Overview of FreeSurfer and TRACULA

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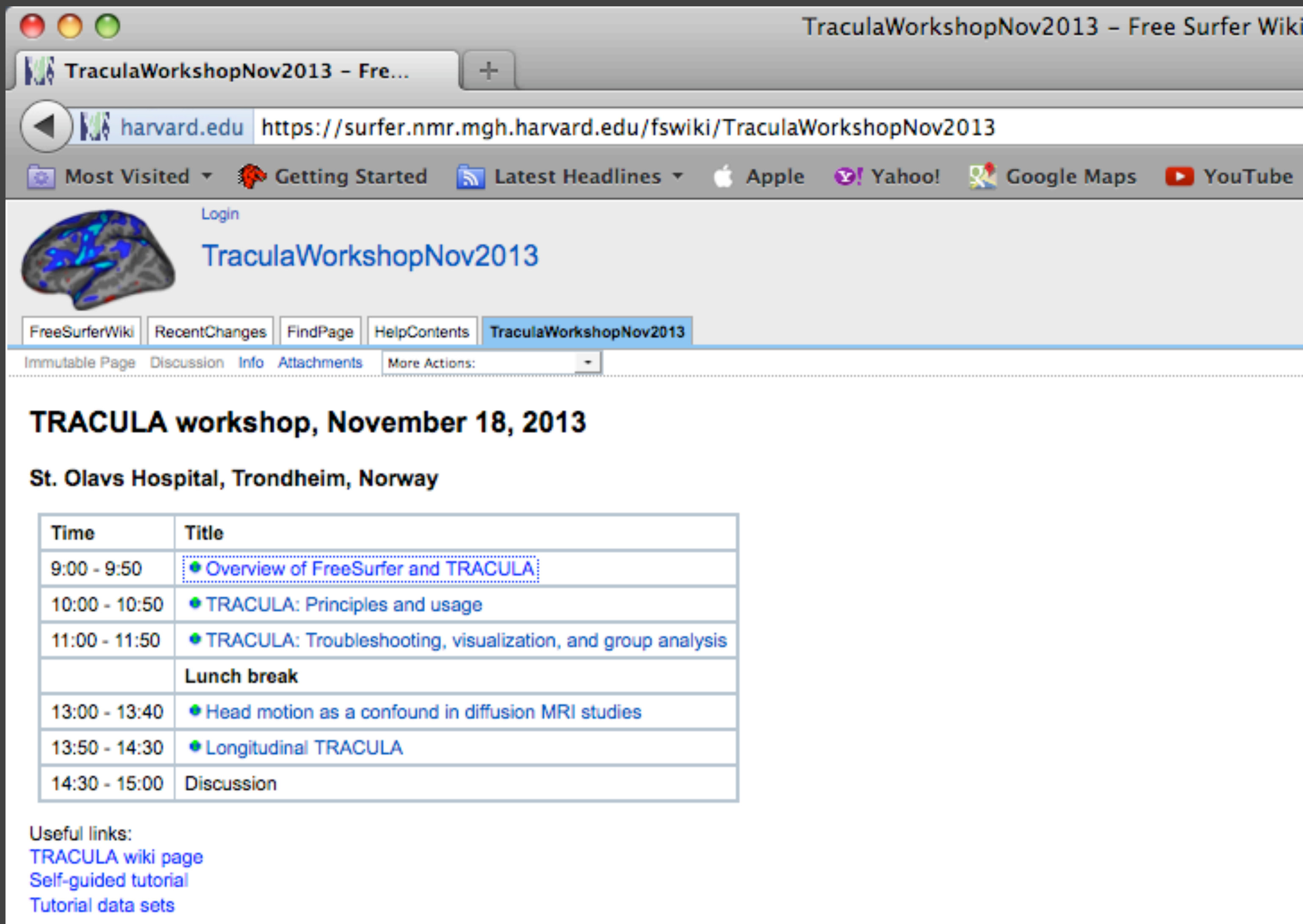
Schedule



TRACULA workshop, November 18, 2013

St. Olavs Hospital, Trondheim, Norway

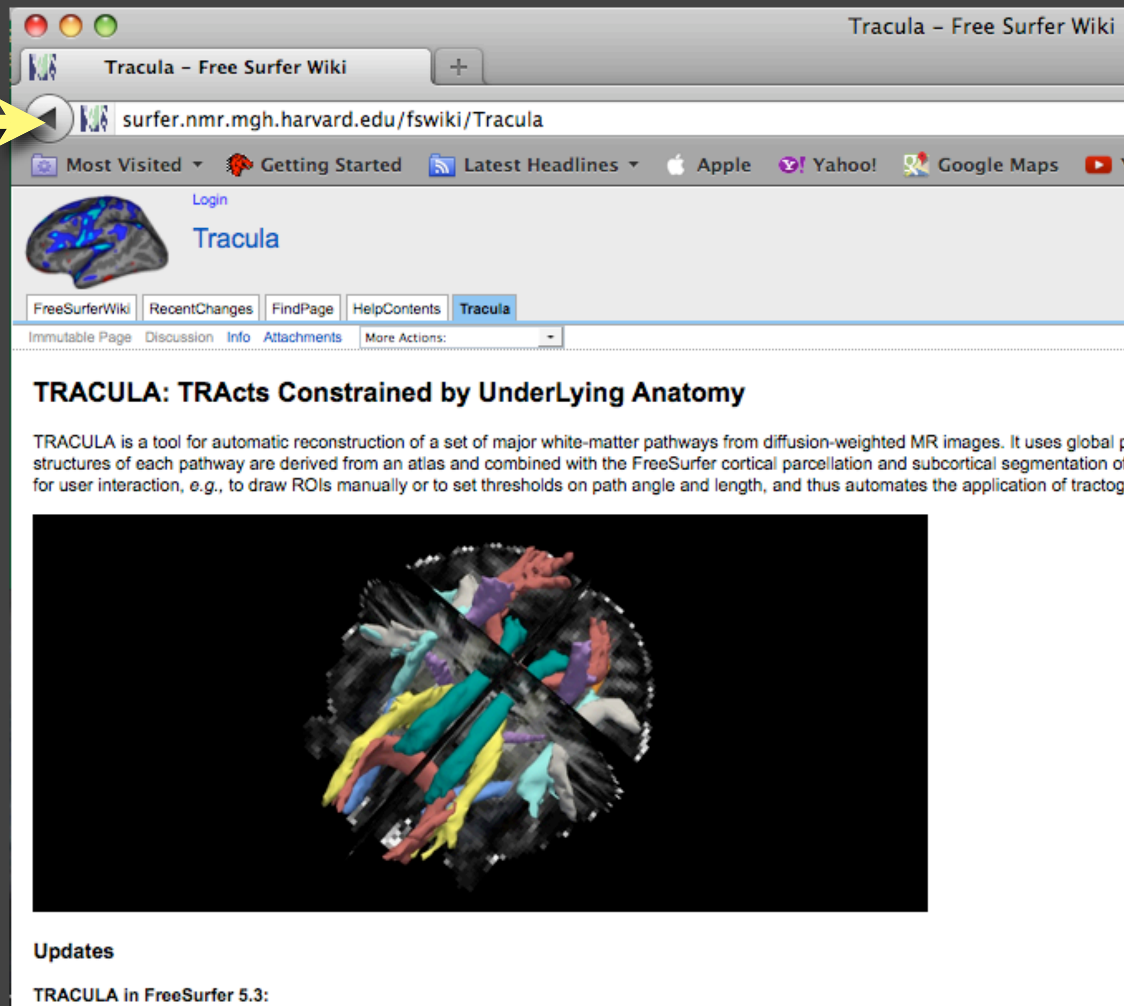
Time	Title
9:00 - 9:50	Overview of FreeSurfer and TRACULA
10:00 - 10:50	TRACULA: Principles and usage
11:00 - 11:50	TRACULA: Troubleshooting, visualization, and group analysis
	Lunch break
13:00 - 13:40	Head motion as a confound in diffusion MRI studies
13:50 - 14:30	Longitudinal TRACULA
14:30 - 15:00	Discussion

Useful links:
TRACULA wiki page
Self-guided tutorial
Tutorial data sets

Documentation and support

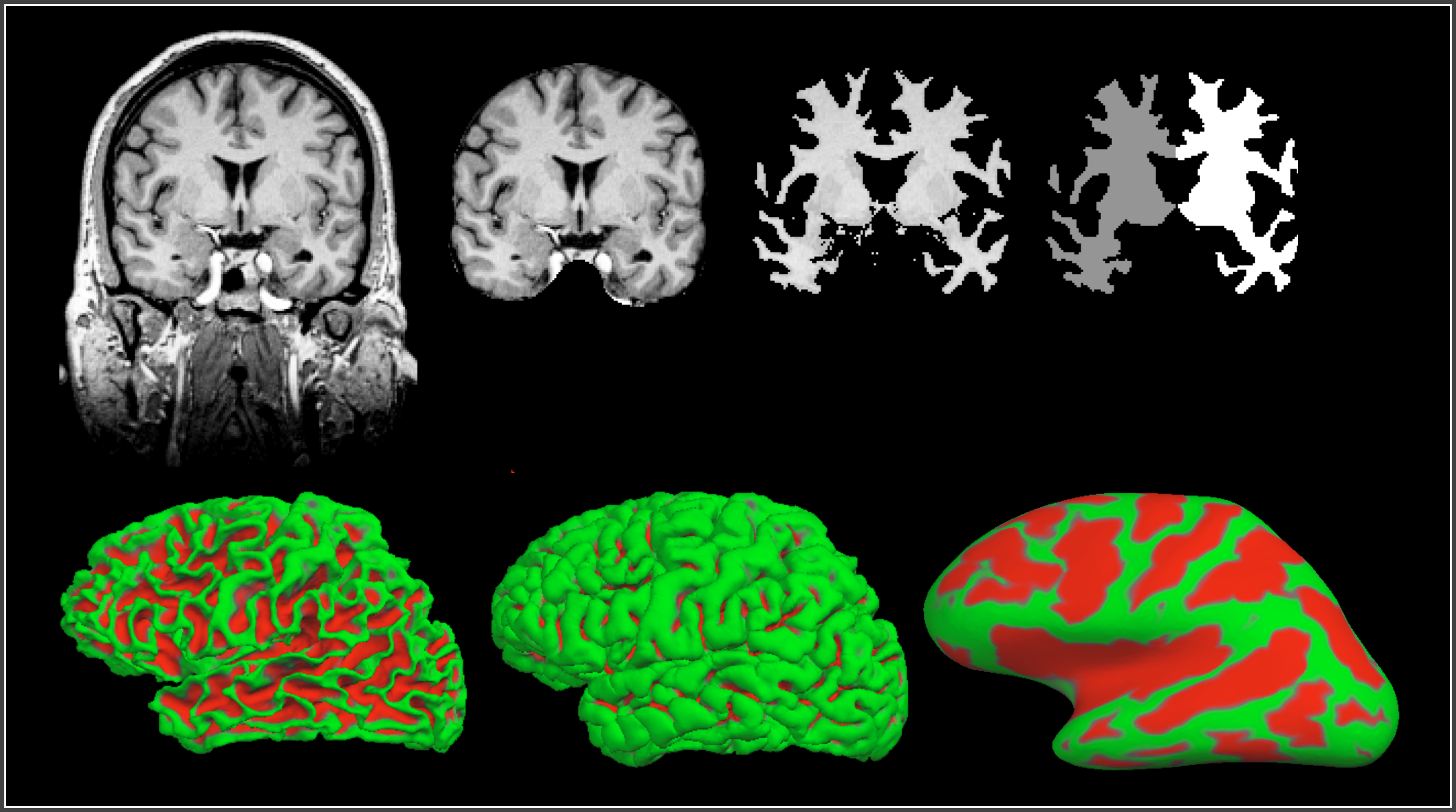
Wiki page:

