Elastography of Biological Tissue

Direct Inversion Methods that Allow for Local Shear Modulus Variations

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Outline

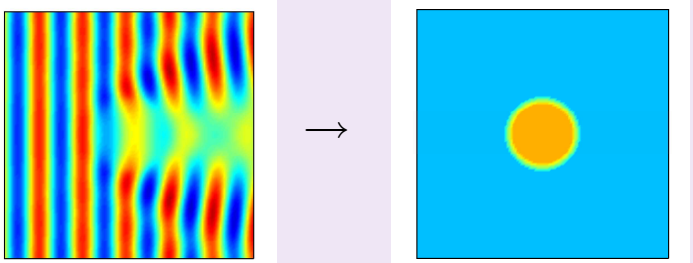
Definition

Magnetic Resonance Elastography (MRE) is a medical imaging technique used to non-invasively 'measure' stiffness in biological tissue.

The technique is indirect:

- Motions are induced through the tissue by applying a known stress.
- A sequence of strain images are captured using MRI.
- The strains are related to stiffness through a tissue model.
- The model is inverted to generate an elastogram.

Strain Images to Elastogram



Motivation: Why tissue stiffness?

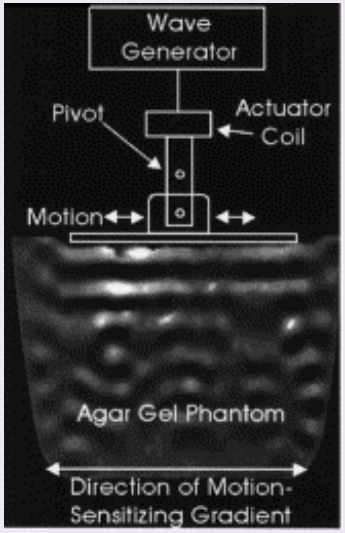
- Stiffness is a common indicator for tissue damage or disease.
  - Tumours, scarring, cirrhosis, hyperthyroidism, muscle atrophy.
- Conventional imaging techniques typically measure density.

> "It is generally agreed that no other physical parameter of tissue is changed by pathological or physiological processes to as great an extent as its elasticity" (Manduca, 2001)

- Palpation has been used as a primary diagnostic tool for millennia.
- Manual palpation is limited to surface tissues.
- Elastography is a form of palpation by imaging.

Outline

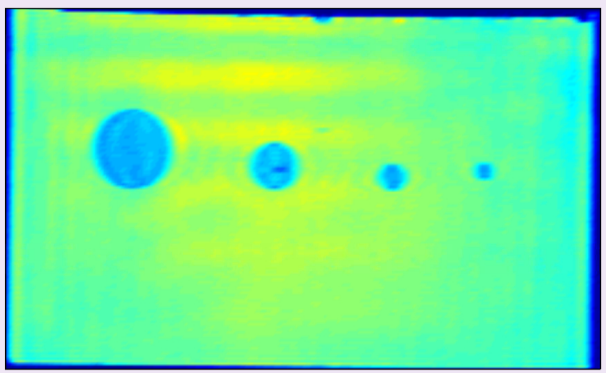
Experiment

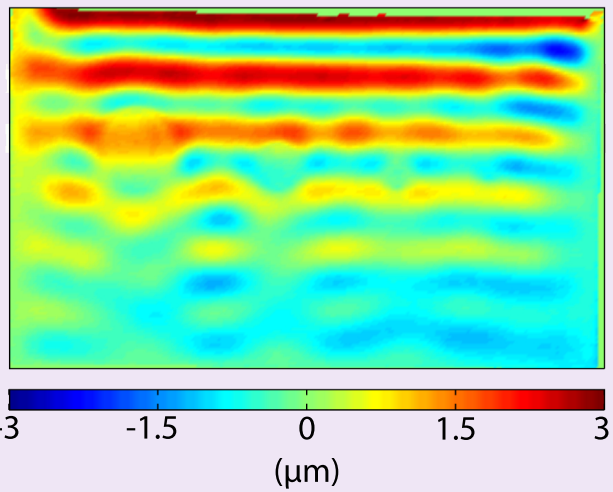


Experiment procedure:

- A contact is placed near the tissue of interest.
- An actuator (motor) forces sinusoidal shear motions.
- Shear waves are induced through the tissue.
- Displacements caused by waves are measured using MRI with motion-encoding gradients and a phase-difference technique.

