MR elastography for brain biomechanics

Philip Bayly

Erik Clayton, Aaron Feng, Ravi Namani, Traci Abney, Ruth Okamoto, Andrew Knutsen, Guy Genin

Mechanical Engineering and Materials Science
Washington University in St. Louis
Basic idea of elastography

Visualize mechanical waves in tissue

Wave speed and wavelength depend on elastic modulus (stiffness)

Elastic modulus depends on tissue type/age/pathology
Motivation

Computer simulation and mathematical modeling are critical to understanding and preventing TBI

- Confidence in simulations is limited
- Brain/skull are difficult to model
- Predictions are difficult to verify

Experimental data is needed to define and validate computer models.

Courtesy of Martin Ostoja-Starszewski (University of Illinois)
Outline

• Impact and traumatic brain injury
  • Response of brain to skull acceleration
• MR elastography and brain stiffness
  • Visualization of shear waves in brain tissue
Overview of the Brain
MR tagging

- Subject 1: Adult male

- Resolution
  - Spatial: 1.5 mm
  - Temporal: 6 ms
  - Tag spacing: 8 mm

- 2 cm above reference plane

- Angular acceleration
  - \(\sim 250 \text{ rad/s}^2\)
MR tagging: absolute brain-skull motion

- Adult male
- Resolution
  - Spatial: 1.5 mm
  - Temporal: 6 ms
  - Tag spacing: 8 mm
- Linear acceleration
  - ~30 m/s²
MR measurement of shear waves: phase contrast

Pulse sequence

Oscillating gradients

Phase accumulation proportional to displacement.

Visualize µm-amplitude harmonic motion
Requires MR compatible actuation

Spatiotemporal Images of Shear Wave Propagation
Container of Gelatin w/ Soft Inclusion
Harmonic actuator (~20 µm peak-to-peak)

(Erik Clayton)
MR elastography basic principle

Given: \( \mathbf{u}_T(x, y, z, t) \)

Find: shear modulus \( \mu \)

Fit \( \mu \) to shear wave equation (minimize LSE)

Simplest case:
linear elastic, homogeneous, isotropic,

\[
\rho \frac{\partial^2 \mathbf{u}_T(x, y, z, t)}{\partial t^2} - \mu \nabla^2 \mathbf{u}_T(x, y, z, t) = 0
\]

18 mm

Gelatin – heterogeneous
400 Hz
MR elastography: Helmholtz decomposition

Isolate transverse wave component of displacement

\[ u = u_T + u_L \]
\[ \nabla \cdot u_T = 0, \]
\[ \nabla \times u_L = 0, \]

Helmholtz decomposition performed in spatial frequency domain*

\[ U(k,t) = \mathcal{F}(u(x,t)) \]
\[ U_T(k,t) = -\frac{k \times (k \times U(k,t))}{k \cdot k} \]
\[ u_T(x,t) = \mathcal{F}^{-1}(U_T(k,t)) \]

Dilatation and distortion components

linear elastic, isotropic, homogeneous

Equation of motion (no body force)

\[ \rho \frac{\partial^2 u_k}{\partial t^2} = \mu \nabla^2 u_k + (\lambda + \mu) \frac{\partial}{\partial x_k} (\nabla \cdot \mathbf{u}), \]

Shear Dilatation

Divergence (Dilatational)

\[ \frac{\partial^2}{\partial t^2} (\nabla \cdot \mathbf{u}) = \frac{\lambda + 2\mu}{\rho} \nabla^2 (\nabla \cdot \mathbf{u}), \]

Curl (Shear)

\[ \frac{\partial^2}{\partial t^2} (\nabla \times \mathbf{u}) = \frac{\mu}{\rho} \nabla^2 (\nabla \times \mathbf{u}), \]

Distortion (rotation) describes shear wave motion

\[ \Gamma_z = \frac{1}{2} \left( \frac{\partial u_y}{\partial x} - \frac{\partial u_x}{\partial y} \right) \]

