Introduction to diffusion MRI

Slides prepared by: Anastasia Yendiki

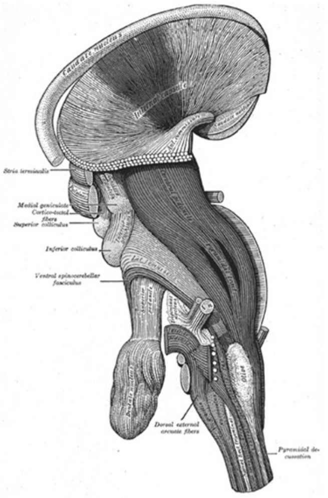
HMS/MGH/MIT Athinoula A. Martinos Center for
Biomedical Imaging

White-matter imaging

From the National Institute on Aging

- Axons measure ~μm in width
- They group together in bundles that traverse the white matter

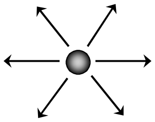
- We cannot image individual axons but we can image bundles with diffusion MRI
- Useful in studying neurodegenerative diseases, stroke, aging, development…



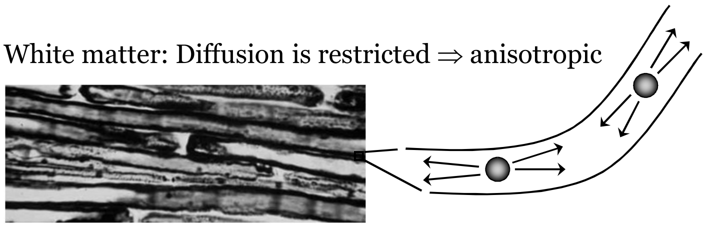
From *Gray's Anatomy: IX. Neurology*

Diffusion in brain tissue

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

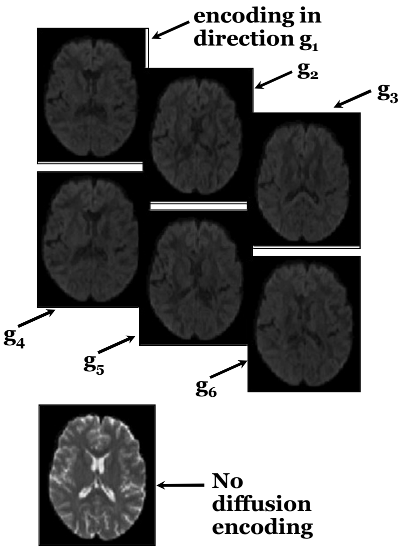


- White matter: Diffusion is restricted ⇒ anisotropic



Diffusion MRI

- 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



Diffusion encoding in direction $\mathbf{g}_1$

$\mathbf{g}_2$

$\mathbf{g}_3$

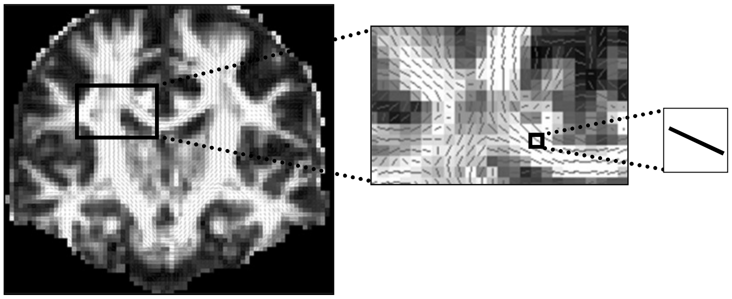
$\mathbf{g}_4$

$\mathbf{g}_5$

$\mathbf{g}_6$

No diffusion encoding

How to represent diffusion



- At every voxel we want to know:
  - Is this in white matter?
  - If yes, what pathway(s) is it part of?
    - What is the orientation of diffusion?
    - What is the magnitude of diffusion?
- A grayscale image cannot capture all this!

Tensors

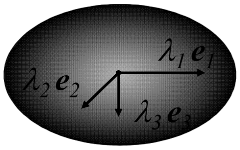
- One way to express the notion of direction is a tensor *D*
- A tensor is a 3 × 3 symmetric, positive-definite matrix:

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

- *D* is symmetric 3 × 3 ⇒ 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 $\boldsymbol{e}_1, \boldsymbol{e}_2, \boldsymbol{e}_3$.



