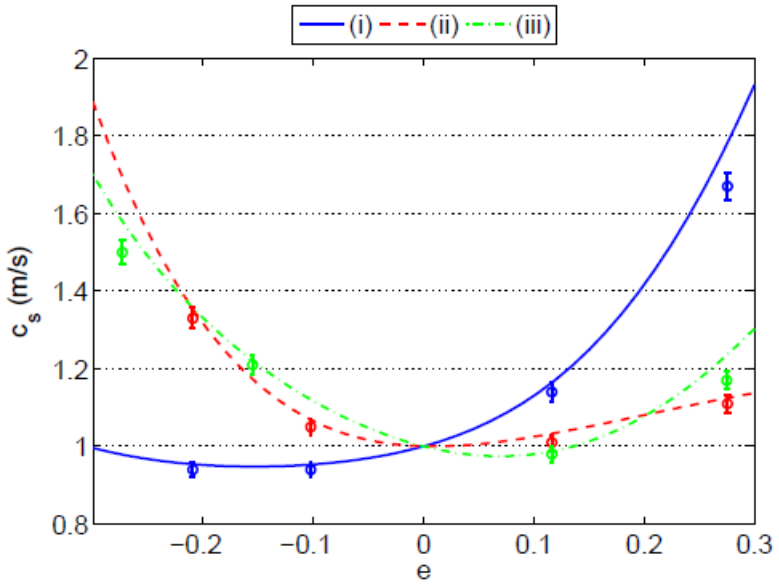


(b) In this configuration, wave type *iii* is measured

$$\rho c_i^2 \approx \mu + \left(3\mu + \frac{A}{4}\right)e + \left(5\mu + \frac{7A}{4} + 3D\right)e^2$$

$$\rho c_{ii}^2 \approx \mu - \left(3\mu + \frac{A}{4}\right)e + \left(5\mu + \frac{7A}{4} + 3D\right)e^2$$

$$\rho c_{iii}^2 \approx \mu + \frac{A}{4}e + (2\mu + A + 3D)e^2$$



Tissue non-linearity – analytical identification

- Combination of non-linear waves + acoustoelasticity can provide relationships to analytically identify non-linear parameters.

- Theoretically, this combined method is more robust to noise.

- Limits: plane waves – experimental issues → can be overcome by numerical simulation of wave propagation
  - Effect of boundary conditions on reconstructed parameters
  - Effect of heterogeneities
  - …

Outline

1. Introduction

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[W. Ye PhD thesis]

3. **Investigation of steady-state in MRE**

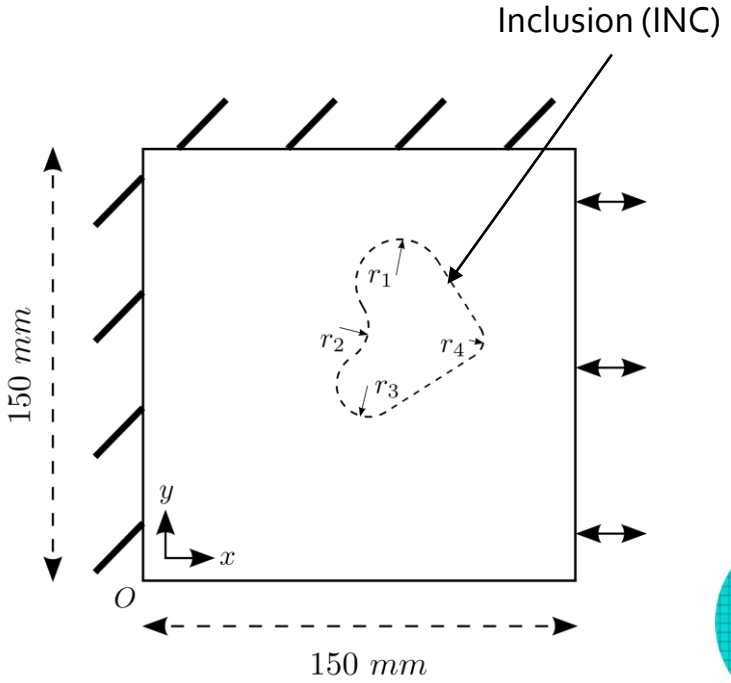
[Q. Du PhD thesis]

4. Conclusions

Investigation of steady-state in MRE

- Can simulation of wave propagation provide good practices in MRE acquisition, i.e.

  After how many cycles can we expect the tissue to reach a steady-state ?