Fitting steps: more details

Fit displacement or curl as a linear function of Laplacian, in a neighborhood around each voxel

\[ U_k(x) = \left( \frac{-G^*}{\rho \omega^2} \right) \nabla^2 U_k(x) \]

\[ \Gamma_k(x) = \left( \frac{-G^*}{\rho \omega^2} \right) \nabla^2 \Gamma_k(x) \]
Virtual fields method

- Fabrice Pierron (Uni Southampton)
- Nathanael Connesson (Uni Grenoble)
- 3D volume – gel cube in vibration (400 Hz)

Piezo actuator

Rod

Specimen in cube

Mounted in the bore of a 11.7 T MRI facility
Virtual fields method

- $f=400$ Hz, $0.5 \times 0.5 \times 0.5$ mm
- 8 images shifted by period fractions of $1/8$, $2/8$ etc.
- Displacement map: $u$ in mm

With Fabrice Pierron (Southampton) / Nathanael Connesson (Grenoble)
Virtual fields method

- Identification
  - Viscoelastic model
  - Isotropy, incompressibility

Zero virtual displacements on all edges
Optimized piecewise virtual fields

\[-\int \sigma_{ij} \varepsilon_{ij}^* \, dV = \int \rho a_i u_i^* \, dV\]

G', G''

3D map of local complex modulus!

With Fabrice Pierron (Southampton) / Nathanael Connesson (Grenoble)
Phantom studies: validation

• Gelatin
  – 70 g glycerol + 70 g water + 4 g gelatin

• Material properties and geometry:
  – Stable
  – Prescribed
  – Predictable
Magnetic Resonance Elastography @ 4.7 T


**PS:** GRE-MRE (Clayton/Bayly)
**TR/TE:** 200/13.75, **FA:** 30°, **nt:** 2
**DM:** 192 x 192 x 11 x 8
**t_{acq}:** 20 minutes/frequency
Raw MRE data

Linear elastic isotropic wave equation

\[-\rho \omega^2 u_i = \mu u_{i,jj} + (\lambda + \mu) u_{j,ji}\]

MRE to DST comparison: good agreement of $G'$ and $G''$

Agreement within 10% at frequency overlap

MOUSE BRAIN
Small animal MRE is important

• Advantages
  – Can perform studies on animals that cannot be performed on humans
    • injury, aging, development, therapeutic intervention, genetics
  – Correlate mechanical properties with histology
  – Reduce technology development costs

• Challenges
  – Requires high spatial resolution
Shear waves induced in brain via *actuated* bite bar

Mouse Brain MRE
Multi-frequency Study

**PS:** SE-MRE (Kroenke/Bayly)
**TR/TE:** 1000/27.5, **nt:** 2
**DM:** 128 x 128 x 29 x 4 (8)
**t_{acq}:** 22 (45) minutes/frequency

4.7 T Varian Consol
Acquired Res.: 250 x 250 x 250 µm

Mouse Brain MRE
Multi-frequency Study

600 Hz

800 Hz

1200 Hz

1800 Hz

4.7 T Varian Consol
Acquired Res.: 250 x 250 x 250 µm
Motion Encoding Cycles: 4 (600 Hz), 5 (800 Hz), 8 (1200 Hz), 10 (1800 Hz)
M.E. Gradient Amp.: +/-18 G/cm
Through-image-plane motion sensitized
Frequency dependence of brain tissue in vivo

<table>
<thead>
<tr>
<th>Frequency (Hz)</th>
<th>Storage modulus, $G'$</th>
<th>Loss modulus, $G''$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atay et al (2008)</td>
<td>1200</td>
<td>13.8</td>
</tr>
<tr>
<td>Diguet et al (2009)</td>
<td>1000</td>
<td>7.36</td>
</tr>
<tr>
<td>Schregel et al (2010)</td>
<td>1000</td>
<td>≈5.40</td>
</tr>
<tr>
<td>Murphy et al (2010)</td>
<td>1500</td>
<td>26.0</td>
</tr>
<tr>
<td></td>
<td>22.0</td>
<td>–</td>
</tr>
</tbody>
</table>