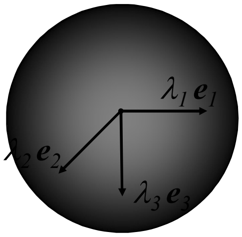
$$D = \underbrace{\lambda_1}_{\text{eigenvalue}} \underbrace{\boldsymbol{e}_1}_{\text{eigenvector}} \cdot \boldsymbol{e}_1{}' + \lambda_2 \boldsymbol{e}_2 \cdot \boldsymbol{e}_2{}' + \lambda_3 \boldsymbol{e}_3 \cdot \boldsymbol{e}_3{}'$$

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

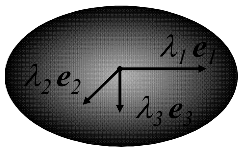
Physical interpretation

- Eigenvectors express diffusion direction
- Eigenvalues express diffusion magnitude

Isotropic diffusion:
$\lambda_1 \approx \lambda_2 \approx \lambda_3$



Anisotropic diffusion:
$\lambda_1 >> \lambda_2 \approx \lambda_3$

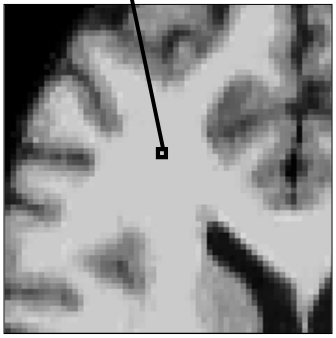


- One such ellipsoid at each voxel: Likelihood of water molecule displacements at that voxel

Diffusion tensor imaging (DTI)

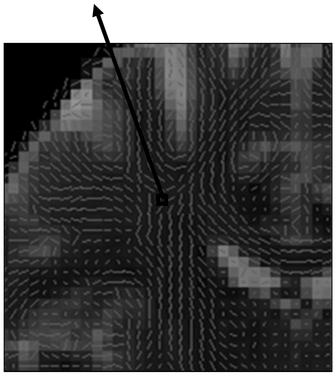
Image:

An intensity value at each voxel



Tensor map:

A tensor at each voxel



Direction of eigenvector corresponding to greatest eigenvalue

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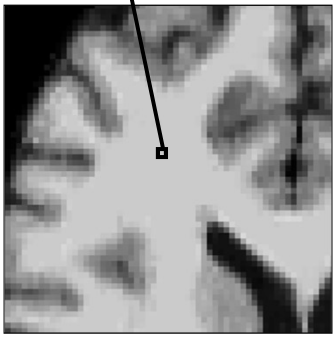
Diffusion tensor imaging (DTI)

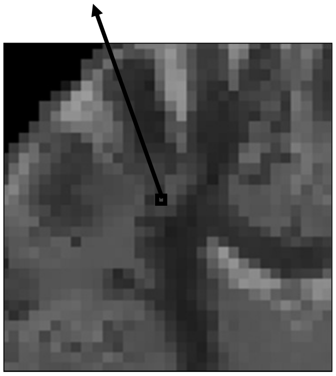
Image:

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

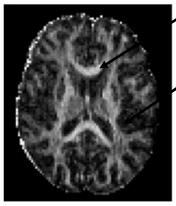
Summary measures

Faster diffusion

Slower diffusion

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

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



Anisotropic diffusion

Isotropic diffusion

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

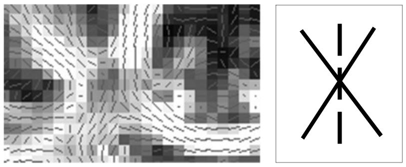
$$\mathrm{FA}(j)^2 = \frac{3}{2}\,\frac{[\lambda_1(j)-\mathrm{MD}(j)]^2 + [\lambda_2(j)-\mathrm{MD}(j)]^2 + [\lambda_3(j)-\mathrm{MD}(j)]^2}{\lambda_1(j)^2 + \lambda_2(j)^2 + \lambda_3(j)^2}$$

More summary measures

- Axial diffusivity: Greatest of the 3 eigenvalues
  $\mathrm{AD}(j) = \lambda_1(j)$
- Radial diffusivity: Average of 2 lesser eigenvalues
  $\mathrm{RD}(j) = [\lambda_2(j) + \lambda_3(j)]/2$
- Inter-voxel coherence: Average angle b/w the major eigenvector at some voxel and the major eigenvector at the voxels around it

