

Imaging Shear Stiffness Tissue Properties Using Inverse Methods When Measurements Are Time Dependent.

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Given:

- 1) Displacement data on a set of grid points on an image plane or a sequence of closely spaced image planes.
- 2) One or more components of the elastic vector are measured.
- 3) Either : time traces of the displacement data are given; or : amplitude of a time harmonic excitation is given.

Use :

(1) Mathematical model that governs the displacement;

(2) Smart algorithms that maximize information retrieval from the data.

To :

- (1) Create useful images that identify small inclusions or low contrast changes or new information rich shear wave related physical properties;
- (2) Motivate new applications or, in some cases, design of experiment.

Images of University of Rochester Data (Parker)

Holographic Wave Movie

MR Data (R. Ehman, Mayo Clinic)

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Fink (ESPCI) Data

Movie of Displacement Data from Transient Elastography Experiment

Amplitude Image

Give models for

Isotropic Elastic Model – time dependent Given $\underline{u}(x,t)$ $\nabla(\lambda \nabla \cdot \underline{u}) + \nabla \cdot (\mu (\nabla \underline{u} + (\nabla \underline{u})^T)) = \rho \underline{u}_{tt}$ single frequency Given $\hat{u}(x,\omega)$ $\nabla(\lambda \nabla \cdot \hat{u}) + \nabla \cdot (\mu (\nabla \hat{u} + (\nabla \hat{u})^T)) + \omega^2 \rho \hat{u} = 0$ wave equation – time dependent Given $u(x, t)$ $\nabla \cdot (\mu \nabla u) = \rho u_{tt}$ single frequency Given $\hat{u}(x,\omega)$ $\nabla \cdot (\mu \nabla \hat{u}) + \omega^2 \rho \hat{u} = 0$ $\nabla \cdot \underline{u} = \frac{\partial}{\partial x_1} u_1 + \frac{\partial}{\partial x_2} u_2 + \frac{\partial}{\partial x_3} u_3, \quad \nabla f = (f_{x_1}, f_{x_2}, f_{x_3})$ Notation:

Approximations – Given $u(x,t)$ or $\hat{u}(x,\omega)$

A. Locally constant assumption:

Isotropic elastic model

time dependent $\nabla p + \mu[\Delta \underline{u} + \nabla (\nabla \cdot \underline{u})] = \rho \underline{u}_{tt}, \quad p = \lambda \nabla \cdot \underline{u},$ single frequency $\nabla \hat{p} + \mu [\triangle \hat{u} + \nabla (\nabla \cdot \hat{u})] + \omega^2 \rho \hat{u} = 0$ time dependent wave equation $\mu \triangle u = \rho u_{tt}$ single frequency $\mu \triangle \hat{u} + \omega^2 \rho \hat{u} = 0$

B. Geometric Optics Approximation.

$$
u = [M_0 + \frac{1}{i\omega}M_1 + \cdots]e^{i\omega\phi}, \omega \gg 1
$$

$$
\sqrt{\mu/\rho}|\nabla\phi| = 1
$$

 $\sqrt{\mu/\rho}$ = phase wave speed

C. Incompressible-Volume Preserving - $\nabla \cdot \underline{u} = 0$

•

Wave equation:
$$
\rho u_{tt} = \nabla \cdot (\mu \nabla u)
$$

Propagating front:

$$
\nabla \cdot (\mu \nabla u) = \rho u_{tt}
$$

$$
\nabla \mu \cdot \nabla \hat{u} + \mu \triangle \hat{u} + \omega^2 \rho \hat{u} = \nabla \cdot (\mu \nabla \hat{u}) + \omega^2 \rho \hat{u} = 0
$$

locally constant assumption yields

$$
\tfrac{\mu}{\rho} = \tfrac{-\omega^2 \hat{u}}{\Delta \hat{u}}
$$

or target phase wave speed or arrival time equation (Eikonal equation)

$$
\sqrt{\mu/\rho}|\nabla \phi| = 1 \qquad \qquad \sqrt{\mu/\rho}|\nabla \widehat T| = 1
$$

