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Engineering

MR elastography for brain biomechanics

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MISSOURI


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Basic idea of elastography

Visualize **mechanical waves** in tissue

Wave speed and wavelength depend on **elastic modulus** (stiffness)

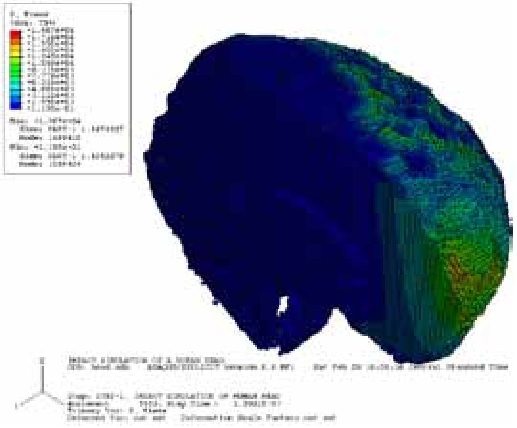
Elastic modulus depends on tissue type/age/pathology

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

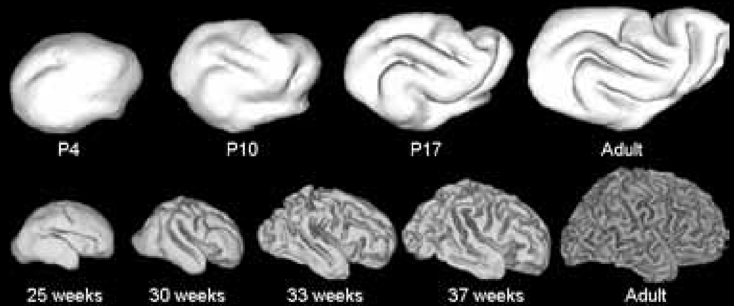
Experimental data is needed to define and validate computer models.



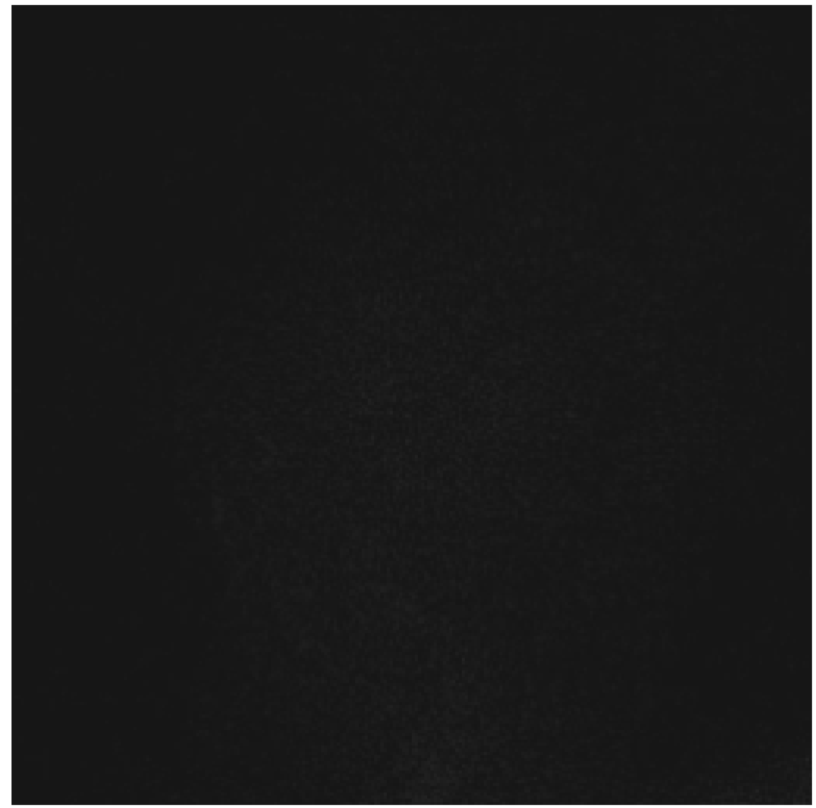
Courtesy of Martin Ostoja-Starszewski (University of Illinois)

Outline

- Impact and traumatic brain injury
  - Response of brain to skull acceleration
- MR elastography and brain stiffness
  - Visualization of shear waves in brain tissue

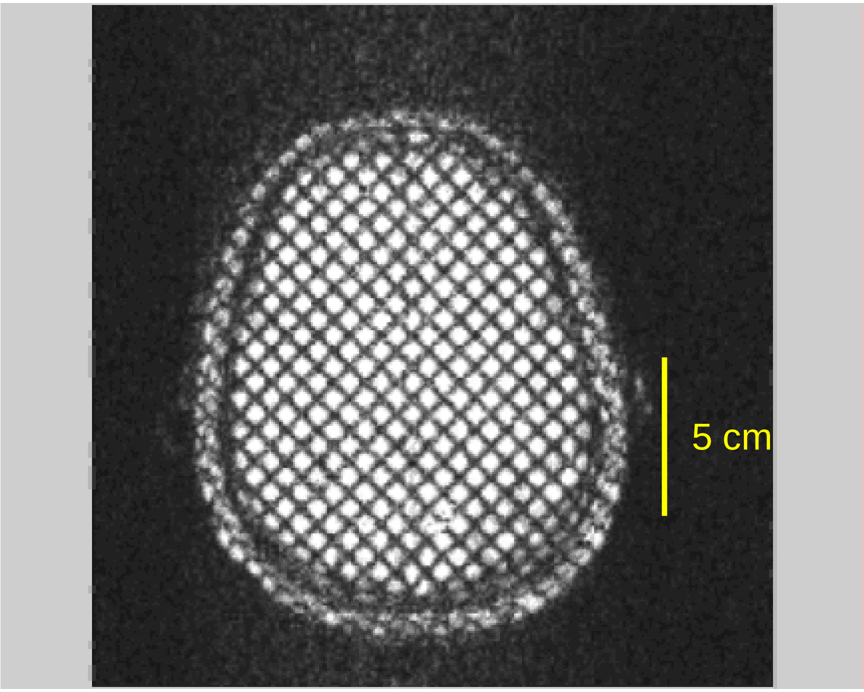


Overview of the Brain



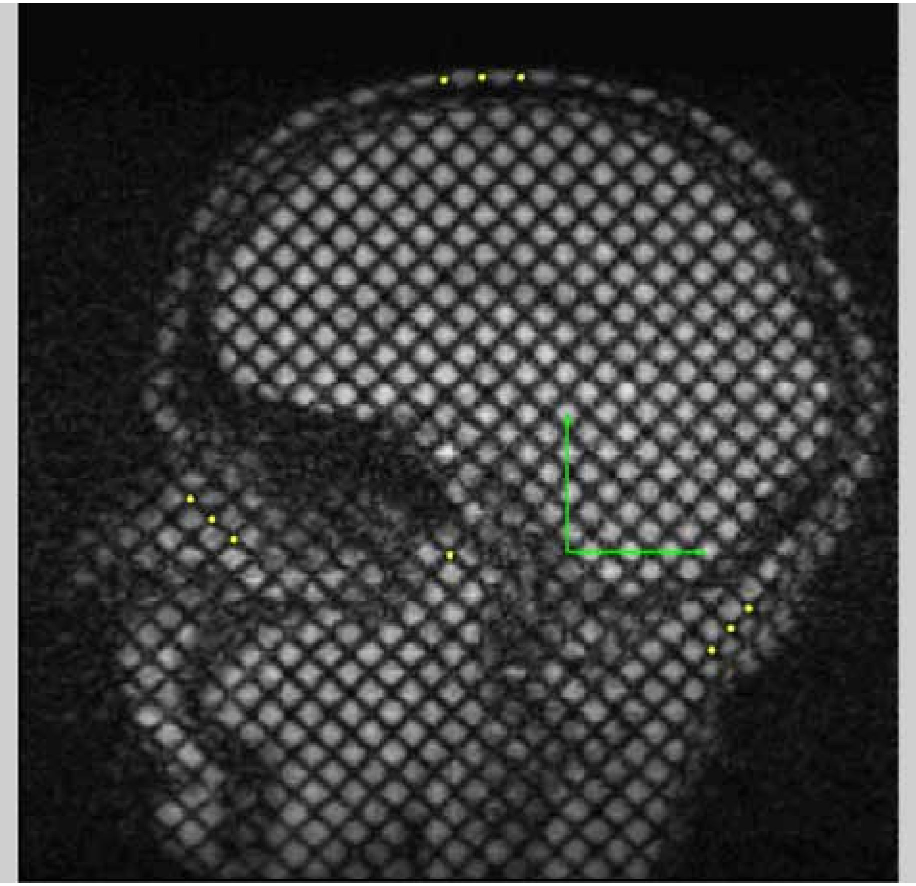
MR tagging

- Subject 1: Adult male
- Resolution
    - Spatial: 1.5 mm
    - Temporal: 6 ms
    - Tag spacing: 8 mm
- 2 cm above reference plane
- Angular acceleration
    - ~250 rad/s^2



MR tagging: absolute brain-skull motion

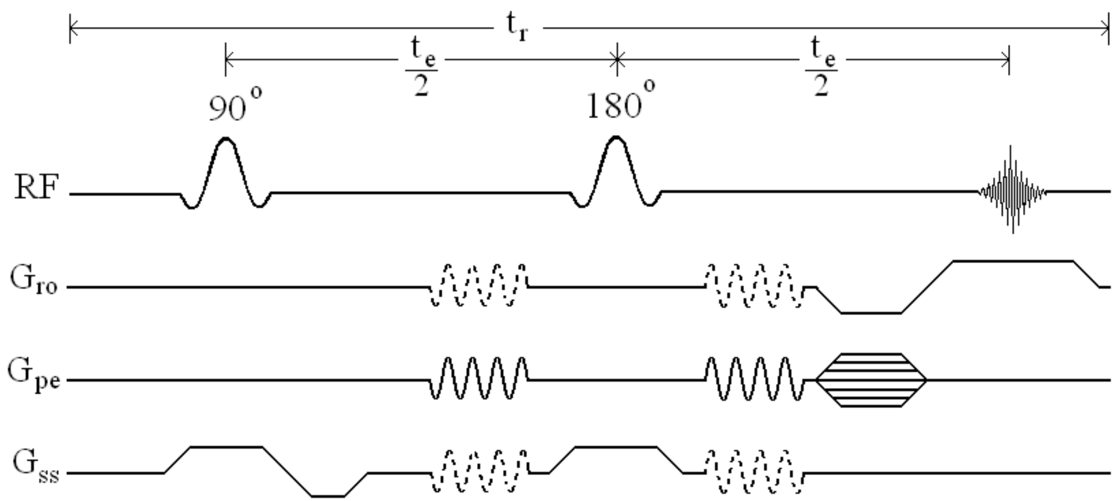
- Adult male
- Resolution
  - Spatial: 1.5 mm
  - Temporal: 6 ms
  - Tag spacing: 8 mm
- Linear acceleration
  - ~30 m/s^2



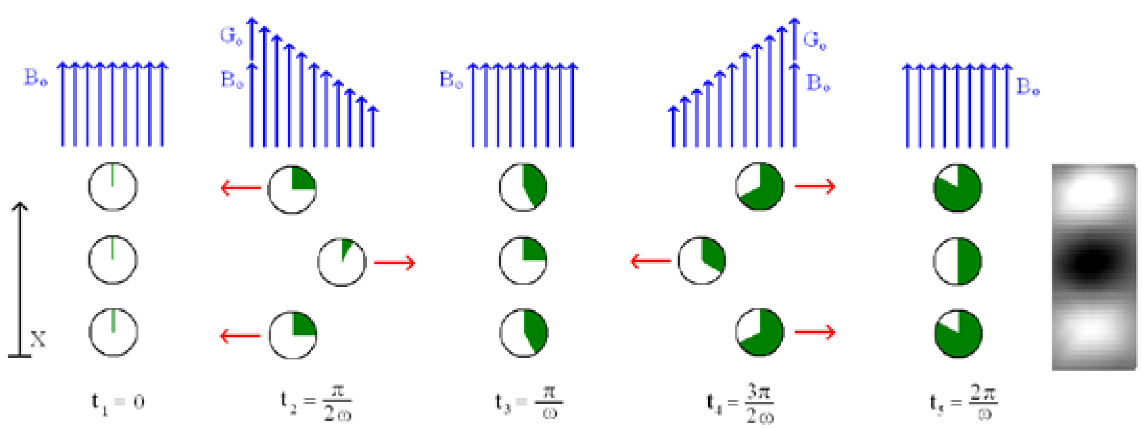
MR measurement of shear waves: phase contrast

Pulse sequence

Oscillating gradients

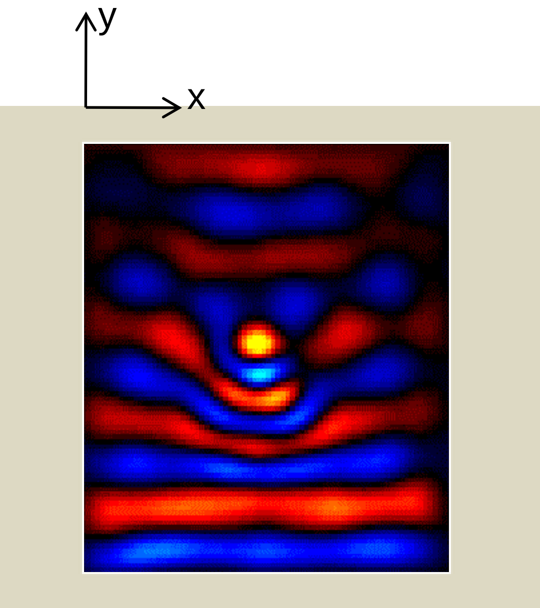


Phase accumulation proportional to displacement.

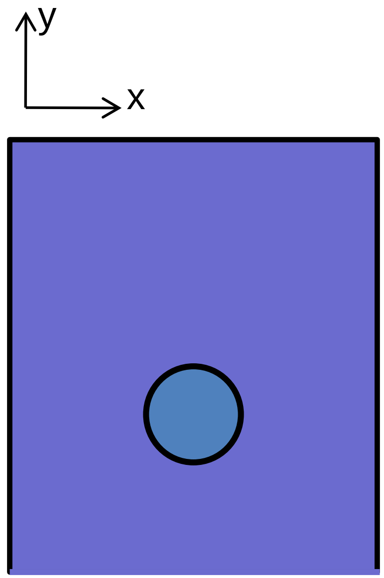


Atay et al. (2008) J Biomech Engrg.

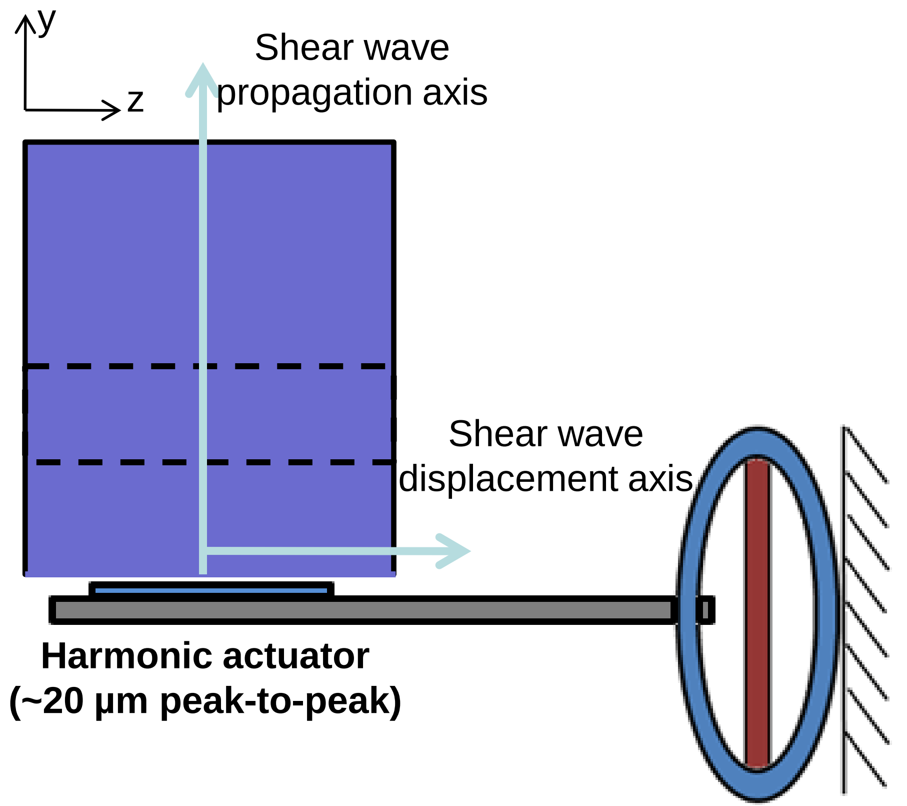
Visualize µm-amplitude harmonic motion Requires MR compatible actuation