Magnitude Image and Displacment Pattern





Tissue Model Assumptions

Linearly viscoelastic isotropic continuum, under oscillatory loading.

General equations of motion (frequency domain)

$$-\omega^2 \rho \, \mathrm{U} = \nabla \cdot \left(\mathcal{M} \left[\nabla \mathrm{U} + \nabla^{\mathrm{T}} \mathrm{U} \right] \right) + \nabla \left(\Lambda \nabla \cdot \mathrm{U} \right) \tag{1}$$

- Displacements, U, are three-dimensional.
- Λ and $\mathcal{M}$ are complex versions of the Lamé parameters.
- Tissue density is usually assumed constant (≈ 1 g/cm^3).
- Due to incompressible nature of soft tissues, the longitudinal component is often negligible ($\nabla \left(\Lambda \nabla \cdot \mathrm{U} \right) \approx 0$). Longitudinal waves travel more quickly through tissue, resulting in very small differences in displacements between neighbouring volume elements.
- Most energy is contained in the first harmonic component of tissue motion.
- Parameter of interest is the complex shear modulus, $\mathcal{M}$, which has been experimentally shown to vary strongly with pathology.

Simplified Tissue Model

$$-\omega^2 \mathrm{U} = \mathcal{M}\nabla\cdot\left(\nabla\mathrm{U} + \nabla^{\mathrm{T}}\mathrm{U}\right) + \nabla\mathcal{M}\cdot\left(\nabla\mathrm{U} + \nabla^{\mathrm{T}}\mathrm{U}\right) \tag{2}$$

Goal of MRE

Estimate the shear modulus from a system of partial differential equations.

Issues:

- Boundary conditions are not known, nor can be measured.
- The problem of finding $\mathcal{M}$ may therefore be ill-posed (have many possible solutions) without first imposing some form of regularization.

Common approach ("AIDE"): assume local homogeneity ($\nabla\mathcal{M} \approx 0$) before inversion.

- From a knowledge of displacement field U, we obtain a solvable algebraic system of equations for $\mathcal{M}$. (Hence "AIDE" = "algebraic inversion of differential equations".)
- However, it limits the local variability of $\mathcal{M}$.
- Approximated solution is invalid in regions where stiffness varies rapidly.
- Sharp local variations often mark boundaries of pathology;
  from a clinical perspective, these regions are the most important.

Outline

- There exist conditions which guarantee a unique solution to

$$-\omega^2 \mathrm{U} = \mathcal{M}\nabla\cdot\left(\nabla\mathrm{U} + \nabla^{\mathrm{T}}\mathrm{U}\right) + \nabla\mathcal{M}\cdot\left(\nabla\mathrm{U} + \nabla^{\mathrm{T}}\mathrm{U}\right),$$

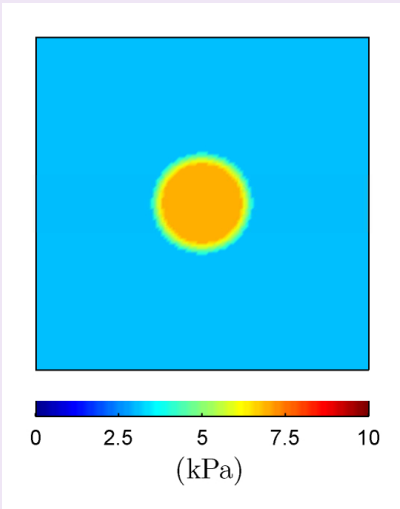
  without the need for regularization.