Finite Difference Methods For $\nabla \cdot (\mu \nabla \hat{u}) + \omega^2 \rho \hat{u} = 0$

- Calculate the derivatives of the data: A. (i) Use centered difference $\hat{u}_x^h(x) = \frac{\hat{u}(x+h) - \hat{u}(x-h)}{2h}$ (too noisy), stepsize=h;
	- (ii) Calculate centered difference for several stepsize $\{h_i\}_{i=1}^n$, Take weighted average or median (see K. Lin's talk) of $\{\hat{u}_x^{n_i}\}_{i=1}^n$. Control noise by bounding the variance.
	- (iii) Use similar idea for second derivatives.
	- B. (i) Start with A (i) above;

(ii) **Smooth by multiplying**
$$
\tilde{u}_x(x) = \frac{1}{\sqrt{2\pi}\sigma} \int_{-\infty}^{\infty} e^{-\frac{(y-x)^2}{2\sigma^2}} \hat{u}_x^h(y) dy
$$

(equivalent to low pass filter).

(iii) Use similar idea for second derivatives.

1. (cont) Calculate derivatives of the data:

C. (i) Assume $\hat{u} = \sum_{i=1}^n a_i \phi_i(x), \{\phi_i\}_{i=1}^n$ polynomials or finite elements.

Choose $\{a_i\}_{i=1}^n$ to minimize

 $\int_{x_0}^{x_1} \left[\sum_{i=1}^n a_i \phi_i(x) - \widehat{u}(x) \right]^2 dx$ (least squares approximation)

(ii)
$$
\hat{u}_x = \sum_{i=1}^n a_i \phi_{i,x}(x)
$$

(iii) Use similar idea for second derivatives.

2. Modify step sizes according to the signal to noise (SNR) ratio and the oscillation of \hat{u} .

Calculate $\,\mu/\rho$ or

I. Locally constant assumption:

 $\mu/\rho = -\omega^2 u^s / \Delta u^s, \Delta u^s, u^s$ smoothed

Advantage : Local algorithm. Disadvantage : (a) neglect $\nabla \mu$ terms and information of other components of elastic vectors. (b) oscillations in u may restrict noise removal.

II. Currently being investigated:

$$
\nabla \mu \cdot \nabla u^s + \mu \triangle u^s + \omega^2 \rho u^s = 0
$$

Wave Speed Reconstruction With Fink's Isotropic Phantom Data By Method A

first assume $\rho \equiv$ constant

Basic Questions: (a) Does elimination of $\nabla \mu \cdot \nabla u^s$ term result in serious imaging error? (b) Can we make a local algorithm in this case?

Calculating Phase Wave Speed or Shear Wave Speed in

$$
\sqrt{\mu/\rho}=1/|\nabla\phi|
$$

$$
\sqrt{\mu/\rho}=1/|\nabla \widehat T|
$$

(Geometric Optics Assumption) (No Locally Constant Assumption)

Methods:

1. Make polynomial approximation of ϕ to calculate derivatives;

2. Use averaging or medians of finite difference approximations to get $\nabla \phi$ or $\nabla \hat{T}$;

3. Distance method (McLaughlin, Renzi) – uses speed = distance / time

$$
\sqrt{\frac{\mu}{\rho}(x)} = \frac{1}{2\Delta t} \left[\min_{T(\hat{x}) = T(x) + \Delta t} |\hat{x} - x| \right]
$$

$$
+\min_{T(\hat{\bar{x}})=T(x)-\Delta t}|\hat{\bar{x}}-x|\big]
$$

slow but reliable.Choose step size according to SNR

Calculating Phase Wave Speed or Shear Wave Speed in

$$
\sqrt{\mu/\rho}=1/|\nabla\phi|
$$

(Geometric Optics Assumption) (No Locally Constant Assumption)

4. Level Curve Method (McLaughlin, Renzi)– Fast method $O(N)$, N number of grid points. (a) Construct higher dimensional function $\psi(x,t)$;

$$
\psi(x, T(x)) = 0
$$
\n**(b)**\n
$$
\psi(y, t) = \pm \min_{T(x) = t} |x - y|;
$$
\n**(c)**\n
$$
\psi_t(x, t)|_{t = \hat{T}(x)} \ge 0;
$$
\n**(d)** Show\n
$$
\psi_t = \sqrt{\mu/\rho}
$$

