HST.583 Functional Magnetic Resonance Imaging: Data Acquisition and Analysis
Fall 2008

HST.583: Functional Magnetic Resonance Imaging: Data Acquisition and Analysis, Fall 2008
Harvard-MIT Division of Health Sciences and Technology
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Diffusion weighted imaging

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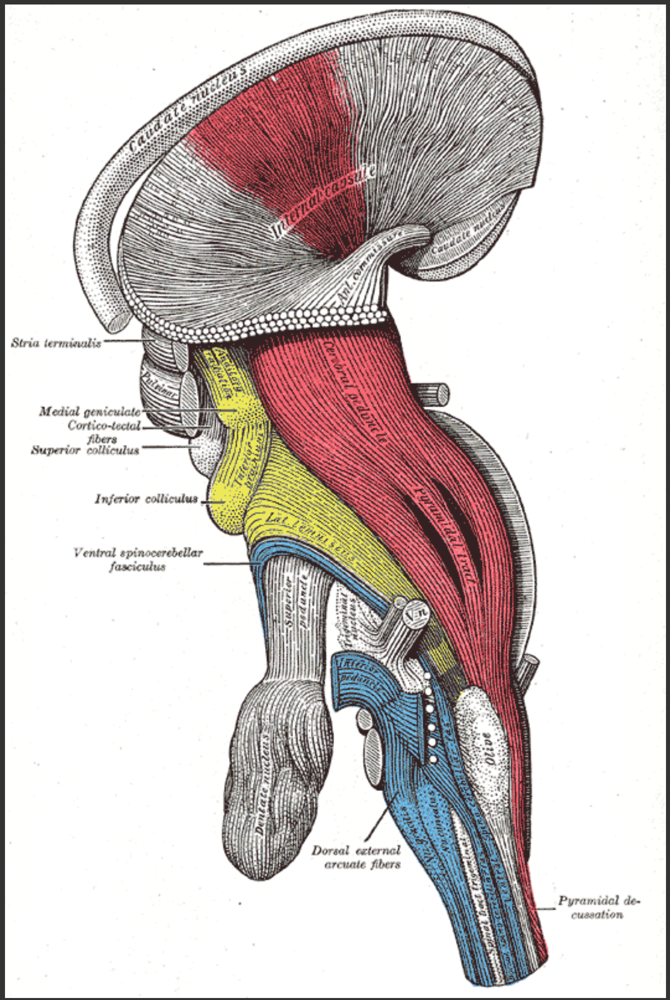
Why diffusion imaging?

- White matter (WM) is organized in fiber bundles

- Identifying these WM pathways is important for:
  - Inferring connections b/w brain regions
  - Understanding effects of neurodegenerative diseases, stroke, aging, development …

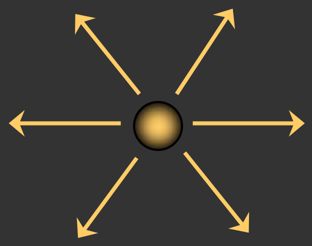


From *Gray's Anatomy: IX. Neurology*

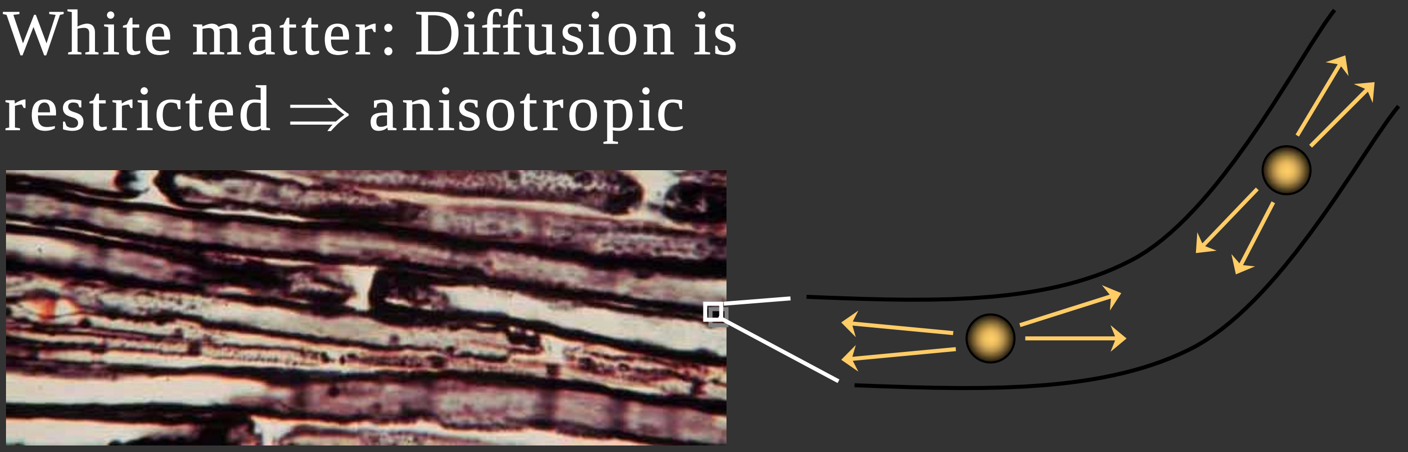
Diffusion in brain tissue

- Differentiate tissues based on the diffusion (random motion) of water molecules within them

