Mathematical and physical foundations of DTI

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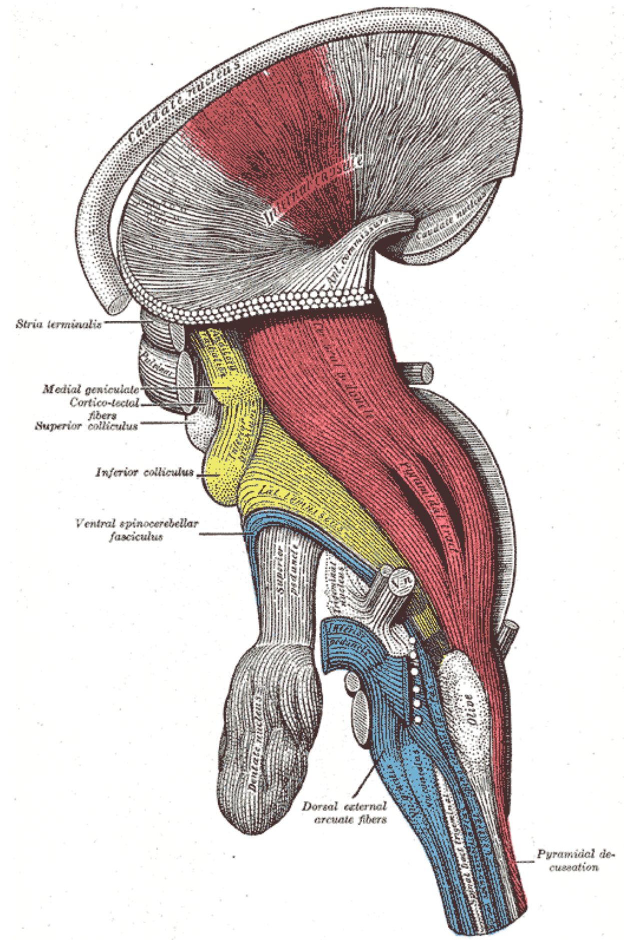
Why diffusion imaging?

- White matter (WM) is organized in fiber bundles

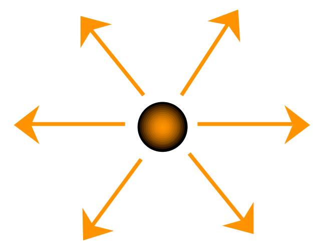
- Identifying these WM pathways is important for:
  - Inferring connections b/w brain regions
  - Understanding effects of neurodegenerative diseases, stroke, aging, development …