- Usage info
- Updates
- Tutorials



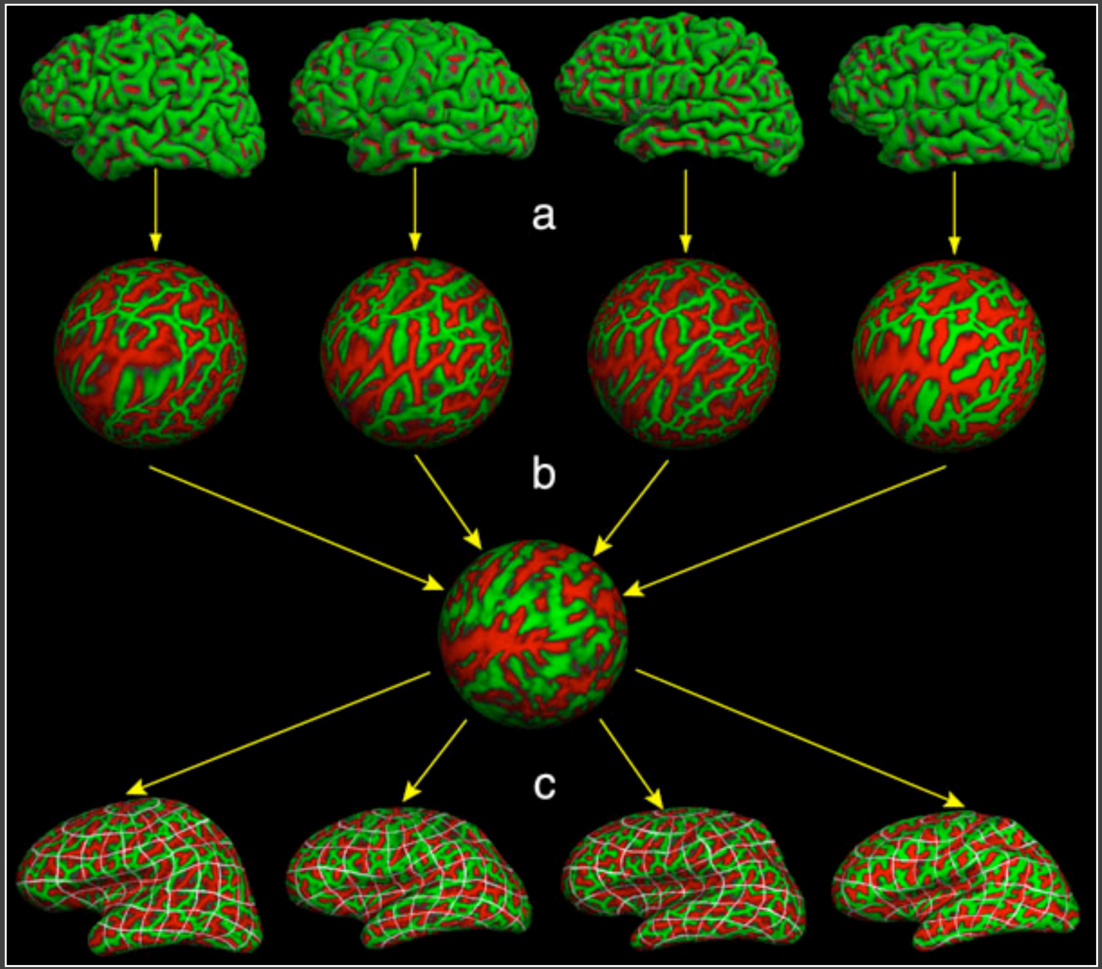
Questions: freesurfer@nmr.mgh.harvard.edu

FreeSurfer



Automated white/grey matter segmentation and surface reconstruction [Dale 1999, Fischl 1999]

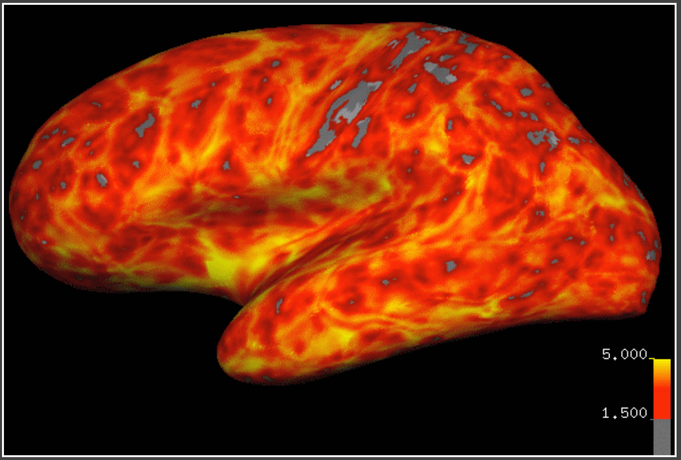
Surface-based coordinate system



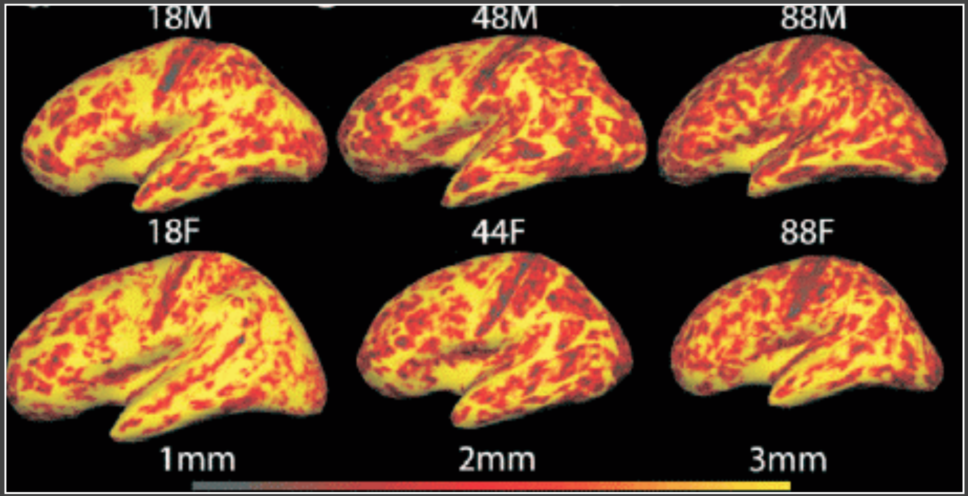
- Align individual brains based on gyral/sulcal patterns [Fischl 1999]

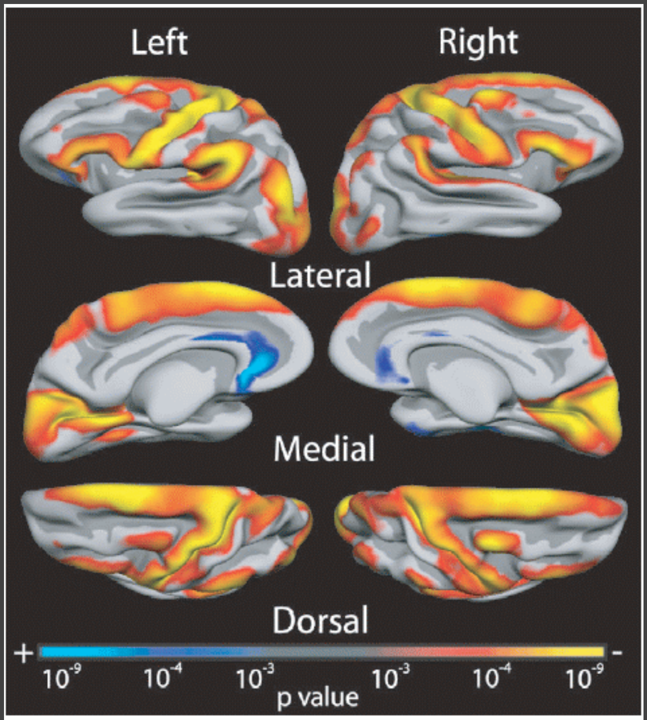
Cortical thickness

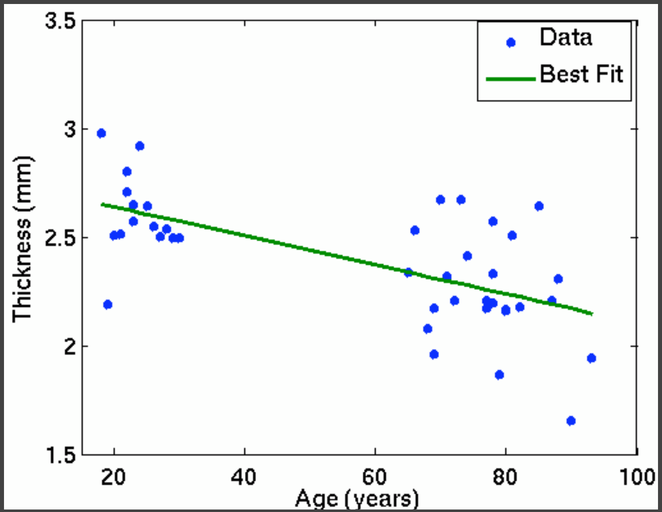
Distance between white and pial surfaces along normal vector (1-5mm)