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Back Up : We have to find ϕ or \widehat{T}

I. Mathematically
$$
\hat{u} = M(x)e^{i\phi(x)}
$$

\n
$$
M = |\hat{u}|
$$
\n
$$
\text{Re } \hat{u}/M = \cos \phi
$$
\n
$$
\text{Re } \hat{u}/\text{ Im } \hat{u} = \cot \phi
$$

II. Phase unwrapping :

$$
\phi(x) = \text{arccot}[\text{Re}\hat{u}/\text{Im}\hat{u}]
$$

Method 1 : Determine arrival time surface by correlation

$$
\hat{T}(x_1) := \hat{T}(x_0) + \Delta \hat{t} \text{ where } x_1 = x_0 + \Delta x \text{ and }
$$

$$
\Delta \hat{t} = \arg \max_{\Delta t} \int u(x_0, t) u(x_1, t - \Delta t) dt.
$$

Method 2 : Take viscoelastic effects into account; See poster of Jens Klein.

Amplitude

Holographic Wave Movie Amplitude Time Traces In Amplitude Time Traces In Amplitude Time Traces In

Method(McLaughlin, Renzi)

- $\bullet\,$ Use cross covariance function to estimate $\,$ arrival times of moving interference pattern
- $\bullet\,$ Use Eikonal equation to find the speed of the $\,$ moving interference pattern

c_s = phase wave speed.

Start with : Isotropic models

Use linear elasticity equation system or acoustic model

Geometric optics approximation

$$
u_1 = ae^{i\omega_1(\phi(x)-t)}
$$

 $u_2 = be^{-i\omega_2 t}$, $\omega_1 - \omega_2 = O(10^{-1})$ At receiver

Measure $|u| = |u_1 + u_2| = a^2 + b^2 + 2ab\cos(\psi(x, t))$

$$
\gamma(x,t) = \omega_1(\phi(x) - t) + \omega_2 t, \quad \omega_2 = \omega_1 + \Delta \omega
$$

$$
\frac{\gamma_t^2}{|\nabla_x \gamma|^2} = \frac{(\Delta \omega)^2 c_s^2}{\omega_1^2}
$$

Holographic Wave Experiment Images

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Create Hybrid Methods: Apply to MR Data Example **(McLaughlin, Renzi, Yoon)**

$$
\mu/\rho\triangle \hat{u} + \omega^2 \hat{u} = 0
$$

\n- Example: Let
$$
\hat{u} = Me^{i\phi}
$$
, Assume μ/ρ is real ⇒ $\sqrt{\mu/\rho} = -\omega^2 M / \left[\triangle M - M |\nabla \phi|^2 \right]$ Step 1: Calculate $\triangle M$ using finite difference averaging; Adjust step size according to SNR.
\n- Step 2: Calculate $|\nabla \phi|^2$ as $1/c^2$ from $c|\nabla \phi| = 1$ using level curve method; Adjust step size according to SNR.
\n- Step 3: Apply local averaging to M.
\n

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Finite Element Methods

• Start with:
$$
\nabla \cdot (\mu \nabla \hat{u}) + \omega^2 \rho \hat{u} = 0
$$

Weak solution formulation

$$
\int_{\partial\Omega} v_j \mu \frac{d\hat{u}}{dn} - \int_{\Omega} \mu \nabla v_j \cdot \nabla \hat{u} + \int_{\Omega} \rho \omega^2 \hat{u} v_j = 0 \qquad \{v_j\}_{j=1}^n \text{-test element}
$$

Advantage: Don't need to take derivatives of μ ;

Basic Method: 1. \hat{u} and its derivatives – calculated as before;

2. Make expansions of
$$
\mu = \sum_{i=1}^n a_i f_i
$$
 ;

3. Find $\{a_i\}_{i=1}^n$ from the n equations.

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Maniatty and Park (Rensselaer) – see talks at conference