Spatiotemporal Images of Shear Wave Propagation



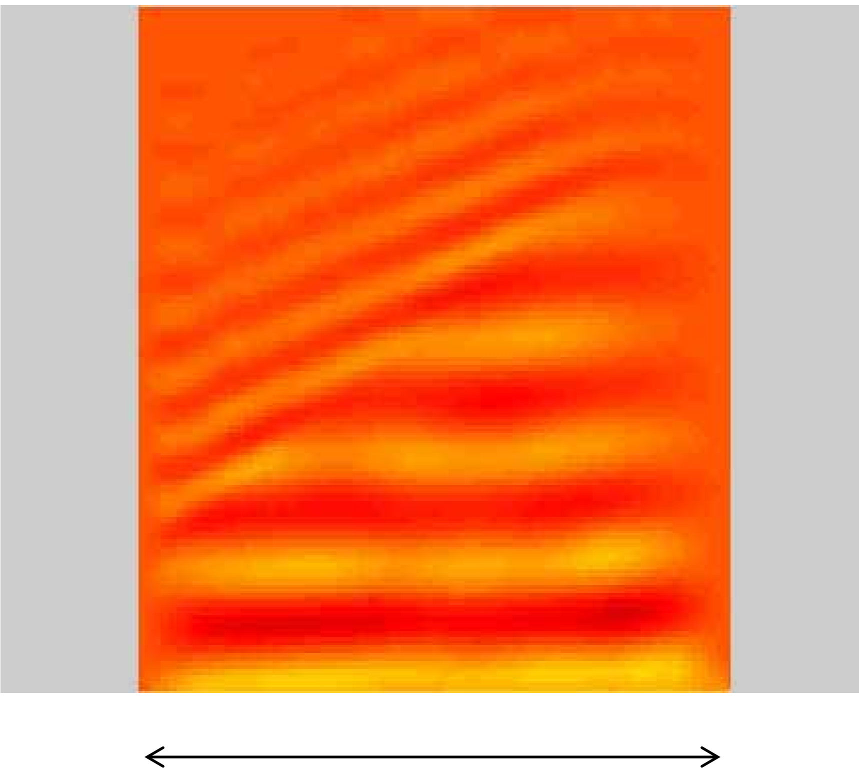
Container of Gelatin w/ Soft Inclusion



Harmonic actuator (~20 µm peak-to-peak)

(Erik Clayton)

MR elastography basic principle



18 mm

Gelatin – heterogeneous
400 Hz

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

Find: shear modulus μ

Fit μ to shear wave equation (minimize LSE)

Simplest case:

linear elastic, homogeneous, isotropic,

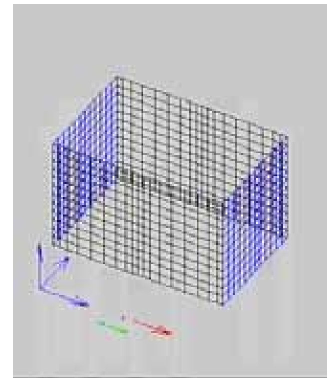
$$\rho \frac{\partial^2 \mathbf{u}_T(x, y, z, t)}{\partial t^2} - \mu \nabla^2 \mathbf{u}_T(x, y, z, t) = \mathbf{0}$$

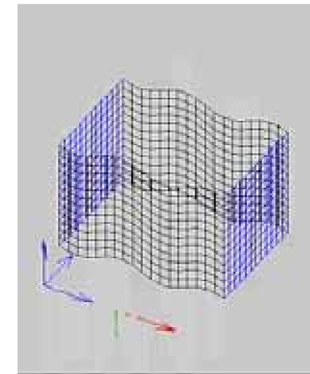
MR elastography: Helmholtz decomposition

Isolate transverse wave component of displacement

$$\mathbf{u} = \mathbf{u}_T + \mathbf{u}_L$$

$$\nabla \cdot \mathbf{u}_T = 0,$$
$$\nabla \times \mathbf{u}_L = 0,$$





Helmholtz decomposition performed in spatial frequency domain*

$$\mathbf{U}(\mathbf{k},t) = \mathcal{F}\left(\mathbf{u}(\mathbf{x},t)\right)$$

$$\mathbf{U}_T(\mathbf{k},t) = -\frac{\mathbf{k} \times \left(\mathbf{k} \times \mathbf{U}(\mathbf{k},t)\right)}{\mathbf{k} \cdot \mathbf{k}}$$

$$\mathbf{u}_T(\mathbf{x},t) = \mathcal{F}^{-1}\left(\mathbf{U}_T(\mathbf{k},t)\right)$$

*Romano et al. Mag Res Med. 2005)

Dilatation and distortion components

linear elastic, isotropic, homogeneous

Equation of motion (no body force)

$$\rho \frac{\partial^2 u_k}{\partial t} = \underbrace{\mu \nabla^2 u_k}_{\text{Shear}} + \underbrace{(\lambda + \mu) \frac{\partial}{\partial x_k} (\nabla \cdot \bar{\mathrm{u}})}_{\text{Dilatation}},$$

Divergence (Dilatational) →

$$\frac{\partial^2}{\partial t^2} (\nabla \cdot \bar{\mathrm{u}}) = \frac{\lambda + 2\mu}{\rho} \nabla^2 (\nabla \cdot \bar{\mathrm{u}}),$$

Curl (Shear) →

$$\frac{\partial^2}{\partial t^2} \boxed{(\nabla \times \bar{\mathrm{u}})} = \frac{\mu}{\rho} \nabla^2 \boxed{(\nabla \times \bar{\mathrm{u}})},$$

Distortion (rotation) describes *shear wave* motion

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

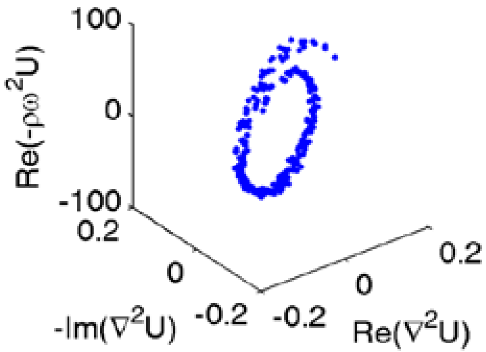
Clayton, Genin, Bayly. Transmission, Attenuation, and Reflection of Shear Waves in the Human Brain. (RSIF 2012)

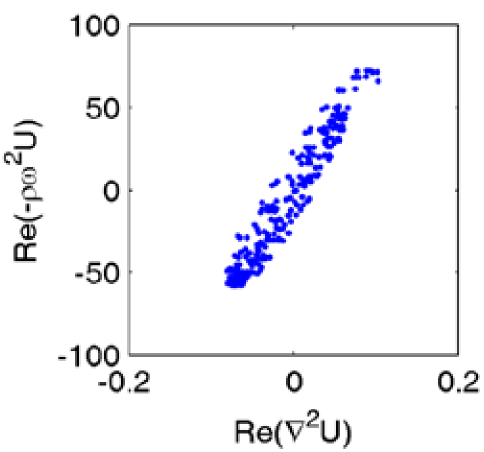
Fitting steps: more details

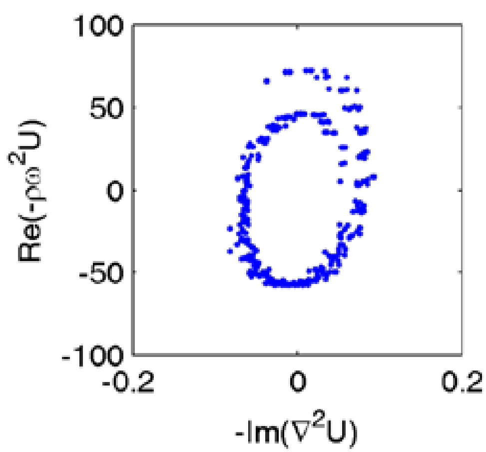
Fit displacement or curl as a linear function of Laplacian, in a neighborhood around each voxel

$$U_k(\mathbf{x}) = \left(\frac{G^*}{\rho\omega^2}\right)\nabla^2 U_k(\mathbf{x})$$

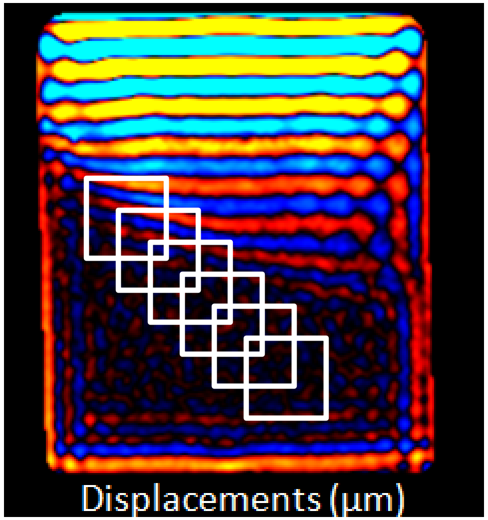
$$\Gamma_k(\mathbf{x}) = \left(\frac{G^*}{\rho\omega^2}\right)\nabla^2 \Gamma_k(\mathbf{x})$$



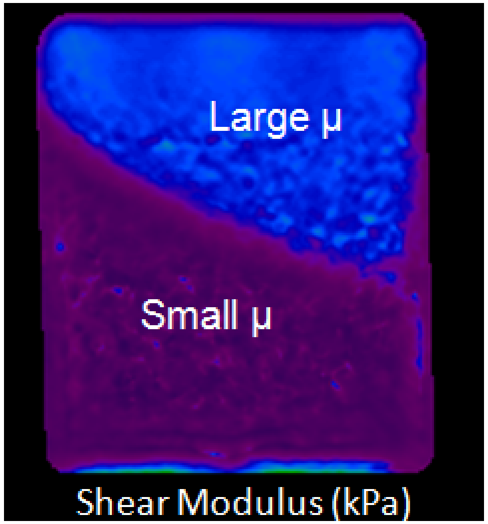




Wave Image

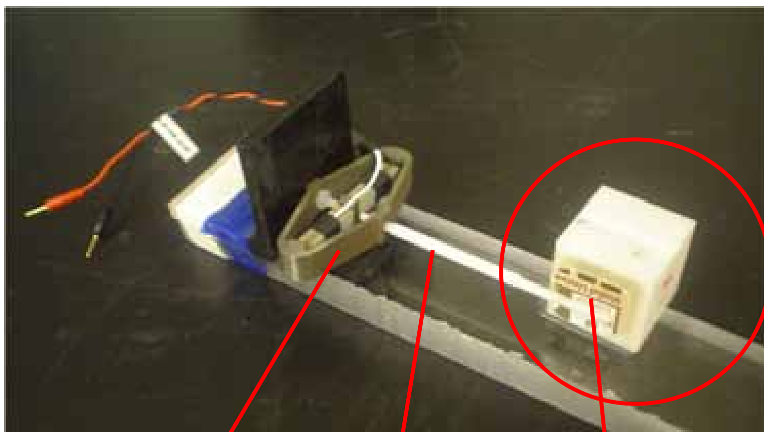


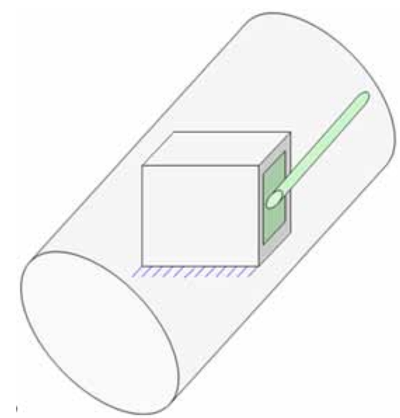
Elastogram



Virtual fields method

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





Piezo actuator

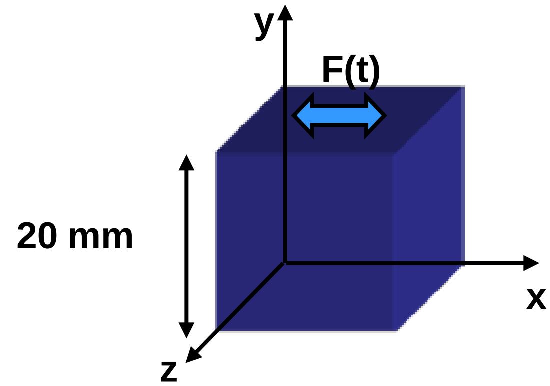
Rod

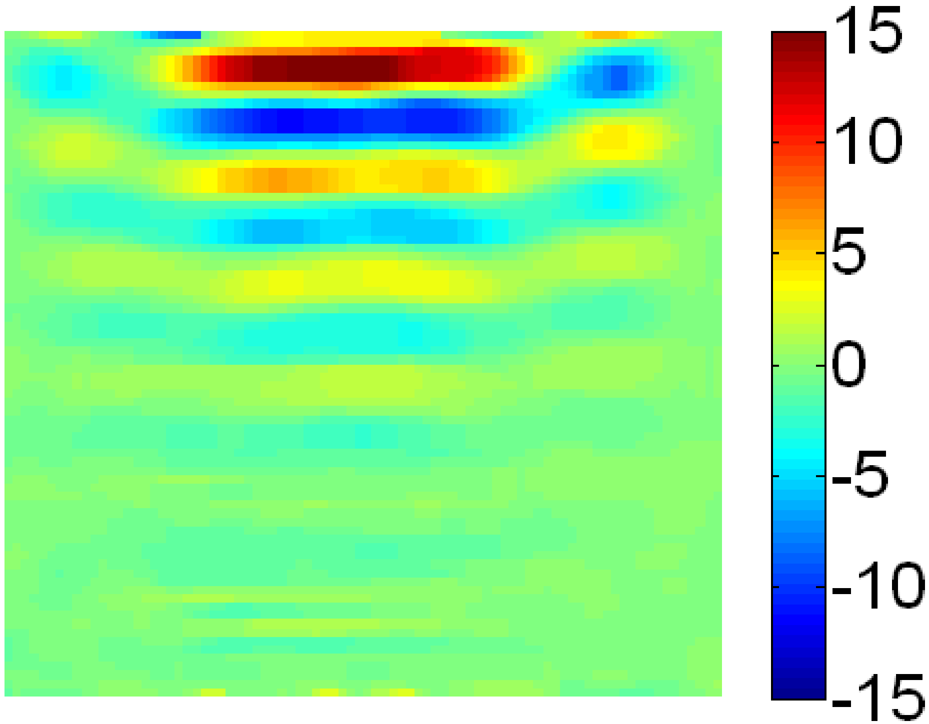
Specimen in cube

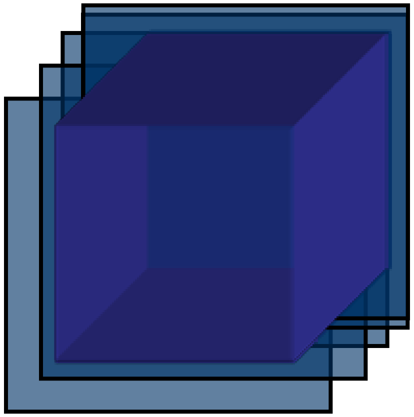
Mounted in the bore of a 11.7 T MRI facility

Virtual fields method

- f=400 Hz, 0.5x0.5x0.5 mm
- 8 images shifted by period fractions of 1/8, 2/8 etc.
  - Displacement map: u in mm

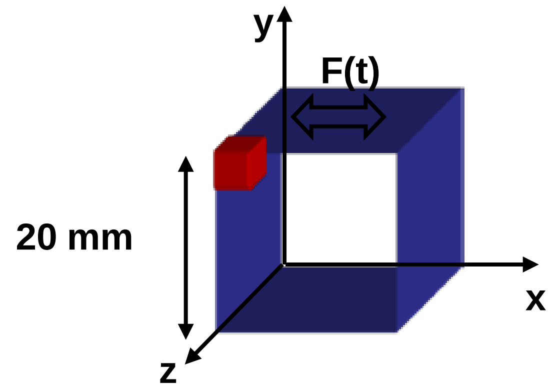






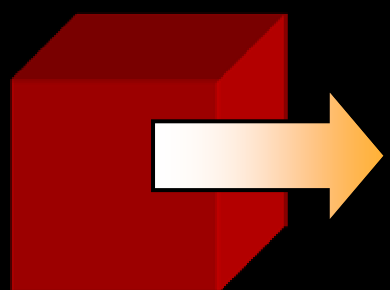
With Fabrice Pierron (Southampton) / Nathanael Connesson (Grenoble)

Virtual fields method



- Identification
  - Viscoelastic model
  - Isotropy, incompressibility

Zero virtual displacements on all edges
Optimized piecewise virtual fields



$$-\int_V \sigma_{ij}\,\varepsilon^*_{ij}\,dV = \int_V \rho\, a_i\, u^*_i\, dV$$

$$G', G''$$

3D map of local complex modulus !