Application: Aging

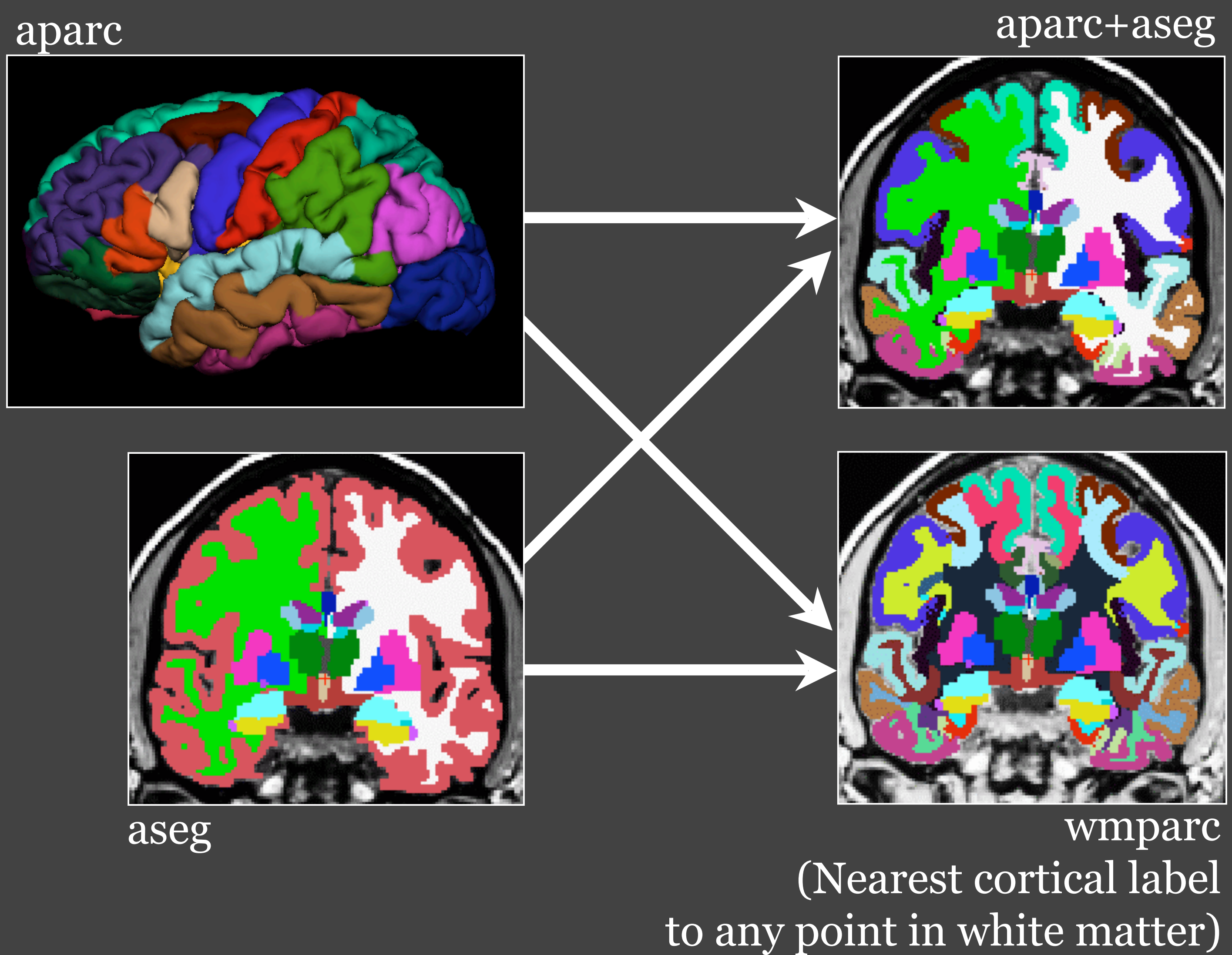






Salat *et al.*, 2004

Cortical/subcortical labels



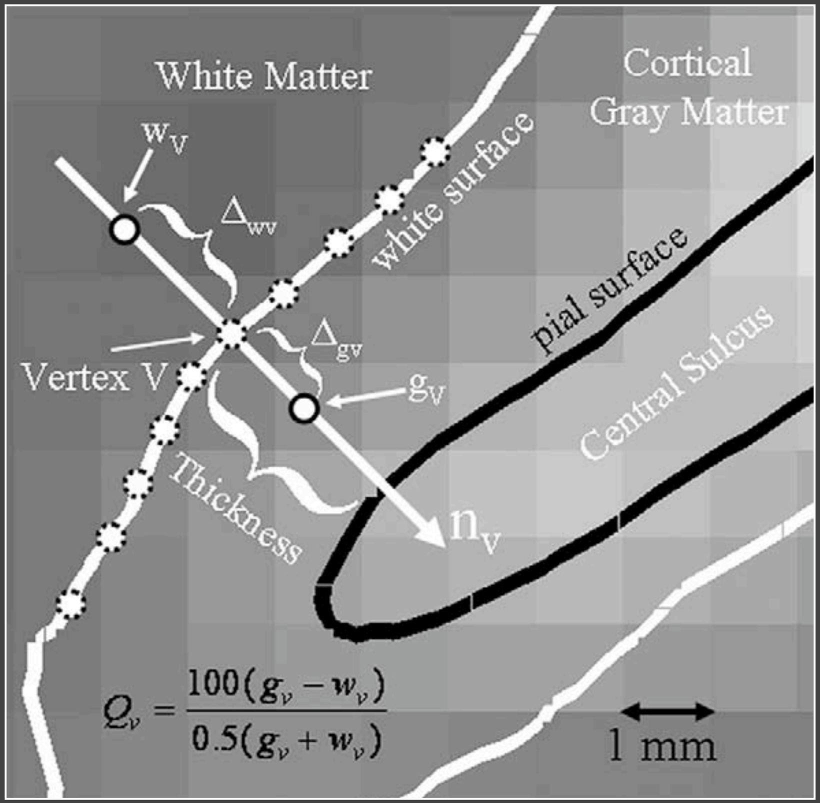
Using surfaces for intra-subject alignment

Boundary-Based Registration (BBR)

Boundary-based registration

Greve and Fischl, 2009

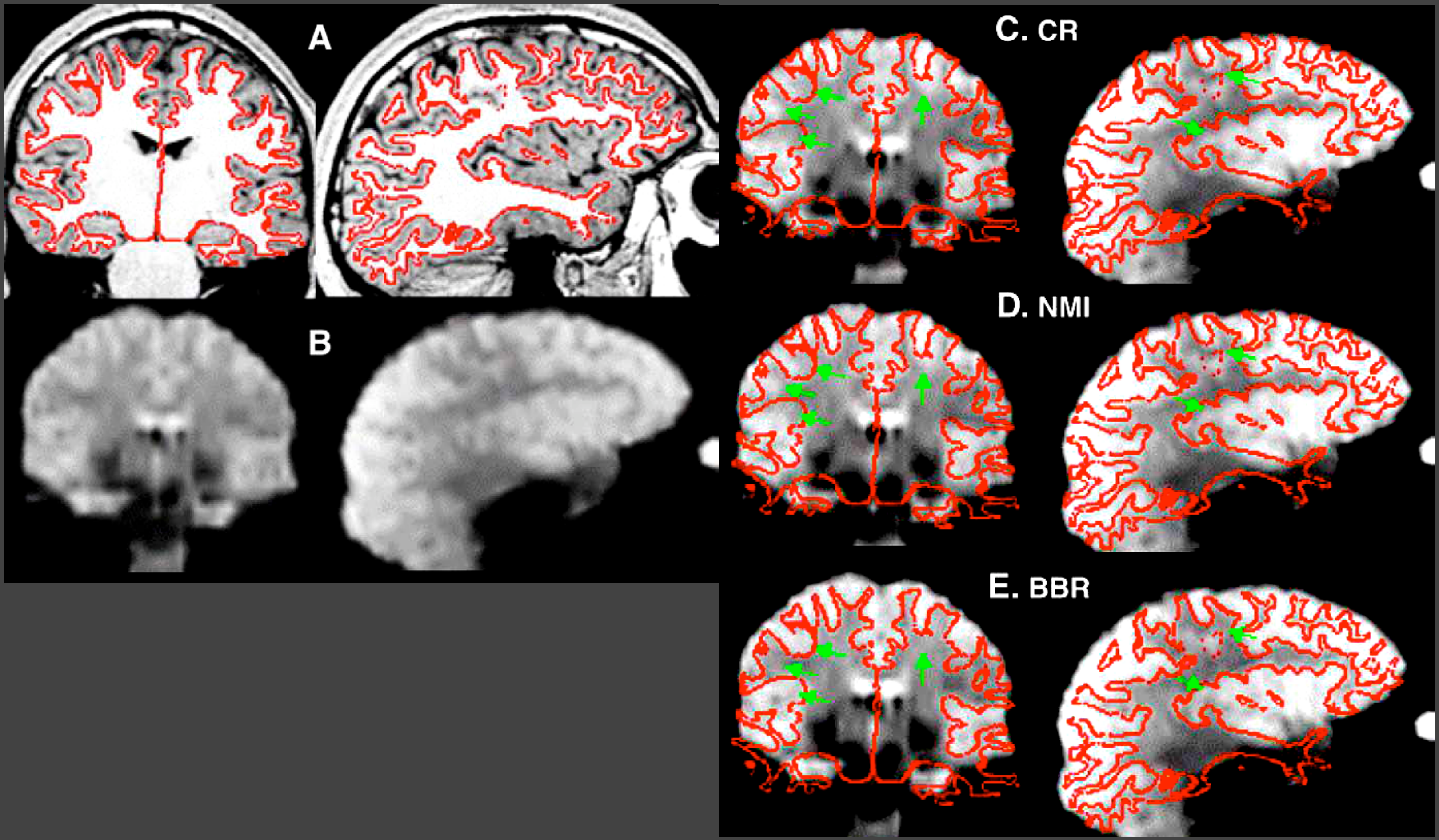
- Goal: Register T_1 (higher resolution and SNR) to EPI (lower resolution and SNR) from the same subject
- EPI can be fMRI or a baseline (low-b) from a diffusion scan
- Most registration methods are intensity-based
- Boundary-based: Exploit the fact that T_1 gives us information on the gray/white boundary
- Optimizes gradient of EPI gray/white contrast perpendicular to the surface



Intensity- vs. boundary-based

Greve and Fischl, 2009

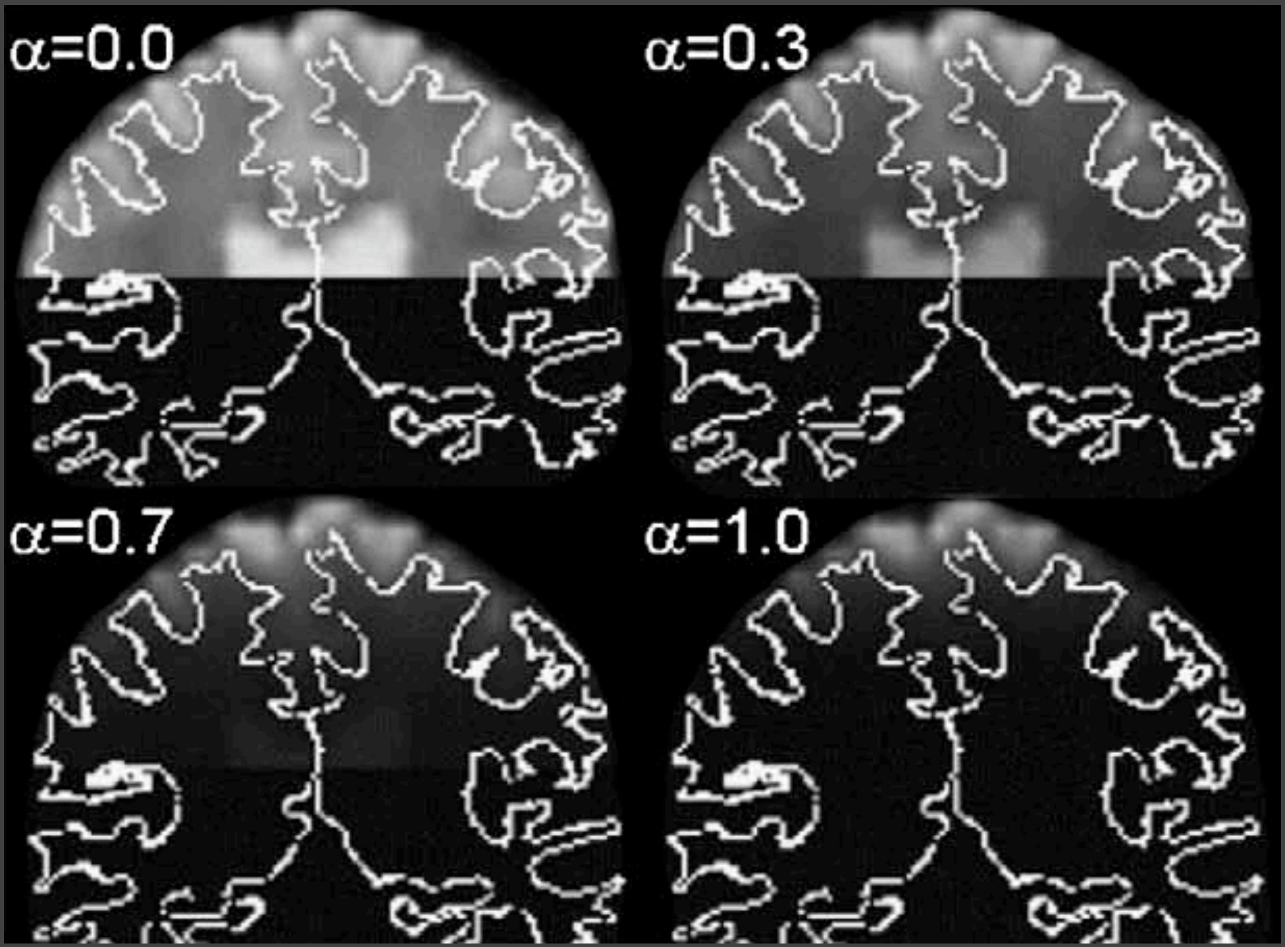
- Compare BBR to methods that use only image intensities: correlation ratio (CR), normalized mutual information (NMI)