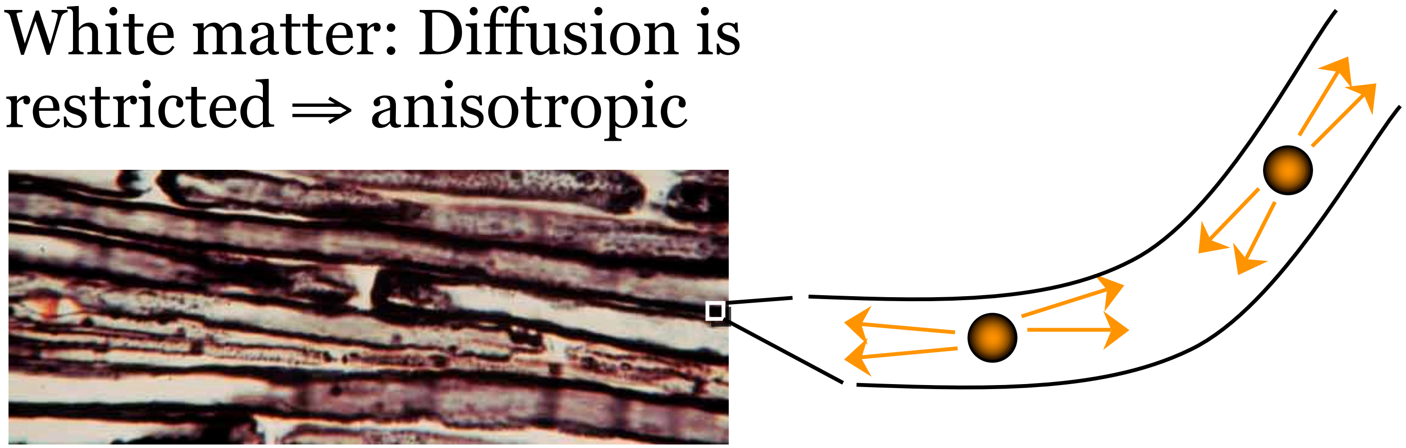
From *Gray's Anatomy: IX. Neurology*

Diffusion in brain tissue

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

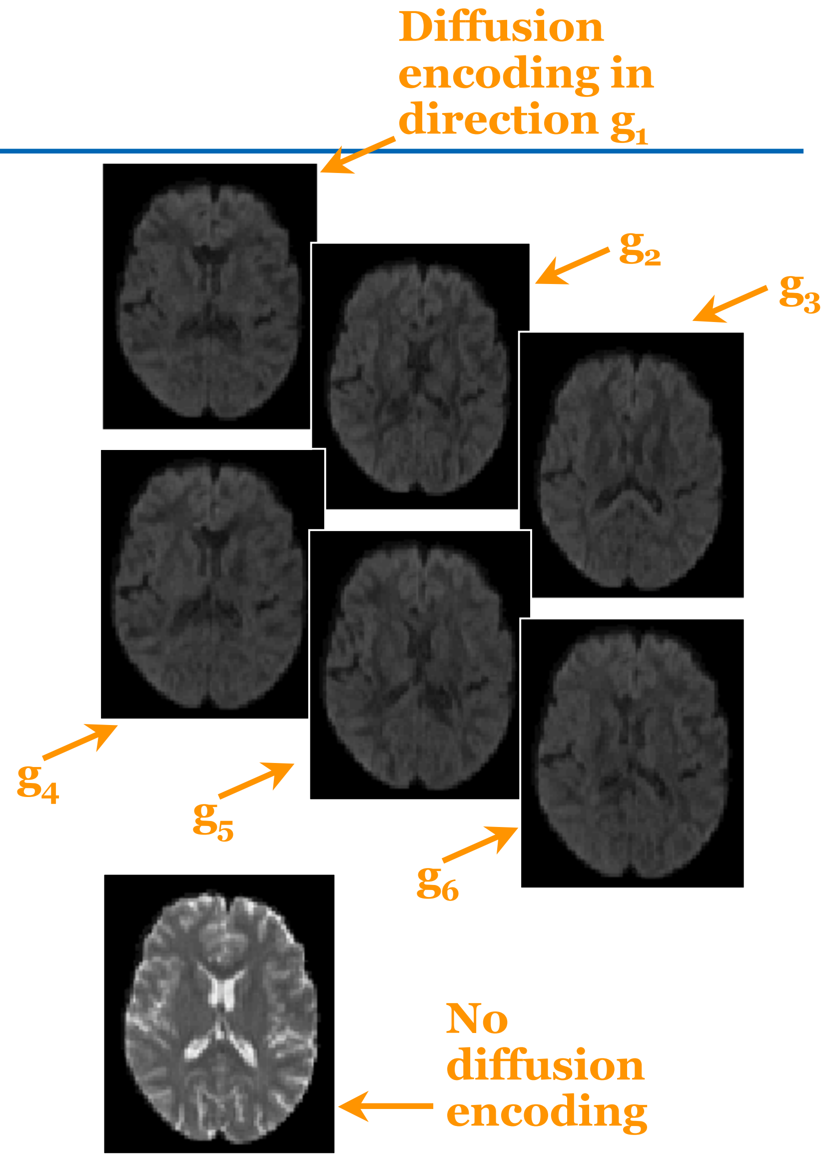


- White matter: Diffusion is restricted ⇒ anisotropic



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

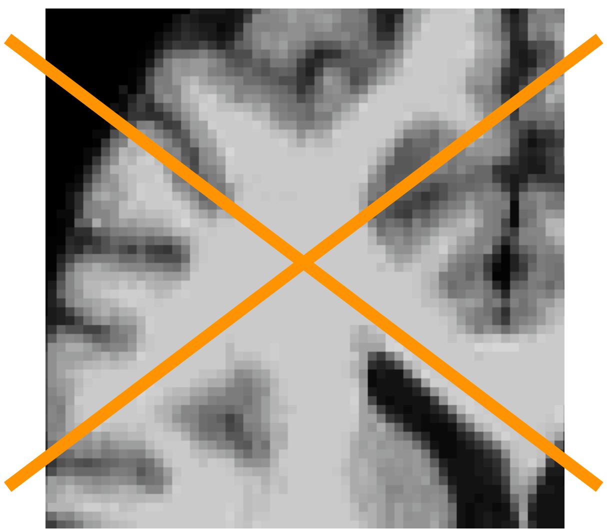


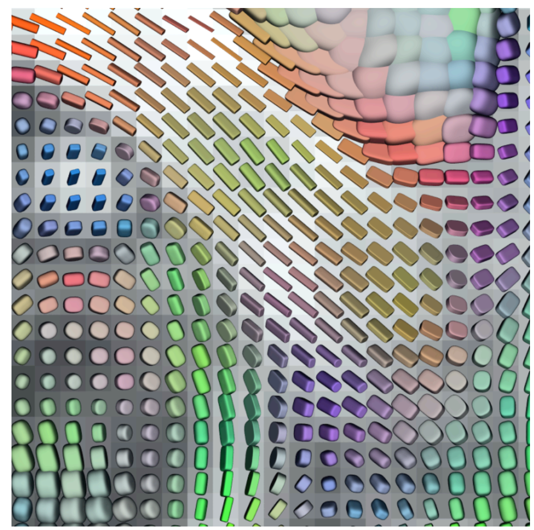
Imaging diffusion

- Image the average direction of water diffusion 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





Courtesy of Gordon Kindlmann

Tensors

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

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

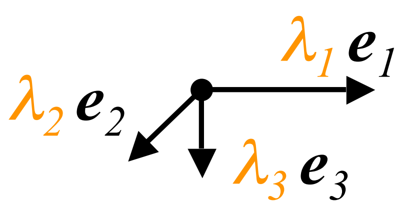
- D is symmetric 3x3 ⇒ It has 6 unique elements
- Suffices to estimate the upper (lower) triangular part

Eigenvalues/vectors

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

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

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

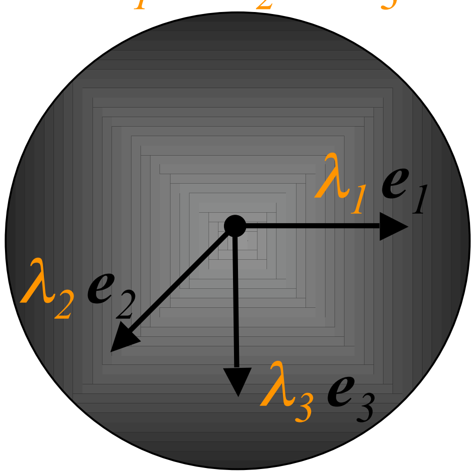


Physical interpretation

- Eigenvectors express diffusion direction
- Eigenvalues express diffusion magnitude

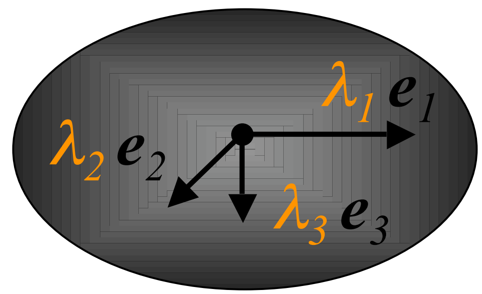
Isotropic diffusion:

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



Anisotropic diffusion:

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



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

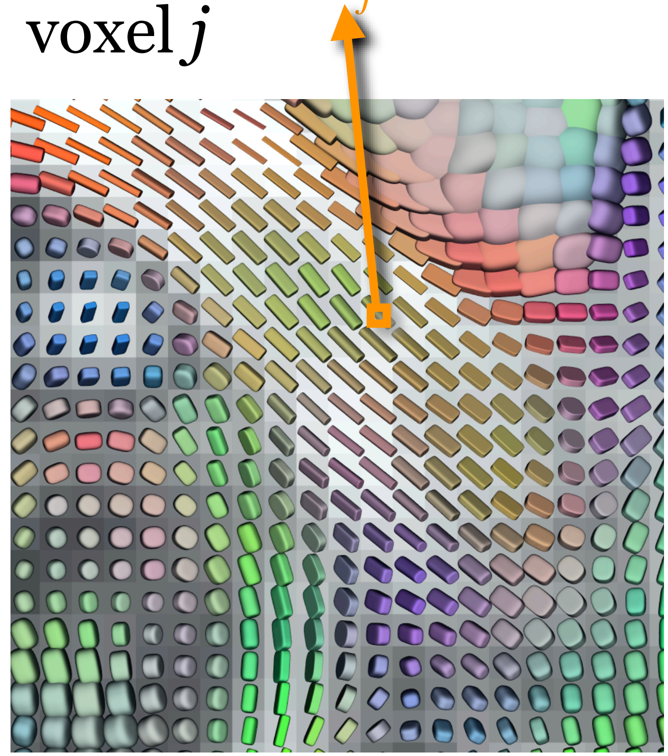
Diffusion tensor imaging

Image:

A **scalar** intensity value f_j at each voxel *j*

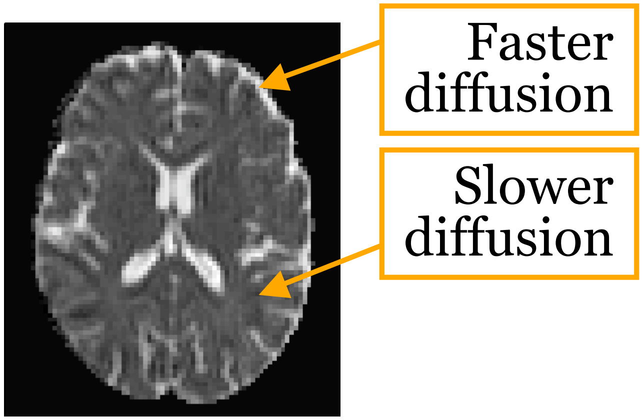
Tensor map:

A **tensor** D_j at each voxel *j*



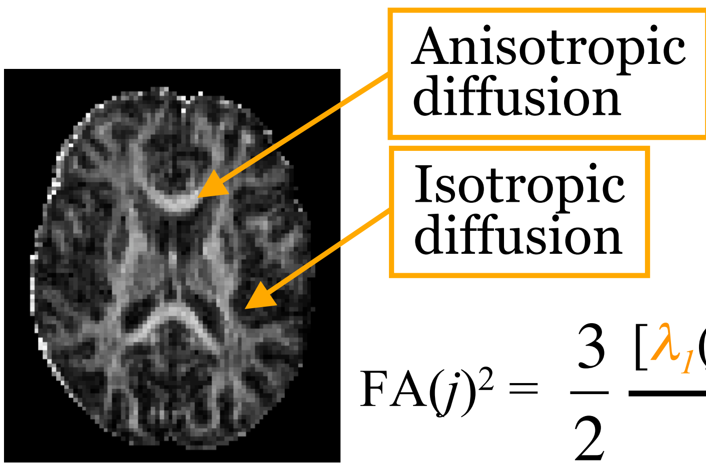
Courtesy of Gordon Kindlmann

Scalar diffusion 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 $0 \le (FA) \le 1$

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

More summary measures

- **Axial diffusivity:** Greatest eigenvalue

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

- **Radial diffusivity:** Average of 2 lesser eigenvalues

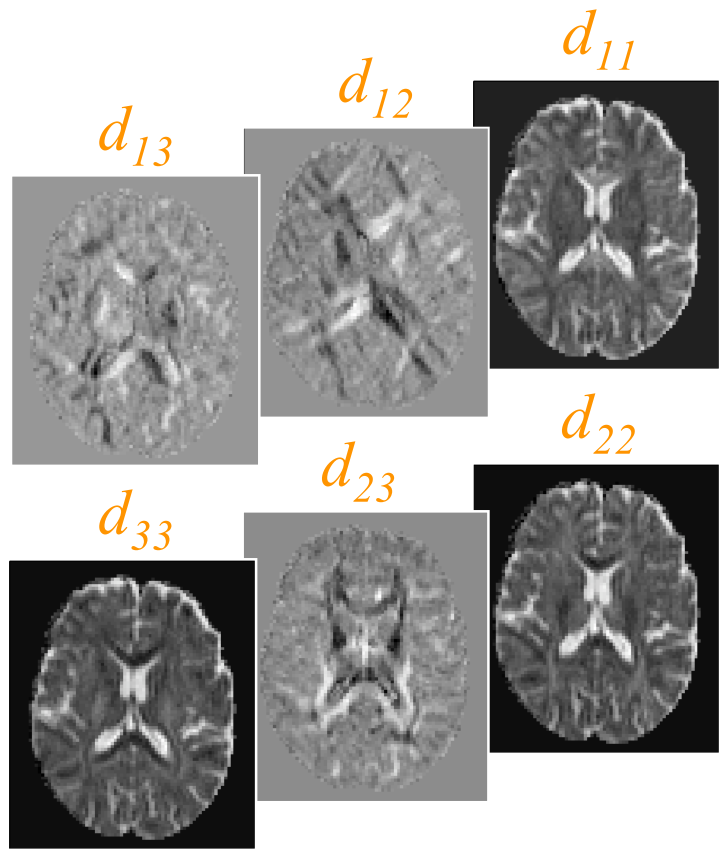
  $RD(j) = [\lambda_2(j) + \lambda_3(j)]/2$