HUMAN BRAIN
Understand human brain response to acoustic pressure load \textit{in vivo}

**Experimental Setup**

- Flexible tubing
- Acoustic actuator
- Pressure transducer
- Passive actuator pads (L/R)

**Motion components**: $u$, $v$, & $w$

**No. Image Slices**: 1

**Temporal Resolution**: 4 point

**Voxel**: $3.0 \times 3.0 \times 3.0 \text{ mm}^3$

**MRE Pulse Sequence**

- **PS**: GRE-MRE (Bolster/Priatna, Siemens)
- **TR/TE**: 133.3/27.5, FA: 25°, nt: 1
- **DM**: $128 \times 128 \times 1 \times 4$
- **$t_{\text{acq}}$$**: 12 minutes/frequency/direction

Clayton, Genin, Bayly. RSIF 2012. (In press)
Spatiotemporal displacement vector data obtained in ~30 min

Clayton, Genin, Bayly. RSIF 2012. (In press)
3D brain displacement data for FE model calibration

Contour: \( v \) – displacement component (\( \mu \text{m} \))

Clayton, Genin, Bayly. RSIF 2012. (In press)
About those two wave propagation modes...

Recall, 2 Wave Modes

\[ \rho \frac{\partial^2 u_k}{\partial t^2} = \mu \nabla^2 u_k + (\lambda + \mu) \frac{\partial}{\partial x_k} (\nabla \cdot \vec{u}), \]

- **Shear**
- **Dilatation**

Divergence (Dilatational)

\[ \frac{\partial^2}{\partial t^2} (\nabla \cdot \vec{u}) = \frac{\lambda + 2\mu}{\rho} \nabla^2 (\nabla \cdot \vec{u}), \]

Curl (Shear)

\[ \frac{\partial^2}{\partial t^2} (\nabla \times \vec{u}) = \frac{\mu}{\rho} \nabla^2 (\nabla \times \vec{u}), \]

Distortion (rotation) describes **Shear Wave** motion

\[ \Gamma = \frac{1}{2} \left( \frac{\partial u_2}{\partial x} - \frac{\partial u_1}{\partial y} \right). \]
Extracranial acoustic pressure induces shear waves in the brain

\[ \Gamma = \frac{1}{2} \left( \frac{\partial u_2}{\partial x} - \frac{\partial u_1}{\partial y} \right) \]

S014 MREB016
45 Hz
Displacements
Scaled x2000

Clayton, Genin, Bayly. RSIF 2012. (In press)
What happens when the frequency changes?
Increasing frequency leads to lower amplitudes and shorter wavelengths.
Shear wave motion tells us more

\[ \mathbf{v}(\mathbf{r}_0) = \sum_{p=1}^{16} |\Gamma_p(\mathbf{r}_0)| \cdot (\cos \theta_p \mathbf{e}_1 + \sin \theta_p \mathbf{e}_2). \]

\[ f_p(\theta_{mn}) = \begin{cases} 
\cos^2 (\theta_{mn} - \theta_p), & \|\theta_{mn} - \theta_p\| \leq \pi/8 \\
0, & \|\theta_{mn} - \theta_p\| > \pi/8 
\end{cases} \]
Propagation vector fields show energy flux and dissipation.