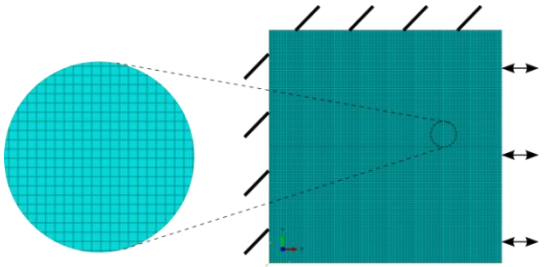


Heterogeneous model:

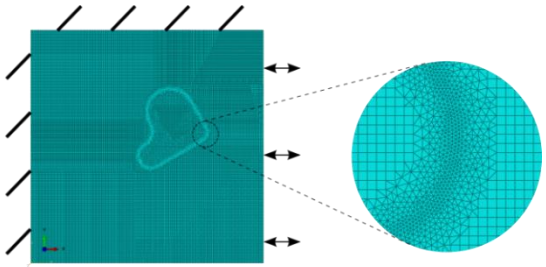
- 2 viscoelastic soft materials
- Longitudinal harmonic excitation
- Inclusion described by eXtended-FEM (X-FEM)

[Du et al., JASA, 2022]

X-FEM mesh



FEM mesh

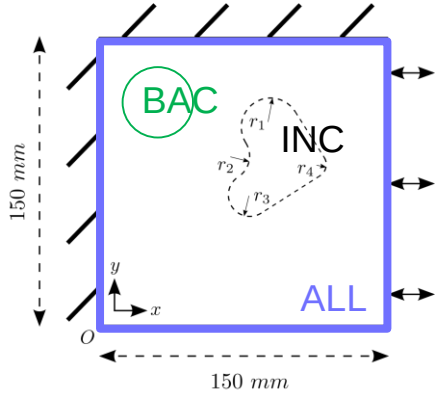


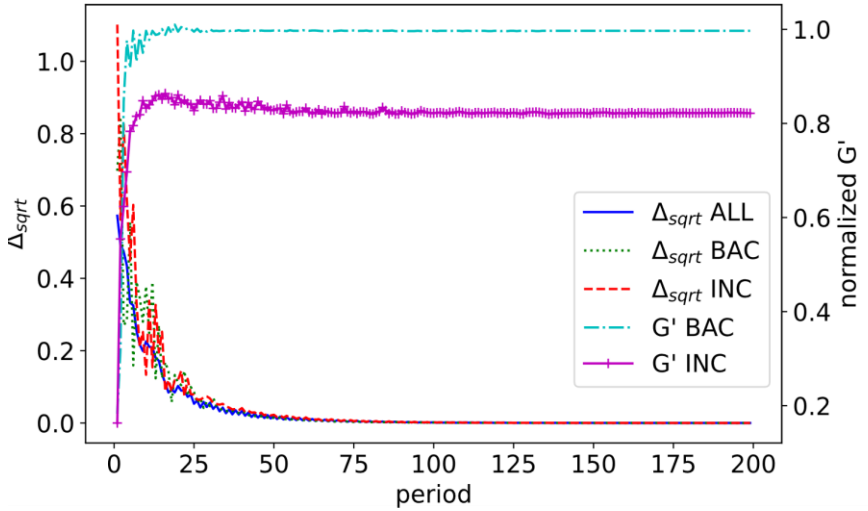
Investigation of steady-state in MRE

- Steady-state metric

$$\Delta_{sqrt}(T_i) = \frac{1}{Nu_0}\sum_{j=1}^{N}\sqrt{[u_x^j(T_{i+1}) - u_x^j(T_i)]^2 + [u_y^j(T_{i+1}) - u_y^j(T_i)]^2}$$

- Direct reconstruction method based on the resolution of the wave equation on the curl-based displacement field (using MREJ plug-in of ImageJ)