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

Back to the tensor

- Remember: A tensor has six unique values

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

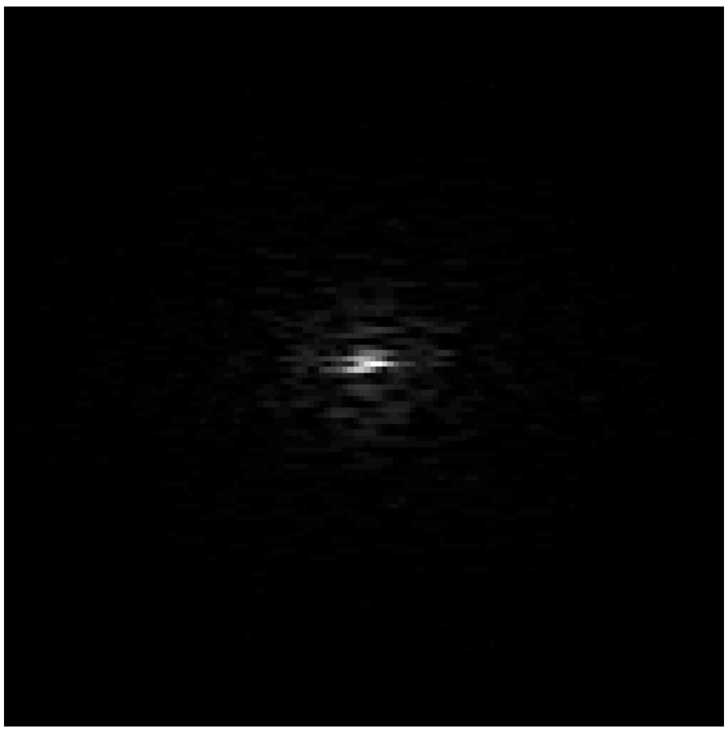


- Must estimate six times as many values at each voxel

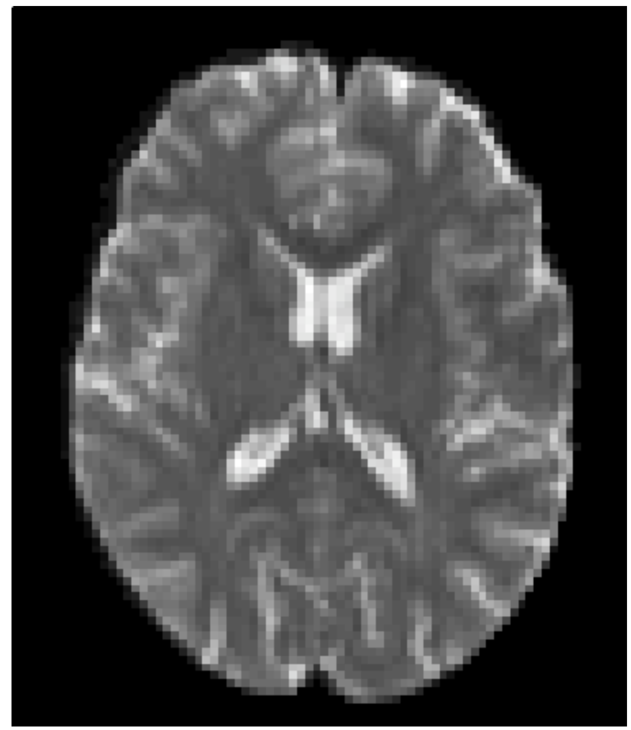
⇒ Must collect (at least) six times as much data!