Partial field of view

Greve and Fischl, 2009

- Very challenging for intensity-based methods

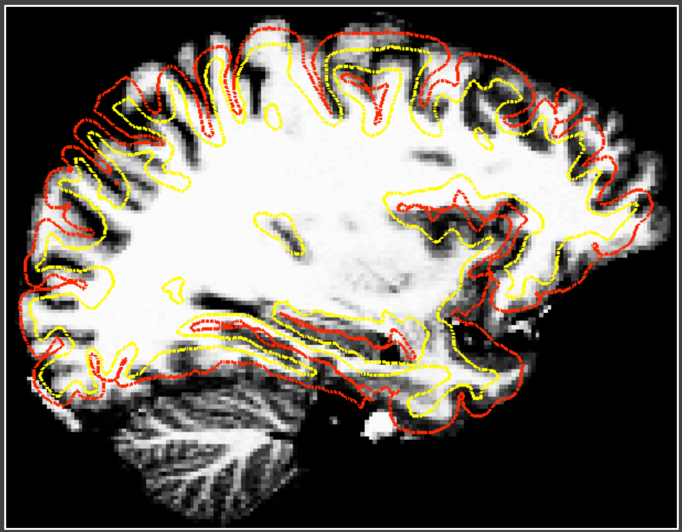


Using surfaces for inter-subject alignment

Combined Volume & Surface (CVS) registration

Inter-subject registration

Work by Lilla Zöllei and Gheorghe Postelnicu

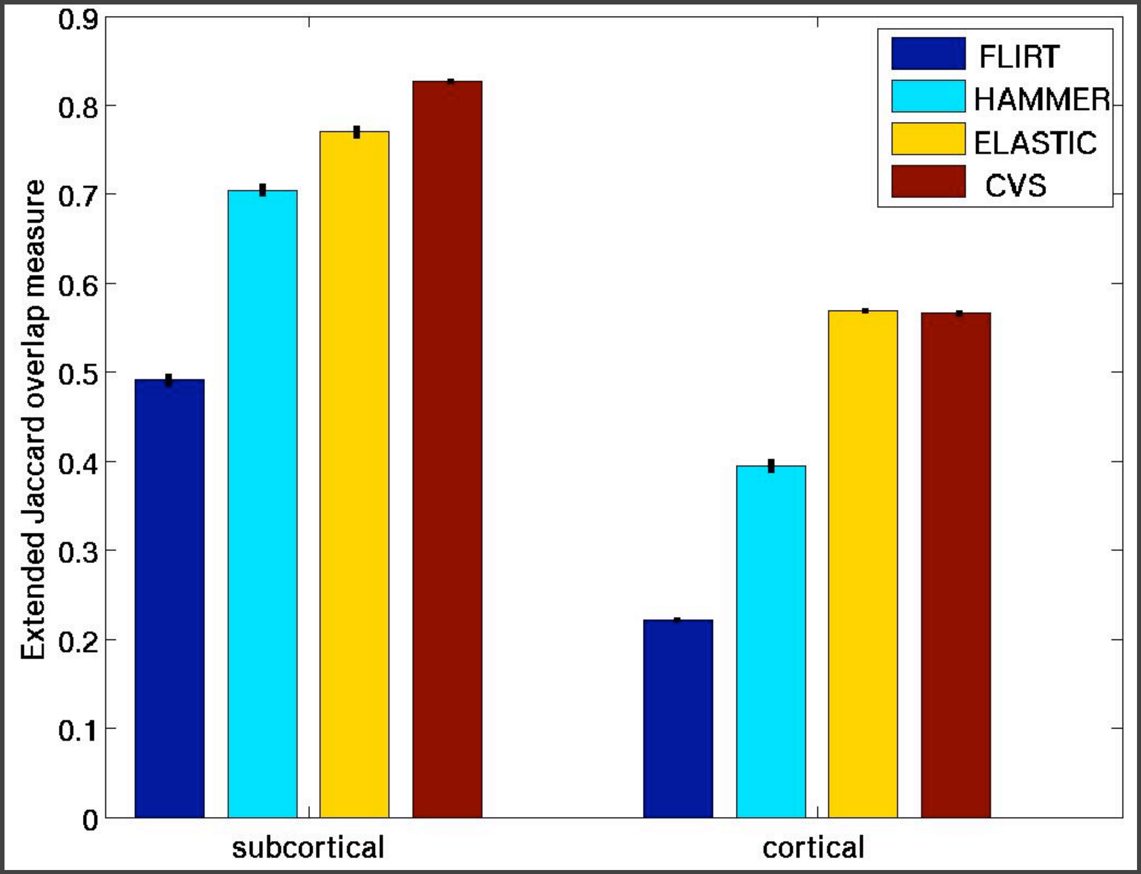


- Volumetric (3D)
  - – Poor for cortical folds
  - + Applies to entire brain
- Surface-based (2D)
  - + Excellent for cortical folds
  - – Doesn't apply to non-cortical structures
- CVS: Combined Volume and Surface
  1. Surface-based registration on the cortex
  2. Propagate into the volume via elastic transform
  3. Initialize intensity-based volumetric registration

Accuracy comparison

Slides by Lilla Zöllei

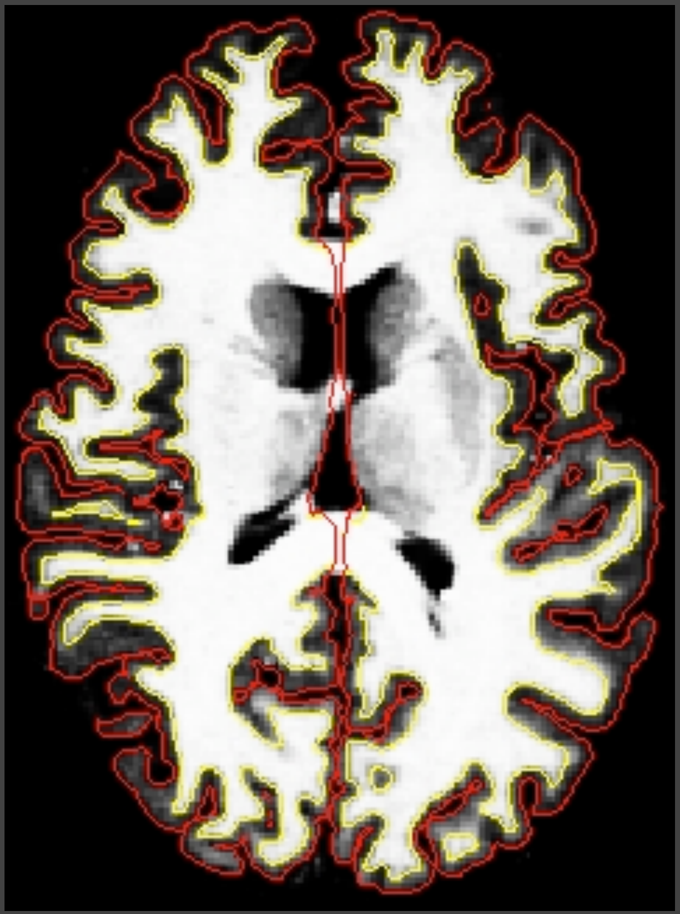
- 40 adult subjects with manually segmented cortex
- Leave-one-out, extended Jaccard overlap metric

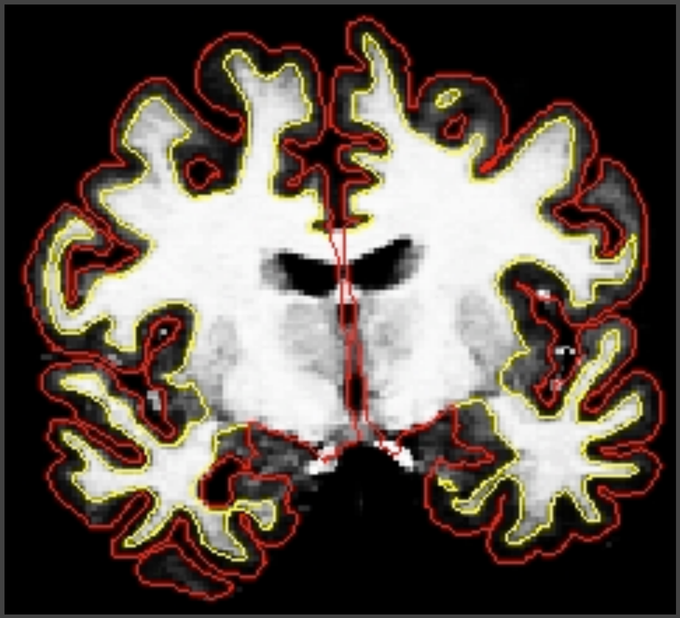


Data courtesy of Dr. R. Buckner, MGH

Template

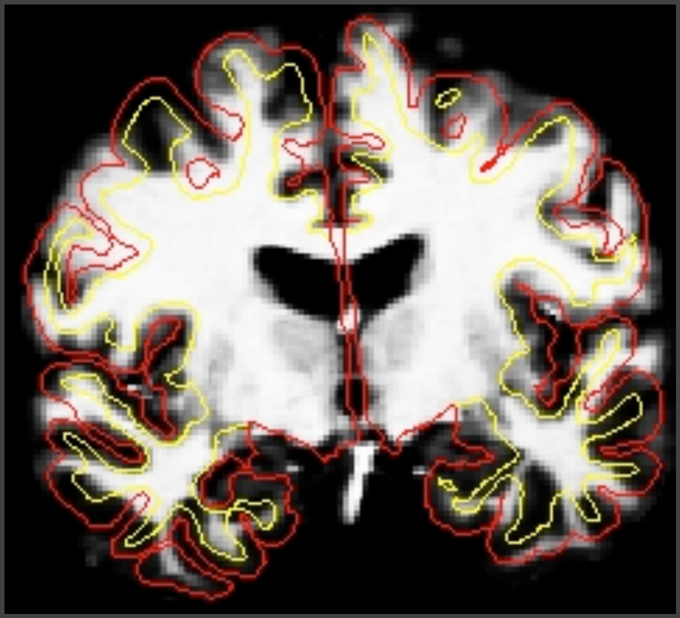
Slides by Lilla Zöllei





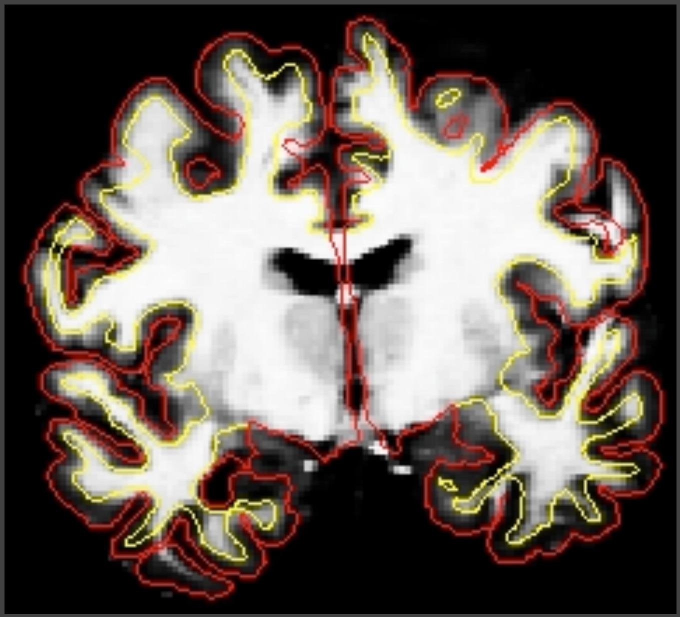
FSL/FLIRT (affine)