Propagation vector field: \( \vec{v}(\vec{r}_0) \)

Divergence of propagation vector field: \( \nabla \cdot \vec{v}(\vec{r}_0) \)

Clayton, Genin, Bayly. RSIF 2012. (In press)
Structural membranes are energy conduits

Gray's Anatomy

Clayton, Genin, Bayly. RSIF 2012. (In press)
Local spatial frequency estimation

Recall equation of motion (shear wave components)

\[- \rho \omega^2 U_j(x) = G^* \nabla^2 U_j(x)\]

Estimate local frequency and attenuation

Displacement \[U_j(x) = U_{0j} e^{ik \cdot x}\]

Curl \[\Gamma_j(x) = \Gamma_{0j} e^{ik \cdot x}\]

Estimate complex modulus from local wavelength and attenuation

\[G^* = \frac{\rho \omega^2}{\kappa^2 - \alpha^2 + i2\alpha \kappa}\]
Viscoelastic properties of brain tissue in vivo

\[ \begin{bmatrix} k^2 - \alpha^2 & 2\alpha k \\ -2\alpha k & k^2 - \alpha^2 \end{bmatrix} \begin{bmatrix} G' \\ G'' \end{bmatrix} = \begin{bmatrix} \rho \omega^2 \\ 0 \end{bmatrix} \]

<table>
<thead>
<tr>
<th>Frequency (Hz)</th>
<th>G' (kPa)</th>
<th>G'' (kPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grey</td>
<td>White</td>
<td>Grey</td>
</tr>
<tr>
<td>45</td>
<td>2.8</td>
<td>3.7</td>
</tr>
<tr>
<td>0.51</td>
<td>0.76</td>
<td>0.23</td>
</tr>
<tr>
<td>60</td>
<td>3.1</td>
<td>3.3</td>
</tr>
<tr>
<td>0.33</td>
<td>0.09</td>
<td>0.30</td>
</tr>
<tr>
<td>80</td>
<td>4.4</td>
<td>4.7</td>
</tr>
<tr>
<td>0.25</td>
<td>0.55</td>
<td>0.22</td>
</tr>
</tbody>
</table>
MR elastography in brain

<table>
<thead>
<tr>
<th>Material</th>
<th>G' 45 Hz</th>
<th>G' 60 Hz</th>
<th>G' 80 Hz</th>
<th>G'' 45 Hz</th>
<th>G'' 60 Hz</th>
<th>G'' 80 Hz</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gray matter</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White matter</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Displacement Animations
• For visualizing wave propagation in the foot-head direction, MRE displacement data is resliced and animated perpendicular to image acquisition planes.
z-component of curl and $\varepsilon_{xy}$ computed for third slice
Shear strain amplitudes and dilatation

\[ |\varepsilon_{xy}|, \quad |\varepsilon_{xz}|, \quad |\varepsilon_{yz}|, \quad \frac{1}{3} |\text{trace}(\varepsilon)| \]
Mechanical Anisotropy

Mechanical Isotropy

Mechanical Anisotropy

Fiber Alignment
Diffusion tensor imaging detects anisotropic diffusion of water (anisotropic structure)
• DTI data is processed using method of Shimony et al (Radiology 212:770-784, 1999) to compute MD, FA, and eigenvectors.
• DTI slice planes are the same as the MRE slice planes.
• Arrow plots used to code regions with fractional anisotropy above a threshold of 0.25.
• Arrow direction/color indicate direction of eigenvector of maximum diffusion and length indicates magnitude of FA.
DTI + MRE process
MR elastography

• MRE provides estimates of brain stiffness *in vivo*
  – Characterizes linear behavior (small deformations)
  – Provides estimates of complex shear modulus

• MRE provides measurements of displacement and strain due to acoustic excitation
  – Complements tagging studies
  – Illuminates effects of anatomy on motion
Acknowledgements

• Group members
  • R Namani, AK Knutsen, AA Sabet, SM Atay, CL Mac Donald, TS Cohen, CC Kessens, EE Black, Erik Clayton, Aaron Feng,

• Collaborators
  • LA Taber, JJ Neil, J Ackerman, CD Kroenke, Fabrice Pierron
  • GM Genin, DL Brody, RJ Okamoto

• Funding
  • NIH: Grants R21 NS045237, R01 NS055951, R21 EB005834
  • NSF: Grant DMS-0540701
  • McDonnell Center for Higher Brain Function
  • McDonnell Center for Cellular and Molecular Neurobiology