MRI data acquisition

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

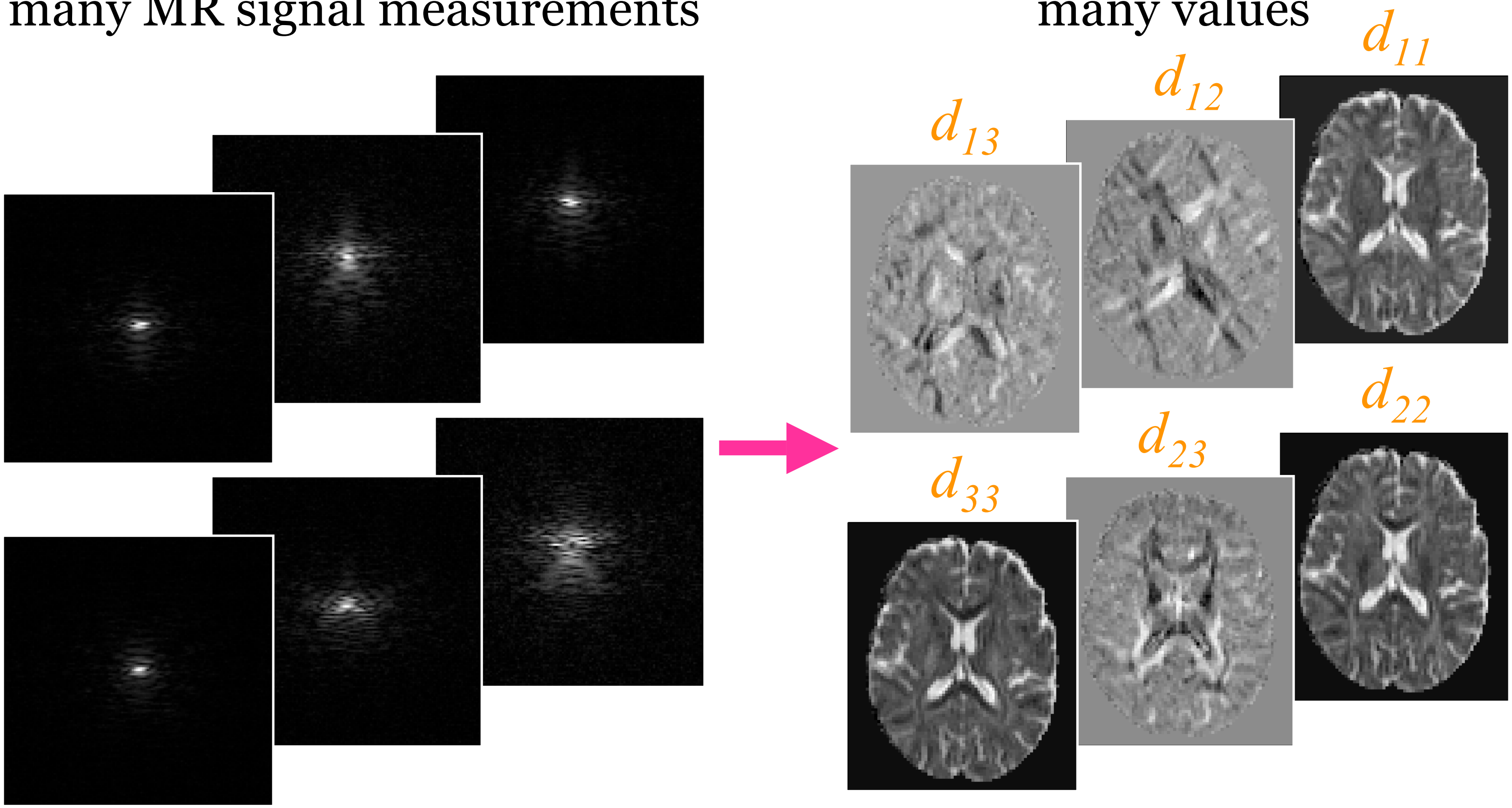


Reconstruct an **image** of transverse magnetization



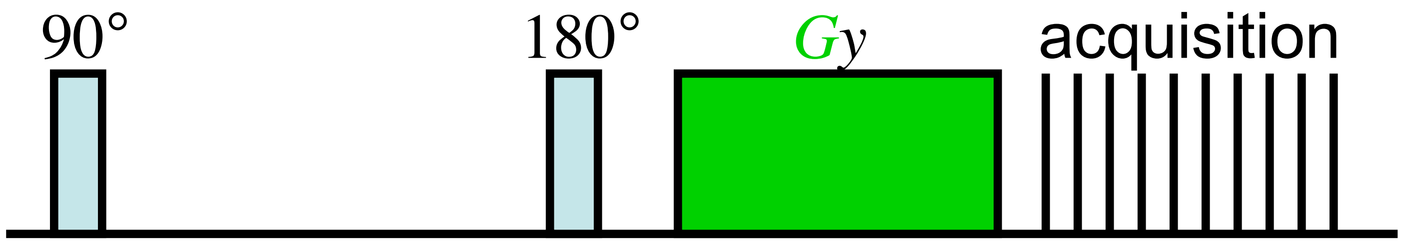
DT-MRI data acquisition

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

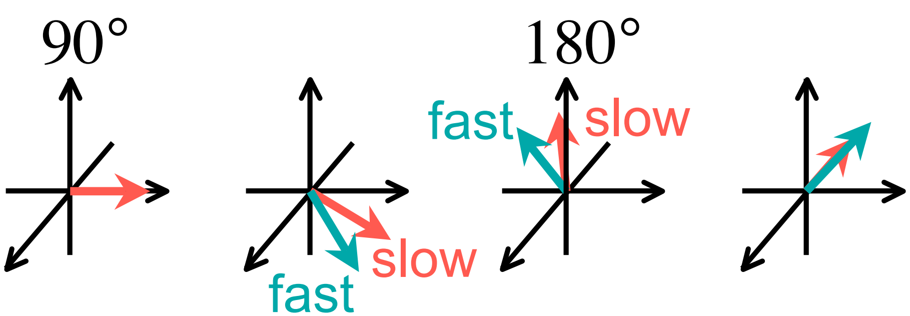


Spin-echo MRI

- Use a 180° pulse to refocus spins:



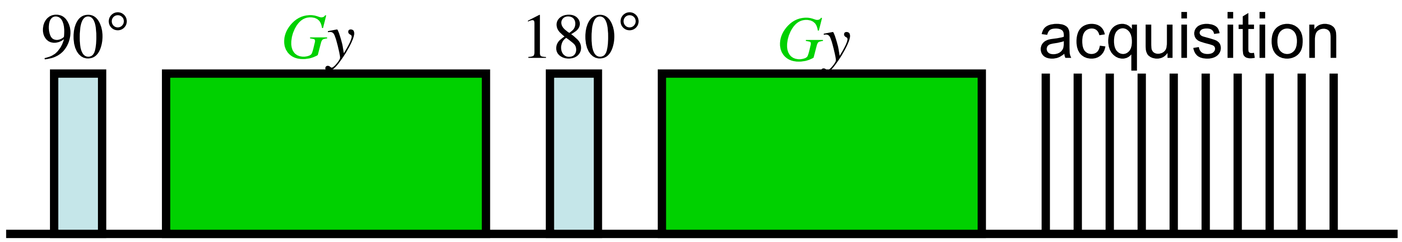
- Apply a field gradient *Gy* for location encoding