Slides by Lilla Zöllei



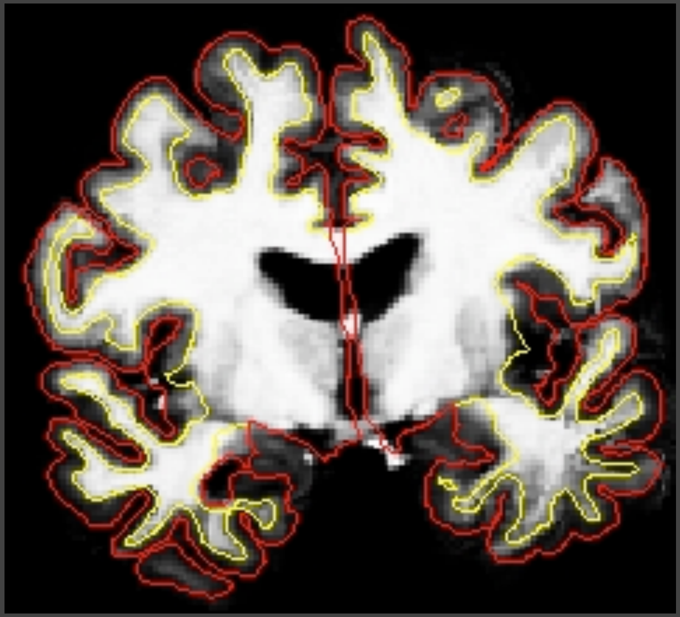
HAMMER (volumetric + gray/white)

Slides by Lilla Zöllei



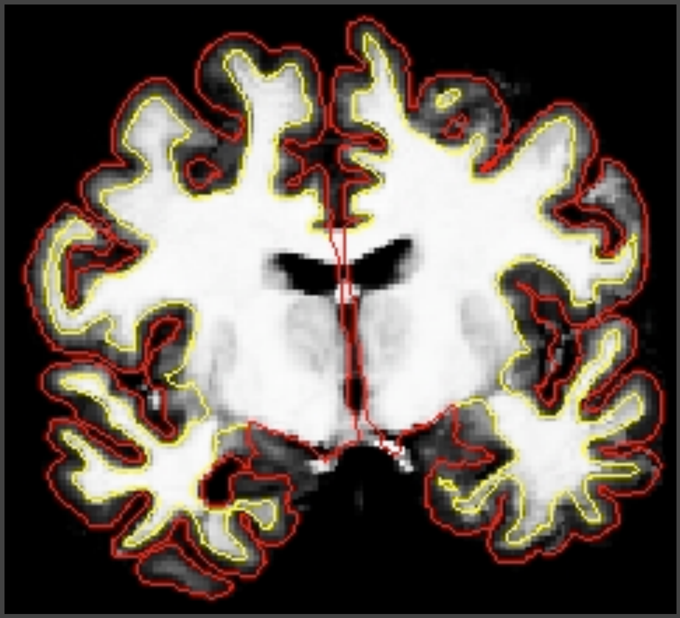
Elastic only

Slides by Lilla Zöllei



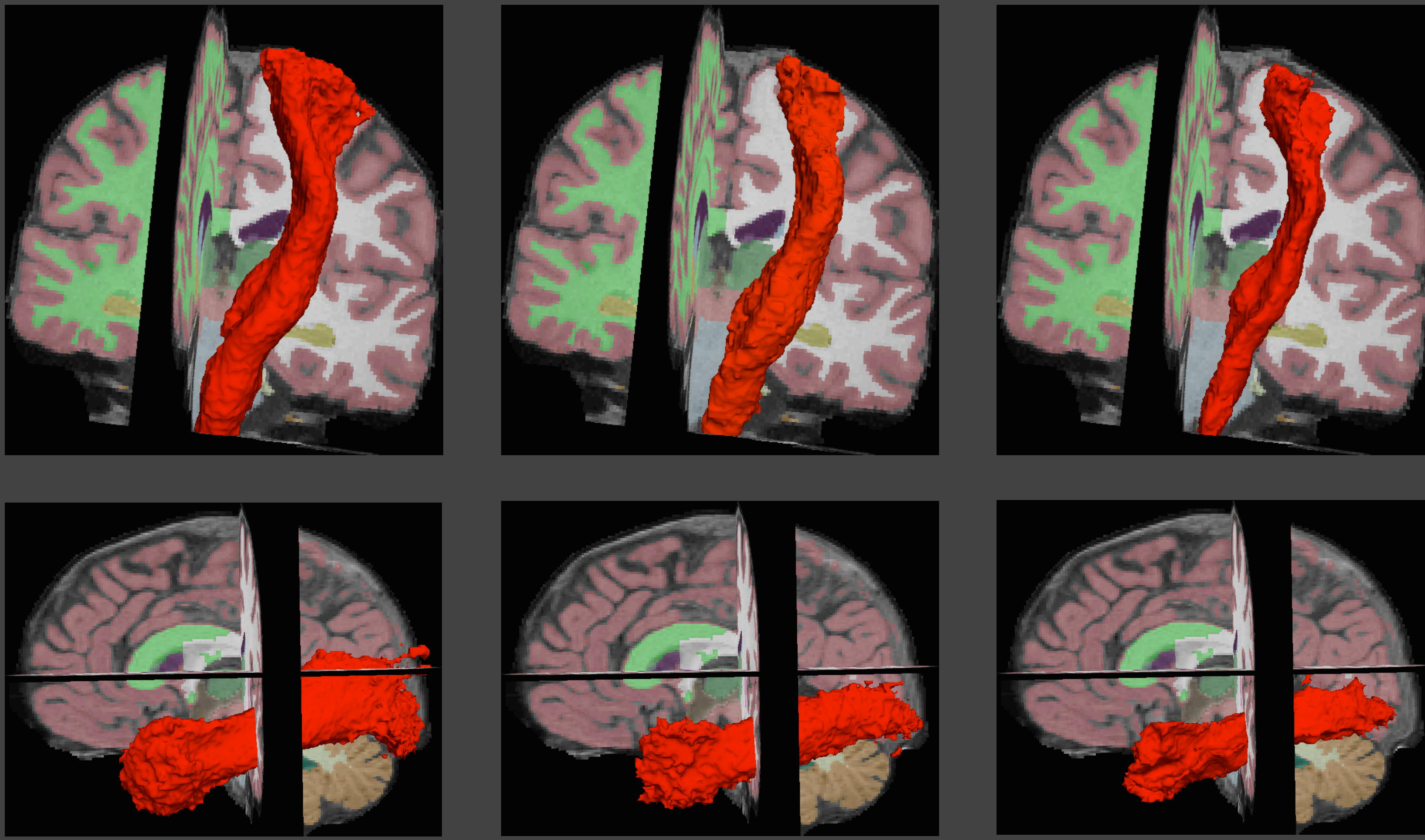
CVS (elastic + intensity-based)

Slides by Lilla Zöllei



Alignment of training paths

Zöllei et al, 2010



FLIRT (affine) TBSS/FNIRT (nonlinear) CVS (nonlinear)

Using anatomical segmentation for automated tractography

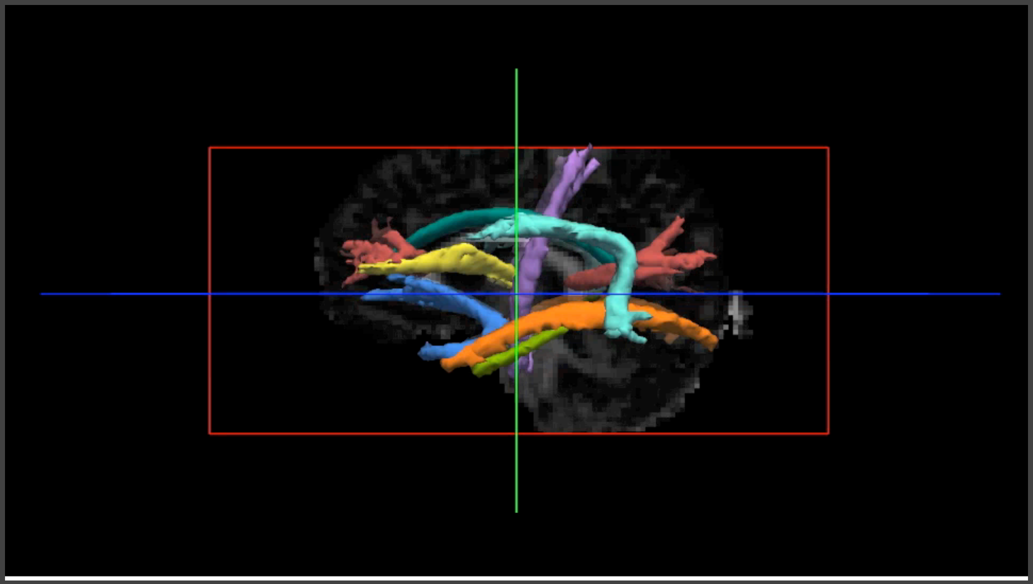
TRActs Constrained by UnderLying Anatomy
(TRACULA)

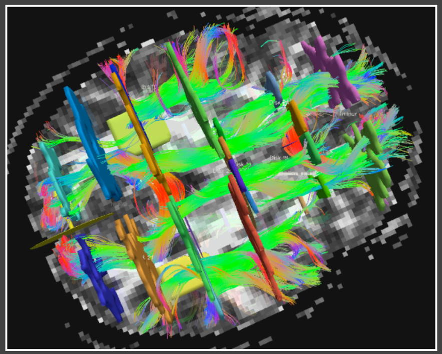
Automated pathway reconstruction

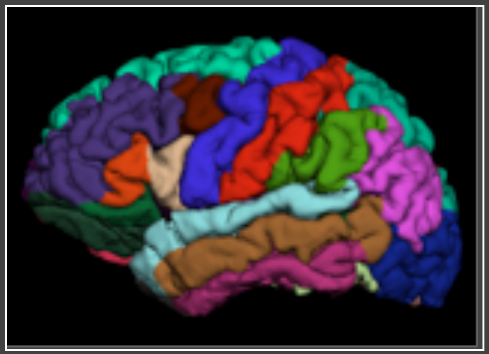
[Yendiki et al 2011]