  - For example: $\operatorname{rank}\left\{\left[\nabla\mathrm{U} + \nabla^{\mathrm{T}}\mathrm{U}\right]\right\} < \operatorname{rank}\left\{\left[\begin{array}{cc} \nabla\cdot\left[\nabla\mathrm{U} + \nabla^{\mathrm{T}}\mathrm{U}\right] & \left[\nabla\mathrm{U} + \nabla^{\mathrm{T}}\mathrm{U}\right] \end{array}\right]\right\},$

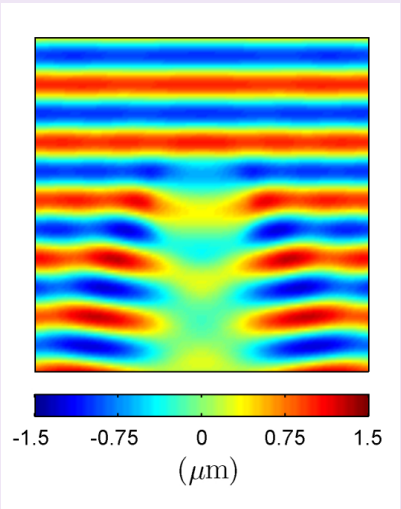
    or $\quad \nabla\times\left[\left[\nabla\mathrm{U} + \nabla^{\mathrm{T}}\mathrm{U}\right]^{-1}\nabla\cdot\left(\nabla\mathrm{U} + \nabla^{\mathrm{T}}\mathrm{U}\right)\right] \neq 0$

- In such cases, imposing local homogeneity only distorts the solution.

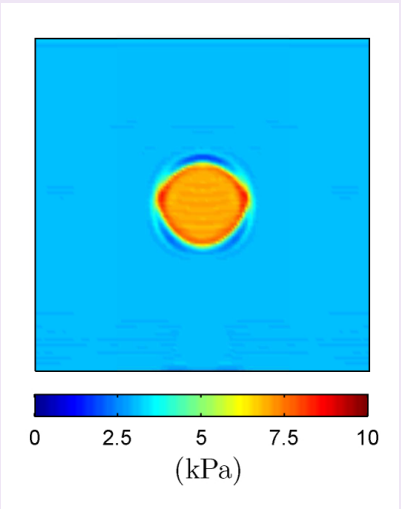
Distortions caused by local homogeneity assumption



True stiffness



Displacement pattern



Distorted solution

In an attempt to avoid distorting the solution unnecessarily, we reformulate the inverse problem as follows:

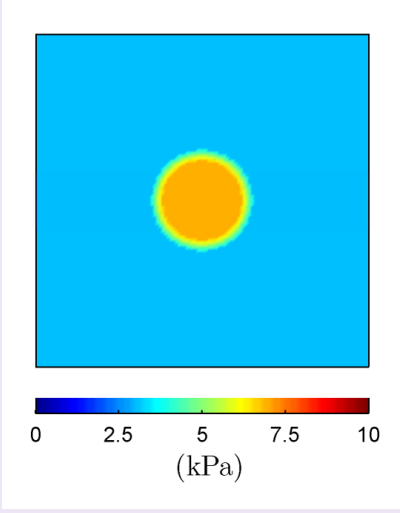
Equality-Constrained Optimization

$$\begin{aligned} &\text{Minimize} && \mathrm{f}(\mathcal{M}) = \|\nabla\mathcal{M}\|^2 \ , \\ &\text{subject to} && -\omega^2 \mathrm{U} = \mathcal{M}\nabla\cdot\left(\nabla\mathrm{U} + \nabla^{\mathrm{T}}\mathrm{U}\right) + \nabla\mathcal{M}\cdot\left(\nabla\mathrm{U} + \nabla^{\mathrm{T}}\mathrm{U}\right). \end{aligned}$$

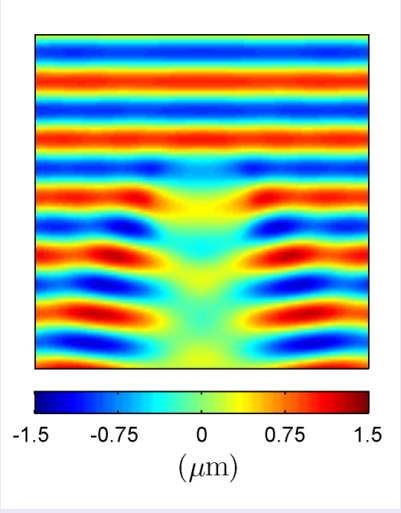
- The equality constraint guarantees that the original PDE system is satisfied.
- Minimization isolates a particular solution when multiple ones exist.
- Note: When the solution is unique, minimization has no effect.

