NA-MIC
National Alliance for Medical Image Computing
http://na-mic.org

Mathematical and physical foundations of DTI

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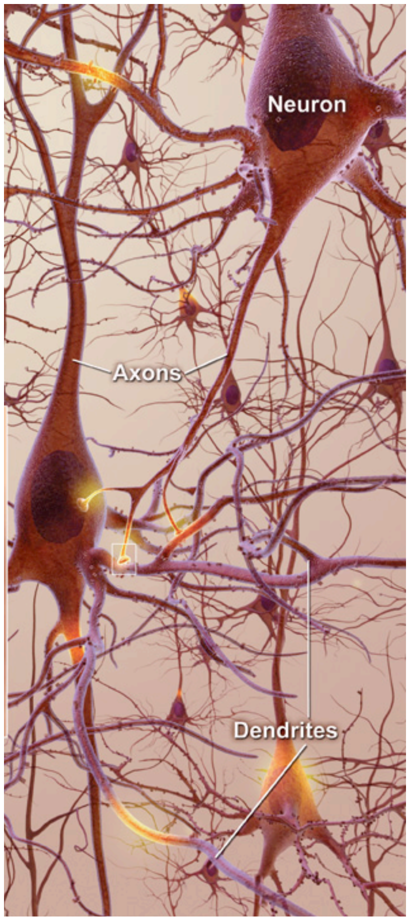
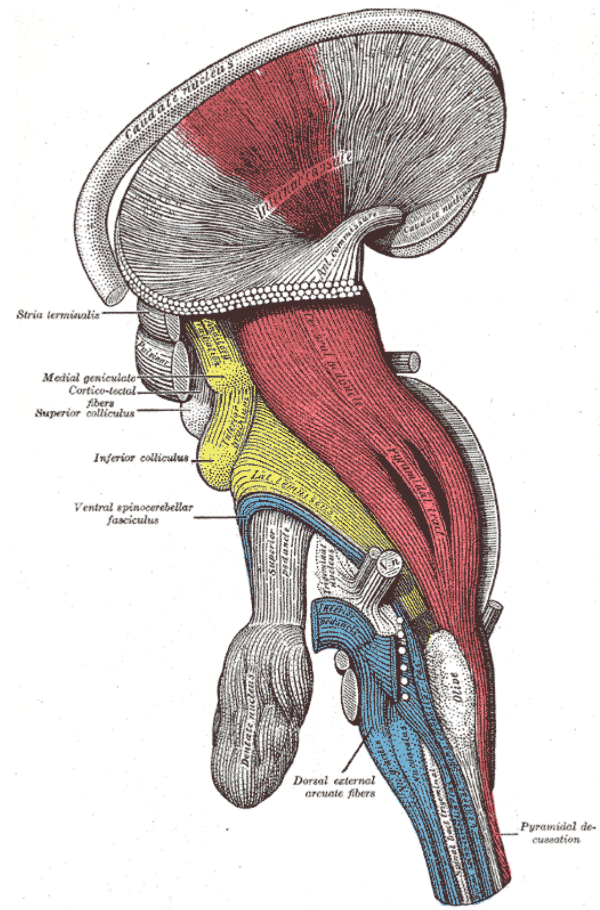
White-matter imaging