- • Subzone Method:
	- A. Eliminate boundary term; (only for acoustic model) B. Assume μ does not vary in normal direction in outer layer;

C. Assume $\rho \equiv$ constant;

D. Make finite element expansion for μ .

Full Elastic Model

•We obtain

$$
\int_{\Omega} p \nabla \cdot v_j + \frac{1}{2} \int_{\Omega} \mu \left[\nabla \hat{u} + (\nabla \hat{u})^T \right] \cdot \left[\nabla v_j + (\nabla v_j)^T \right] + \omega^2 \int_{\Omega} \rho \hat{u} \cdot v
$$

=
$$
\int_{\partial \Omega} \left[p \frac{dv}{dn} + \mu v_j \cdot \left[\nabla \hat{u} + (\nabla \hat{u})^T \right] \cdot n \right] d\sigma = \int_{\partial \Omega} T v_j d\sigma
$$

Apply subzone method : Now find $p =$ pressure and μ .

traction

Pressure Isn't Zero In Heterogeneous Case

•Recovery of μ with synthetic data – multiple inclusion;

Consider Anisotropic Models

- Muscle tissue has fibers ; z
- Elastic properties of cancerous tissue may be anisotropic (preliminary studies) ; \bullet
- More correct models give better results ;
- Distinguish cancerous from benign tissue.

Model for Transversely Isotropic Medium

(fiber in x_3 direction)

$$
\boxed{\rho \vec{u}_{tt} = \nabla \cdot \sigma = \nabla \cdot (\mathcal{C} \epsilon)} \qquad \epsilon = \frac{1}{2} (\nabla \vec{u} + \nabla \vec{u}^T), \mathcal{C} = (c_{ijkl})
$$

By relabelling $(11, 22, 33, 23, 31, 12) \rightarrow (1, 2, 3, 4, 5, 6), \sigma = \mathcal{C}\epsilon$ is represented by

$$
c_{11} = (1 - n\nu_{fp}^2)D, \quad c_{13} = \nu_{fp}(1 + \nu_p)D, \quad c_{33} = \frac{1}{n}(1 - \nu_p^2)D, \quad E_p, E_f = \text{Young's moduli}
$$

$$
c_{44} = \mu_{fp}, \quad c_{66} = \frac{E_p}{2(1 + \nu_p)}, \quad D := \frac{E_p}{(1 + \nu_p)(1 - \nu_p - 2n\nu_{fp}^2)}.
$$

Transversely Isotropic Medium

Incompressible condition:
$$
0 = \nabla \cdot \vec{u} = \text{tr}(\epsilon) \epsilon = \frac{1}{2} (\nabla \vec{u} + \nabla \vec{u}^T)
$$

For transversely isotropic medium: $1 = \nu_p + n \nu_{fp}$, $1 = 2 \nu_{fp}$

Identify Or identify E_p, E_f = Young's moduli μ_{fp} =shear modulus \vec{f} = fiber direction

 $c_{44} = \mu_{fp}$ $c_{66} = \frac{E_f E_p}{(4E_f - E_p)}$ $n = E_p/E_f$ \vec{f} = fiber direction

direction orthogonal to lines of constant phase.

Wave Fronts in Measured Data

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Anisotropic Case: Propagating Fronts

Arrival Time:

\n
$$
SH(x) = \inf\{t \in (0, T) : u(x, s) = 0, s \le t\}
$$

Theorem: If C_{44} , C_{66} , $\rho \in C^1(\overline{\Omega})$ and T_{SH} is Lipschitz continuous, then $C_{SH}^2 = \frac{C_{66}}{Q} + \left(\frac{C_{44}}{Q} - \frac{C_{66}}{Q}\right) \frac{(\nabla T_{SH} \cdot f)^2}{|\nabla T_{GH}|^2}.$ \vec{f} fiber direction $C_{SH}^2 |\nabla T_{SH}|^2 = 1.$ θ_{SH} ∇T_{SH} Goal 1: Given T_{SH} find C_{SH} . normal to the front

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In Isotropic and Anisotropic Cases:

Goal 1: Find speed in direction orthogonal to front; Anisotropic Case:

Goal A: Given \vec{f} , C_{66}/ρ and $\nabla T_{SH} \angle \vec{f}$, image $\sqrt{C_{44}/\rho}$; Goal B: Given \vec{f} , $\nabla T_{SH} \perp \vec{f}$, image $\sqrt{C_{66}}/\rho$;

Goal C: Given multiple T_{SH} , find $\sqrt{C_{44}/\rho}$, $\sqrt{C_{66}/\rho}$, \vec{f} .