The above procedure is analogous to the method of total variation minimization in image processing.

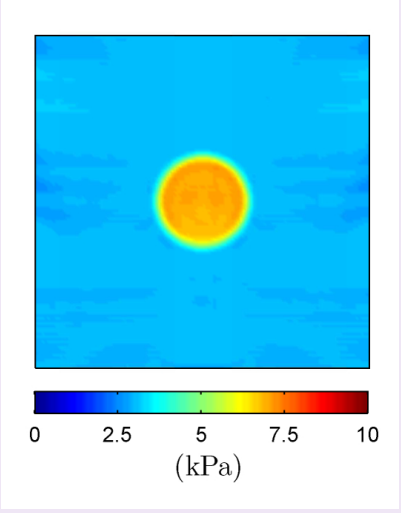
Solution obtained through constrained optimization



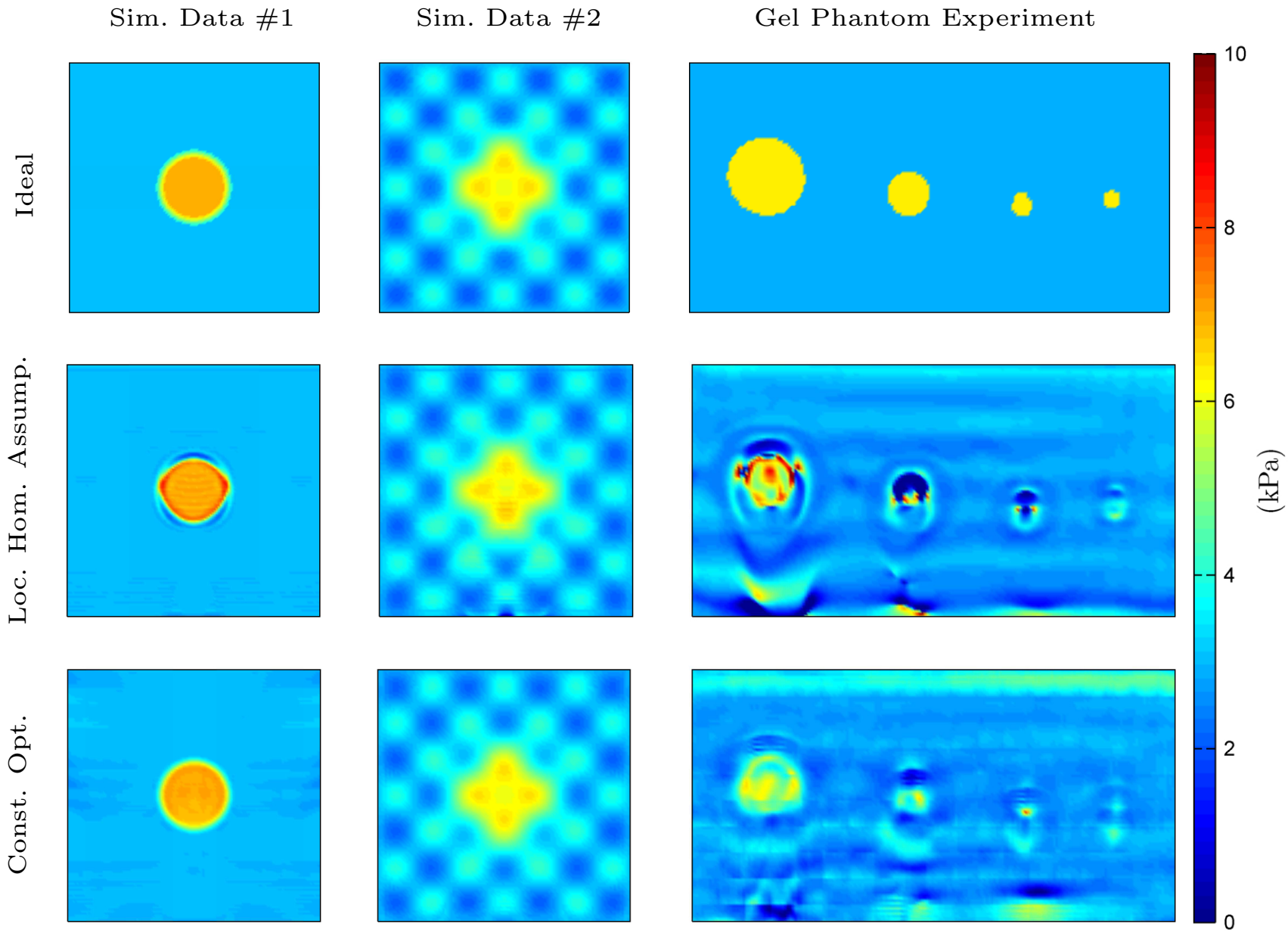
True stiffness



Displacement pattern



Undistorted solution


Sim. Data #1
Sim. Data #2
Gel Phantom Experiment
Ideal
Loc. Hom. Assump.
Const. Opt.
10
8
6
4
2
0
(kPa)

The previous method reduces distortions, but is quite computationally expensive and can be sensitive to noise.

Alternative: introduce Green's functions.

A very brief description: Let L be a differential operator and consider the boundary value problem

$$\mathrm{Lu(x)} = \mathrm{f(x)} \quad + \quad \text{boundary conditions on } \mathrm{u(x)}. \tag{3}$$

Here, f(x) is given and we must solve for u(x). Then the solution u(x) is given by

$$\mathrm{u(x)} = \int \mathcal{G}(\mathrm{x}, \mathrm{y})\mathrm{f(y)}\, \mathrm{dy}, \tag{4}$$

where $\mathcal{G}(\mathrm{x}, \mathrm{y})$ is the Green's function associated with L and the boundary conditions. $\mathcal{G}$ defines the inverse operator of L:

$$\mathrm{Lu} = \mathrm{f} \quad \Rightarrow \quad \mathrm{u} = \mathrm{L}^{-1}\mathrm{f}. \tag{5}$$

Well-known example, relevant to our problem