With Fabrice Pierron (Southampton) / Nathanael Connesson (Grenoble)

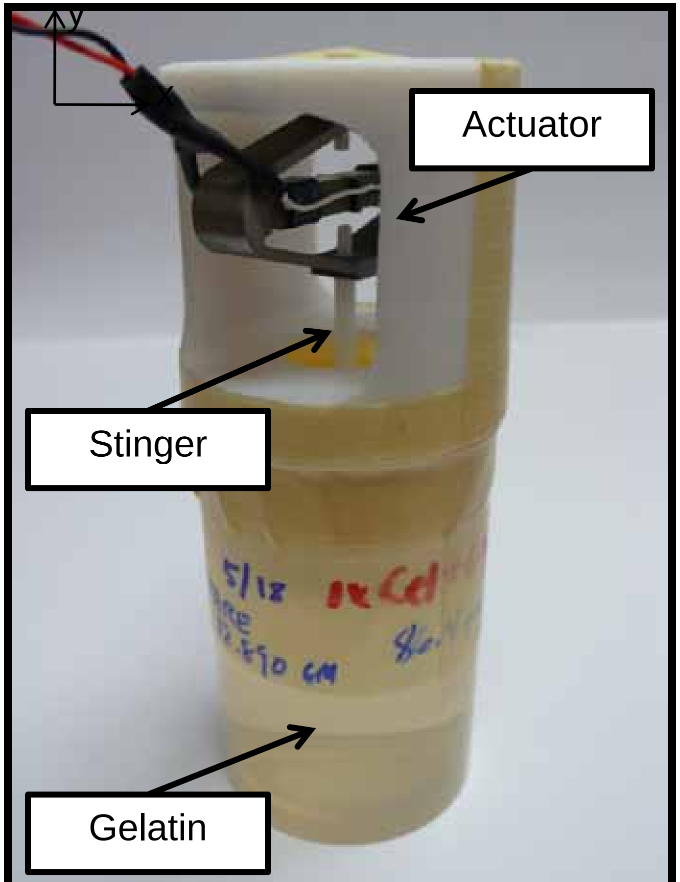
Phantom studies:validation

- Gelatin
  - 70 g glycerol + 70 g water + 4 g gelatin

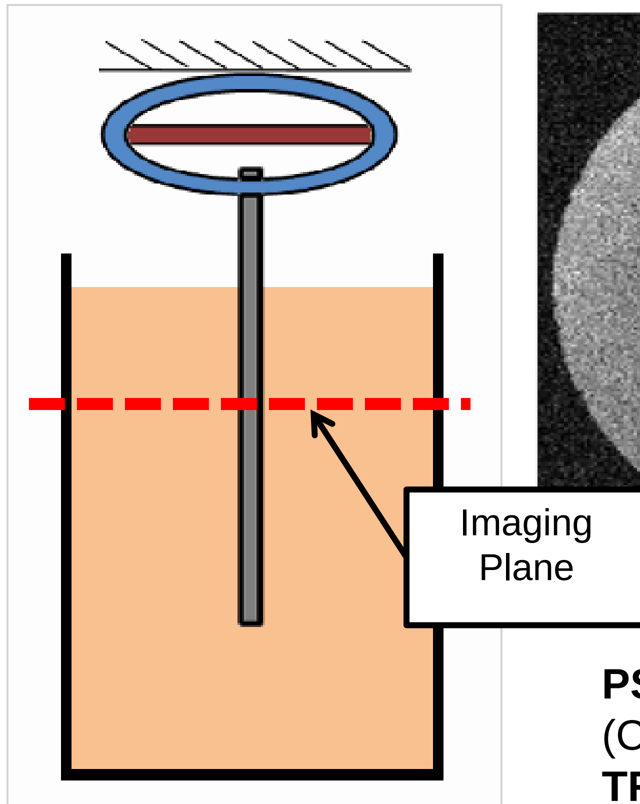
- Material properties and geometry:
  - Stable
  - Prescribed
  - Predictable

Gelatin-based phantom

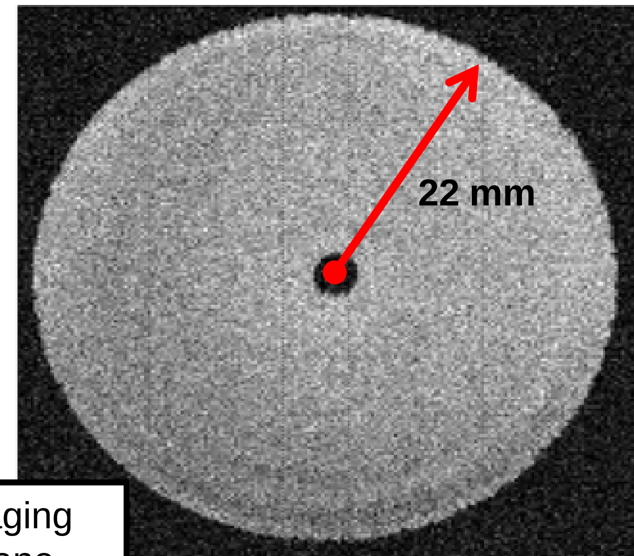
Magnetic Resonance Elastography @ 4.7 T



Setup Schematic



Magnitude Image

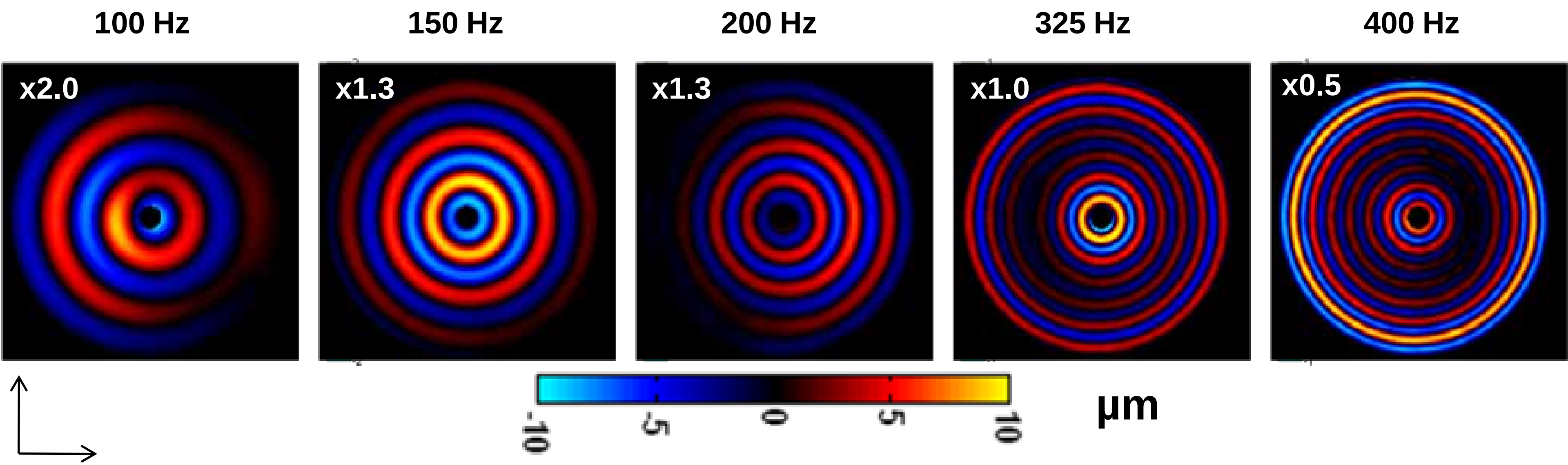


250µm x 250µm x 500µm

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

Okamoto, Clayton, Bayly. (2011) Phys. Med. Biol. 56, 6379-6400.

Raw MRE data

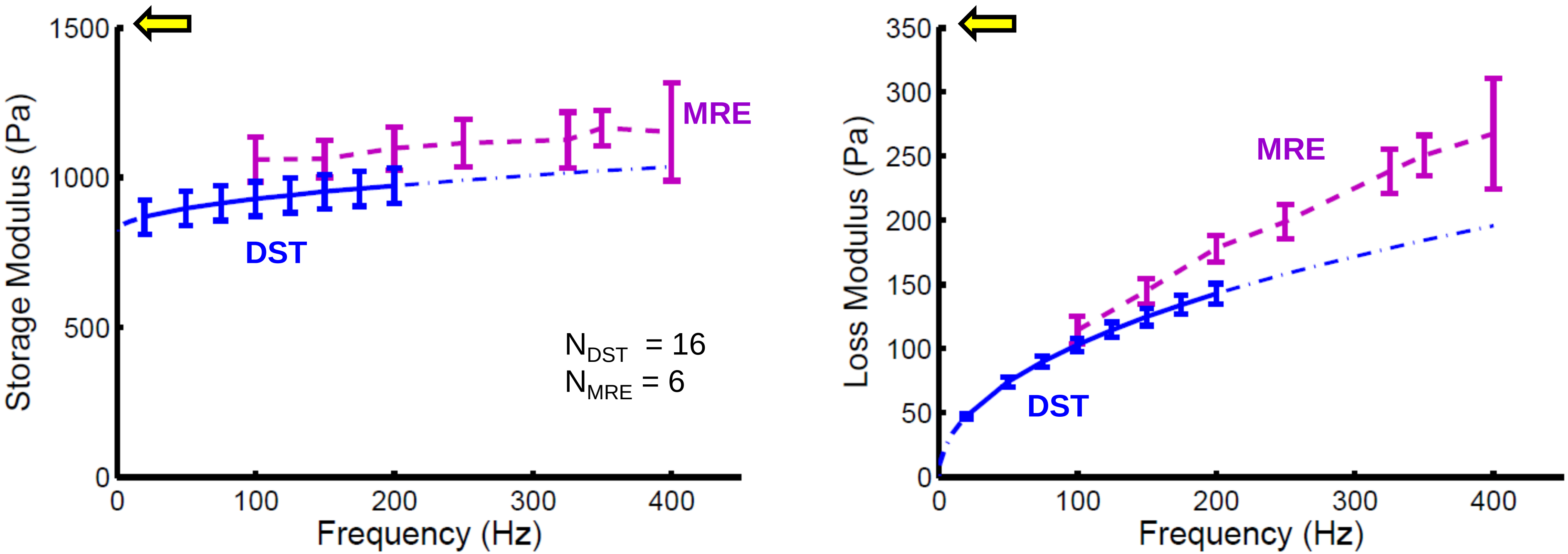


Linear elastic isotropic wave equation

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

Okamoto, Clayton, Bayly. (2011) Phys. Med. Biol. 56, 6379-6400.

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



Agreement within 10% at frequency overlap

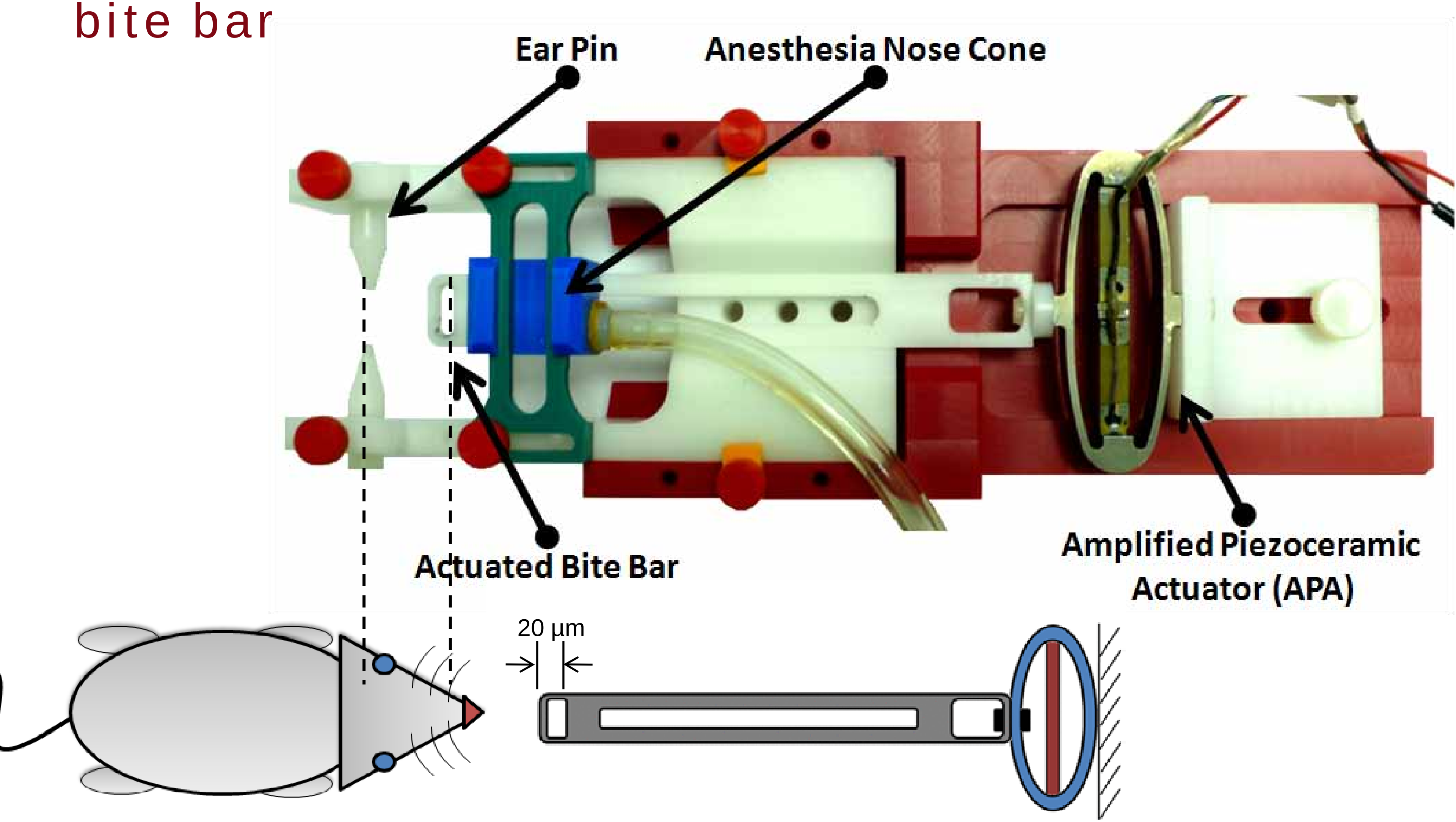
Okamoto, Clayton, Bayly. (2011) Phys. Med. Biol. 56, 6379-6400.

MOUSE BRAIN

Small animal MRE is important

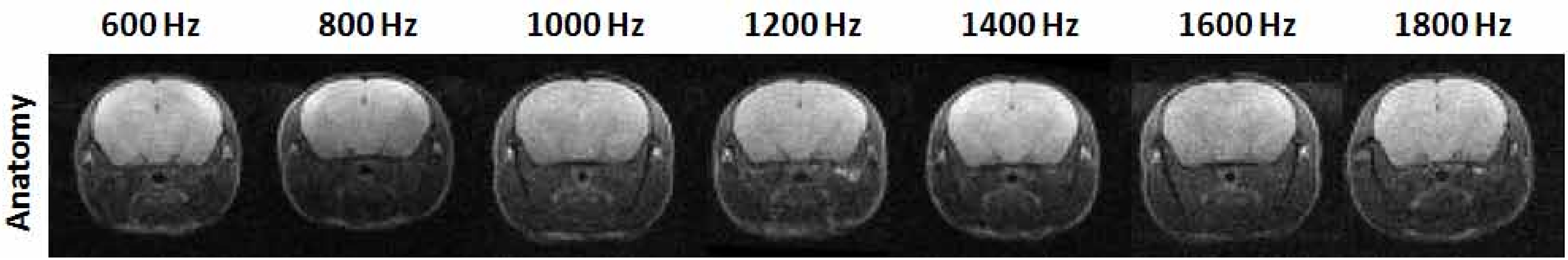
- Advantages
  - Can perform studies on animals that cannot be performed on humans
    - injury, aging, development, therapeutic intervention, genetics
  - Correlate mechanical properties with histology
  - Reduce technology development costs
- Challenges
  - Requires high spatial resolution

Shear waves induced in brain via *actuated* bite bar



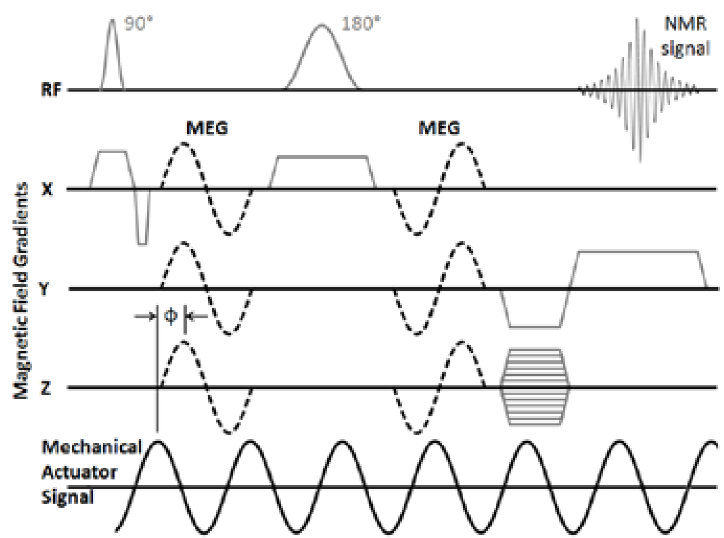
Clayton, Garbow, Bayly. (2011) Phys. Med. Biol. 56, 2391-2406.