- Gray matter: Diffusion is unrestricted $\Rightarrow$ isotropic

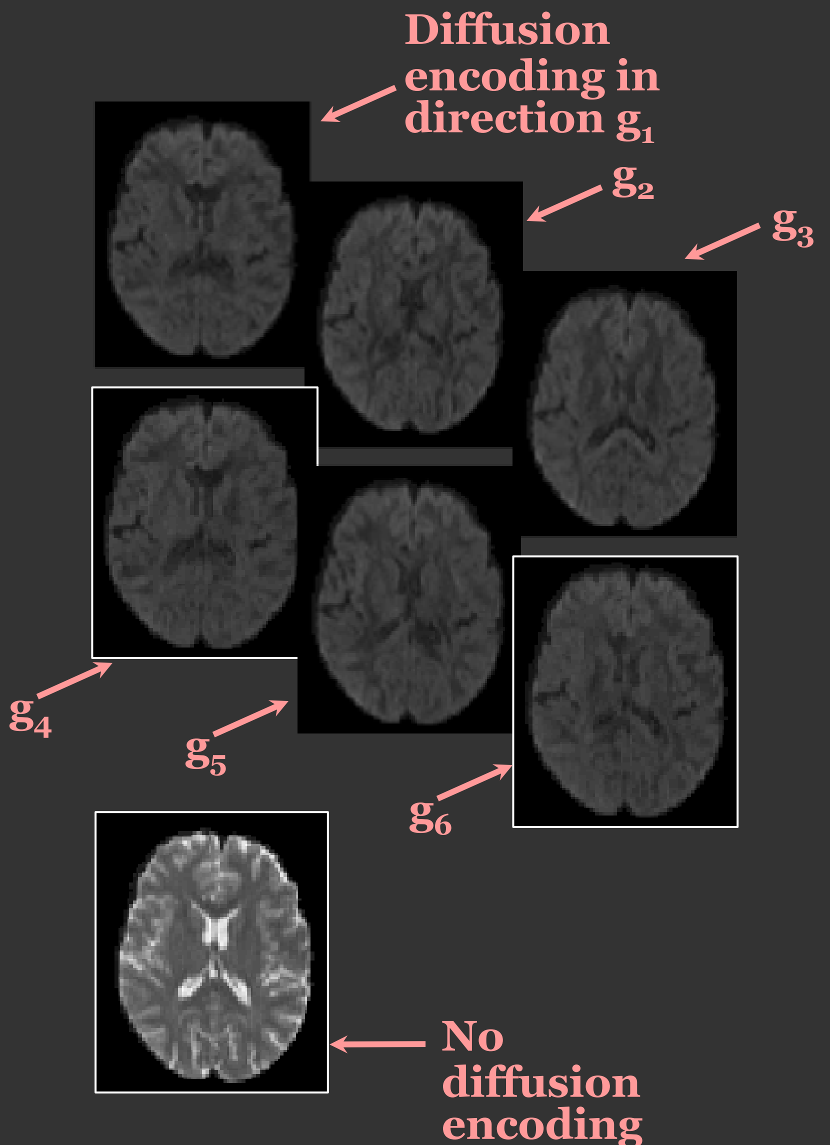


- White matter: Diffusion is restricted $\Rightarrow$ anisotropic



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



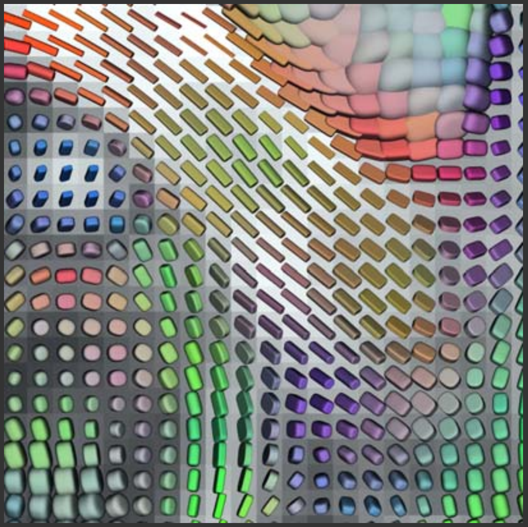
Imaging diffusion

- Image the direction in which water molecules diffuse at each voxel in the brain

  $\Rightarrow$ Infer WM fiber orientation at each voxel

- Clearly, direction can't be described by a usual grayscale image

Grayscale brain image removed due to copyright restrictions.



Courtesy of Gordon Kindlmann. Used with permission.

Tensors

- We express the notion of "direction" mathematically by a tensor D
- A tensor is a 3x3 symmetric, positive-definite matrix:

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

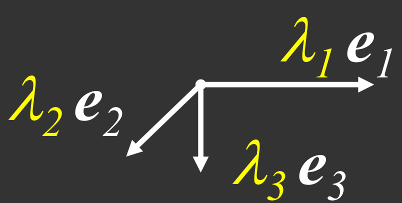
- D is symmetric 3x3 $\Rightarrow$ It has 6 unique elements
- Suffices to estimate the upper (lower) triangular part

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 $\boldsymbol{e}_1, \boldsymbol{e}_2, \boldsymbol{e}_3$.

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

$$\boldsymbol{e}_1 = \begin{bmatrix} e_{1x} \\ e_{1y} \\ e_{1z} \end{bmatrix}$$

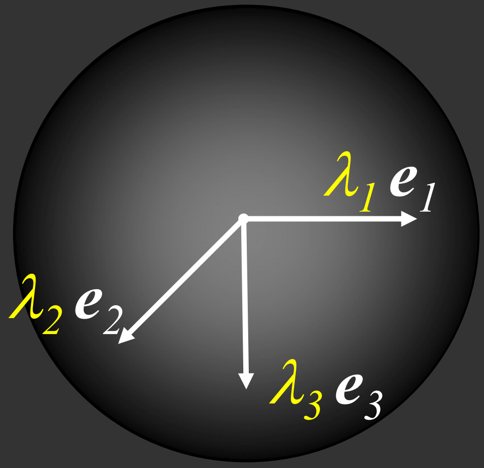


Physical interpretation

- Eigenvectors express diffusion direction
- Eigenvalues express diffusion magnitude

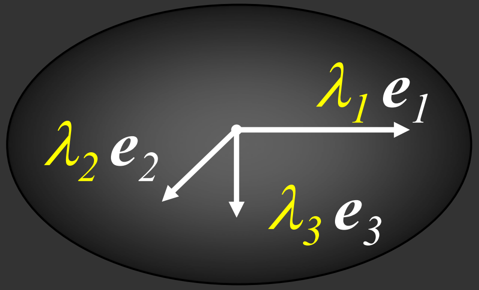
Isotropic diffusion:

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



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)

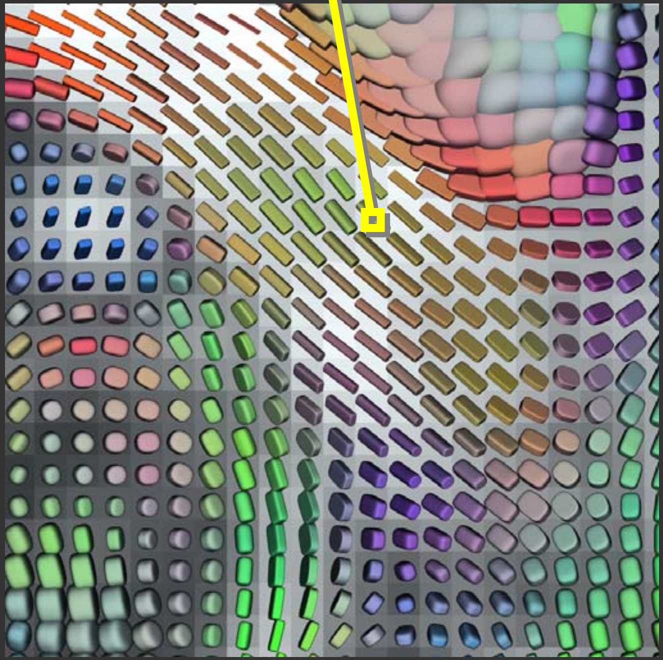
Image:

A scalar intensity value f_j at each voxel j

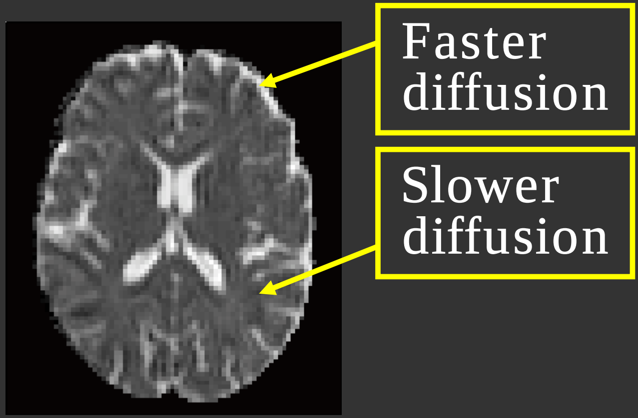
Grayscale brain image removed due to copyright restrictions.

Tensor map:

A tensor $\boldsymbol{D}_j$ at each voxel j

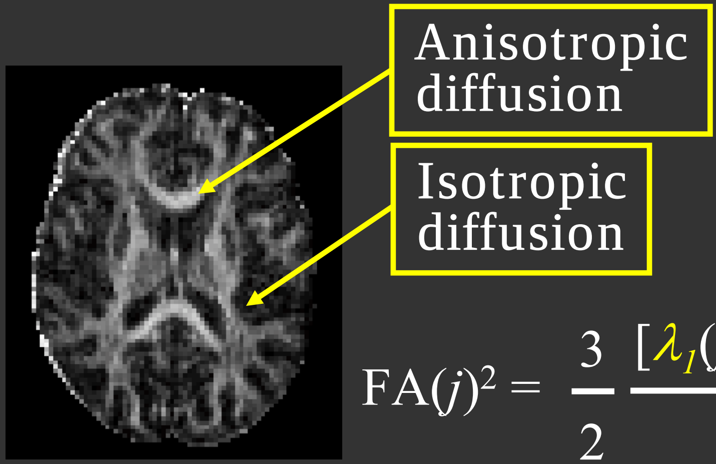


Summary measures



• 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 summary measures

- Axial diffusivity: Greatest eigenvalue

  $\mathrm{AD}(j) = \lambda_1(j)$

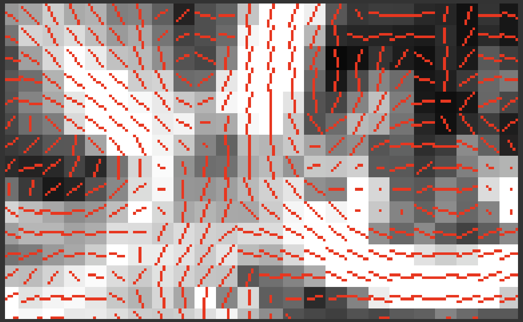
- Radial diffusivity: Average of 2 lesser eigenvalues