$L = \nabla^2$, the Laplacian operator in R^3, with boundary condition $u(x) \to 0$ as $\|x\| \to \infty$. Then the solution to Poisson's equation,

$$\nabla^2 u = f, \tag{6}$$

is given by

$$u(x) = \int \mathcal{G}(x, y) f(y)\, dy, \quad \text{where} \quad \mathcal{G}(x, y) = -\frac{1}{4\pi \|x - y\|}. \tag{7}$$

In electrostatics, $u(x)$ is the potential function associated with the electrostatic charge distribution $f(x)$. Note that

$$u = \mathcal{G} * f \quad \text{(convolution with } \mathcal{G}\text{)}. \tag{8}$$

Pros:
- Solution is simply a convolution of the data with a Green's function.
- Convolution is fast and robust.

Cons:
- The true Green's function depends on the data, so must be solved numerically.
- All Green's functions depend on boundary conditions, which are unknown.

For preliminary results, the model was simplified so that the Green's function was independent of the data but still dependent on boundary conditions. This was done by introducing data windows (boxcar functions).

Further Simplified Tissue Model

$$-\omega^2 \mathrm{U} = \nabla^2 (\mathcal{M}\mathrm{U}) \tag{9}$$

- Boundaries are initially assumed to have a constant stiffness value.
- These boundary values can then be updated iteratively.