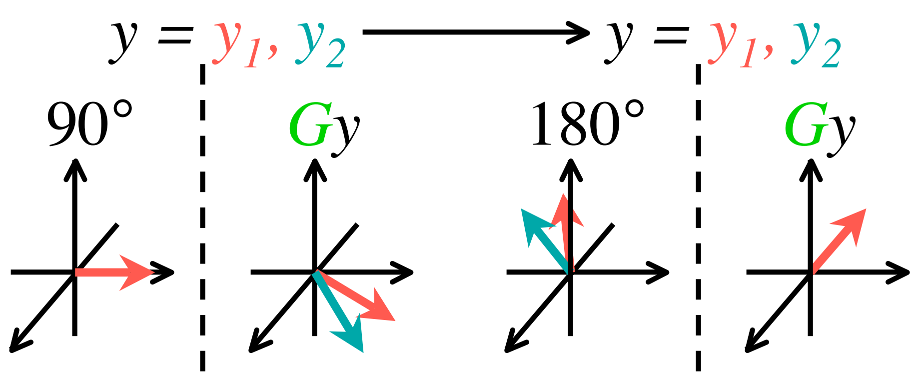
Measure transverse magnetization at each location -- depends on tissue properties (T_1,T_2)

Diffusion-weighted MRI

- Apply two gradient pulses:



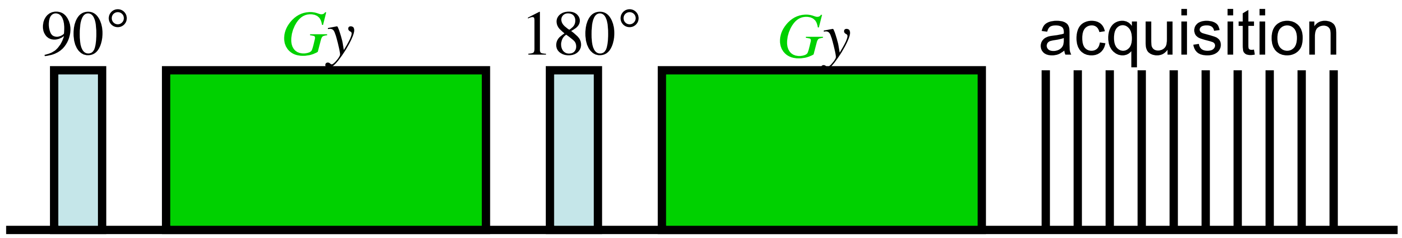
- **Case 1: If spins are not diffusing**



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

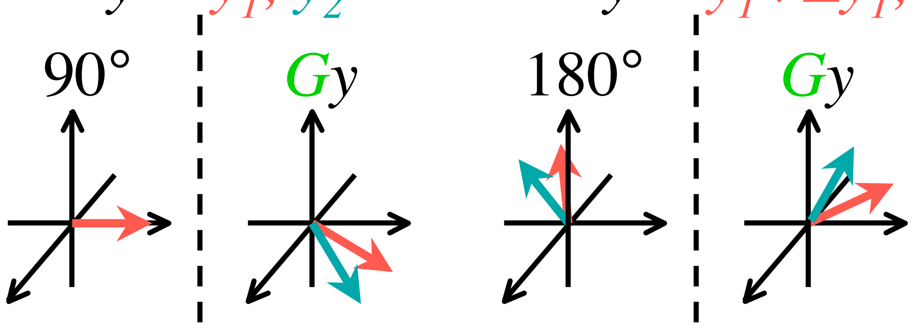
Diffusion-weighted MRI

- Apply two gradient pulses:



- **Case 2: If spins are diffusing**

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

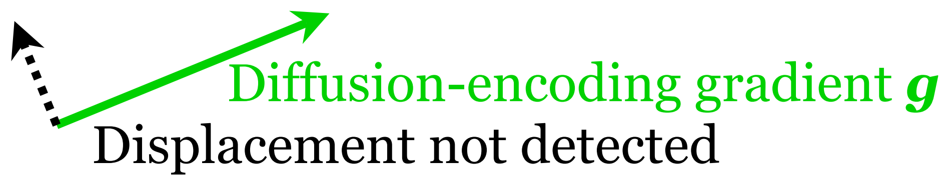


Displacement in $y \Rightarrow$
Dephasing $\Rightarrow$
Signal attenuation

Choice 1: Directions

- Diffusion direction || Applied gradient direction
  ⇒ Maximum signal

- Diffusion direction ⊥ Applied gradient direction
  ⇒ No signal



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

How many directions?

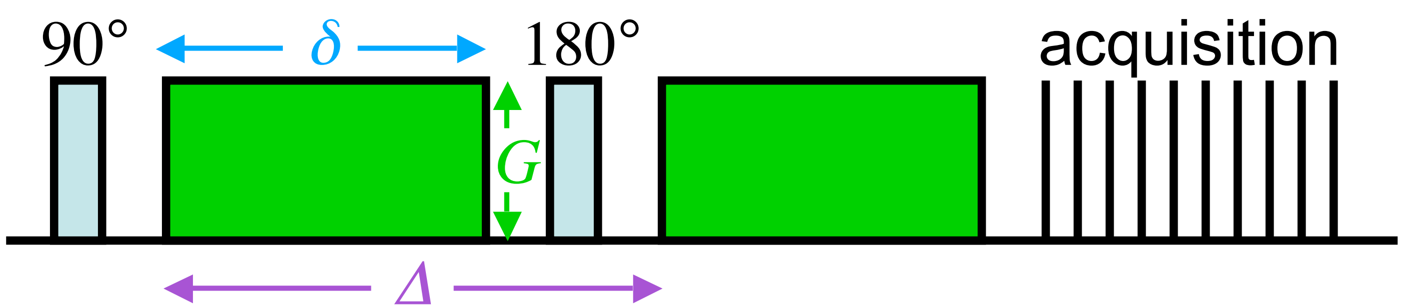
- Six diffusion-weighting directions are the minimum, but usually we acquire more
- Acquiring more directions leads to:
  + More reliable estimation of tensors
  – Increased imaging time ⇒ Subject discomfort, more susceptible to artifacts due to motion, respiration, etc.
- Typically diminishing returns beyond a certain number of directions [Jones, 2004]

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?