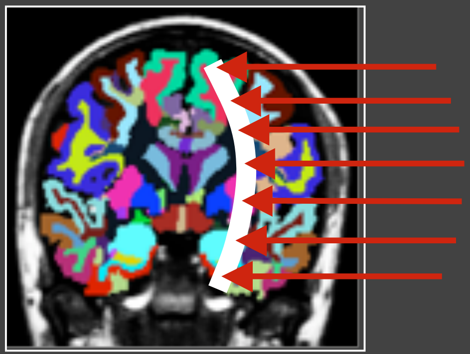
- TRACULA (TRActs Constrained by UnderLying Anatomy)

- Algorithm trained on the likelihood of each pathway passing by each anatomical structure



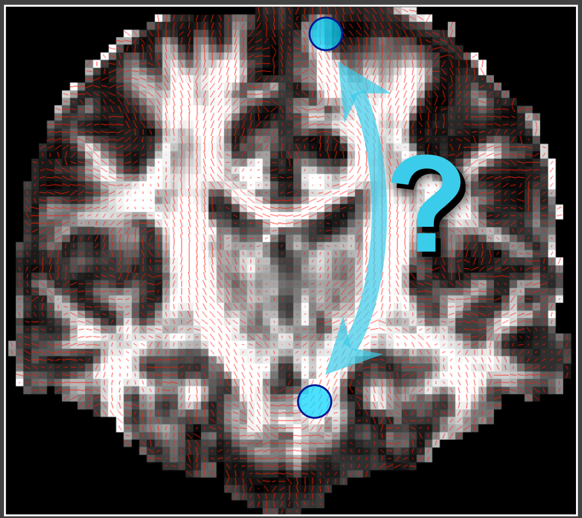






Tractography studies

- Exploratory tractography:
  - Example: *Show me all regions that the motor cortex is connected to*
  - Seed region can be anatomically defined (motor cortex) or functionally defined (region activated in an fMRI finger-tapping task)



- Tractography of known pathways:
  - Example: *Show me the corticospinal tract*
  - Use prior anatomical knowledge of the pathway's terminations and trajectory (connects motor cortex and brainstem through capsule)

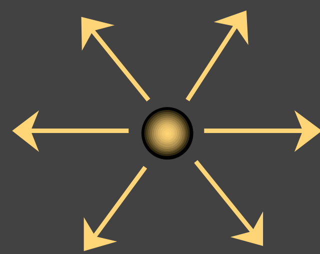
- TRACULA is for the latter type of study

Tractography methods

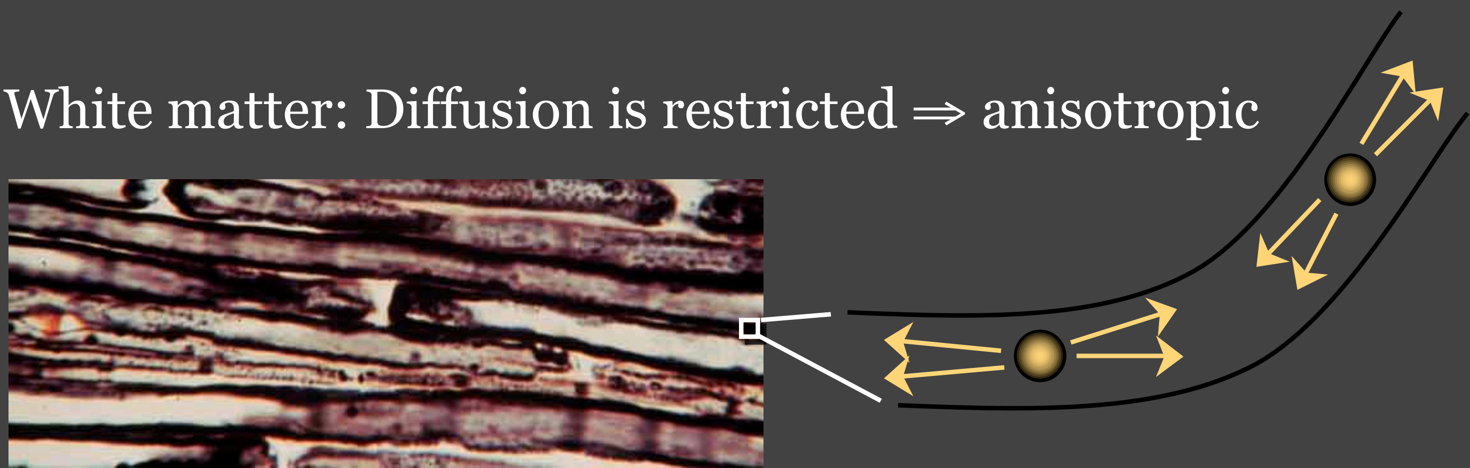
- Every tractography method can be characterized by:
  - Which model of diffusion does it use?
    - Representation of local orientation of diffusion at every voxel that is fit to image data (tensor, ball-and-stick, etc.)
  - Is it deterministic or probabilistic?
    - Deterministic estimates only the most likely orientation
    - Probabilistic also estimates the uncertainty around that
  - Is it local or global?
    - Local fits the pathway to the data one step at a time
    - Global fits the entire pathway at once
- TRACULA does global probabilistic tractography with the ball-and-stick model

Diffusion in brain tissue

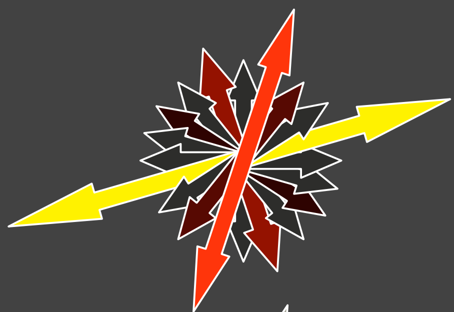
- Differentiate between tissues based on the diffusion (random motion) of water molecules within them
- Gray matter: Diffusion is unrestricted ⇒ isotropic



- White matter: Diffusion is restricted ⇒ anisotropic

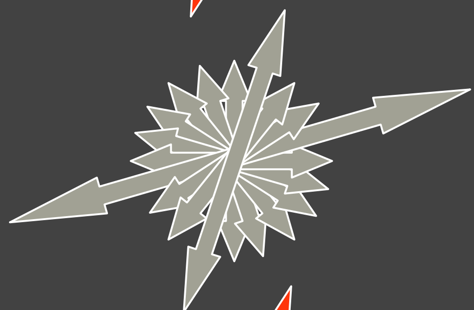


Models of diffusion



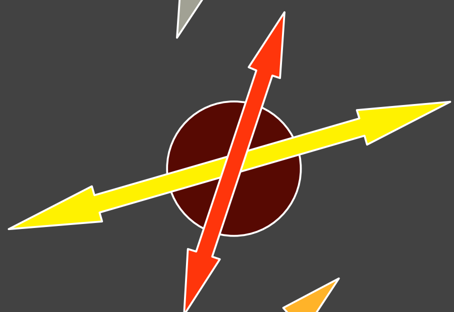
Diffusion spectrum: — DSI

Full distribution of orientation and magnitude



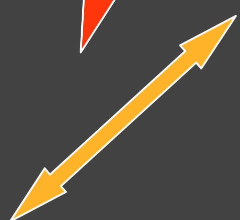
Orientation distribution function (ODF): — Q-ball

No magnitude info



Ball-and-stick: — FSL (bedpostX)

Orientation and magnitude for up to N anisotropic compartments (default N=2)

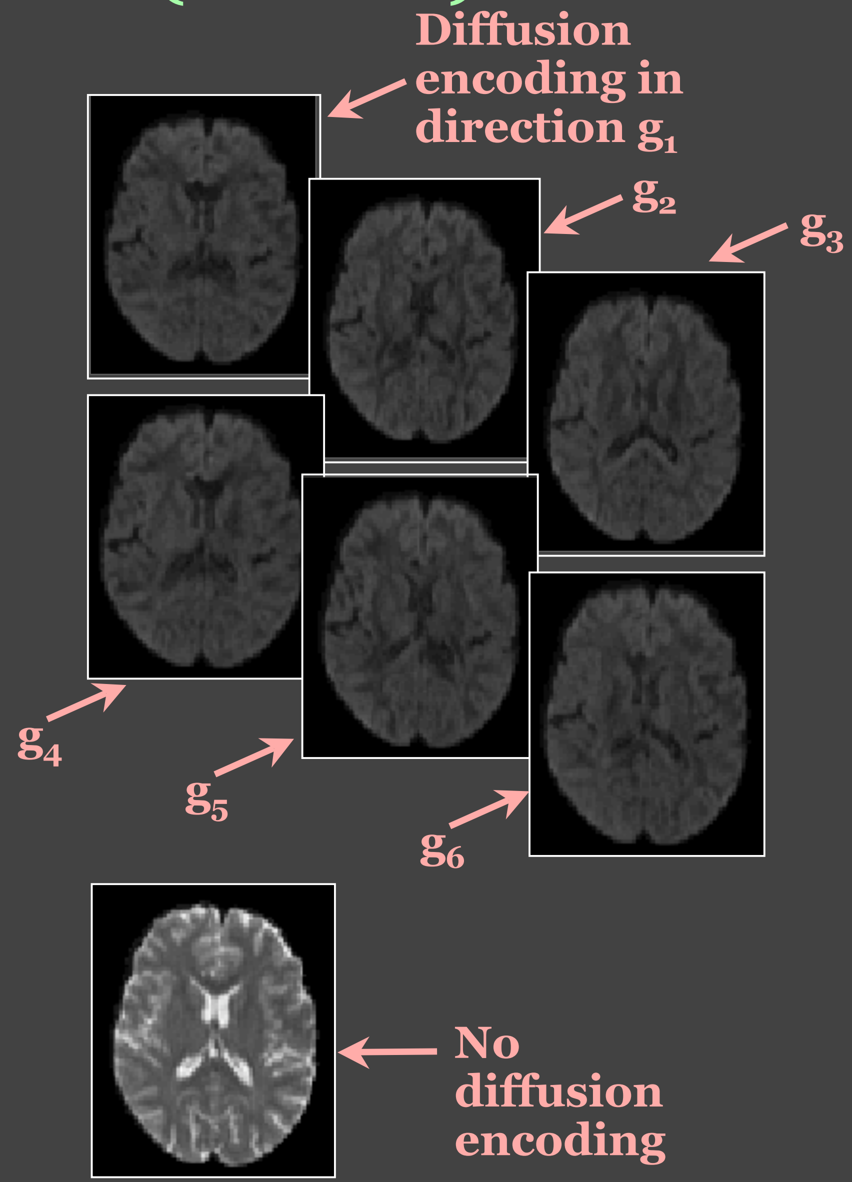


Tensor: — DTI

Single orientation and magnitude

Diffusion MRI (dMRI)

- Magnetic resonance imaging can provide "diffusion encoding"
- Magnetic field strength is varied by gradients in different directions
- Image intensity is attenuated depending on water diffusion in each direction
- Compare with baseline images to infer on diffusion process



Tensors

- One way to express the notion of direction is a tensor D

- A tensor is a 3x3 symmetric, positive-definite matrix:

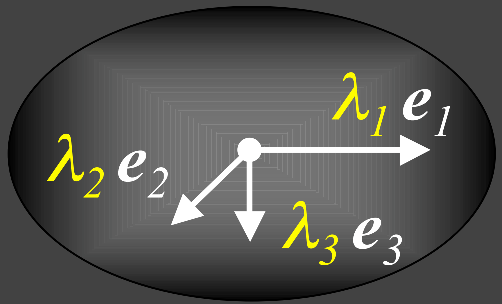
$$D = \begin{bmatrix} d_{11} & d_{12} & d_{13} \\ d_{12} & d_{22} & d_{23} \\ d_{13} & d_{23} & d_{33} \end{bmatrix}$$

- D is symmetric 3x3 ⇒ It has 6 unique elements

- Suffices to estimate the upper (lower) triangular part

Eigenvalues & eigenvectors

- The matrix D is positive-definite $\Rightarrow$
  - It has 3 real, positive eigenvalues $\lambda_1, \lambda_2, \lambda_3 > 0$.
  - It has 3 orthogonal eigenvectors $\boldsymbol{e}_1, \boldsymbol{e}_2, \boldsymbol{e}_3$.



$$D = \lambda_1 \boldsymbol{e}_1 \cdot \boldsymbol{e}_1' + \lambda_2 \boldsymbol{e}_2 \cdot \boldsymbol{e}_2' + \lambda_3 \boldsymbol{e}_3 \cdot \boldsymbol{e}_3'$$

eigenvalue (λ_1) eigenvector ($\boldsymbol{e}_1$)

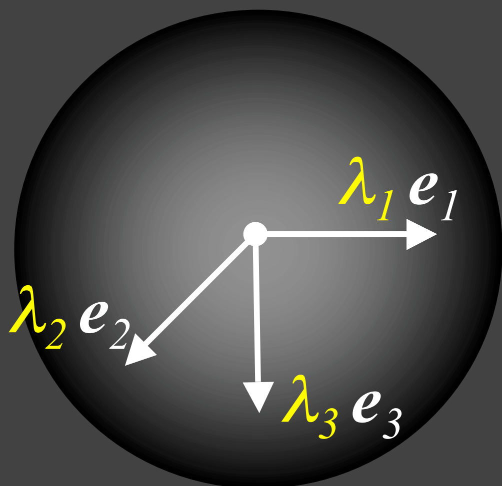
$$\boldsymbol{e}_i = \begin{bmatrix} e_{ix} \\ e_{iy} \\ e_{iz} \end{bmatrix}$$

Physical interpretation

- Eigenvectors express diffusion direction
- Eigenvalues express diffusion magnitude

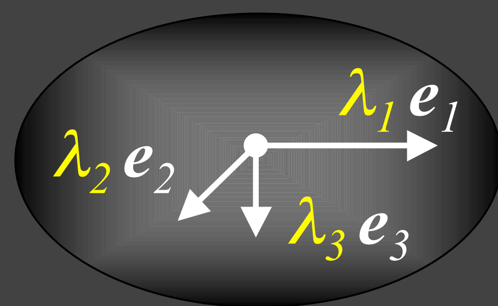
Isotropic diffusion:

$\lambda_1 \approx \lambda_2 \approx \lambda_3$



Anisotropic diffusion:

$\lambda_1 >> \lambda_2 \approx \lambda_3$

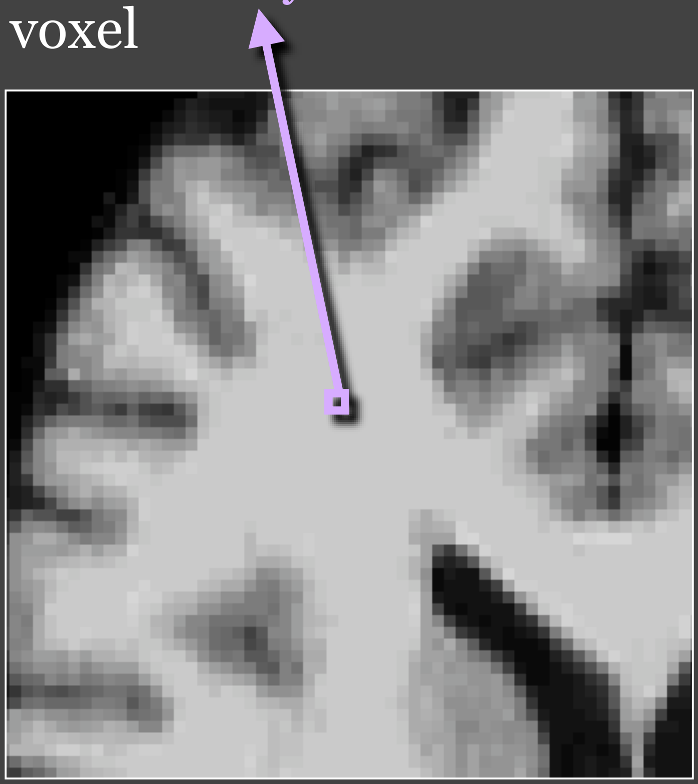


- One such ellipsoid at each voxel: Likelihood of water molecule displacements at that voxel

Diffusion tensor imaging (DTI)

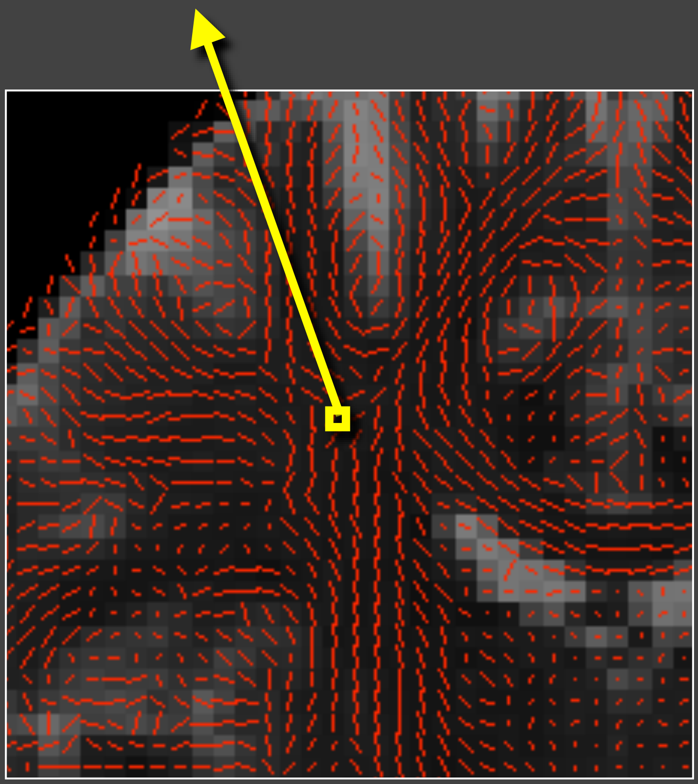
Image:

An intensity value at each voxel



Tensor map:

A tensor at each voxel

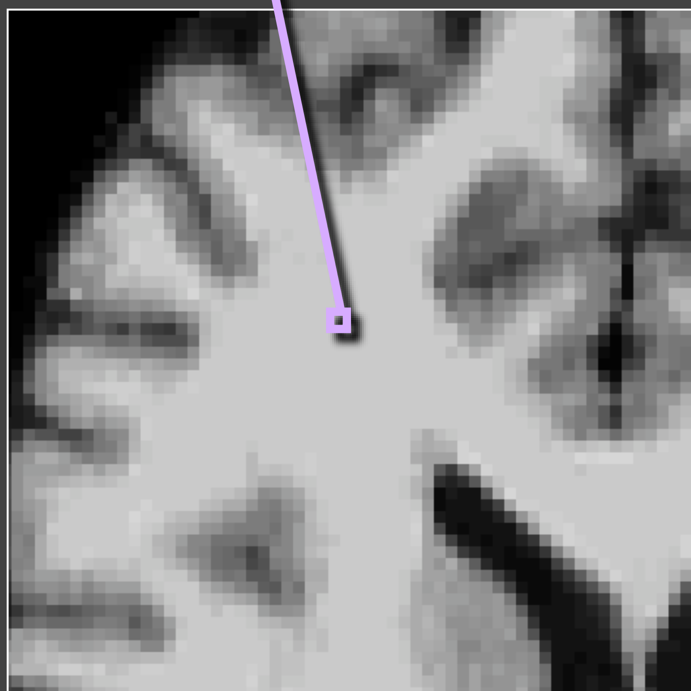


Direction of eigenvector corresponding to greatest eigenvalue

Diffusion tensor imaging (DTI)

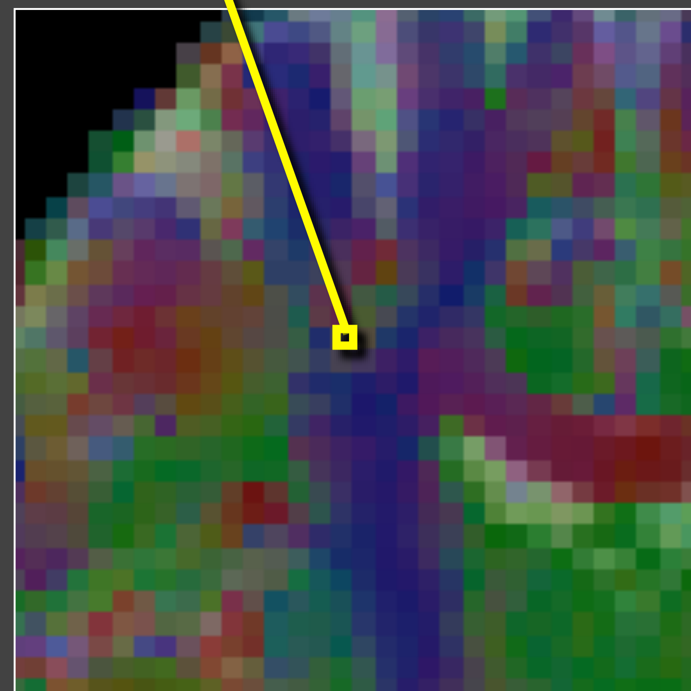
Image:

An intensity value at each voxel



Tensor map:

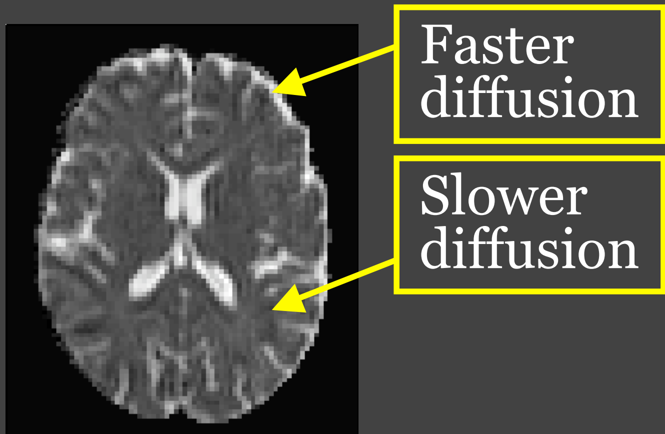
A tensor at each voxel



Direction of eigenvector corresponding to greatest eigenvalue

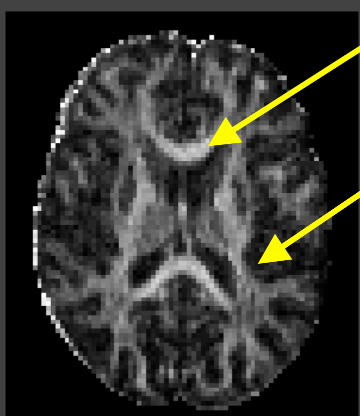
Red: L-R, Green: A-P, Blue: I-S

Tensor-based measures of diffusion



• Mean diffusivity (MD):
Mean of the 3 eigenvalues

$$MD(j) = [\lambda_1(j)+\lambda_2(j)+\lambda_3(j)]/3$$



• Fractional anisotropy (FA):
Variance of the 3 eigenvalues, normalized so that $0 \leq (FA) \leq 1$

$$FA(j)^2 = \frac{3}{2} \frac{[\lambda_1(j)-MD(j)]^2 + [\lambda_2(j)-MD(j)]^2 + [\lambda_3(j)-MD(j)]^2}{\lambda_1(j)^2 + \lambda_2(j)^2 + \lambda_3(j)^2}$$