Brief description of Green's function method

- First of all, we need to introduce Laplacian operator into elasticity equation. Return to general equation of motion, once again ignorning longitudinal component,

$$-\omega^2 \rho \mathrm{U} = \nabla \cdot (\mathcal{M} \nabla \mathrm{U}) + \nabla \cdot (\mathcal{M} \nabla^{\mathrm{T}} \mathrm{U}). \tag{10}$$

- Claim: Final term is negligible. Once again local homogeneity of $\mathcal{M}$ to obtain

$$-\omega^2 \mathrm{U} = \nabla^2 (\mathcal{M} \mathrm{U}). \tag{11}$$

  We now have our desired Laplacian operator.

- It's now tempting to convolve with (free-space) Green's function $\mathcal{G}$ and then deconvolve:

$$-\omega^2 \mathcal{G} * \mathrm{U} = \mathcal{G} * \nabla^2 (\mathcal{M} \mathrm{U}) = \mathcal{M} \mathrm{U} \quad \Rightarrow \quad \mathcal{M} = -\omega^2 \frac{\mathcal{G} * \mathrm{U}}{\mathrm{U}}. \tag{12}$$

  Unfortunately, this is valid only for solutions that vanish at extremes – not the situation for windowed data.

- Multiply function U window function W with compact support (i.e., an $n_1 \times n_2 \times n_3$-pixel block):

$$-\omega^2(\mathrm{WU}) = \nabla^2(\mathcal{M}\mathrm{WU}) \tag{13}$$

Now convolve with Green's function to yield the expression,

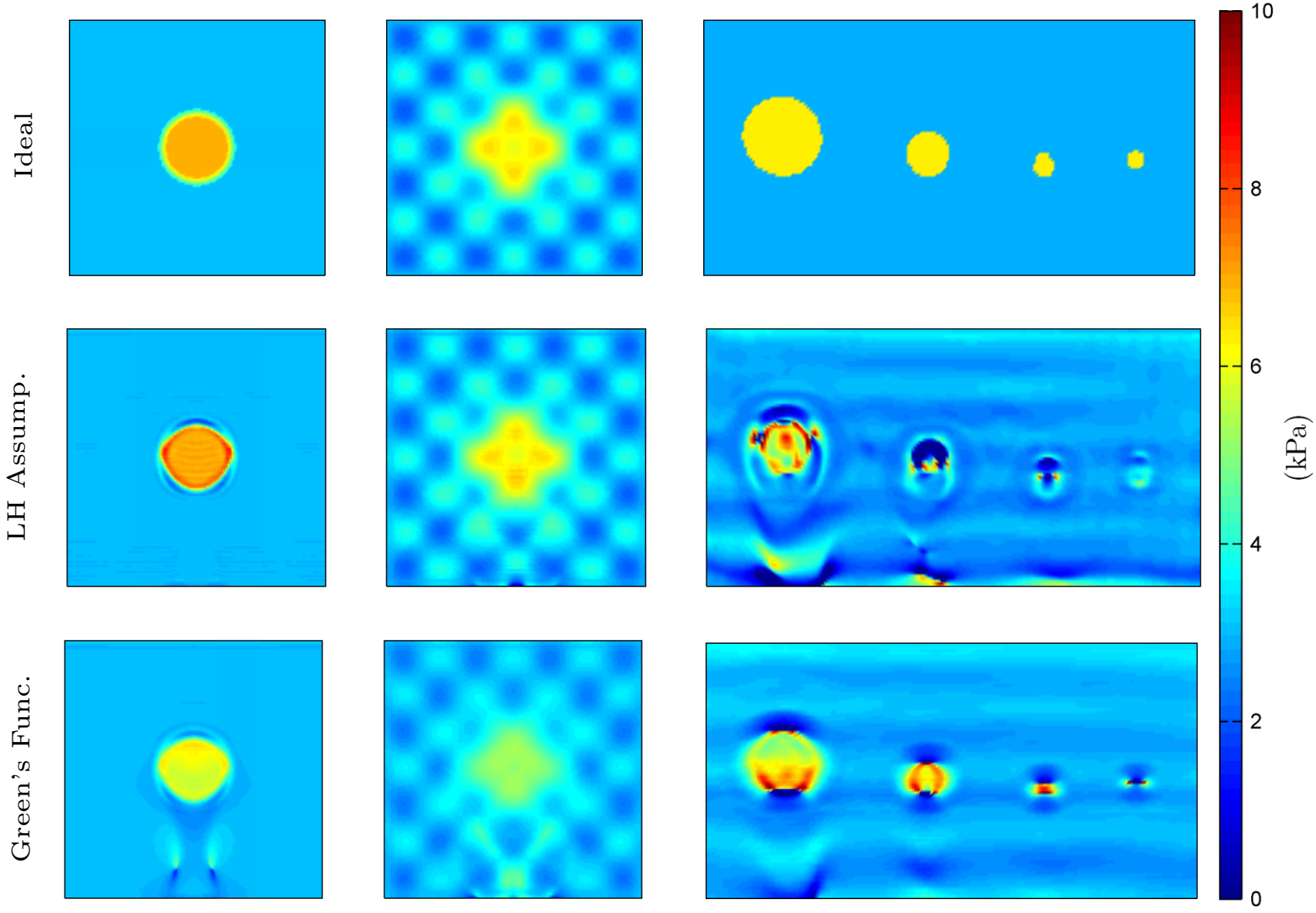
$$\begin{aligned} -\omega^2\mathcal{G} * (\mathrm{WU}) &= \mathcal{M}\mathrm{WU} - \mathcal{G} * (2\nabla\mathrm{W} \cdot \nabla(\mathcal{M}\mathrm{U}) + \mathcal{M}\mathrm{U}\nabla^2\mathrm{W}) && (14)\\ &= \mathcal{M}\mathrm{WU} + \mathcal{L}_{\mathcal{B}}(\mathcal{M}). && (15) \end{aligned}$$