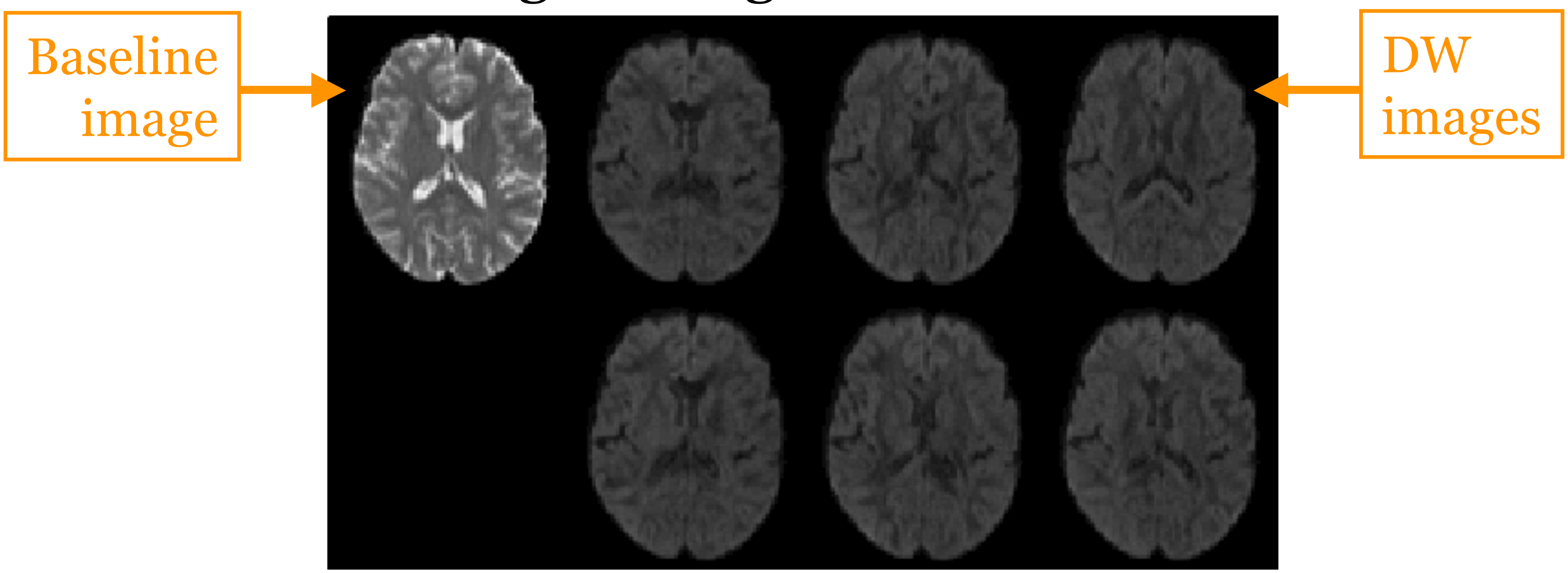
- Typical values for DTI ~ 1000 sec/mm^2
- Increasing the b-value leads to:
  - \+ Increased contrast b/w areas of higher and lower diffusivity in principle
  - – Decreased signal-to-noise ratio ⇒ Less reliable estimation of tensors in practice
- Data can be acquired at multiple b-values for trade-off
- Repeat same acquisition several times and average to increase signal-to-noise ratio

Diffusion tensor model

- $f_j^{b,\mathbf{g}} = f_j^0 \, e^{-b\mathbf{g}'\cdot\mathbf{D}_j\cdot\mathbf{g}}$
  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
- Reconstruct images from acquired data:
  - $f_j^{b,\mathbf{g}}$ 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 DW 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
- Eigendecomposition is sensitive to noise, may result in negative eigenvalues

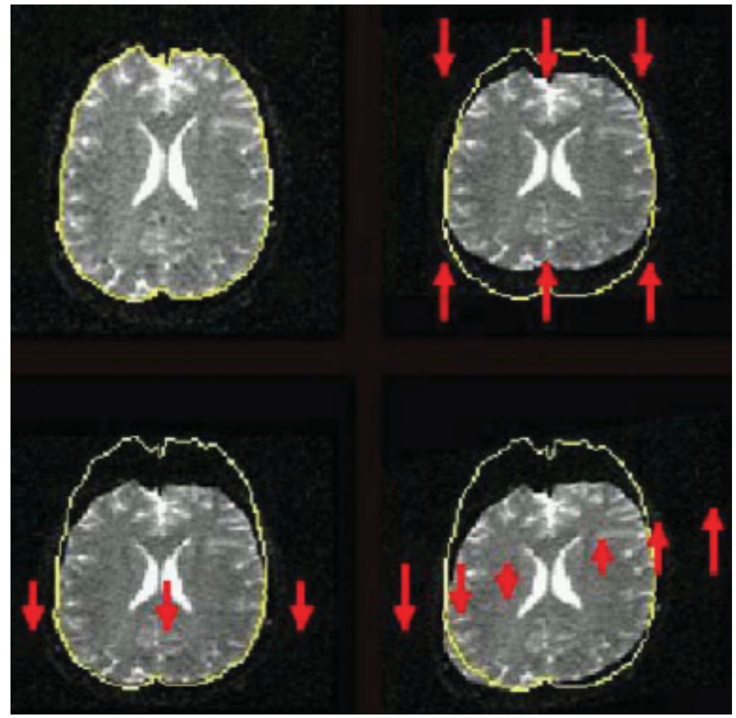


Field inhomogeneities

- 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

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



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

Distortion correction

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

Tensor estimation

- $f_j^{b,\mathbf{g}} = f_j^0 \, e^{-b\mathbf{g}'\cdot\mathbf{D}_j\cdot\mathbf{g}}$