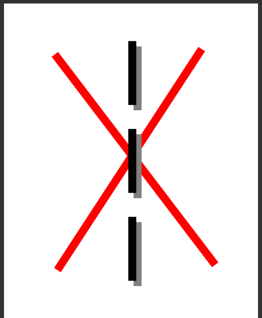
  $\mathrm{RD}(j) = [\lambda_2(j) + \lambda_3(j)]/2$

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

Other models of diffusion

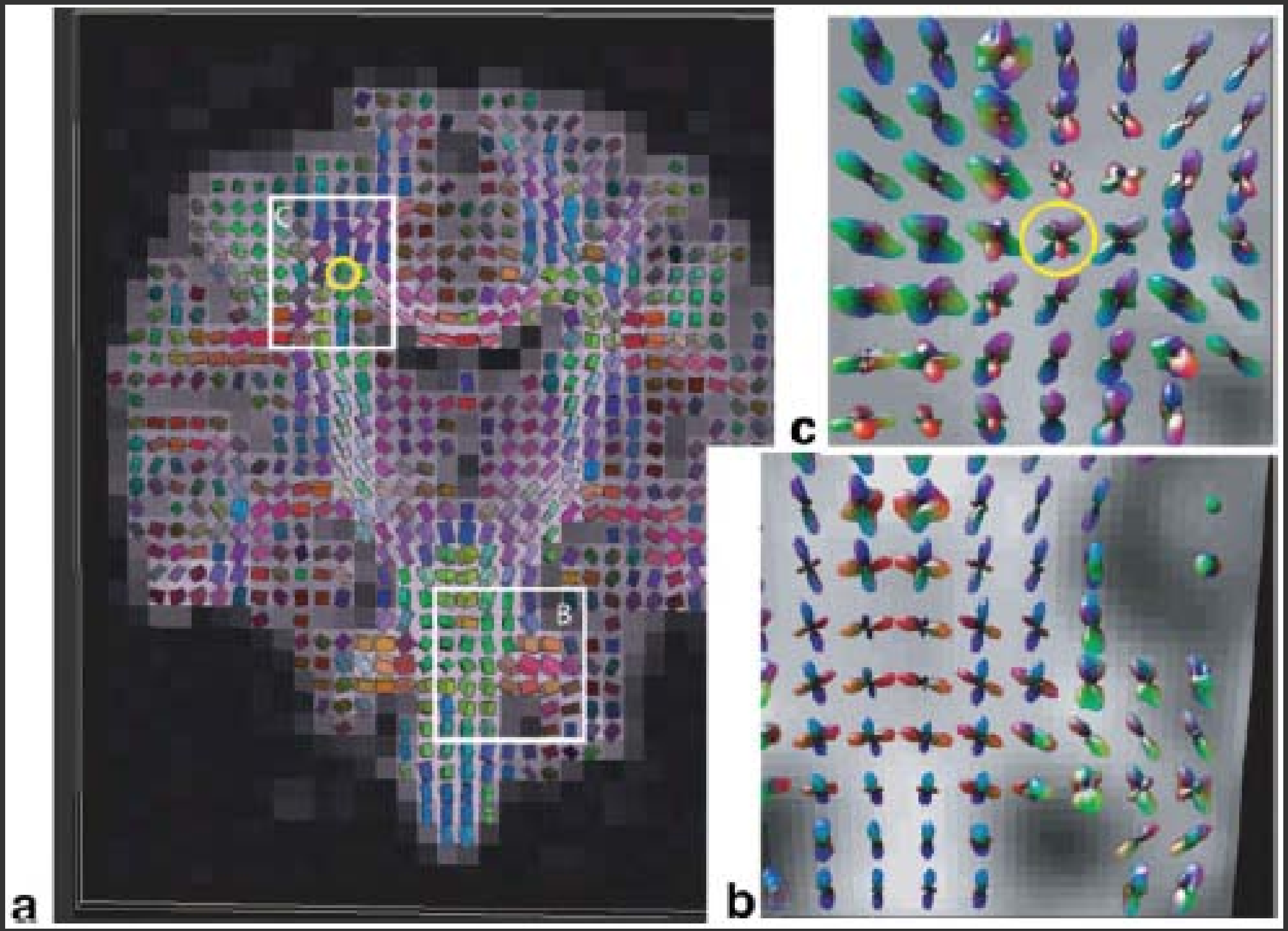
- The tensor is an imperfect model: What if more than one major diffusion direction in the same voxel?





- High angular resolution diffusion imaging (HARDI)
  - A mixture of the usual (“rank-2”) tensors [Tuch’02]
  - A tensor of rank > 2 [Frank’02, Özarslan’03]
  - An orientation distribution function [Tuch’04]
  - A diffusion spectrum (DSI) [Wedeen’05]
- More parameters at each voxel ⇒ More data needed

Example: DTI vs. DSI

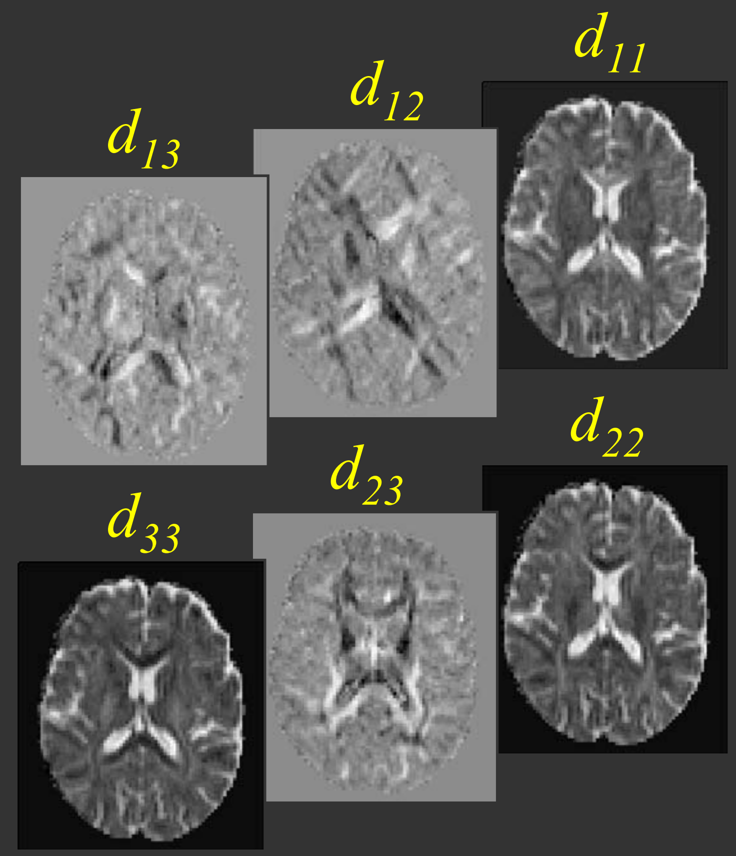


Source: Wedeen, V. J. *et al.,* "Mapping complex tissue architecture with diffusion spectrum magnetic resonance imaging." *MRM* 54, no. 6 (2005): 1377-1386.