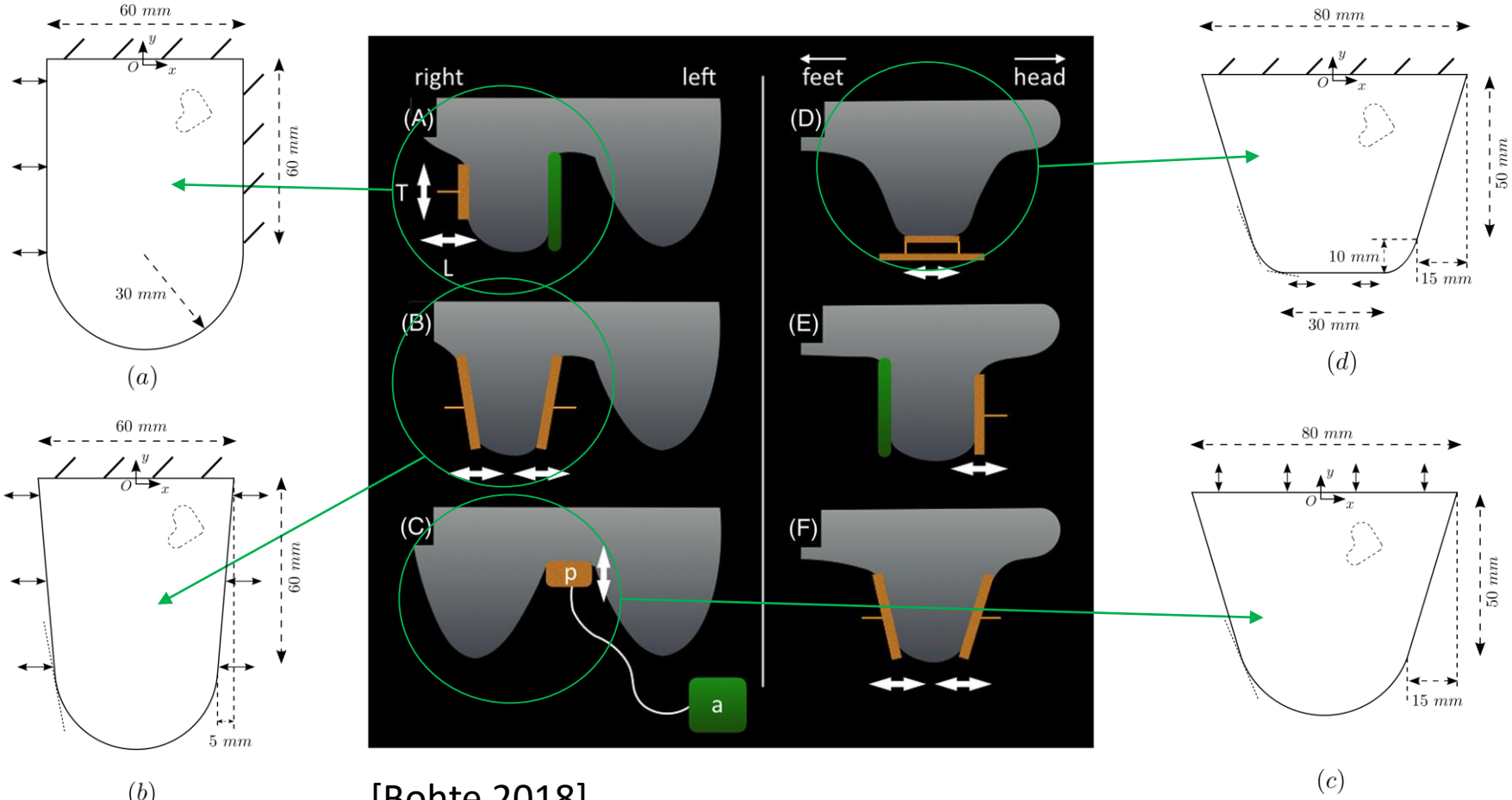
→ G′ estimation converged after 25 cycles

→ $\Delta_{sqrt} \approx 0.1$ seems a reasonable threshold.

MREJ: Xiang et al., Comput Biol Med, 2013

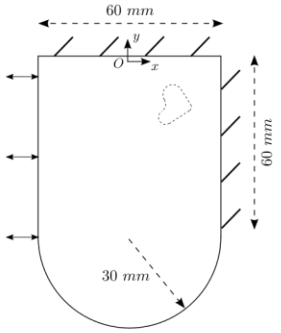
Investigation of steady-state in MRE: application to breast MRE

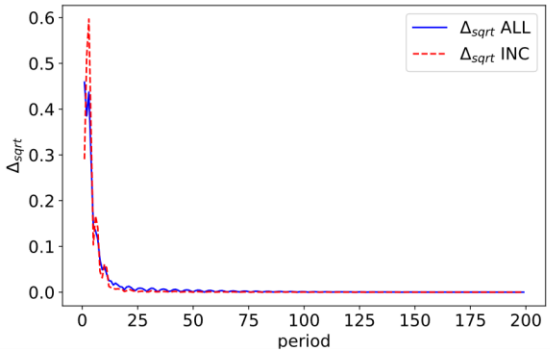
- Different breast MRE existing configurations