More tensor-based measures

- Axial diffusivity: Greatest of the 3 eigenvalues

  $AD(j) = \lambda_1(j)$

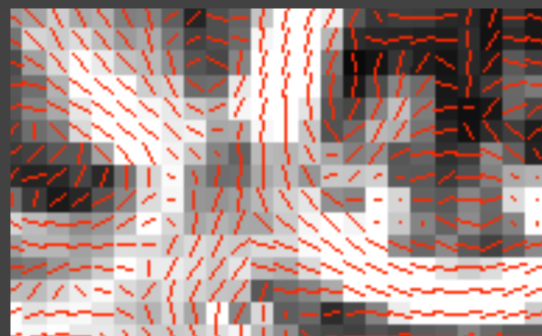
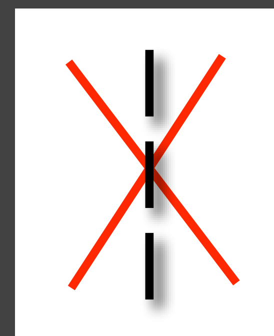
- Radial diffusivity: Average of 2 lesser eigenvalues

  $RD(j) = [\lambda_2(j) + \lambda_3(j)]/2$

- Inter-voxel coherence: Average angle b/w the major eigenvector at some voxel and the major eigenvector at the voxels around it

Beyond the tensor

- The tensor is an imperfect model: What if more than one major diffusion direction in the same voxel?

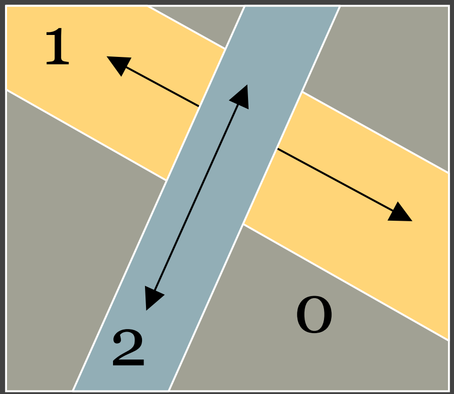
- High angular resolution diffusion imaging (HARDI): More complex models to capture more complex microarchitecture
  - Mixture of tensors [Tuch'02]
  - Higher-rank tensor [Frank'02, Özarslan'03]
  - Ball-and-stick [Behrens'07]
  - Orientation distribution function [Tuch'04]
  - Diffusion spectrum [Wedeen'05]

Non-tensor measures of diffusion

- From the orientation distribution function (ODF) [Tuch'04]:
  - Peak directions
  - Generalized fractional anisotropy (GFA)

$$\mathrm{GFA}^2 = \frac{n\ \Sigma_i[\mathrm{ODF}(\theta_i) - \Sigma_i\ \mathrm{ODF}(\theta_i)/n]^2}{(n\text{-}1)\ \Sigma_i\ \mathrm{ODF}(\theta_i)^2}$$

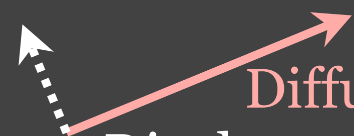
- From the ball-and-stick model [Behrens'07]:
  - Orientation angles of each anisotropic compartment (1, 2, …)
  - Volume of each anisotropic compartment
  - Overall diffusivity in the voxel



Choice 1: Gradient directions

- True diffusion direction || Applied gradient direction
  ⇒ Maximum attenuation

- True diffusion direction ⊥ Applied gradient direction
  ⇒ No attenuation



- To capture all diffusion directions well, gradient directions should cover 3D space uniformly

How many directions?

- Acquiring data with more gradient directions leads to:
  + More reliable estimation of diffusion measures
  – Increased imaging time ⇒ Subject discomfort, more susceptible to artifacts due to motion, respiration, etc.

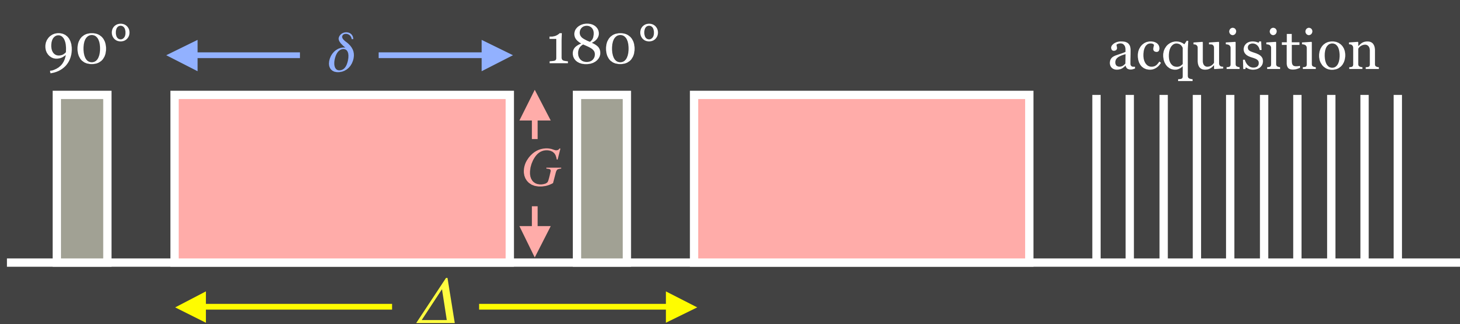
- DTI:
  – Six directions is the minimum
  – Usually a few 10's of directions
  – Diminishing returns after a certain number [Jones, 2004]
- DSI:
  – Usually a few 100's of directions

Choice 2: The b-value

- The b-value depends on acquisition parameters:

$$b = \gamma^2 G^2 \delta^2 (\Delta - \delta/3)$$

  - γ the gyromagnetic ratio
  - G the strength of the diffusion-encoding gradient
  - δ the duration of each diffusion-encoding pulse
  - Δ the interval b/w diffusion-encoding pulses



How high b-value?

- Increasing the b-value leads to:
  + Increased contrast b/w areas of higher and lower diffusivity in principle
  – Decreased signal-to-noise ratio ⇒ Less reliable estimation of diffusion measures in practice

- DTI: b ~ 1000 sec/mm^2
- DSI: b ~ 10,000 sec/mm^2

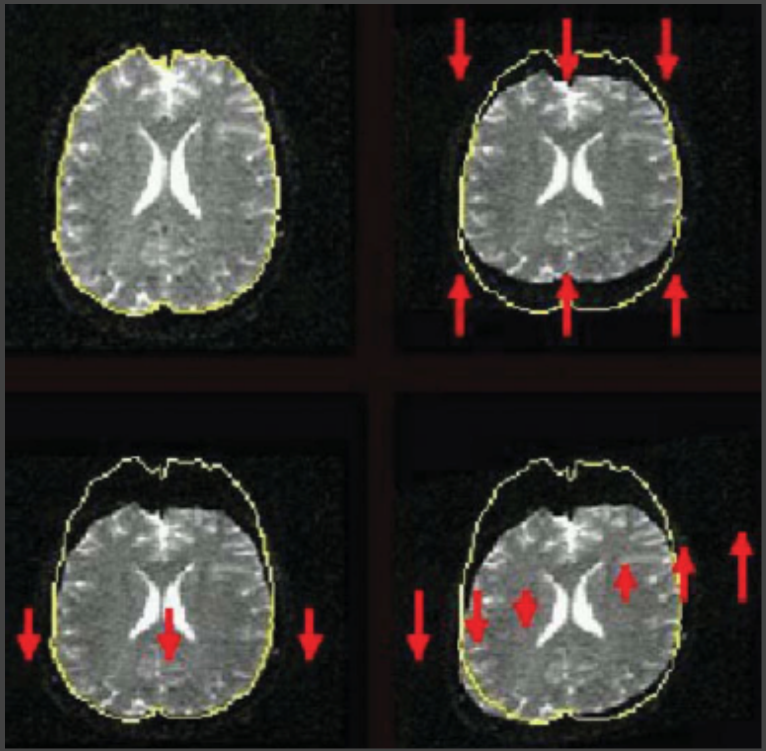
- Data can be acquired at multiple b-values for trade-off
- Repeat acquisition and average to increase signal-to-noise ratio

Distortions: Field inhomogeneities

- Causes:
  - Scanner-dependent (imperfections of main magnetic field)
  - Subject-dependent (changes in magnetic susceptibility in tissue/air interfaces)
- Results:
  - Signal loss in interface areas
  - Geometric distortions (warping) of the entire image

Distortions: Eddy currents

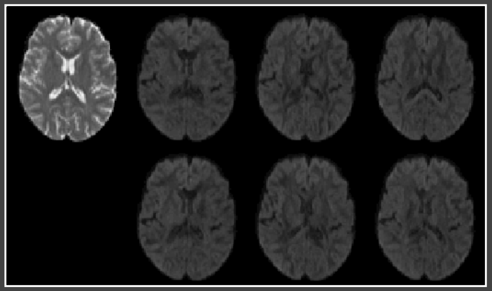
- Cause: Fast switching of diffusion-encoding gradients induces eddy currents in conducting components
- Eddy currents lead to residual gradients that shift the diffusion gradients
- The shifts are direction-dependent, *i.e.*, different for each DW image
- Result: Geometric distortions

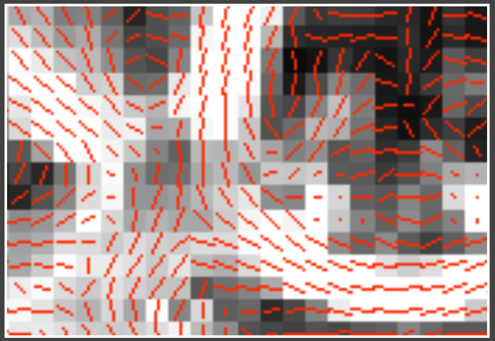


From Le Bihan *et al.*, Artifacts and pitfalls in diffusion MRI, JMRI 2006

Data analysis steps

- Pre-process images to reduce distortions
  - Either register distorted DW images to an undistorted (non-DW) image
  - Or use information on distortions from separate scans (field map, residual gradients)





- Fit a diffusion model at every voxel
  - DTI, DSI, Q-ball, …
- Compute measures of anisotropy/diffusivity and compare them between populations
  - Voxel-based (*e.g.*, TBSS), ROI-based, tract-based
- For tract-based: Reconstruct pathways