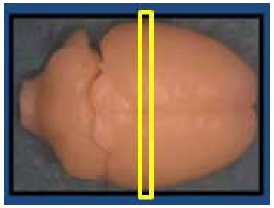
Mouse Brain MRE
Multi-frequency Study



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

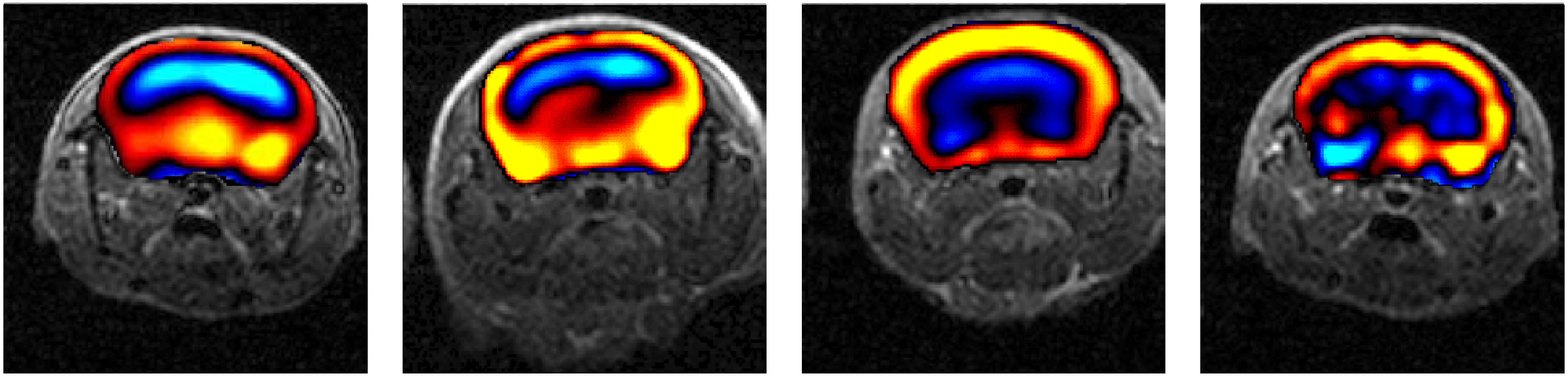




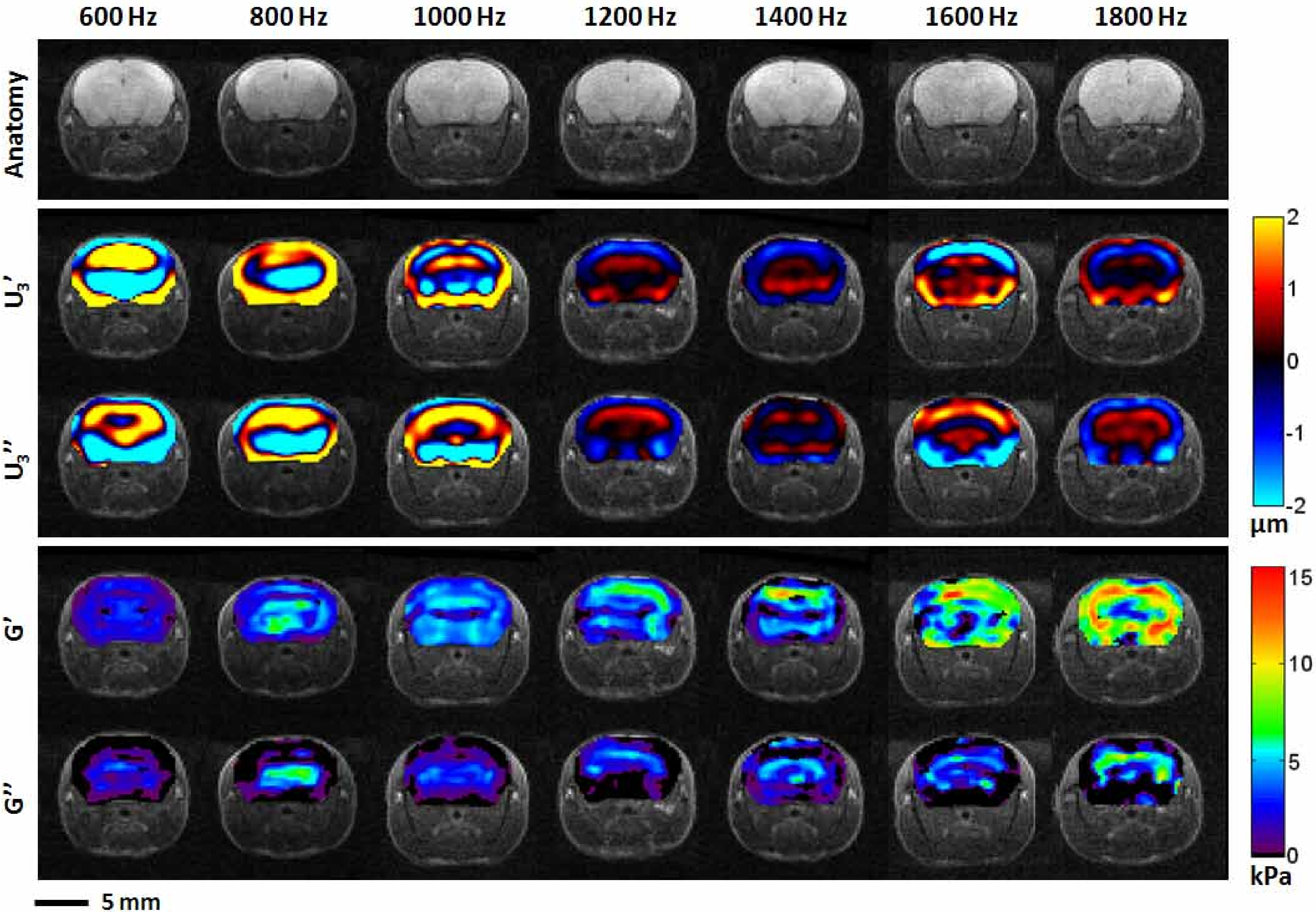
Clayton, Garbow, Bayly. (2011) Phys. Med. Biol. 56, 2391-2406.

Mouse Brain MRE
Multi-frequency Study

600 Hz **800 Hz** **1200 Hz** **1800 Hz**



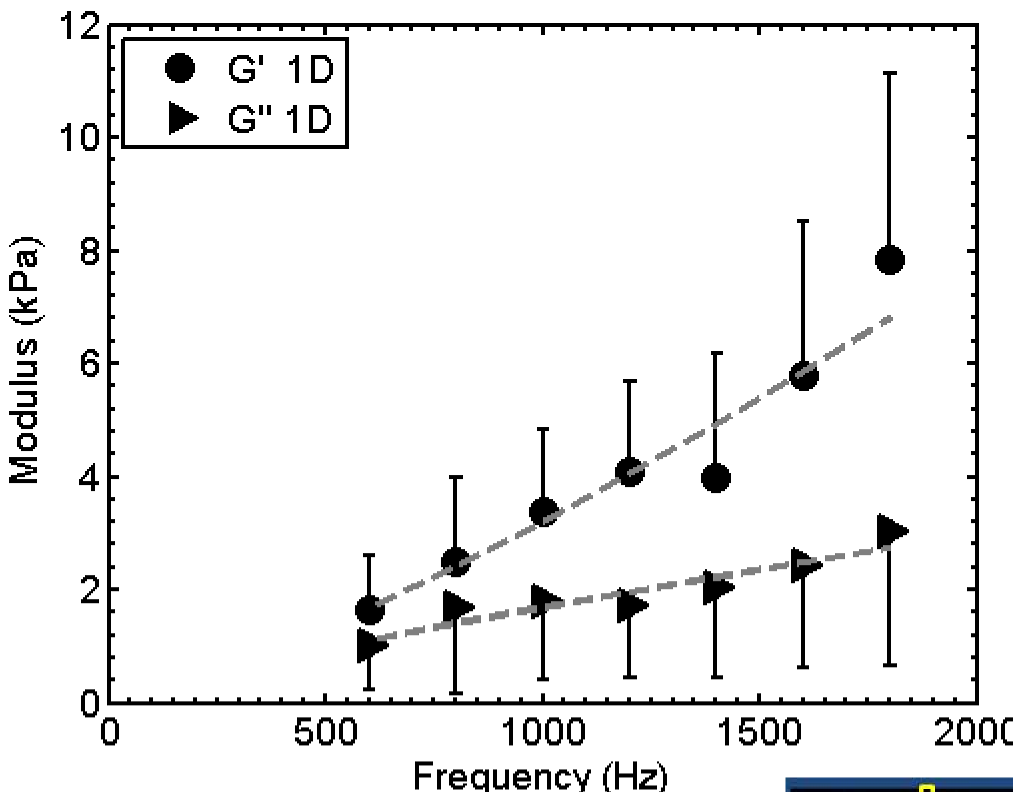
4.7 T Varian Consol
Acquired Res.: 250 x 250 x 250 µm
Motion Encoding Cycles: 4 (600 Hz), 5 (800 Hz), 8 (1200 Hz), 10 (1800 Hz)
M.E. Gradient Amp.: +/-18 G/cm
Through-image-plane motion sensitized

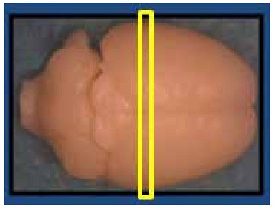


Clayton, Garbow, Bayly. (2011) Phys. Med. Biol. 56, 2391-2406.

Frequency dependence of brain tissue in vivo

	Frequency (Hz)	Storage modulus, *G′* Mean (kPa)	Storage modulus, *G′* Std (kPa)	Loss modulus, *G″* Mean (kPa)	Loss modulus, *G″* Std (kPa)	Strain
Atay *et al* (2008)	1200	13.8	1.49	–	–	C57BL/6
Diguet *et al* (2009)	1000	7.36	0.50	3.33	0.80	C57BL/6
Schregel *et al* (2010)	1000	≈5.40	–	≈1.50	–	C57BL/6
Murphy *et al* (2010)	1500	26.0	–	–	–	WT
		22.0	–	–	–	APP-PS1

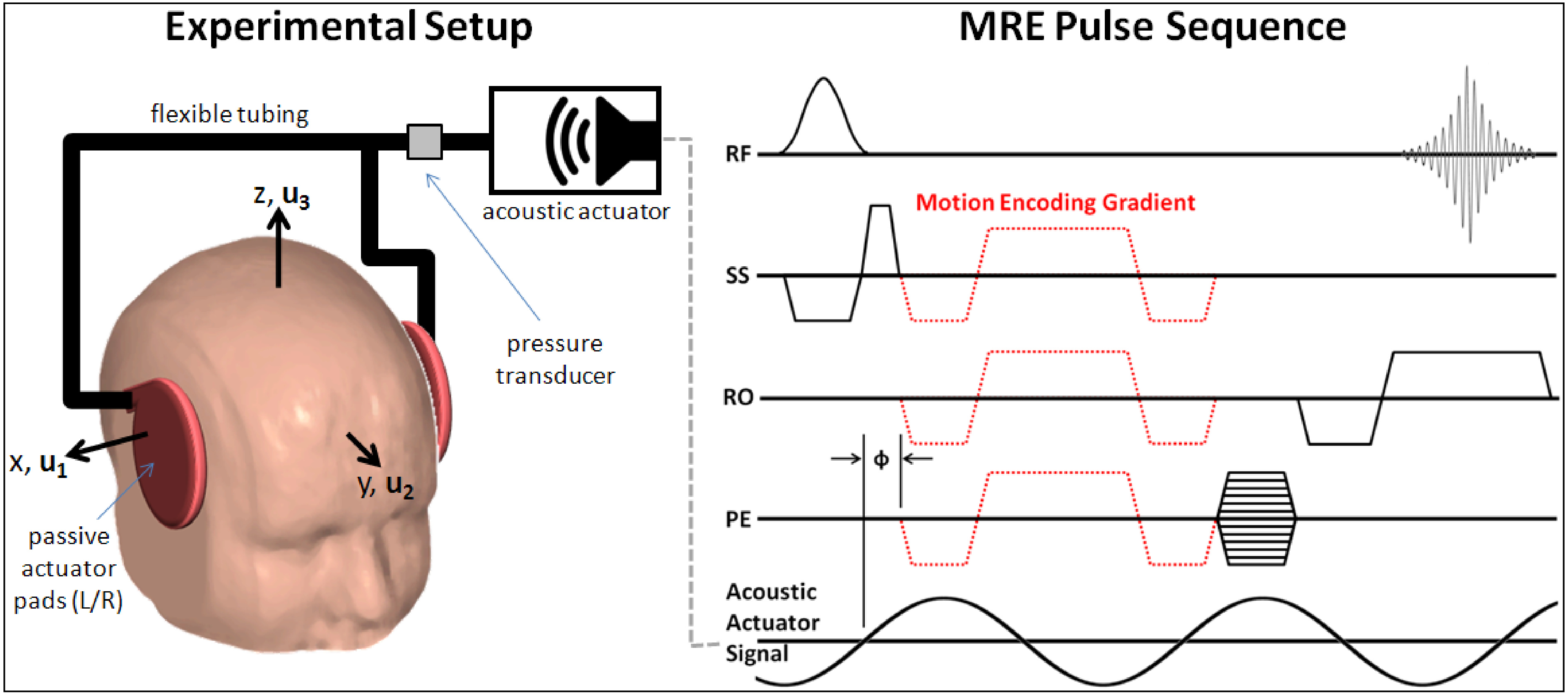




Clayton, Garbow, Bayly. (2011) Phys. Med. Biol. 56, 2391-2406.

HUMAN BRAIN

Understand human brain response to acoustic pressure load *in vivo*

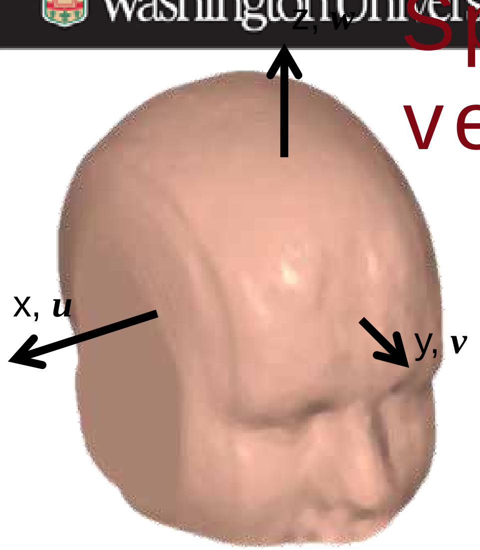


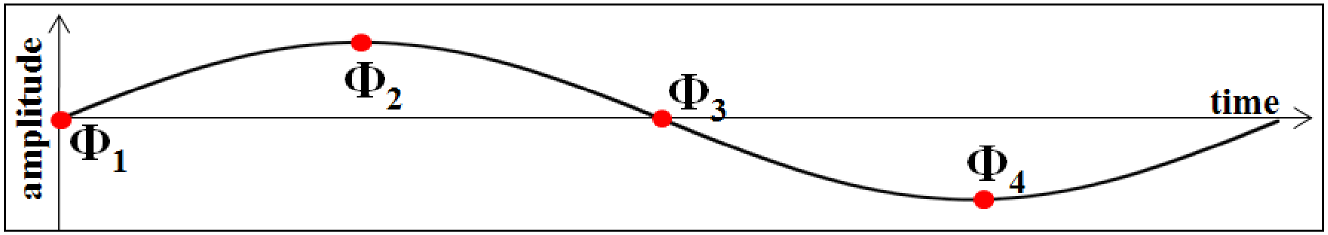
Motion components : u, v, & w
No. Image Slices : 1
Temporal Resolution : 4 point
Voxel : 3.0 x 3.0 x 3.0 mm^3

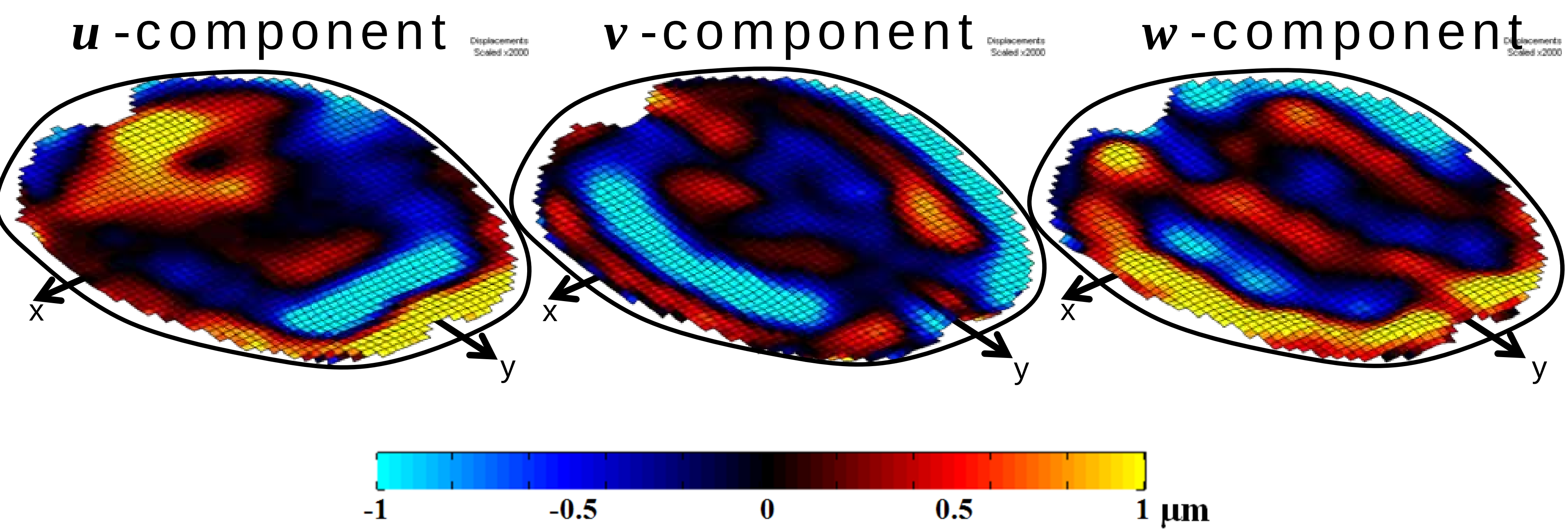
PS: GRE-MRE (Bolster/Priatna, Siemens)
TR/TE: 133.3/27.5, FA: 25^o, nt**:** 1
DM: 128 x 128 x 1 x 4
t_{acq}: 12 minutes/frequency/direction

Clayton, Genin, Bayly. RSIF 2012. (In press)