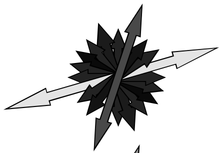
Beyond the tensor

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

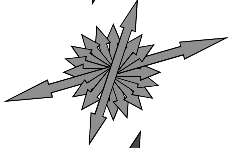


- High angular resolution diffusion imaging (HARDI): More complex models to capture more complex microarchitecture
  - Mixture of tensors [Tuch'02]
  - Higher-rank tensor [Frank'02, Özarslan'03]
  - Ball-and-stick [Behrens'03]
  - Orientation distribution function [Tuch'04]
  - Diffusion spectrum [Wedeen'05]

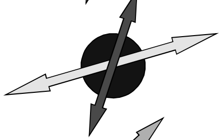
Models of diffusion



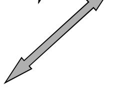
Diffusion spectrum (DSI):
Full distribution of orientation and magnitude



Orientation distribution function (Q-ball):
No magnitude info, only orientation

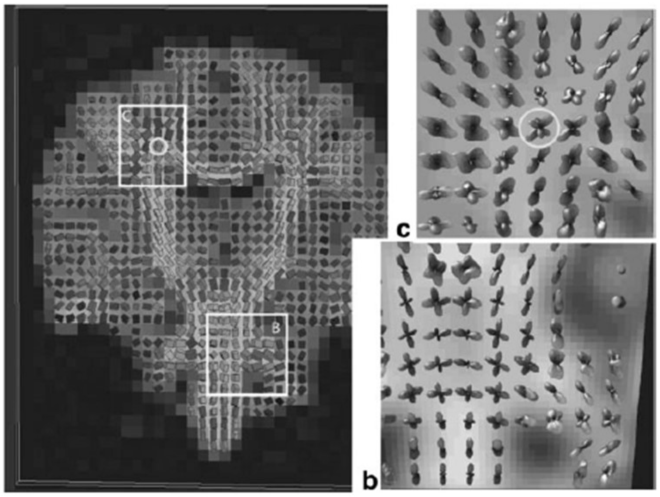


Ball-and-stick:
Orientation and magnitude for up to N anisotropic compartments



Tensor (DTI):
Single orientation and magnitude

Example: DTI vs. DSI



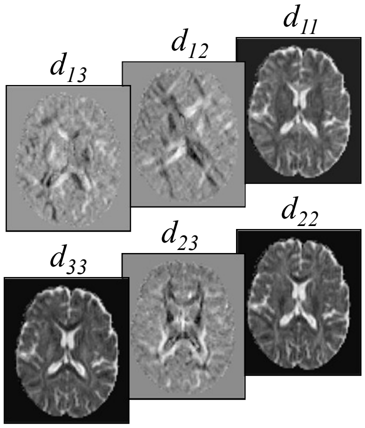
From Wedeen *et al.,* Mapping complex tissue architecture with diffusion spectrum magnetic resonance imaging, MRM 2005

Data acquisition

- Remember: A tensor has six unique parameters

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

- To estimate six parameters at each voxel, must acquire at least six diffusion-weighted images
- HARDI models have more parameters per voxel, so more images must be acquired



Choice 1: Gradient directions

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

Diffusion-encoding gradient ***g***
Displacement detected

- True diffusion direction ⊥ Applied gradient direction
  ⇒ No attenuation

Diffusion-encoding gradient ***g***
Displacement not detected

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

Diffusion-encoding gradient ***g***
Displacement partly detected

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.

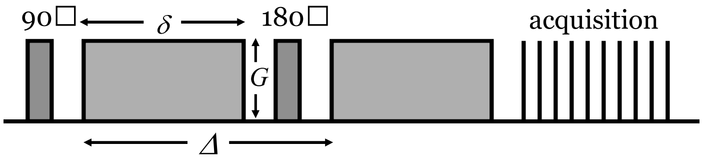
- DTI:
  - Six directions is the minimum
  - Usually a few 10’s of directions
  - Diminishing returns after a certain number [Jones, 2004]
- HARDI/DSI:
  - Usually a few 100’s of directions

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

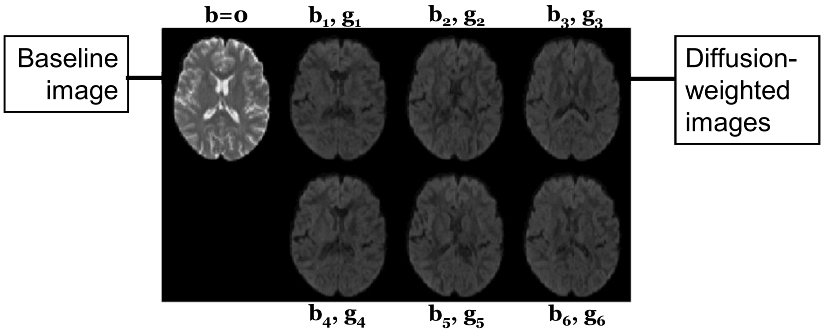
- DTI: b ~ 1000 sec/mm^2
- DSI: b ~ [0, 10,000] sec/mm^2