- Estimate tensor from images:
  - Usually by least squares (implying Gaussian noise statistics)
    [Basser'94, Anderson'01, Papadakis'03, Jones'04, Chang'05, Koay'06]

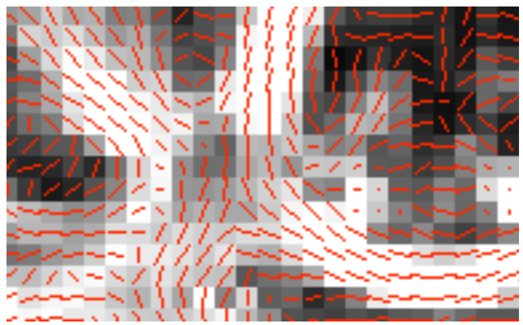
    $$\log(f_j^{b,\mathbf{g}} / f_j^0) = -b\mathbf{g}'\cdot\mathbf{D}_j\cdot\mathbf{g} = -\mathbf{B}\cdot\mathbf{D}_j$$

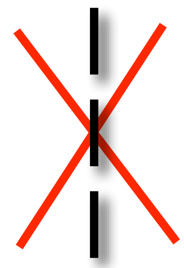
  - Or accounting for Rician noise statistics [Fillard'06]

- Pre-smooth or post-smooth tensor map to reduce noise
  [Parker'02, McGraw'04, Ding'05; Chefd'hotel'04, Coulon'04, Arsigny'06]

Other models of diffusion

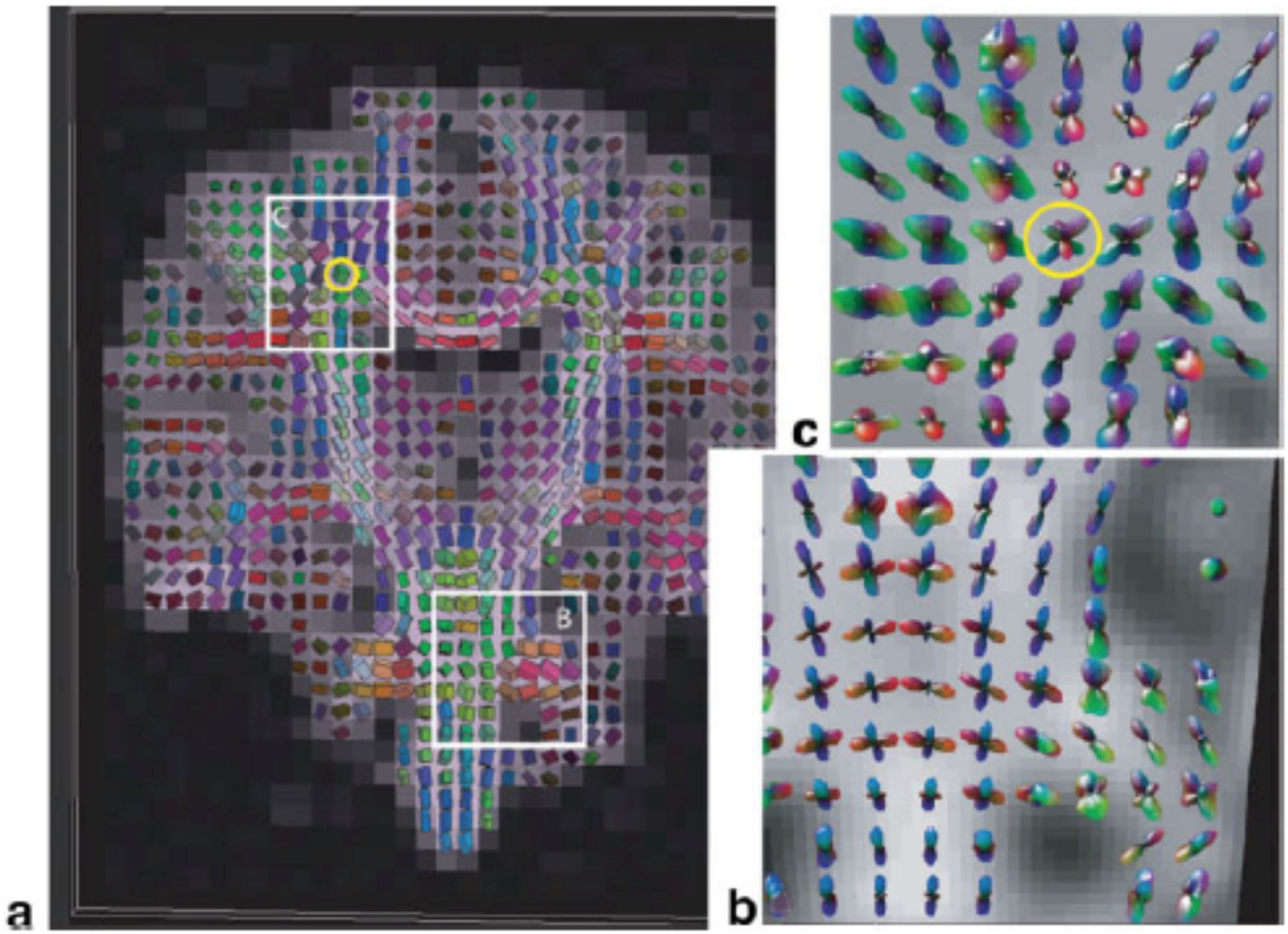
- The tensor is an imperfect model: What if more than one major diffusion direction in the same voxel?





- 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



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