Spatiotemporal displacement vector data obtained in ~30 min

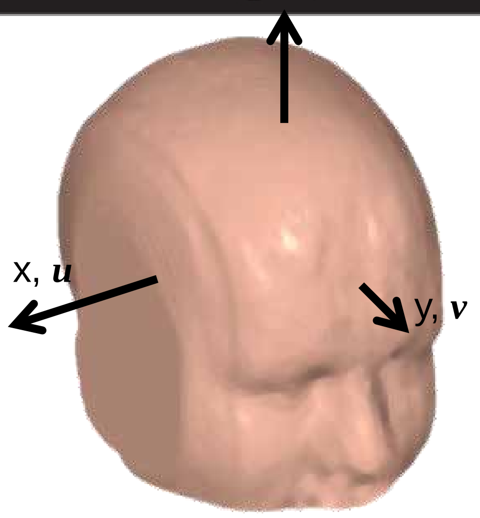


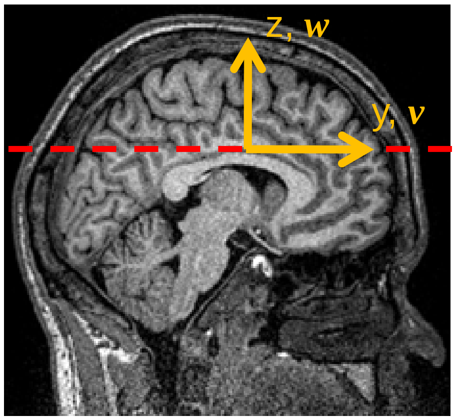


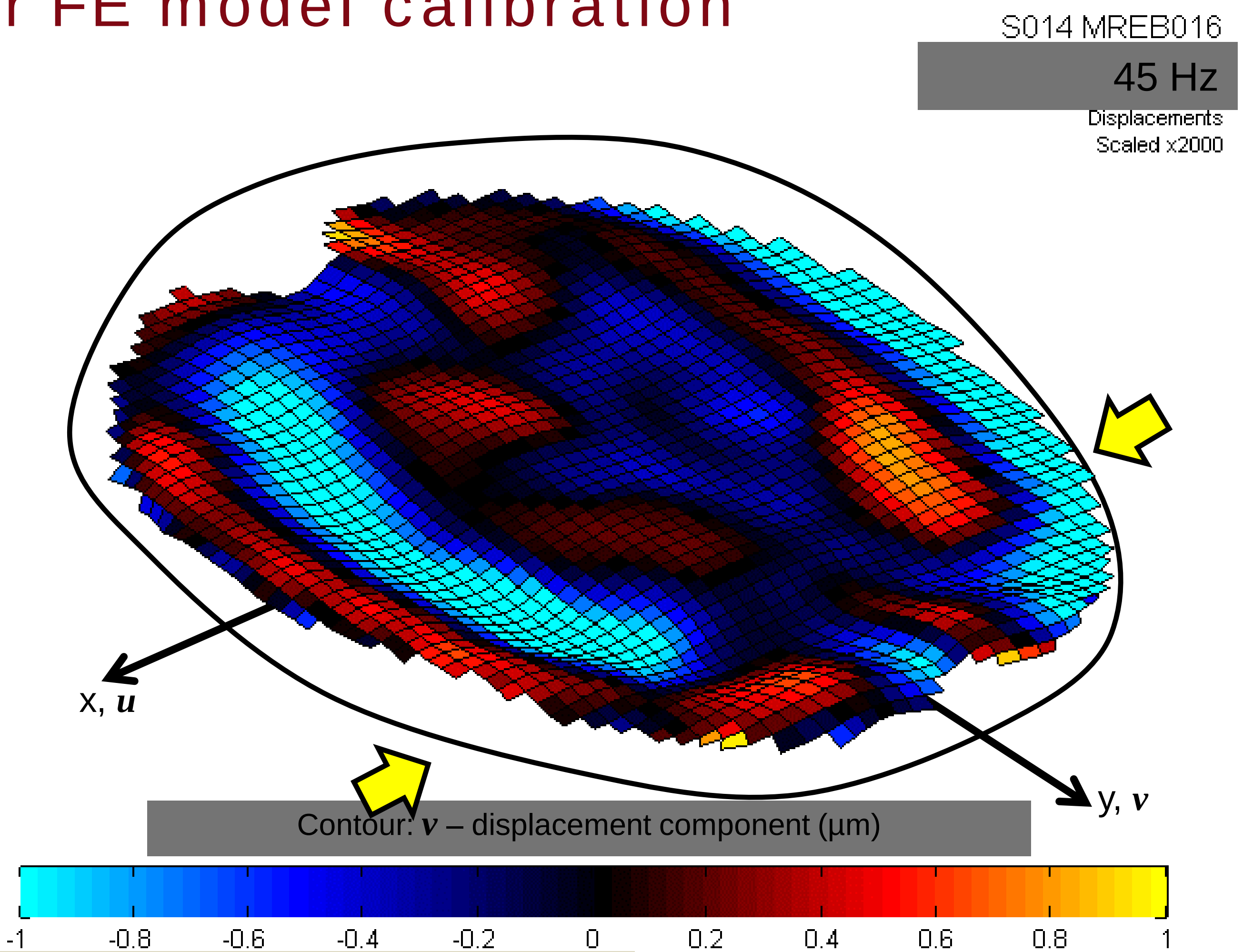


Clayton, Genin, Bayly. RSIF 2012. (In press)

3D brain displacement data for FE model calibration







Clayton, Genin, Bayly. RSIF 2012. (In press)

About those two wave propagation modes…

Recall,
2 Wave Modes

$$\rho \frac{\partial^2 u_k}{\partial t} = \underbrace{\mu \nabla^2 u_k}_{\text{Shear}} + \underbrace{(\lambda + \mu) \frac{\partial}{\partial x_k} (\nabla \cdot \bar{\mathbf{u}})}_{\text{Dilatation}} ,$$

Divergence (Dilatational) →

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

Curl (Shear) →

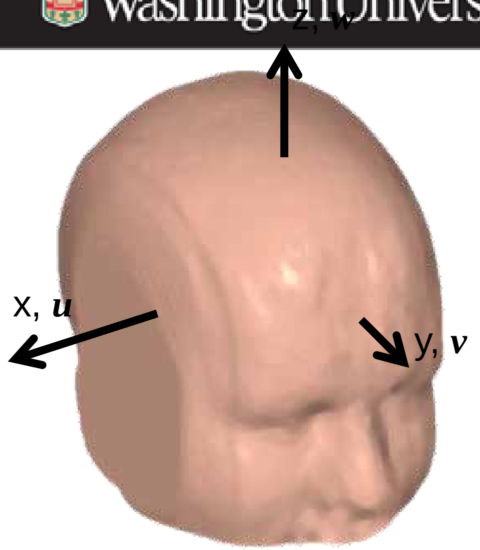
$$\frac{\partial^2}{\partial t^2} \boxed{(\nabla \times \bar{\mathbf{u}})} = \frac{\mu}{\rho} \nabla^2 \boxed{(\nabla \times \bar{\mathbf{u}})} ,$$

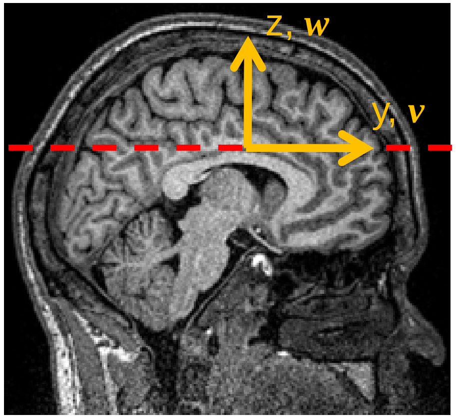
Distortion (rotation) describes *Shear Wave* motion

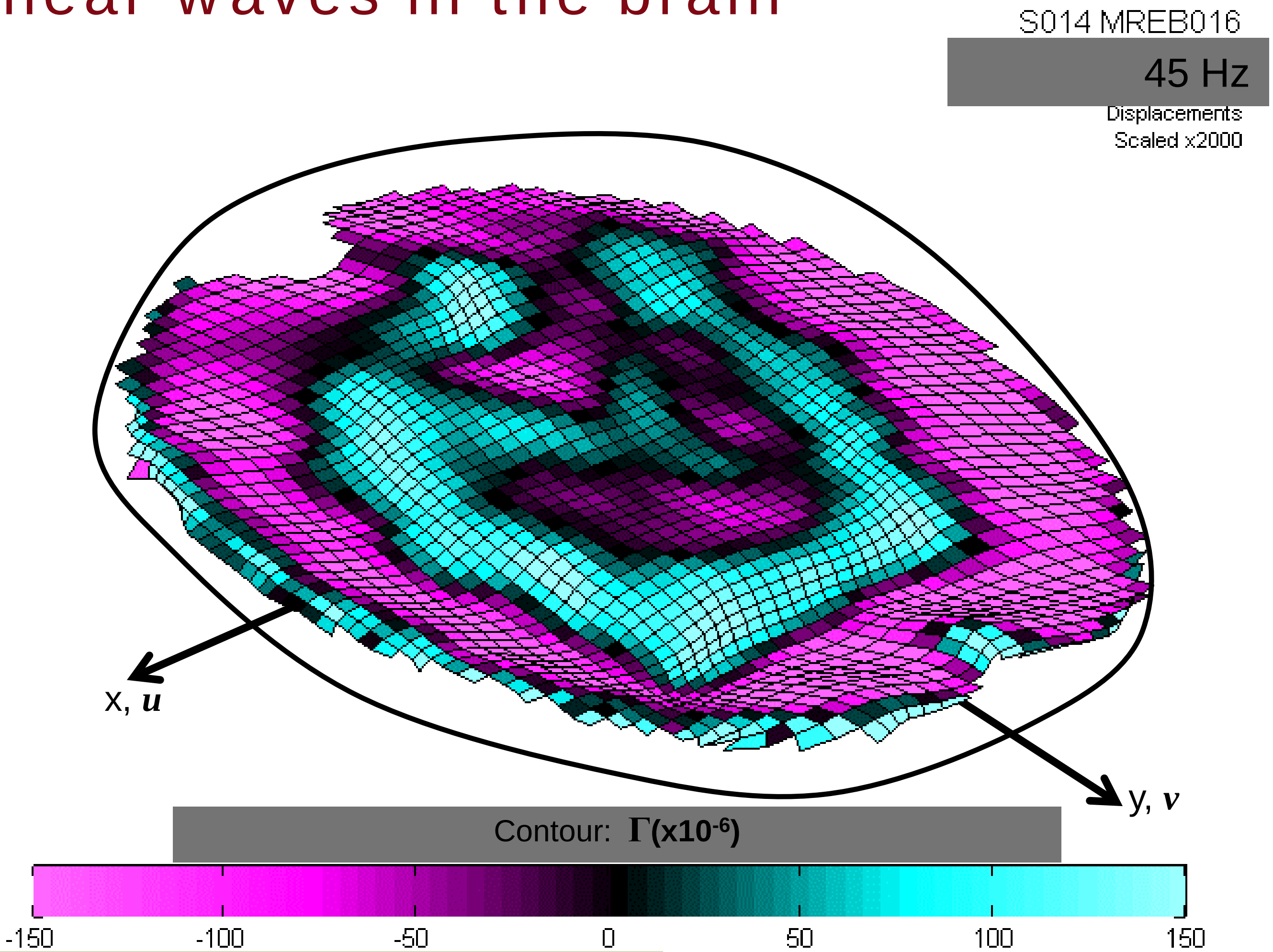
$$\Gamma = \frac{1}{2} \left(\frac{\partial u_2}{\partial x} - \frac{\partial u_1}{\partial y} \right) .$$

Clayton, Genin, Bayly. RSIF 2012. (In press)

Extracranial acoustic pressure induces shear waves in the brain





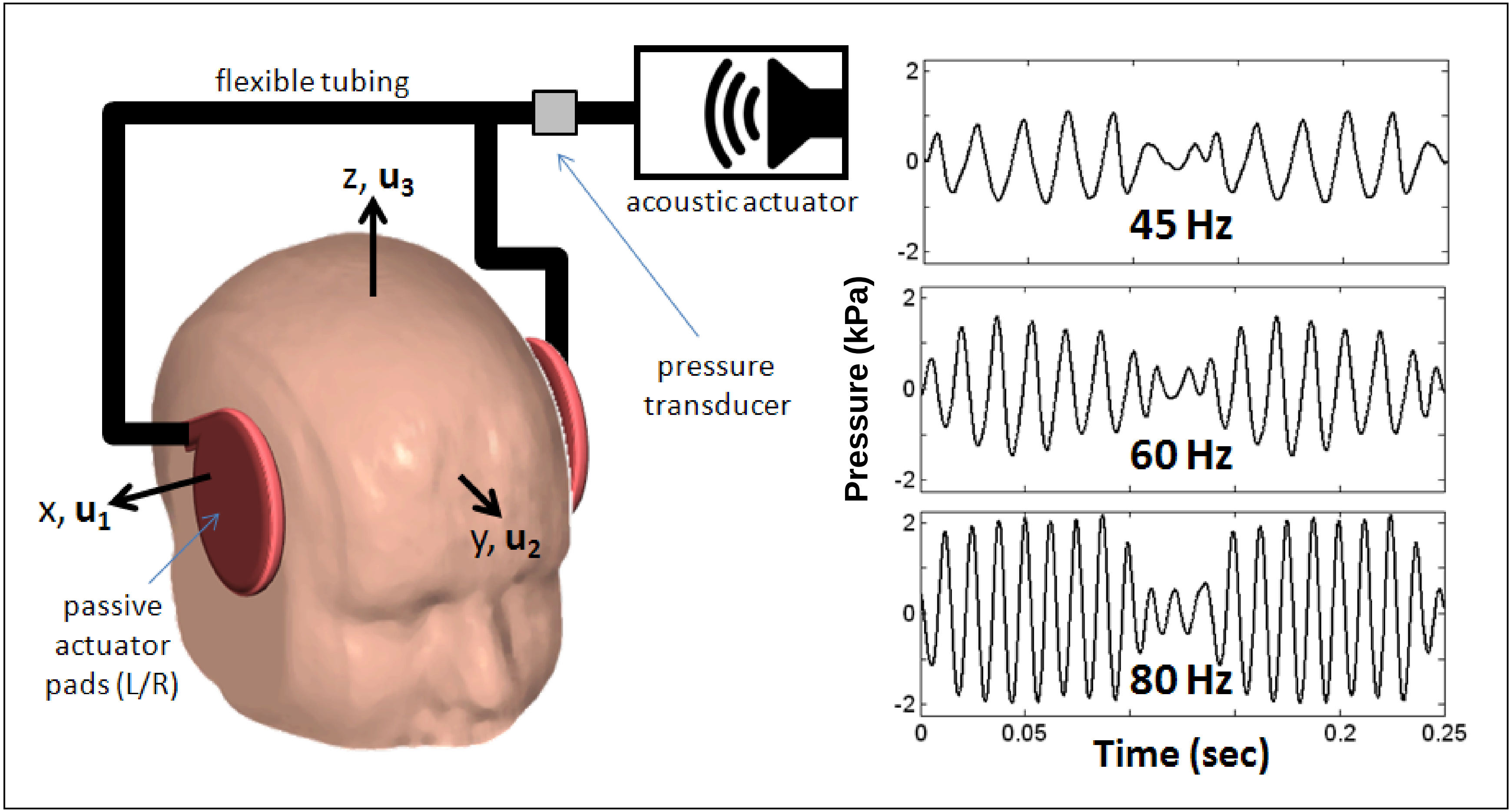


Planar Distortion

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

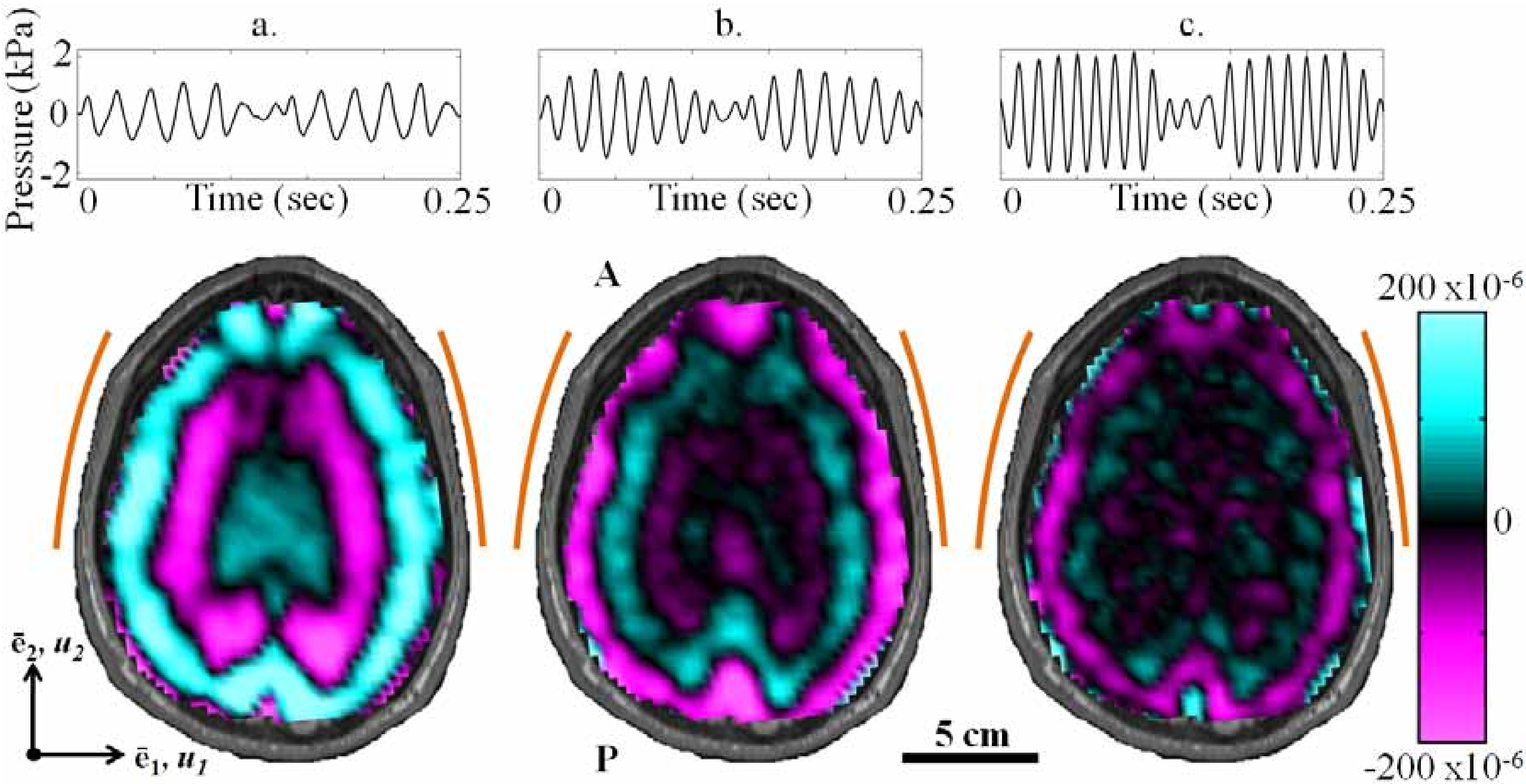
Clayton, Genin, Bayly. RSIF 2012. (In press)

What happens when the frequency changes?