From the National Institute on Aging

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

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

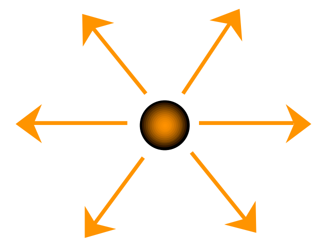


From *Gray's Anatomy: IX. Neurology*

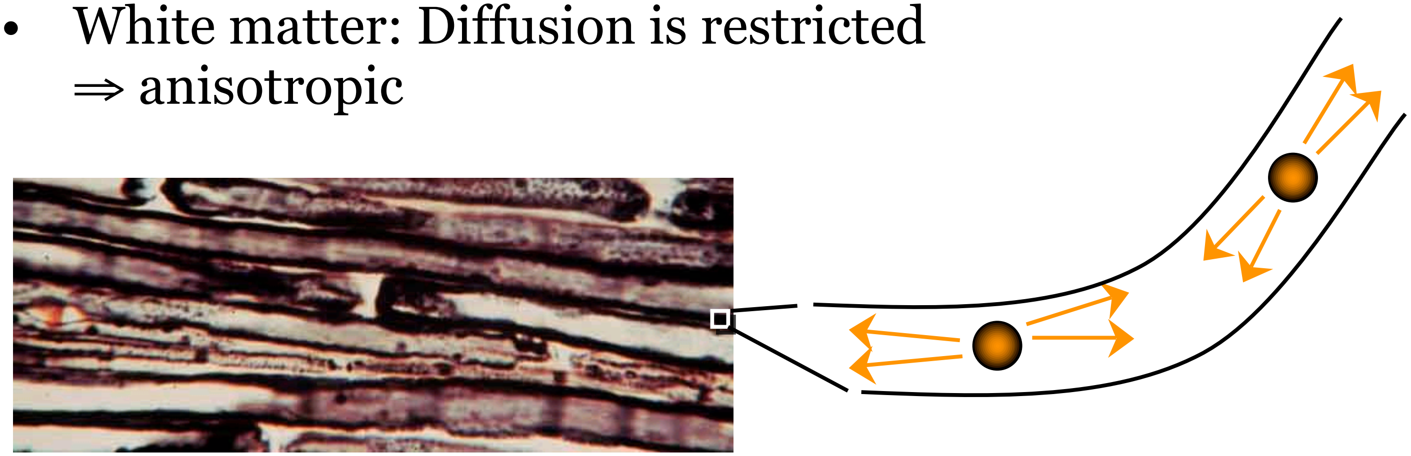
Diffusion in brain tissue

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

- Gray matter: Diffusion is unrestricted
  ⇒ isotropic

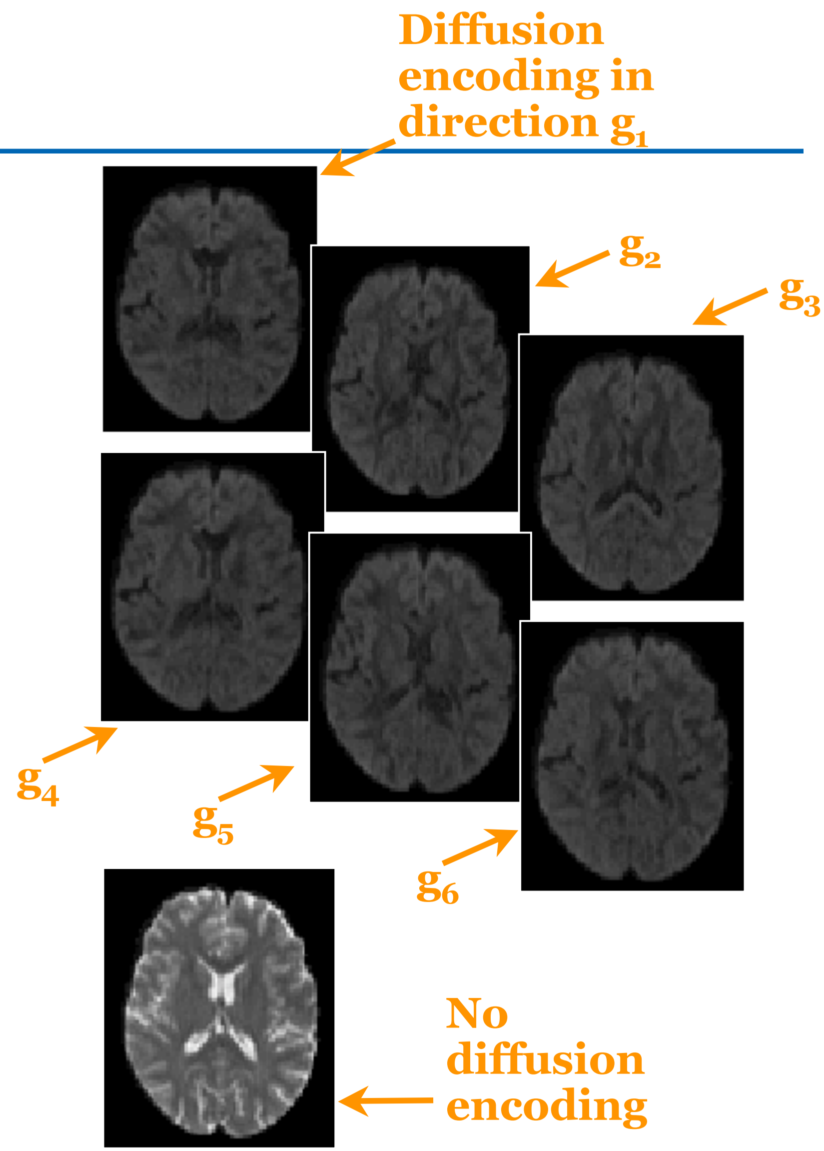


- White matter: Diffusion is restricted
  ⇒ anisotropic

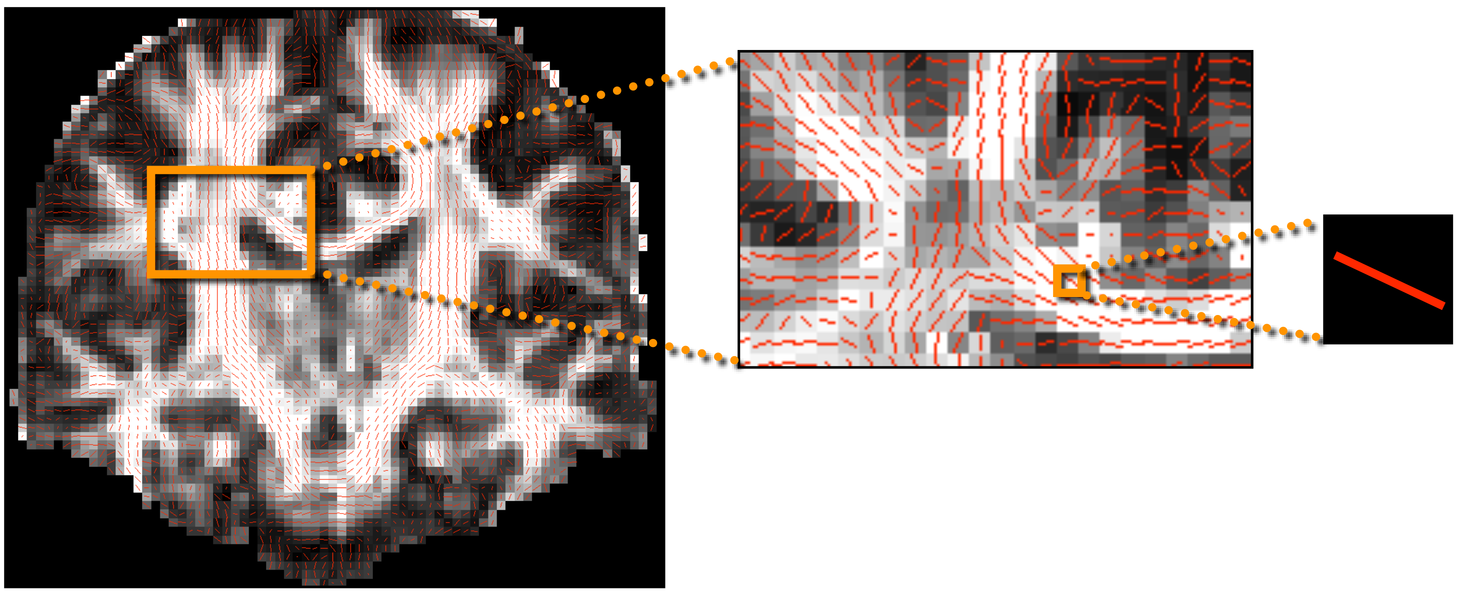


Diffusion MRI

- 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



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" mathematically is 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