Back to the tensor

- Remember: A tensor has six unique values

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



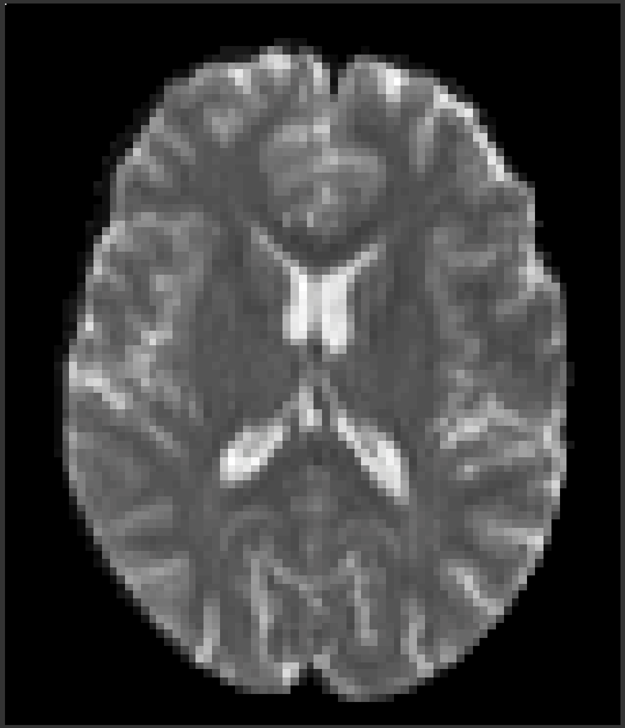
- Must estimate six times as many values at each voxel

$\Rightarrow$ Must collect (at least) six times as much data!

MR data acquisition

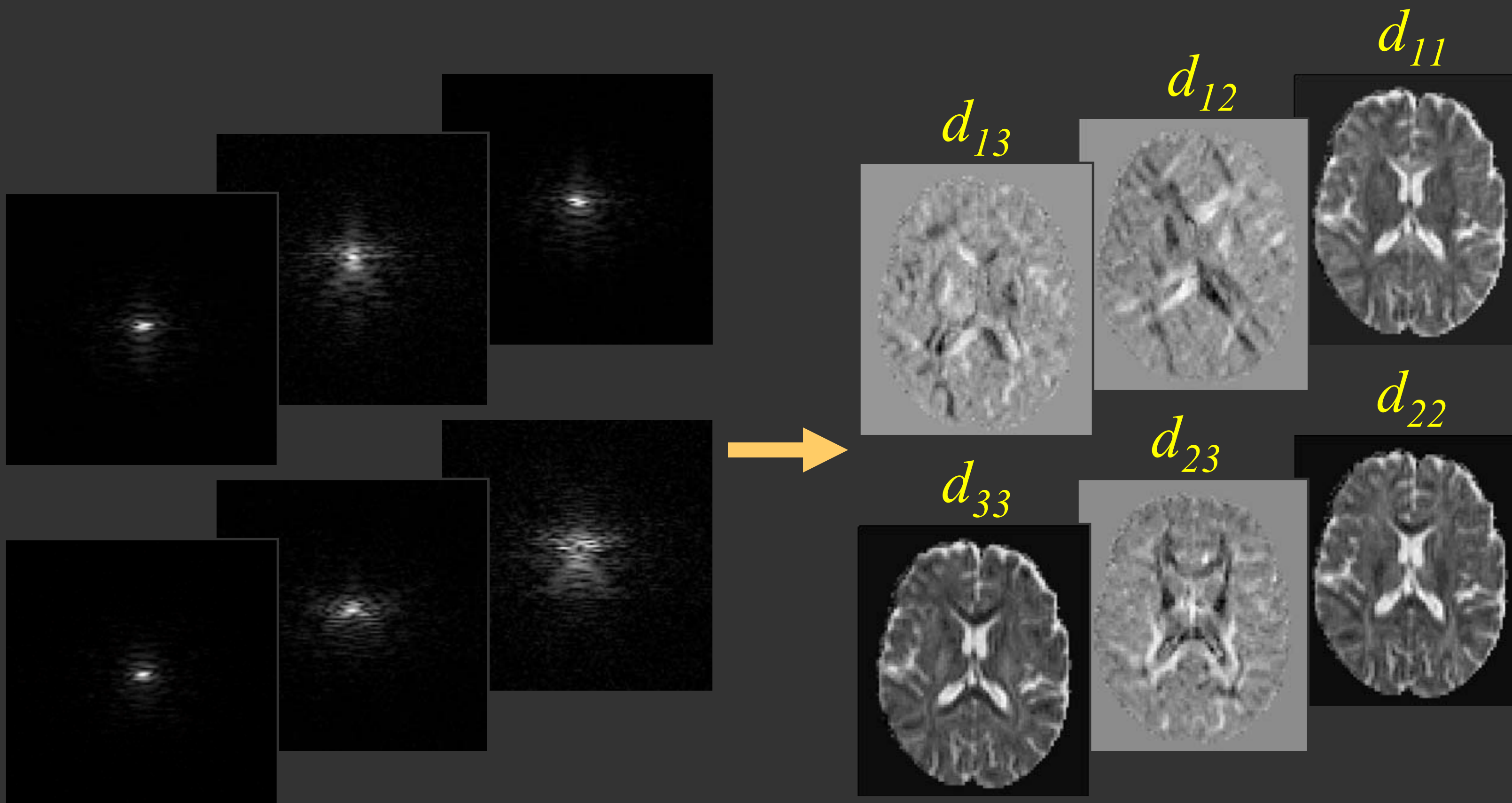
Measure raw MR signal (frequency-domain samples of transverse magnetization)

Reconstruct an image of transverse magnetization



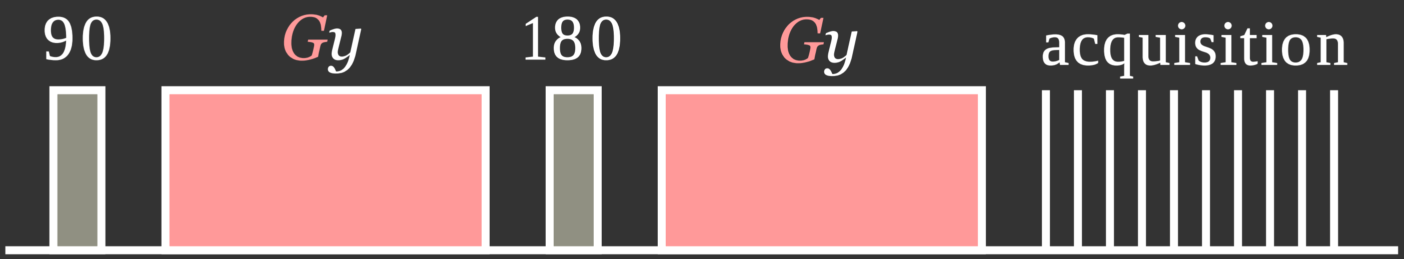
Diffusion MR data acquisition

Must acquire at least 6 times as many MR signal measurements $\Leftarrow$ Need to reconstruct 6 times as many values

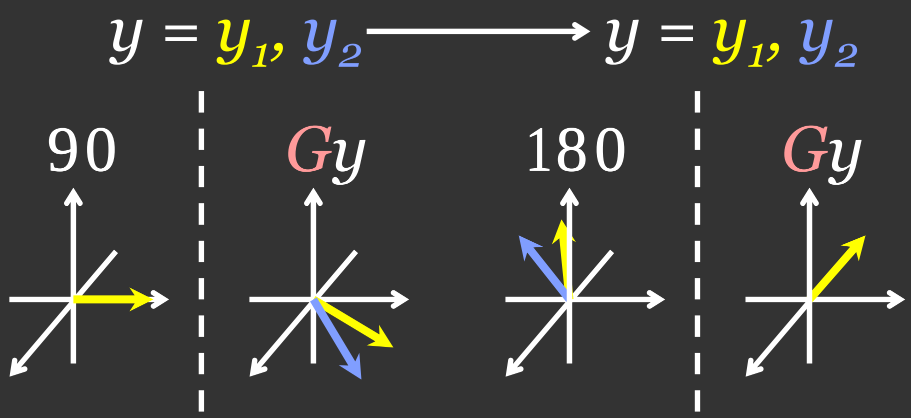


Diffusion encoding in MRI

- Apply two gradient pulses in some direction y:



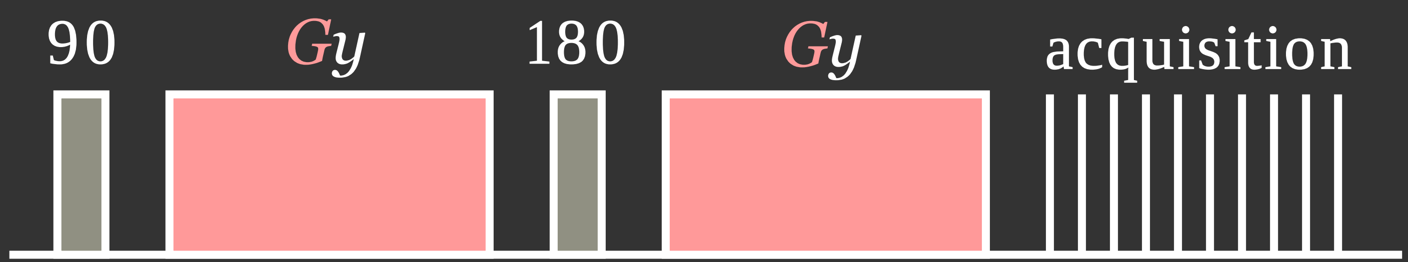
- Case 1: If spins aren't diffusing



No displacement in $y \Rightarrow$
No dephasing $\Rightarrow$
No net signal change

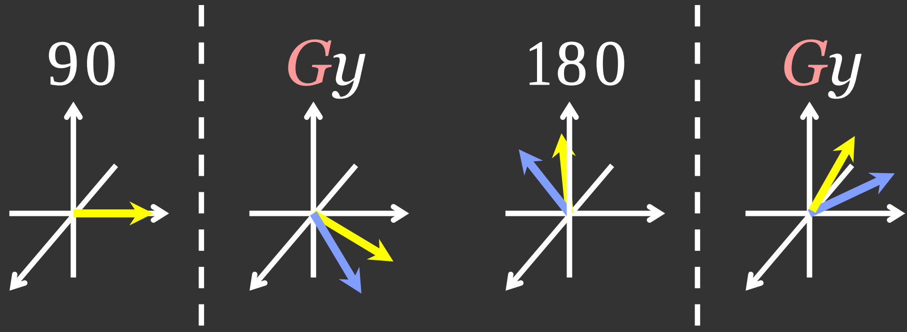
Diffusion encoding in MRI

- Apply two gradient pulses:



- Case 2: If spins are diffusing

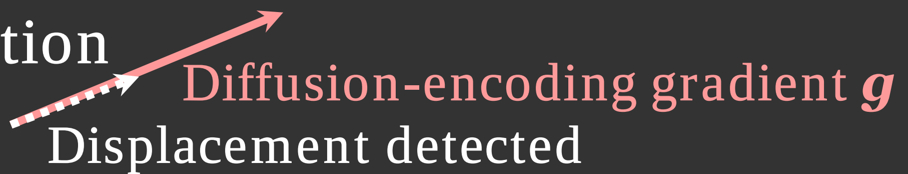
$$y = y_1, y_2 \longrightarrow y = y_1 + \Delta y_1, y_2 + \Delta y_2$$



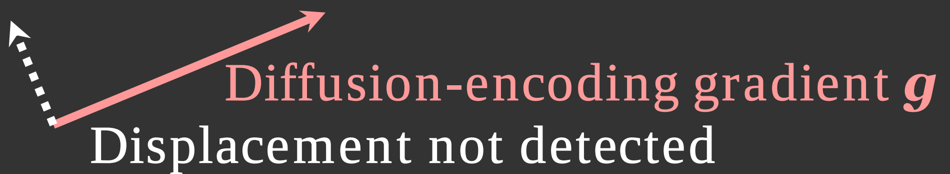
Displacement in $y \Rightarrow$
Dephasing $\Rightarrow$
Signal attenuation

Choice 1: Gradient directions

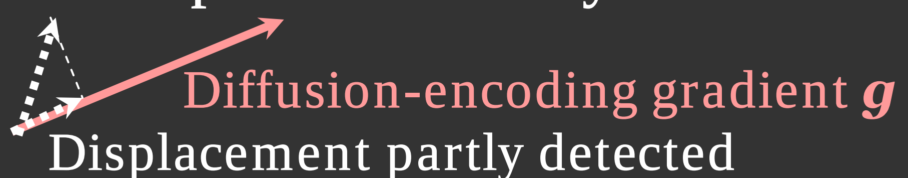
- Spin diffusion direction || Applied gradient direction
  $\Rightarrow$ Maximum attenuation



- Spin diffusion direction $\perp$ Applied gradient direction
  $\Rightarrow$ No attenuation



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



How many directions?

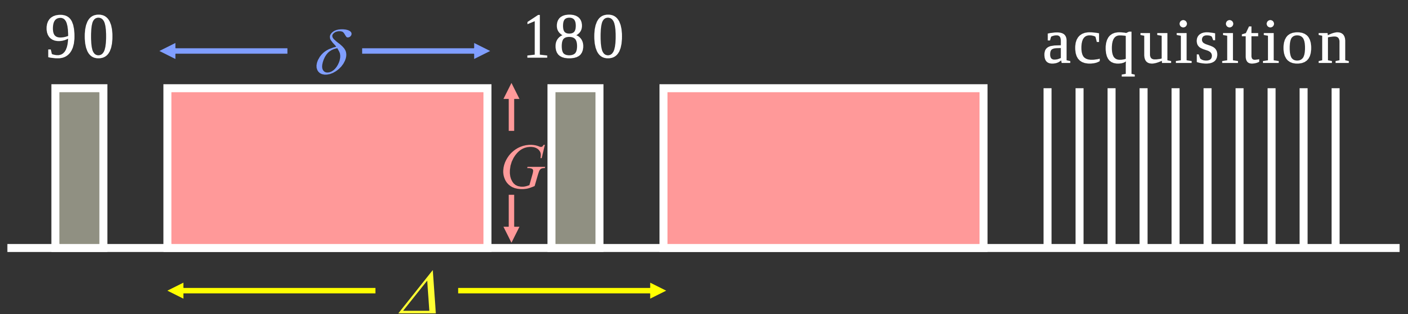
- Acquiring with more gradient directions leads to:
  - \+ More reliable estimation of diffusion measures
  - – Increased imaging time $\Rightarrow$ Subject discomfort, more susceptible to artifacts due to motion, respiration, etc.
- DTI:
  - Six directions is the minimum
  - Usually a few 10's of directions
  - 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?