Clayton, Genin, Bayly. RSIF 2012. (In press)

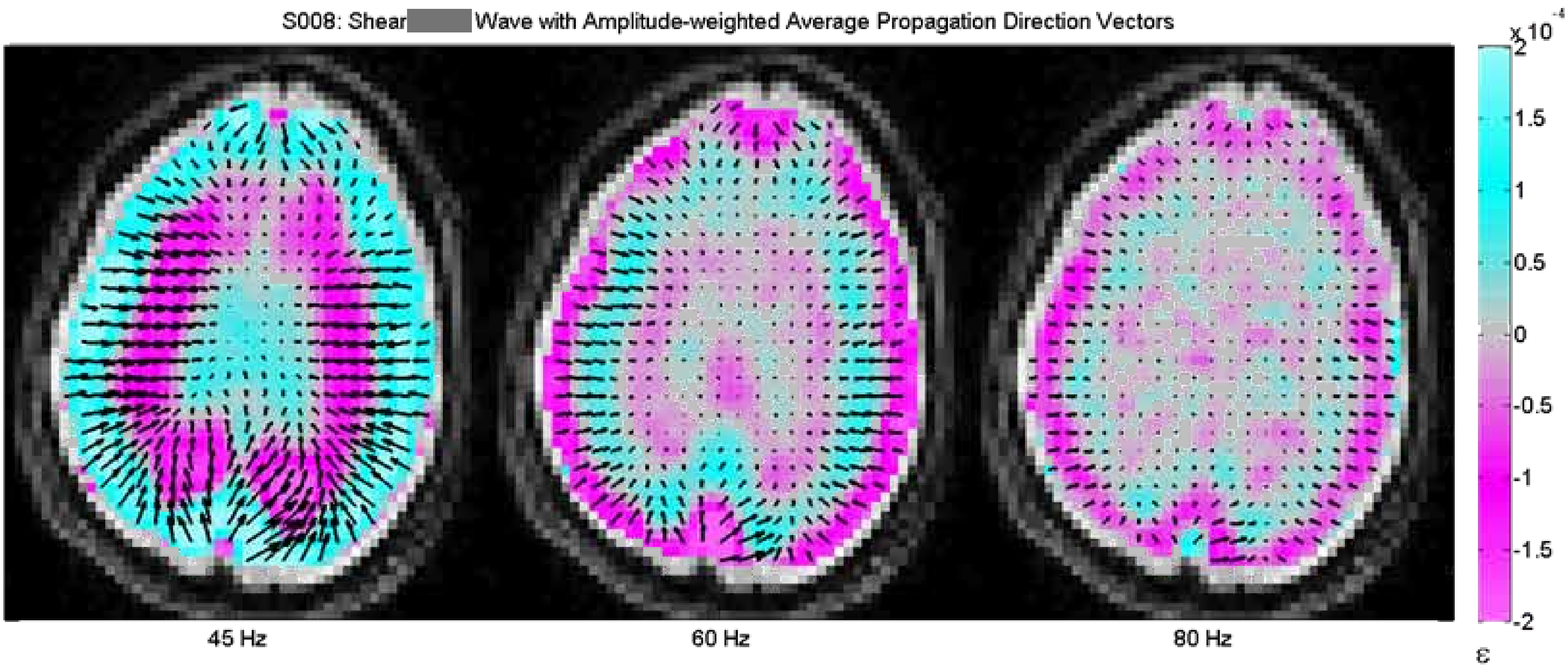
Increasing frequency leads to lower amplitudes and shorter wavelengths



Distortion (Γ)

Clayton, Genin, Bayly. RSIF 2012. (In press)

Shear wave *motion* tells us more



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

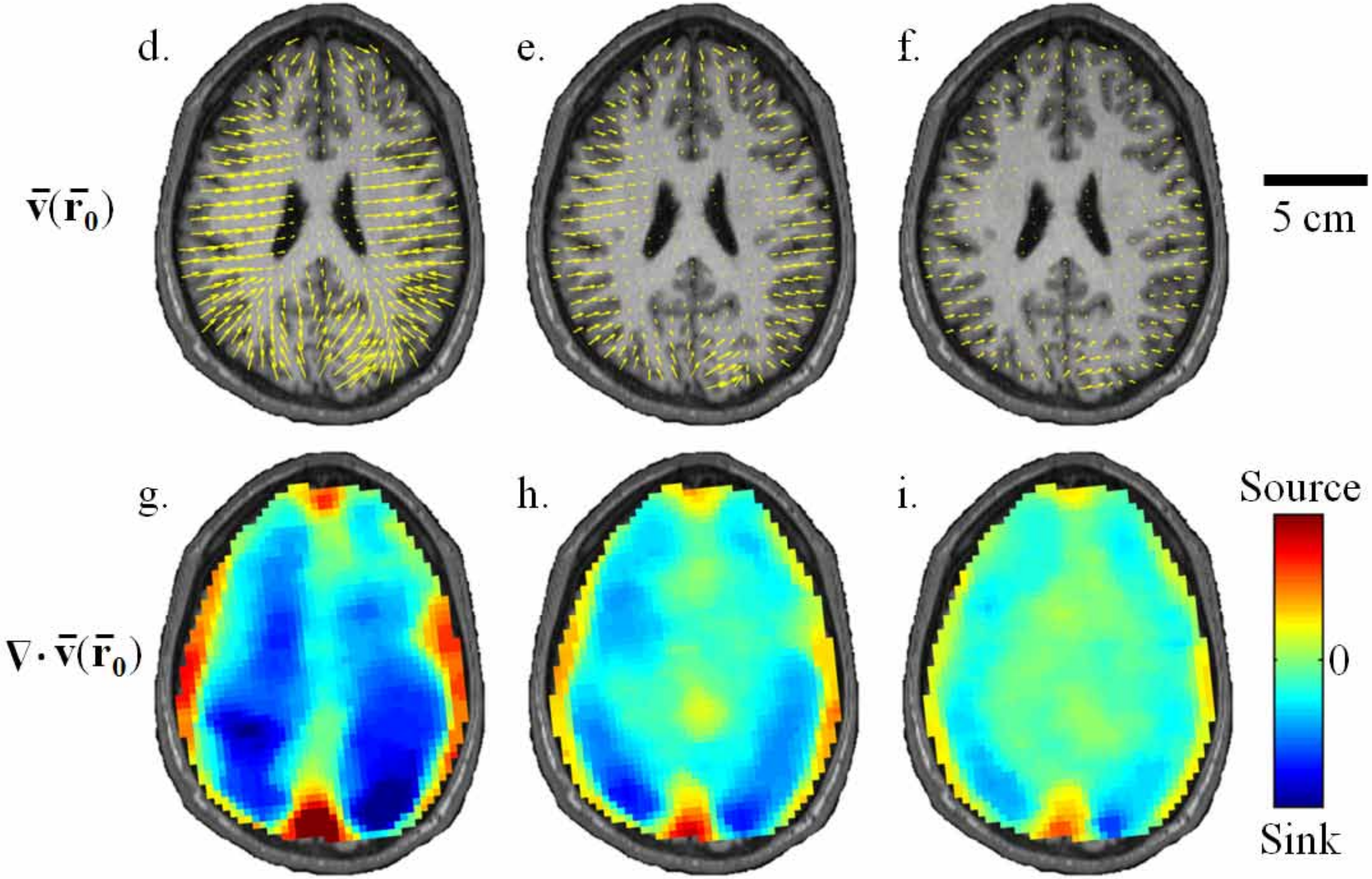
$$f_p(\theta_{mn}) = \begin{cases} \cos^2(\theta_{mn} - \theta_p), & \|\theta_{mn} - \theta_p\| \leq \pi/8 \\ 0, & \|\theta_{mn} - \theta_p\| > \pi/8 \end{cases}$$

Clayton, Genin, Bayly. RSIF 2012. (In press)

Propagation vector fields show energy *flux* and *dissipation*

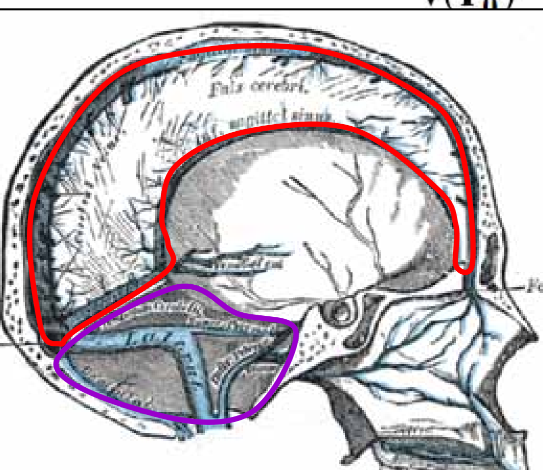
Propagation vector field

Divergence of propagation vector field

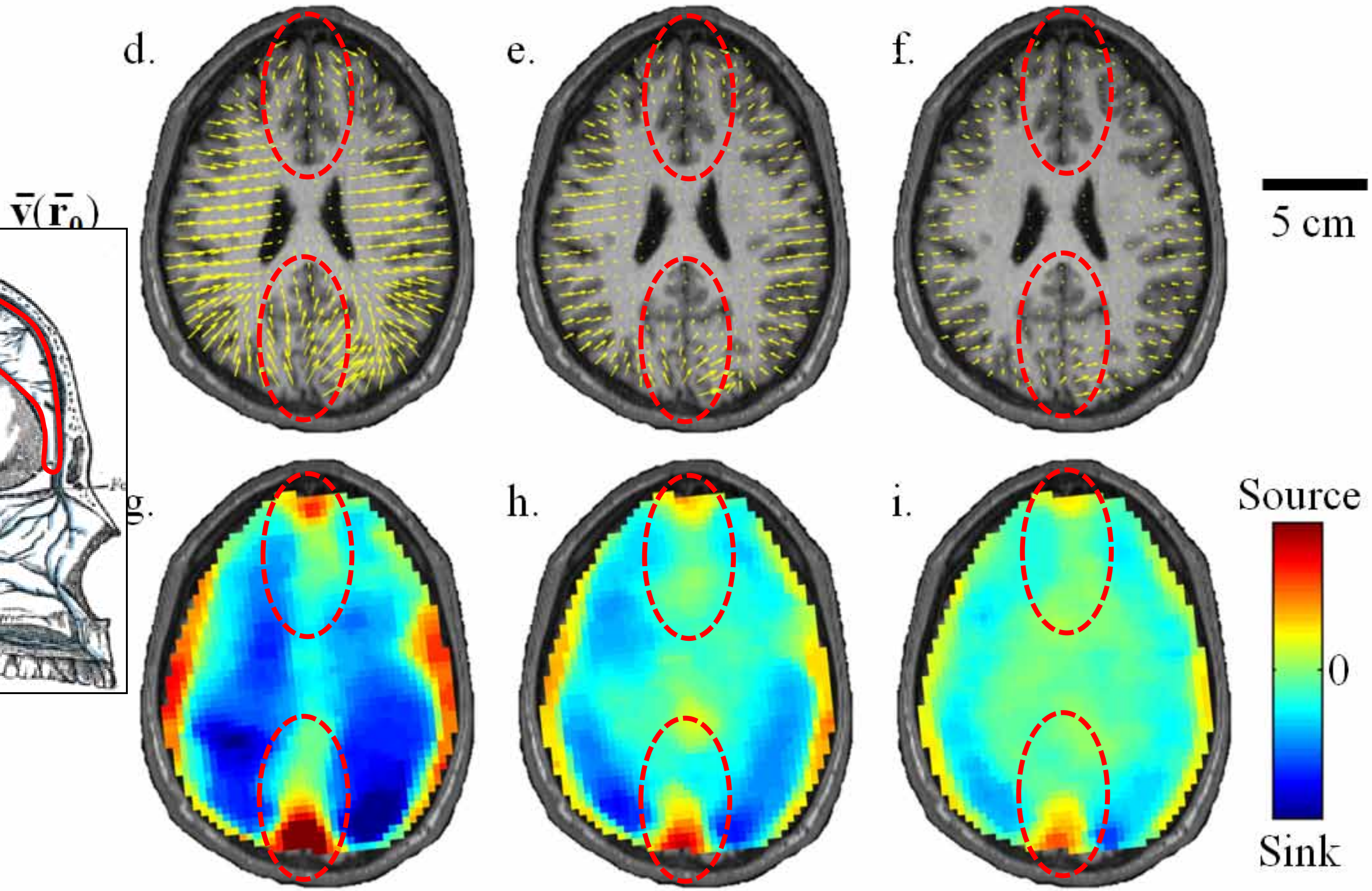


Clayton, Genin, Bayly. RSIF 2012. (In press)

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)

$$-\rho\omega^2 U_j(\mathbf{x}) = G^* \nabla^2 U_j(\mathbf{x})$$

Estimate local frequency and attenuation

Displacement $U_j(\mathbf{x}) = U_{0j} e^{i\mathbf{k}\cdot\mathbf{x}} = U_{0j} e^{i(\boldsymbol{\kappa}+i\boldsymbol{\alpha})\cdot\mathbf{x}}$

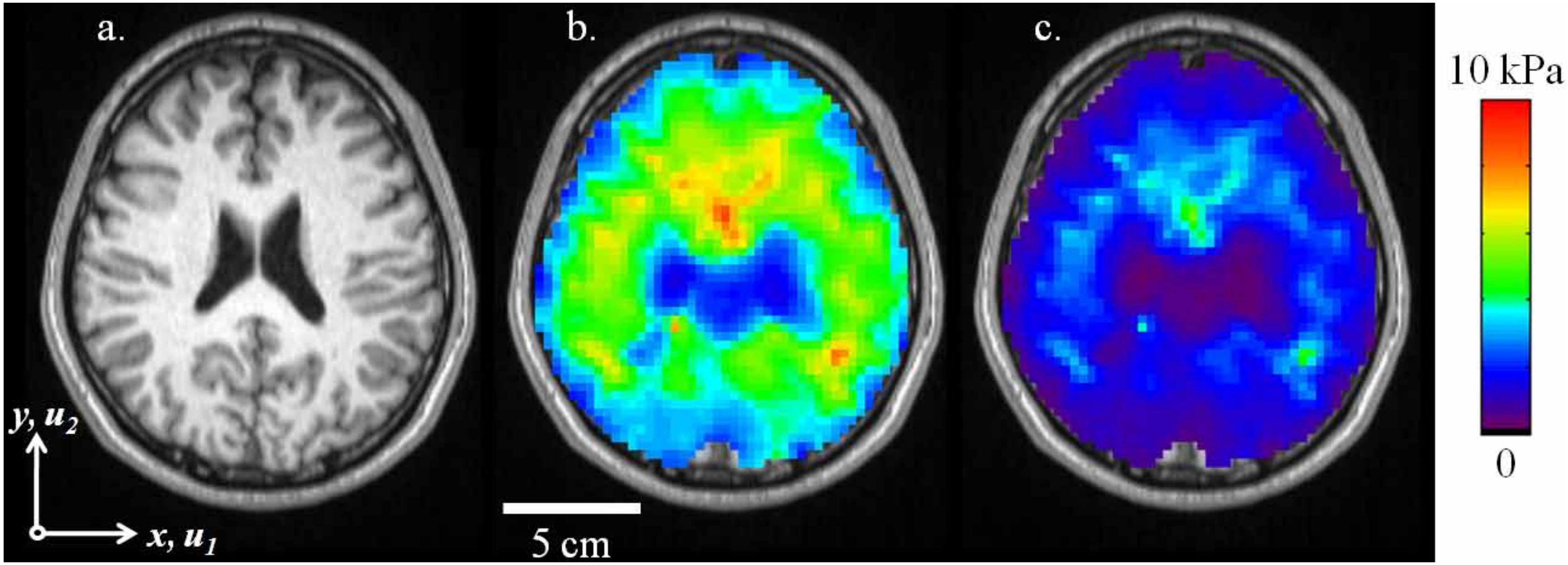
Curl $\Gamma_j(\mathbf{x}) = \Gamma_{0j} e^{i\mathbf{k}\cdot\mathbf{x}} = \Gamma_{0j} e^{i(\boldsymbol{\kappa}+i\boldsymbol{\alpha})\cdot\mathbf{x}}$

Estimate complex modulus from local wavelength and attenuation

$$G^* = \frac{\rho\omega^2}{\kappa^2 - \alpha^2 + i2\alpha\kappa}$$

Manduca et al., Medical image analysis (2001)