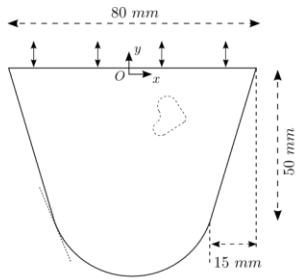


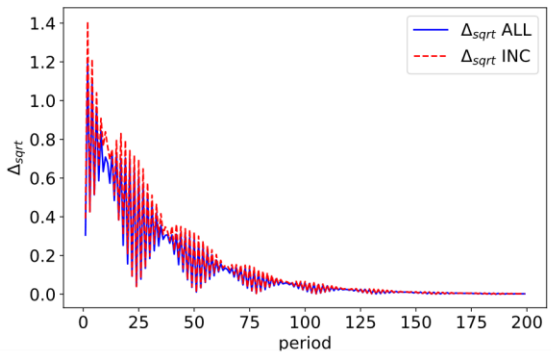
[Bohte 2018]

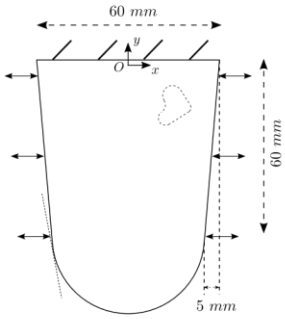
Investigation of steady-state in MRE: application to breast MRE