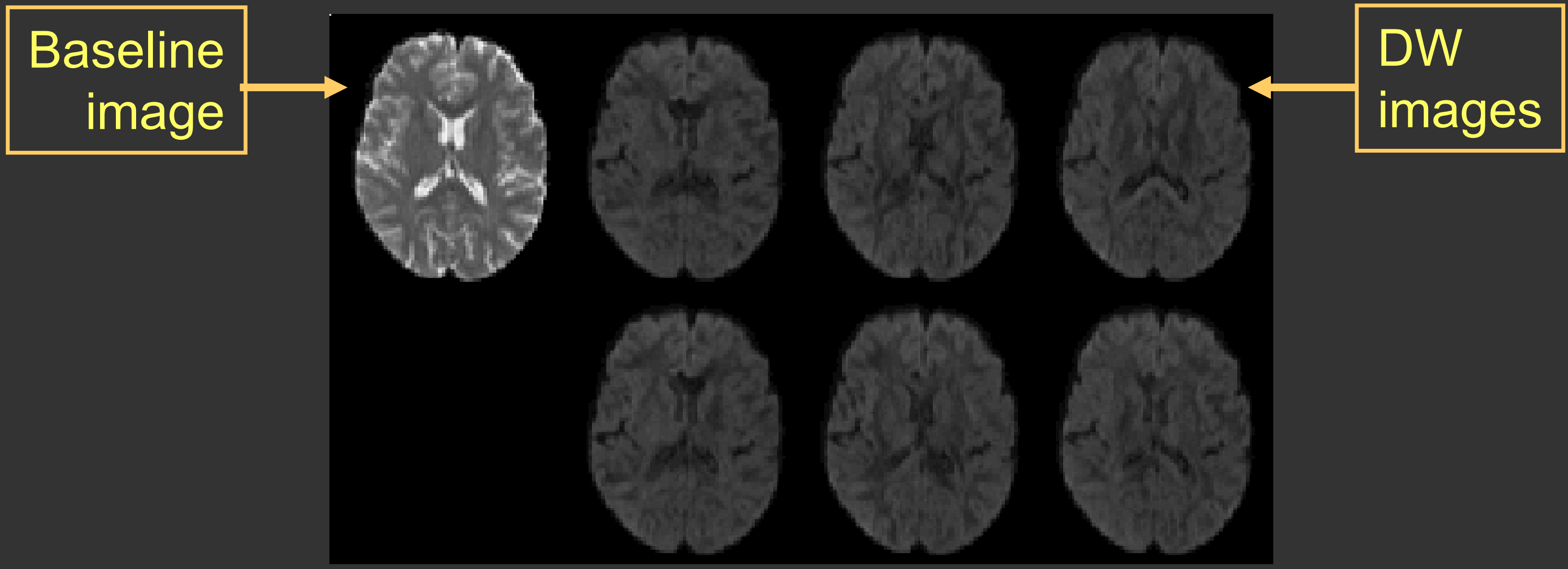
- Increasing the b-value leads to:
  - + Increased contrast b/w areas of higher and lower diffusivity in principle
  - – Decreased signal-to-noise ratio $\Rightarrow$ Less reliable estimation of diffusion measures in practice
- DTI: b ~ 1000 sec/mm^2
- HARDI/DSI: b ~ 10,000 sec/mm^2
- Data can be acquired at multiple b-values for trade-off
- Repeat acquisition and average to increase signal-to-noise ratio

Estimating the tensor

- $f_j^{b,\mathbf{g}} = f_j^0 \, e^{-b\,\mathbf{g}' \cdot \mathbf{D}_j \cdot \mathbf{g}}$
  where the $\mathbf{D}_j$ the diffusion tensor at voxel j
- Design acquisition:
  – b the diffusion-weighting factor
  – $\mathbf{g}$ the diffusion-encoding gradient direction
- Acquire images:
  – $f_j^{b,\mathbf{g}}$ image acquired with diffusion-weighting factor b and diffusion-encoding gradient direction $\mathbf{g}$
  – f_j^0 "baseline" image acquired without diffusion-weighting ($b=0$)
- Estimate unknown diffusion tensor $\mathbf{D}_j$

Noise in diffusion-weighted images

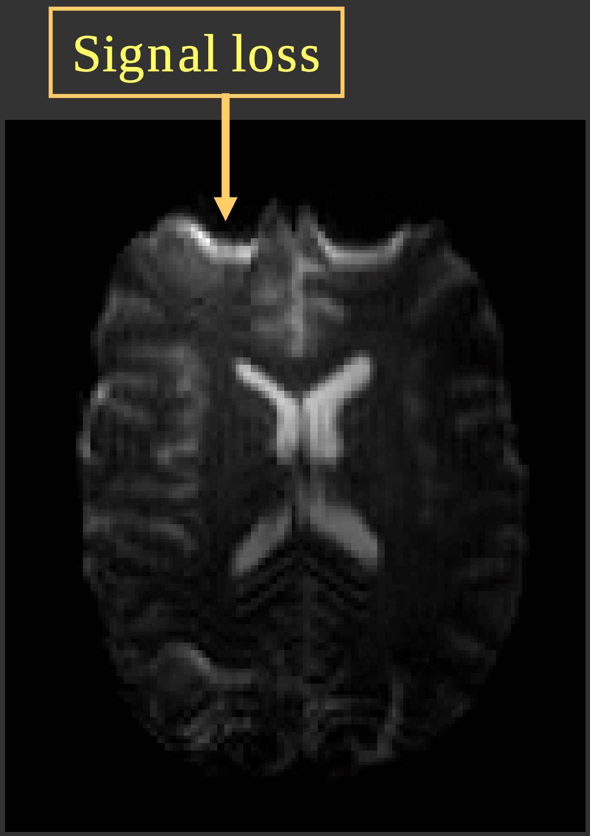
- Due to signal attenuation by diffusion encoding, signal-to-noise ratio in DW images can be an order of magnitude lower than "baseline" image
- Eigenvalue decomposition is sensitive to noise, may result in negative eigenvalues



Distortions: Field inhomogeneities

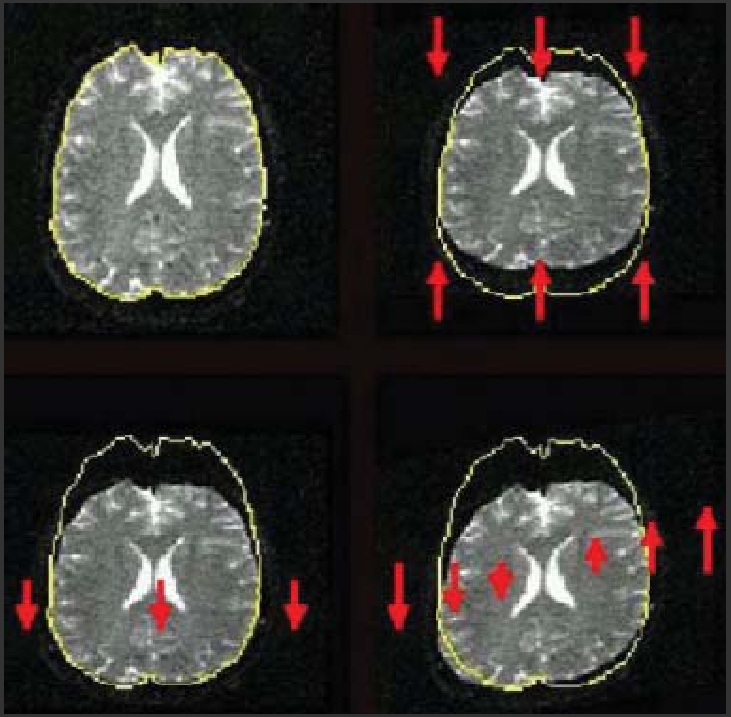
- Causes:
  - Scanner-dependent (imperfections of main magnetic field)
  - Subject-dependent (changes in magnetic susceptibility in tissue/air interfaces)

- Results: Signal loss in interface areas, geometric distortions



Distortions: Eddy currents

- 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
- Results: Geometric distortions



Distortion correction

Post-process images to reduce distortions due to field inhomogeneities and eddy-currents:

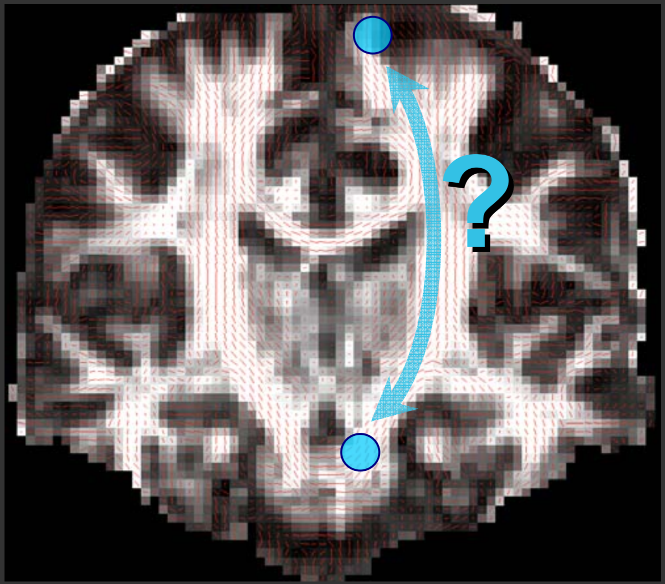
- Either register distorted DW images to an undistorted (non-DW) image
  [Haselgrove'96, Bastin'99, Horsfield'99, Andersson'02, Rohde'04, Ardekani'05, Mistry'06]

- Or use information on distortions from separate scans (field map, residual gradients)
  [Jezzard'98, Bastin'00, Chen'06; Bodammer'04, Shen'04]

Tractography

- What does one do with diffusion data?
  – Statistical analysis on MD, FA, tensors...
  – Tractography: Given the diffusion data, determine "best" pathway between two brain regions

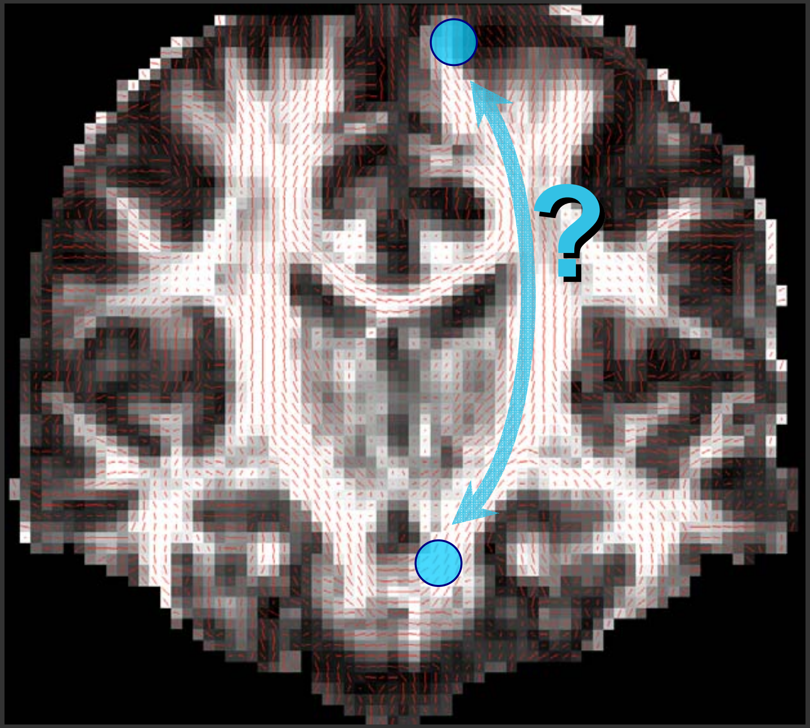
- Challenges in tractography:
  - Noisy, distorted images
  - Pathway crossings
  - High-dimensional space
- Many methods to overcome them...



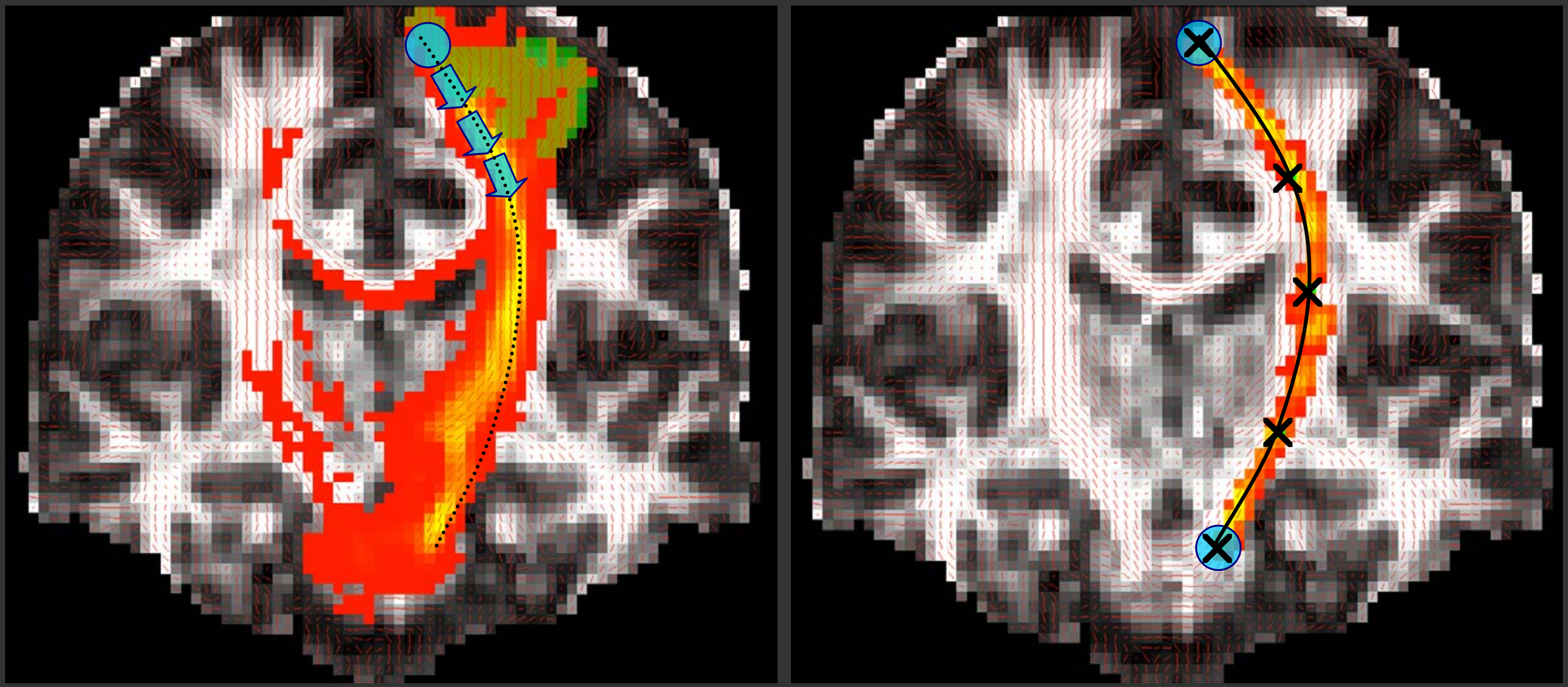
Deterministic vs. probabilistic

- **Deterministic methods:** Model geometry of diffusion data, *e.g.*, tensor/eigenvectors [Conturo '99, Jones '99, Mori '99, Basser '00, Catani '02, Parker '02, O'Donnell '02, Lazar '03, Jackowski '04, Pichon '05, Fletcher '07, Melonakos '07, ...]

- **Probabilistic methods:** Also model statistics of diffusion data [Behrens '03, Hagmann '03, Pajevic '03, Jones '05, Lazar '05, Parker '05, Friman '06, Jbabdi '07, ...]