Viscoelastic properties of brain tissue *in vivo*

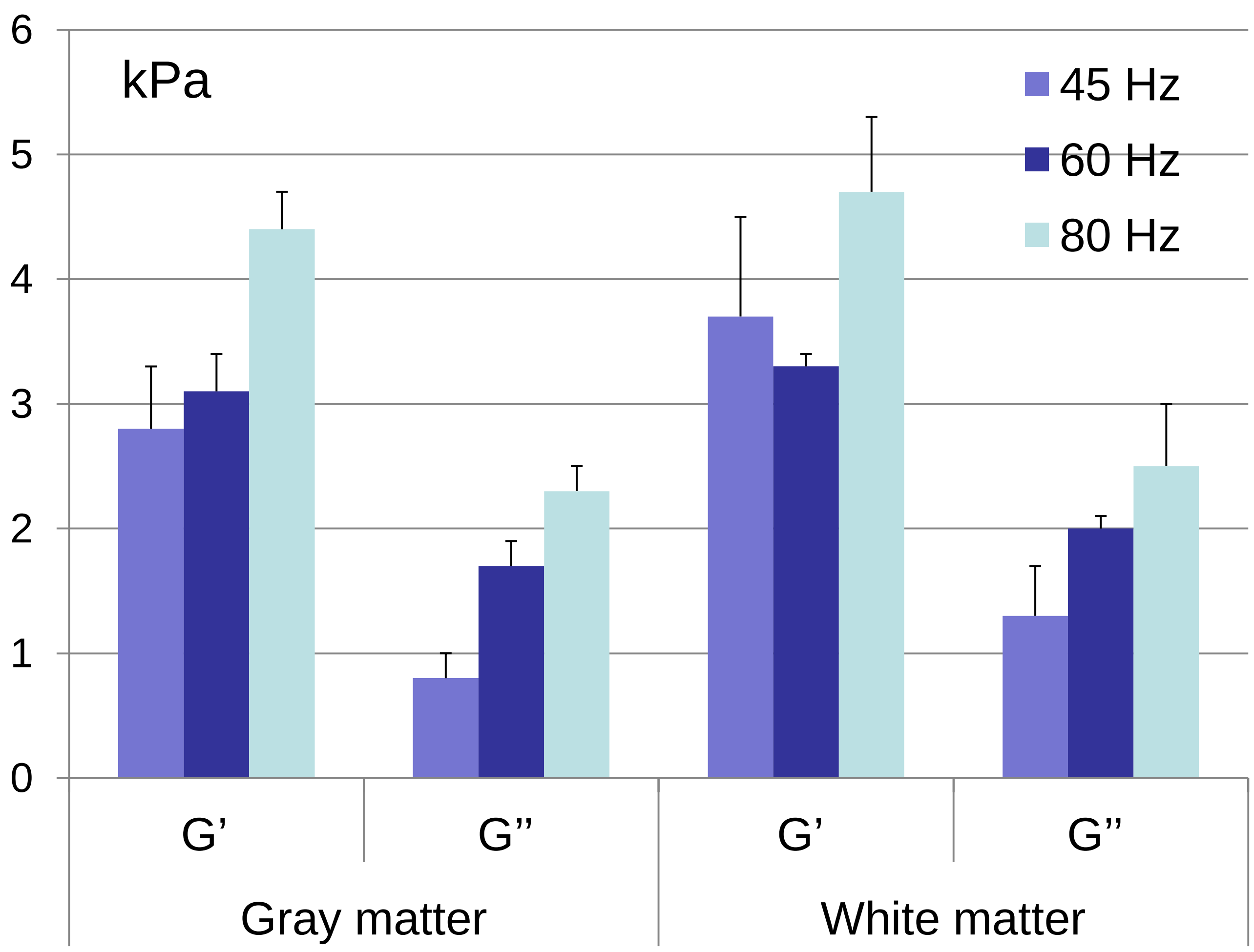


Frequency (Hz)	G' (kPa)		G'' (kPa)	
	Grey	White	Grey	White
45	**2.8**	**3.7**	**0.80**	**1.3**
	0.51	0.76	0.23	0.44
60	**3.1**	**3.3**	**1.7**	**2.0**
	0.33	0.09	0.30	0.08
80	**4.4**	**4.7**	**2.3**	**2.4**
	0.25	0.55	0.22	0.48

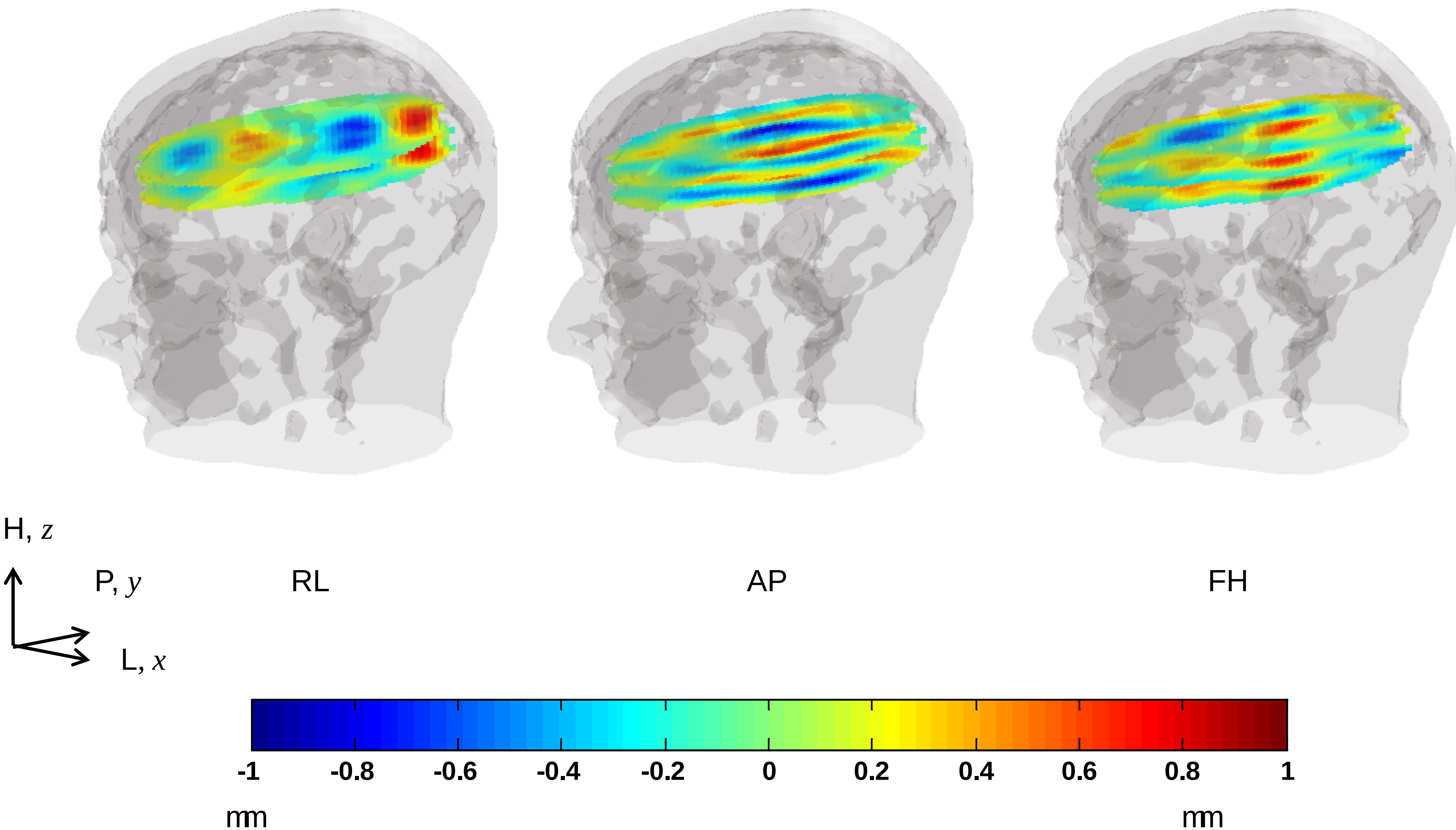
$$\begin{bmatrix} k^2-\alpha^2 & 2\alpha k \\ -2\alpha k & k^2-\alpha^2 \end{bmatrix} \begin{Bmatrix} G' \\ G'' \end{Bmatrix} = \begin{Bmatrix} \rho\omega^2 \\ 0 \end{Bmatrix}$$

Clayton, Genin, Bayly. RSIF 2012.

MR elastography in brain



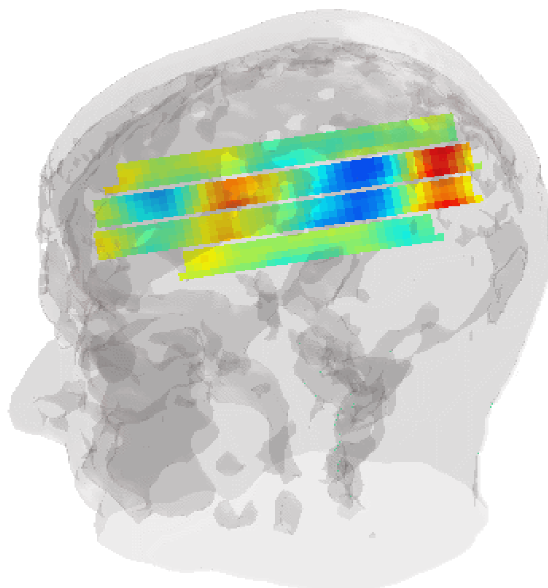
Displacement Animations



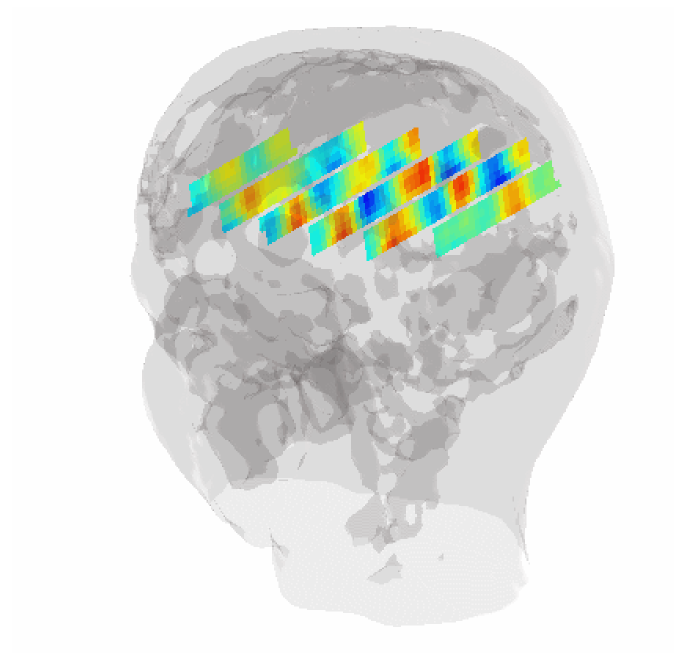
S018-MREB024

Re-sliced Displacement Animations

- For visualizing wave propagation in the foot-head direction, MRE displacement data is resliced and animated perpendicular to image acquisition planeging planes