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

Looking at the data

A diffusion data set consists of:

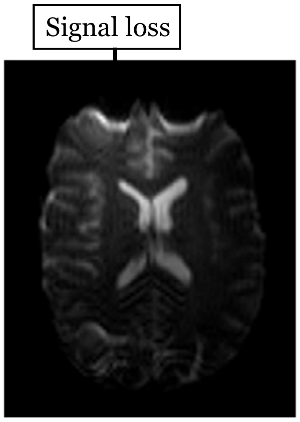
- A set of non-diffusion-weighted a.k.a “baseline” a.k.a. “low-b” images (b-value = 0)
- A set of diffusion-weighted (DW) images acquired with different gradient directions g_1, g_2, … and b-value >0
- The diffusion-weighted images have lower intensity values



Distortions: Field inhomogeneities

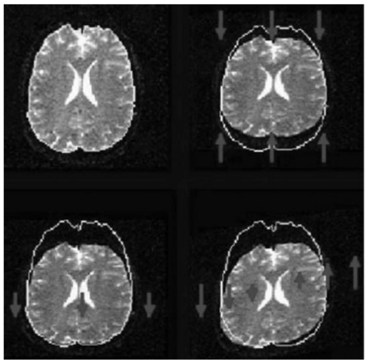
- Causes:
  - – Scanner-dependent (imperfections of main magnetic field)
  - – Subject-dependent (changes in magnetic susceptibility in tissue/air interfaces)

- Results:
  - – Signal loss in interface areas
  - – Geometric distortions (warping) of the entire image



Distortions: Eddy currents

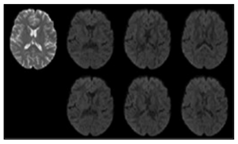
- Cause: Fast switching of diffusion-encoding gradients induces eddy currents in conducting components
- Eddy currents lead to residual gradients that shift the diffusion gradients
- The shifts are direction-dependent, *i.e.,* different for each DW image
- Result: Geometric distortions



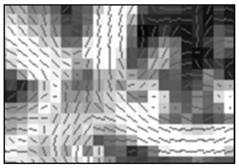
From Le Bihan *et al.,* Artifacts and pitfalls in diffusion MRI, JMRI 2006

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)



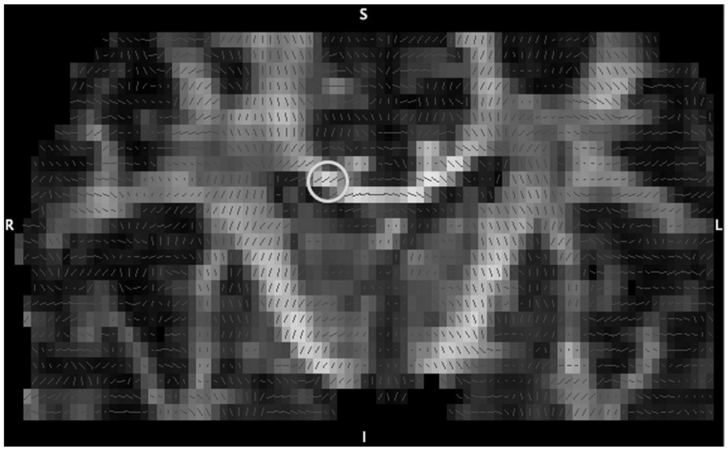
- Fit a diffusion model at every voxel
  - DTI, DSI, Q-ball, …



- Do tractography to reconstruct pathways and/or
- Compute measures of anisotropy/diffusivity and compare them between populations
  - Voxel-based, ROI-based, or tract-based statistical analysis

Caution!

- The FA map or color map is not enough to check if your gradient table is correct - display the tensor eigenvectors as lines
- Corpus callosum on a coronal slice, cingulum on a sagittal slice



Tutorial

- Use **`dt_recon`** to prepare DWI data for a simple voxel-based analysis:
  - Calculate and display FA/MD/... maps
  - Intra-subject registration (individual DWI to individual T1)
  - Inter-subject registration (individual T1 to common template)
  - Use anatomical segmentation (aparc+aseg) as a brain mask for DWIs
  - Map all FA/MD/... volumes to common template to perform voxel-based group comparison