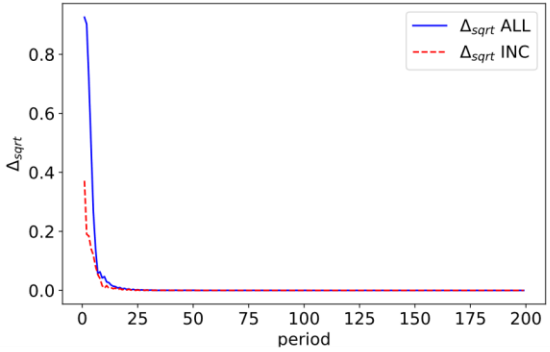


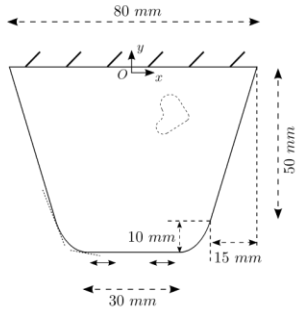


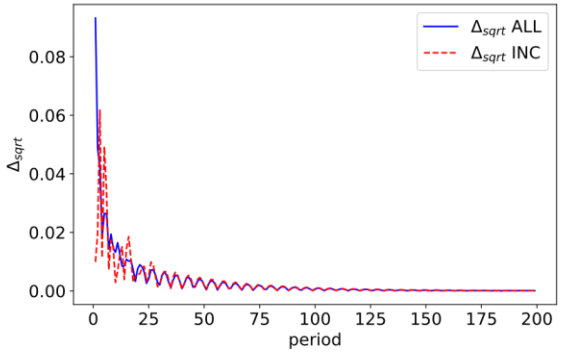








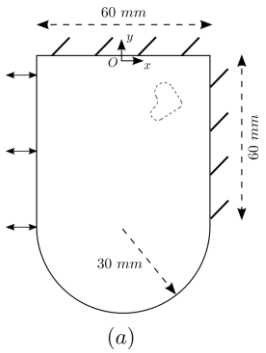


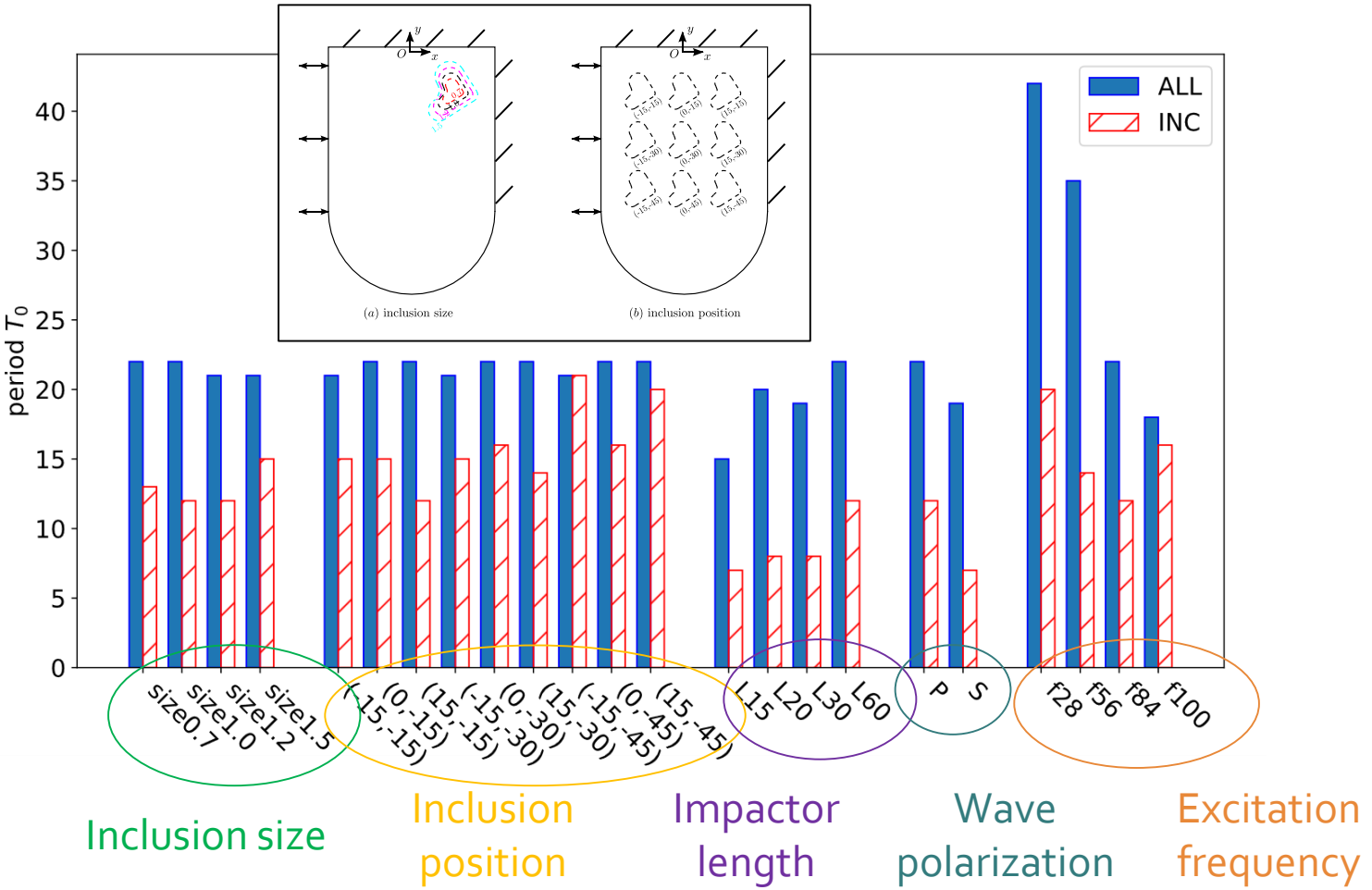


More constrained models reach steady-state earlier.

Investigation of steady-state in MRE: application to breast MRE

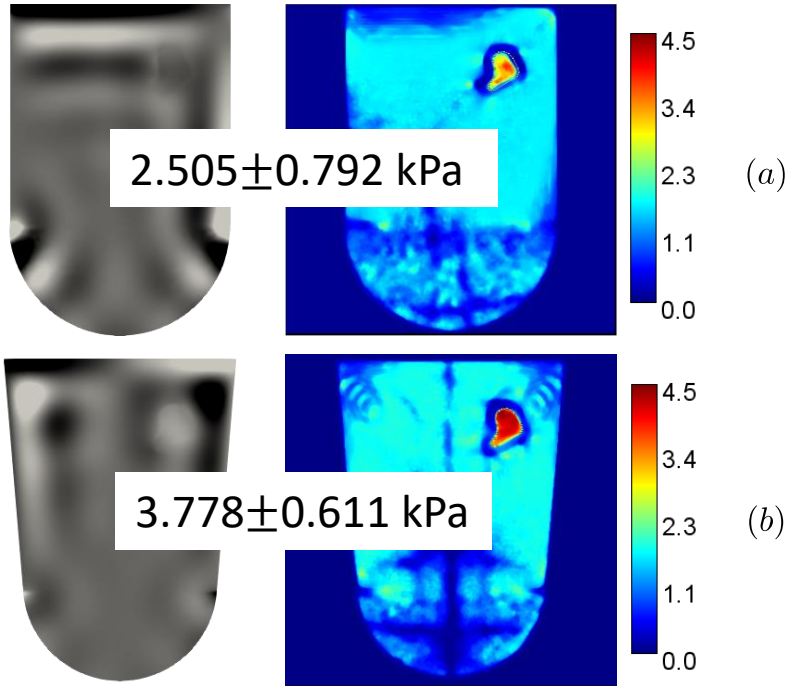
- Influence of impactor and inclusion on steady-state: parametric study