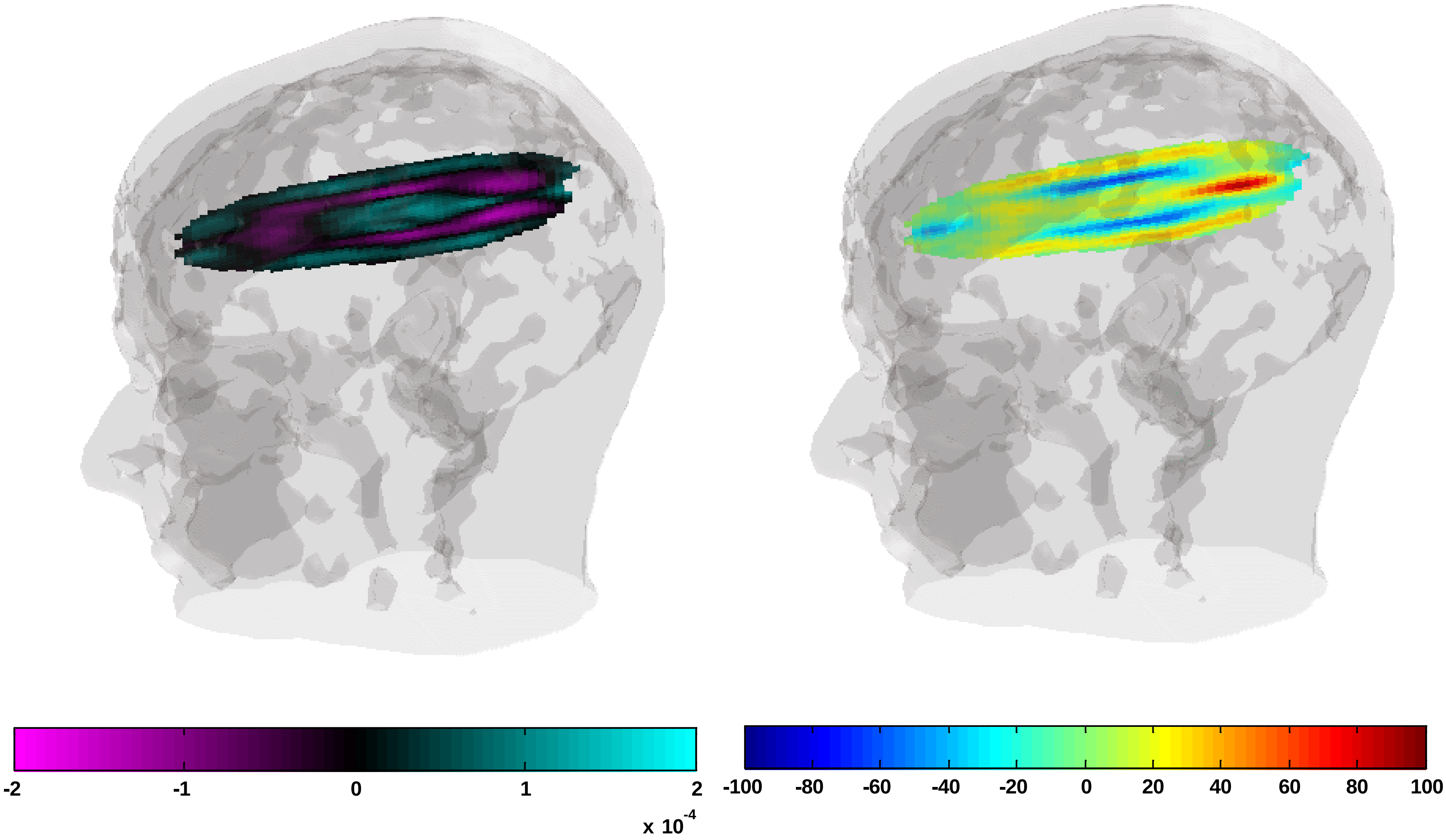


RL displacement
propagates primarily in AP dir

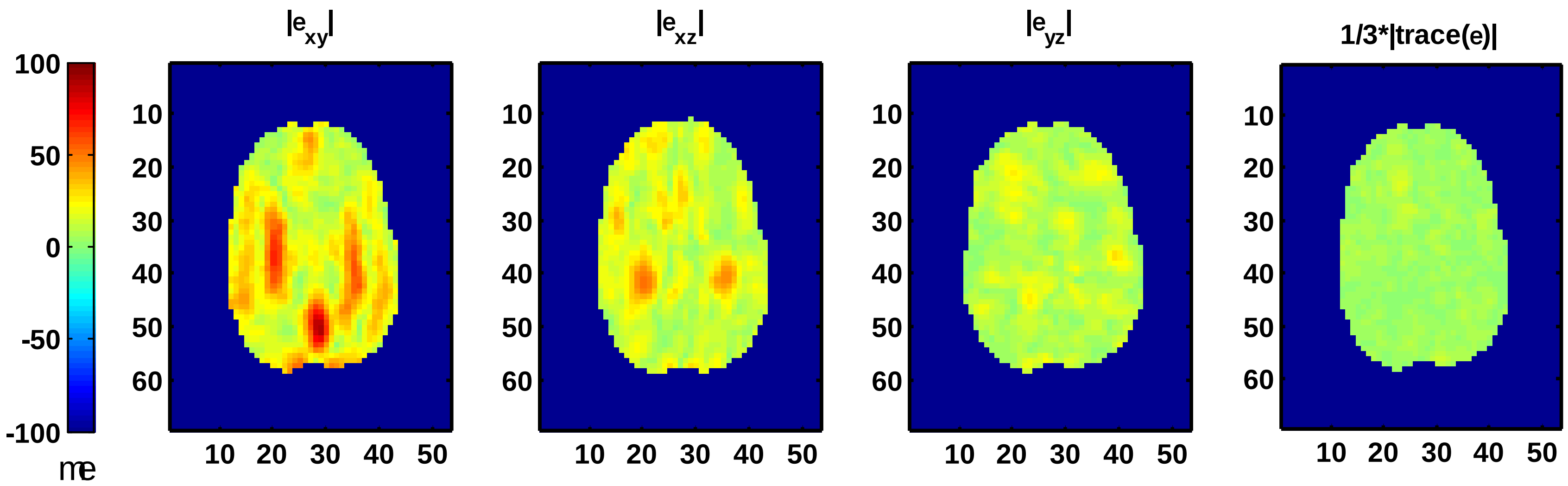


AP displacement
propagates primarily in RL dir

z-component of curl and e_{xy} computed for third slice

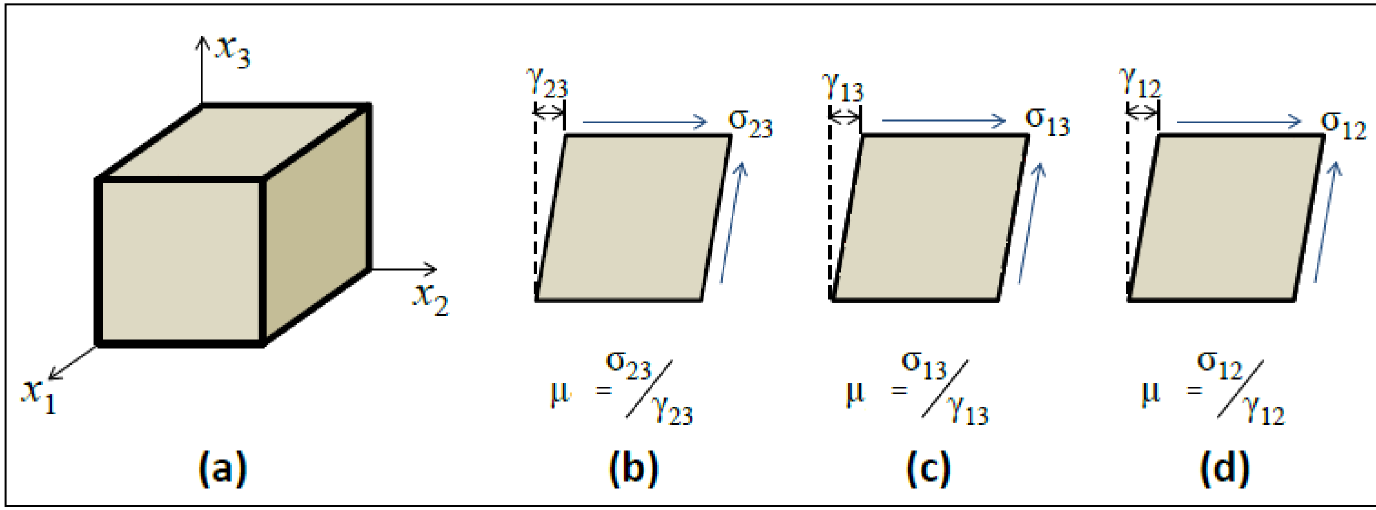


Shear strain amplitudes and dilatation

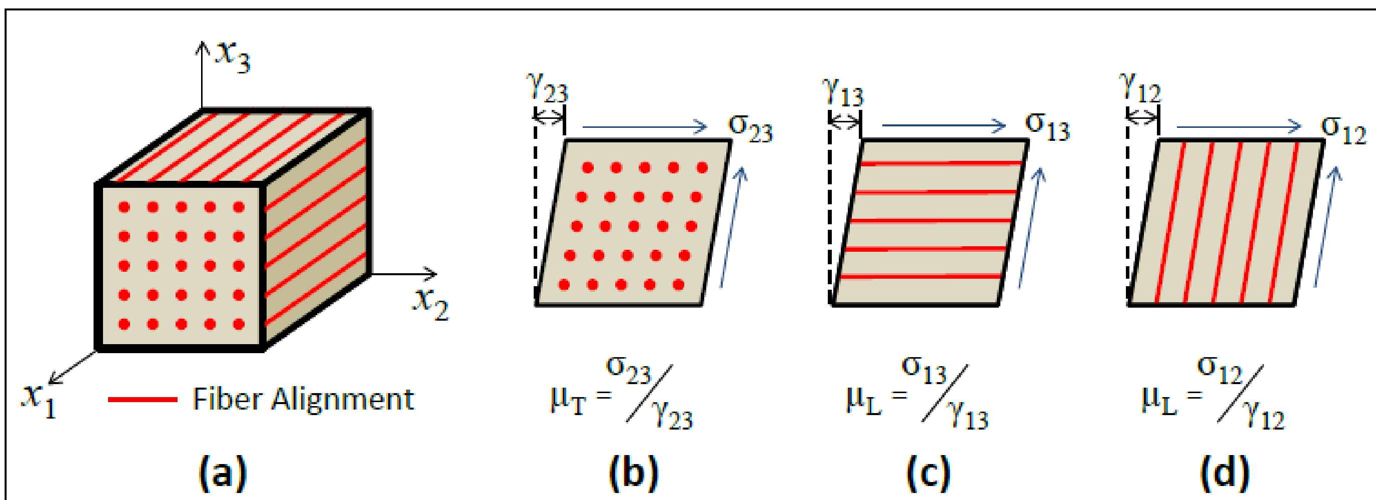


Mechanical Anisotropy ?

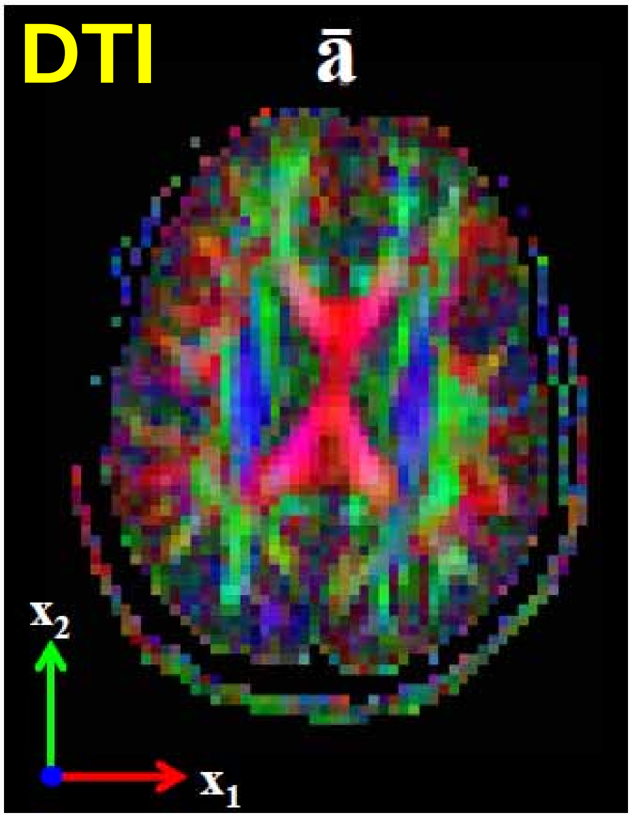
Mechanical Isotropy



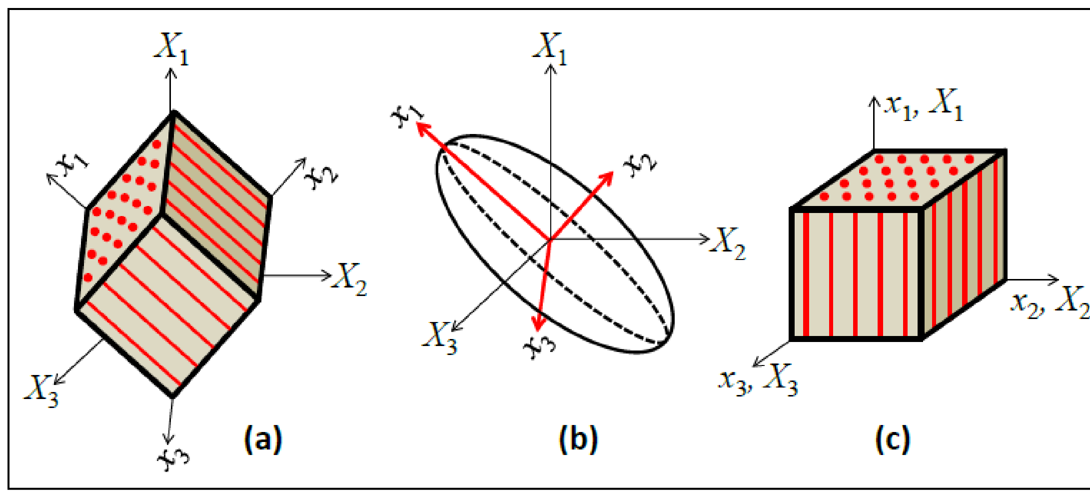
Mechanical Anisotropy



Diffusion tensor imaging

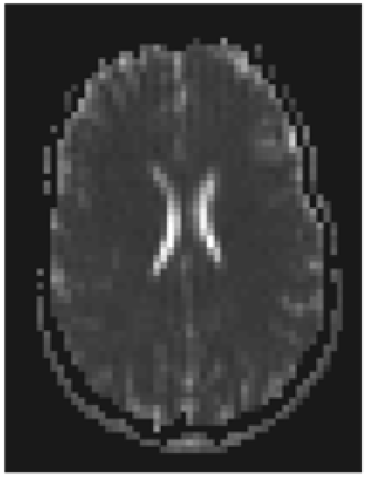


Diffusion tensor imaging detects anisotropic diffusion of water (anisotropic structure)



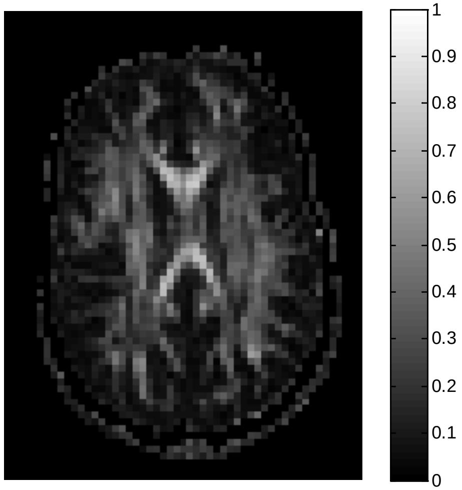
- DTI data is processed using method of Shimony et al (Radiology 212:770-784,1999) to compute MD, FA, and eigenvectors
- DTI slice planes are the same as the MRE slice planes
- Arrow plots used to code regions with fractional anisotropy above a threshold of 0.25.
- Arrow direction/color indicate direction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

S018-MREB024 Mean Diffusivity



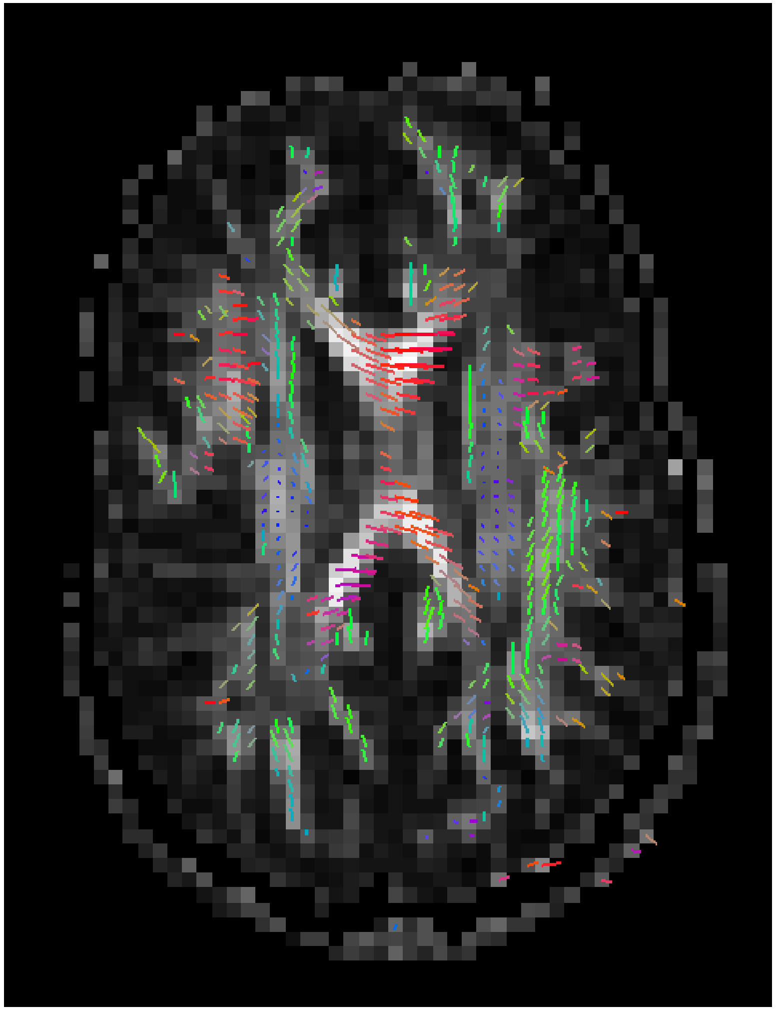
MD (slice 3)

S018-MREB024 Fractional Anisotropy



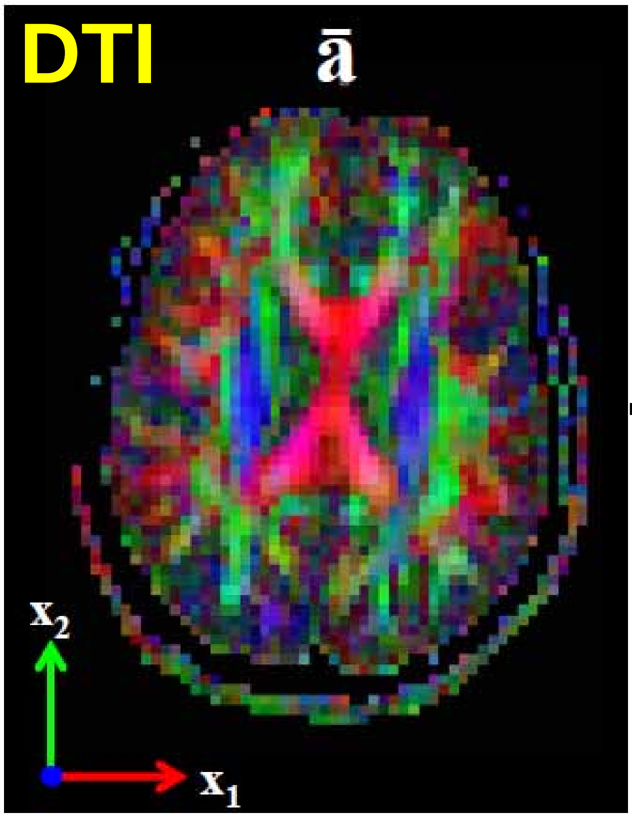
FA (slice 3)

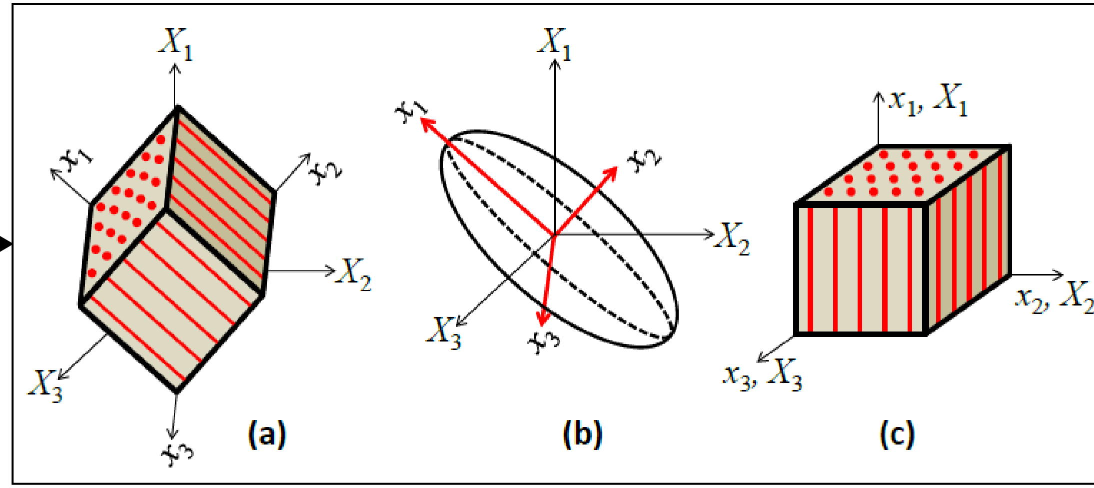
S018-MREB024, DTI vectors, slice 3



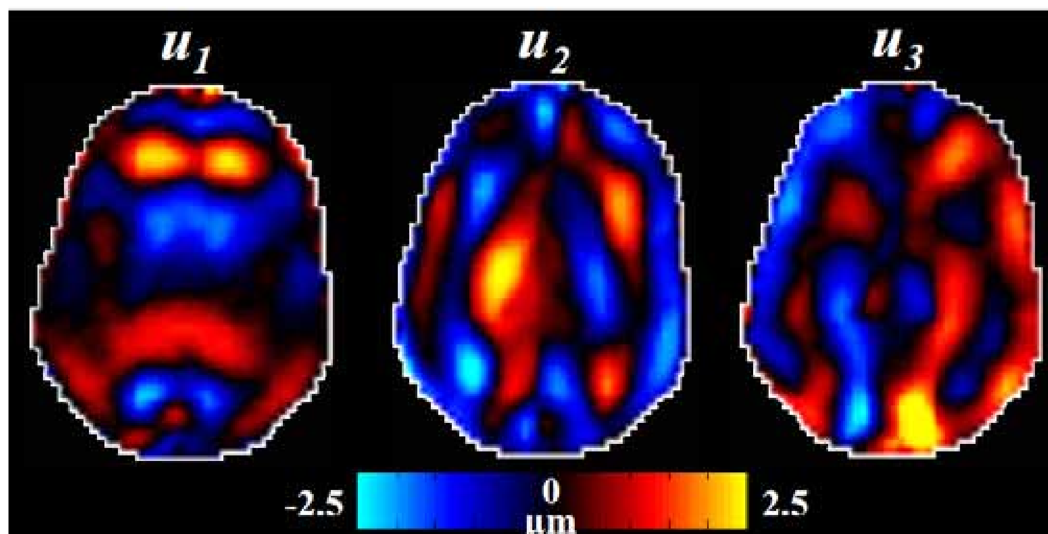
Color coded arrow plot overlaid on FA image

DTI + MRE process





MRE



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

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