Here, $\mathcal{L}_{\mathcal{B}}(\mathcal{M})$ denotes the boundary term. ($\mathcal{L}_{\mathcal{B}}$ is a linear operator.) Unfortunately, the boundary term $\mathcal{L}_{\mathcal{B}}\mathrm{M}$ depends on the values of $\mathcal{M}$ and its derivatives on the boundary of the window W.

- Simplification: Assume that $\mathcal{M}$ is constant over boundary of W yielding first estimate of $\mathcal{M}$:

$$\mathcal{M}^{(1)} = -\frac{\omega^2\mathcal{G} * (\mathrm{WU})}{\mathrm{WU} - \mathcal{G} * (2\nabla\mathrm{W} \cdot \nabla\mathrm{U} + \mathrm{U}\nabla^2\mathrm{W})}. \tag{16}$$

- Then use $\mathcal{M}^{(1)}$ as the starting point for an iteration procedure that produces successive approximations $\mathcal{M}^{(\mathrm{k})}$ that (hopefully!) converge to a fixed point solution $\mathcal{M}$.


Sim. Data #1
Sim. Data #2
Gel Phantom Experiment
Ideal
LH Assump.
Green's Func.
10
8
6
4
2
0
(kPa)

Outline

Conclusions

- A sequence of strain images is converted to an elastogram by inverting a tissue model to find a stiffness parameter.
- The model is a system of PDEs without any known boundary conditions.
- Typically, an approximate solution is found by assuming local homogeneity.
- There are instances when the LH assumption is not required, and imposing it only serves to distort the solution.
- To avoid distortions, the problem was reposed as a constrained optimization.
  - PDE system is imposed as a constraint, allowing for strong local variations.
  - Minimization of the norm is only enforced in regions where solution is not unique.
  - Inversion algorithm is computationally expensive and sensitive to noise.
  - Distortions near boundaries of inclusions were removed.
  - Overall accuracy of the stiffness estimate was increased.
- To reduce sensitivity to noise and decrease computation time, Green's functions were implemented.
  - The model was further simplified so the Green's function was independent of the data.
  - Speed and robustness were drastically increased.
  - Accuracy is limited by the validity of the simplified model.
  - To increase accuracy further, the original PDE system should be used, and the true Green's function solved numerically.