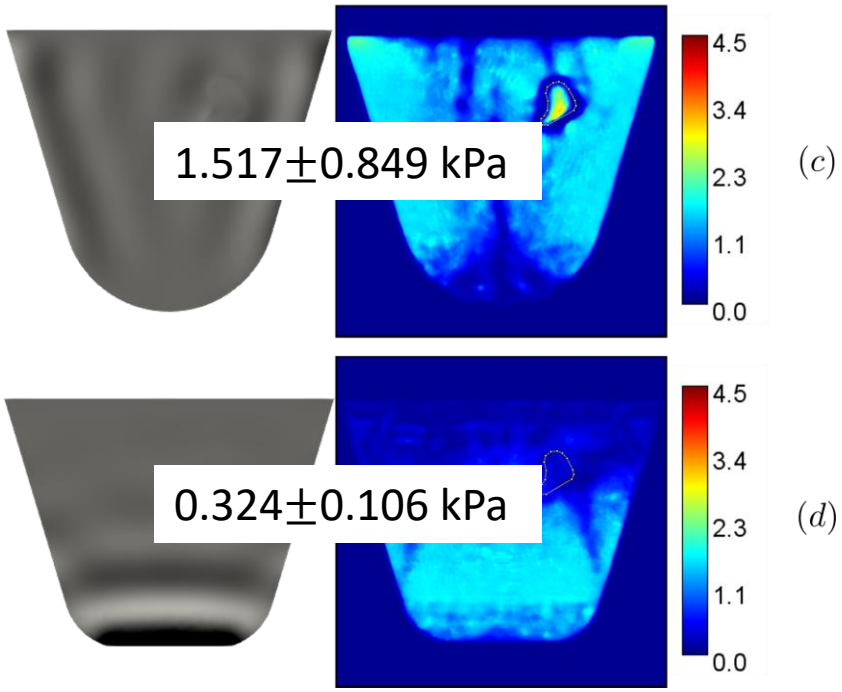




Investigation of steady-state in MRE: application to breast MRE

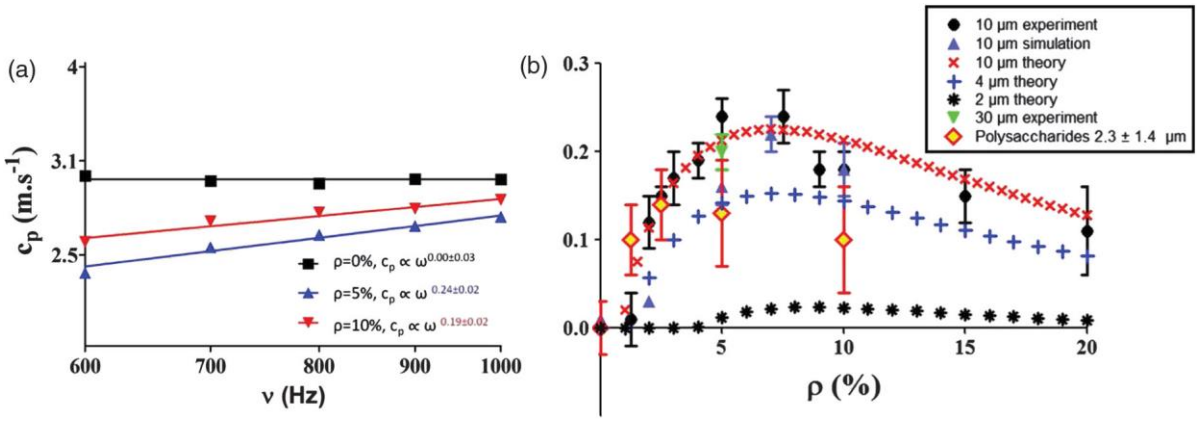
- Reconstruction results for G' (ground truth: 3.88 kPa)





Conclusions & Perspectives

- Steady-state estimation can provide experimental guidelines in terms of impactor, wave polarization, acquisition procedures, etc.
- X-FEM: simpler meshing of interfaces, adapted to multiple and complex interfaces.
- Move to smaller scales: can we detect microstructure (neurons, vasculature) from a macroscopic signal?



Lambert et al., PRL, 2015