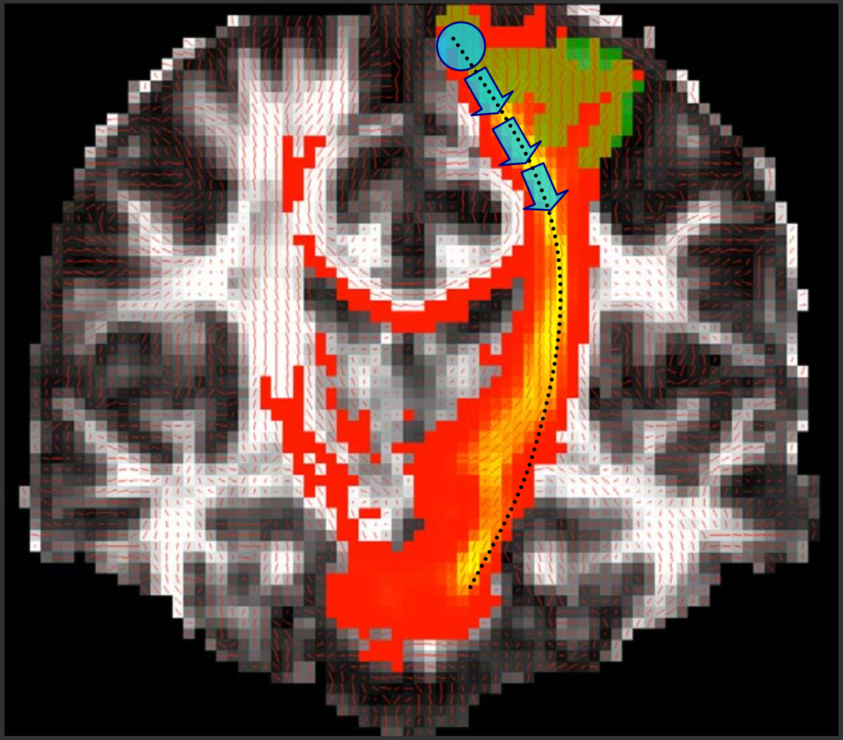


Local vs. global



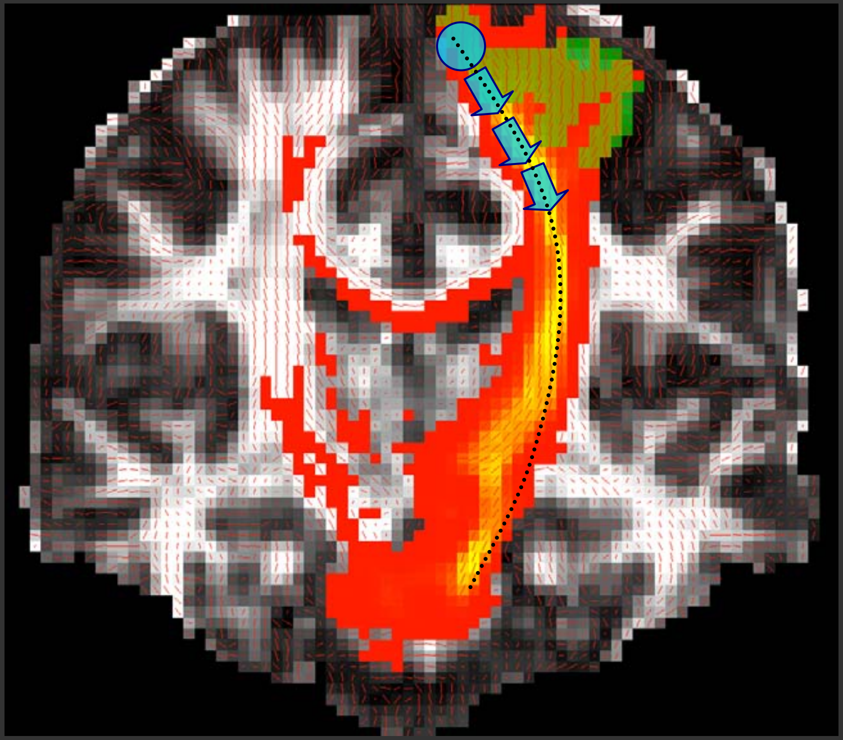
- Local: Uses local information to determine next step, errors propagate from areas of high uncertainty
- Global: Integrates information along the entire path

Local tractography



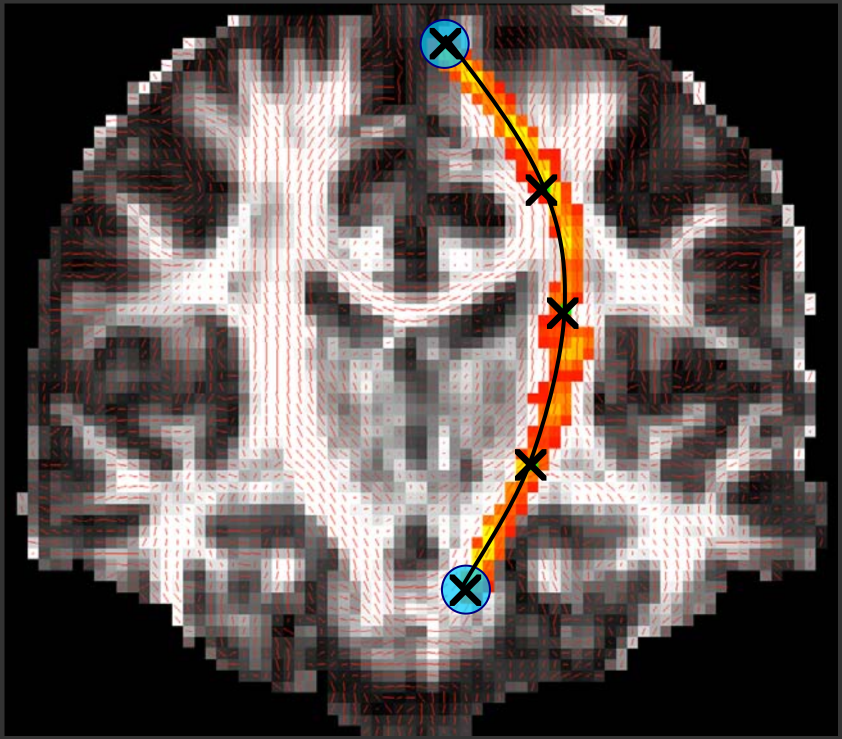
- Define a "seed" voxel or ROI to start the tract from
- Trace the tract by small steps, determine "best" direction at each step
- Deterministic: Only one possible direction at each step
- Probabilistic: Many possible directions at each step (because of noise), some more likely than others

Some issues



- Not constrained to a connection of the seed to a target region
- How do we isolate a specific connection? We can set a threshold, but how?
- What if we want a non-dominant connection? We can define waypoints, but there's no guarantee that we'll reach them.
- Not symmetric between tract "start" and "end" point

Global tractography

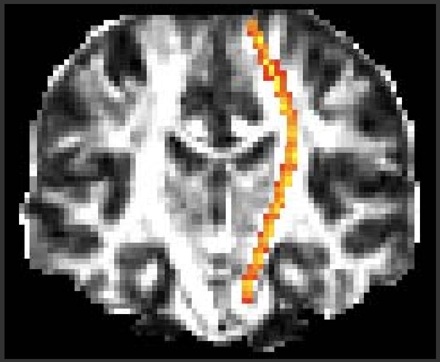


- Define a “seed” voxel or ROI
- Define a “target” voxel or ROI
- Deterministic: Only one possible path
- Probabilistic: Many possible paths, find their probability distribution

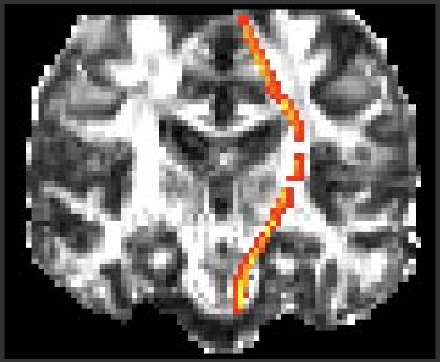
- Constrained to a specific connection
- Symmetric between seed and target regions

Application: Huntington's disease

Data courtesy of Dr. D. Rosas, MGH



Healthy



Huntington's (premanifest)

Huntington's (advanced)