 $C_S|\nabla \widehat{T}| = \sqrt{\frac{\mu}{\rho}}|\nabla \widehat{T}| = 1$ Isotropic:

Anisotropic: $1 = C_{SH}^2 |\nabla T_{SH}|^2 = \frac{C_{66}}{\rho} |\nabla T_{SH}|^2 + \left(\frac{C_{44}}{\rho} - \frac{C_{66}}{\rho}\right) (\nabla T_{SH} \cdot \vec{f})^2$

We can find wave speed in each case

Single Measurement – Downward Component

3D - Basic Equation

$$
C_{SH}^2 = \phi_t^2 = \frac{C_{66}}{\rho} + \left(\frac{C_{44}}{\rho} - \frac{C_{66}}{\rho}\right)(\nabla_x \psi \cdot \vec{f})^2 \quad t = T_{SH}(x)
$$

With four data sets $\{(\nabla_x \psi^j, C_{SH}^j)\}_{i=1}^4$, there are at most four distinct solutions $\{C_{44}^k/\rho,C_{66}^k/\rho,\vec{f}^k\}_{k=1}^4$. (This is a consequence of the nonlinearity)

Basic Property:

 C_{66}/ρ is the root of a fourth degree polynomial.

Numerical Reconstructions With Synthetic Data

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Total Variation Denoising

For all images – can apply smoothing to images.

$$
\min_{\sqrt{\mu/\rho} \in BV} \left[\gamma \int_{\Omega} \left\{ \left(\sqrt{\frac{\mu}{\rho}} \right)_D - \left(\sqrt{\frac{\mu}{\rho}} \right)_F \right\}^2 + \int_{\Omega} \left| \nabla \left(\sqrt{\frac{\mu}{\rho}} \right)_F \right| \right]
$$

with regularized Euler-Lagrange equation **Values from reconstruction Targeted final imaging functional**

$$
\nabla \cdot \left[\frac{\nabla \left(\sqrt{\frac{\mu}{\rho}}\right)_F}{\left|\nabla \left(\sqrt{\frac{\mu}{\rho}}\right)_F\right|+\epsilon}\right] + 2\gamma \left[\left(\sqrt{\frac{\mu}{\rho}}\right)_D - \left(\sqrt{\frac{\mu}{\rho}}\right)_F\right] = 0
$$

Introducing the evolving variable s, solve

$$
\frac{\partial}{\partial s}\sqrt{\frac{\mu}{\rho}}=\nabla\cdot\left[\frac{\nabla\left(\sqrt{\frac{\mu}{\rho}}\right)_F}{\left|\nabla\left(\sqrt{\frac{\mu}{\rho}}\right)_F\right|+\epsilon}\right]+2\gamma\left[\left(\sqrt{\frac{\mu}{\rho}}\right)_D-\left(\sqrt{\frac{\mu}{\rho}}\right)_F\right] \qquad \sqrt{\frac{\mu}{\rho}}\bigg|_{s=0}=\left(\sqrt{\frac{\mu}{\rho}}\right)_D
$$

Conclusion

- • Inverse Problem:
	- 1. Modeling;
	- 2. Identify richest or most usable data sets;
	- 3. Identify acceptable approximations;
	- 4. Smart algorithms.
- • Data:
	- 1. Data smoothing that maximizes information content;
	- 2. Identify rich data subsets.
- \bullet Algorithm Options Covered In This Talk:
	- 1. Finite Difference based local algorithms;
	- 2. Arrival Time algorithms;
	- 3. Finite Element weak solution formulations.