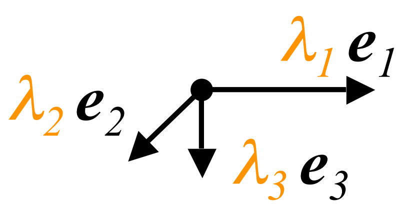
Eigenvalues/vectors

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

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

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

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

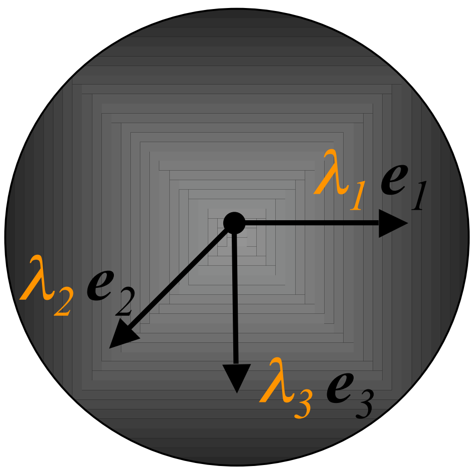


Physical interpretation

- Eigenvectors express diffusion direction
- Eigenvalues express diffusion magnitude

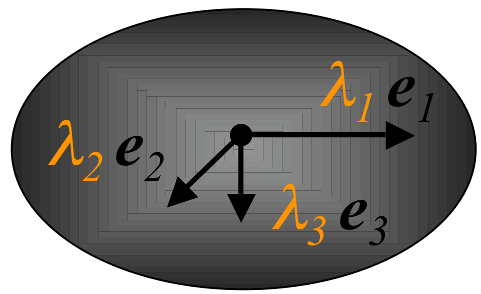
Isotropic diffusion:

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



Anisotropic diffusion:

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

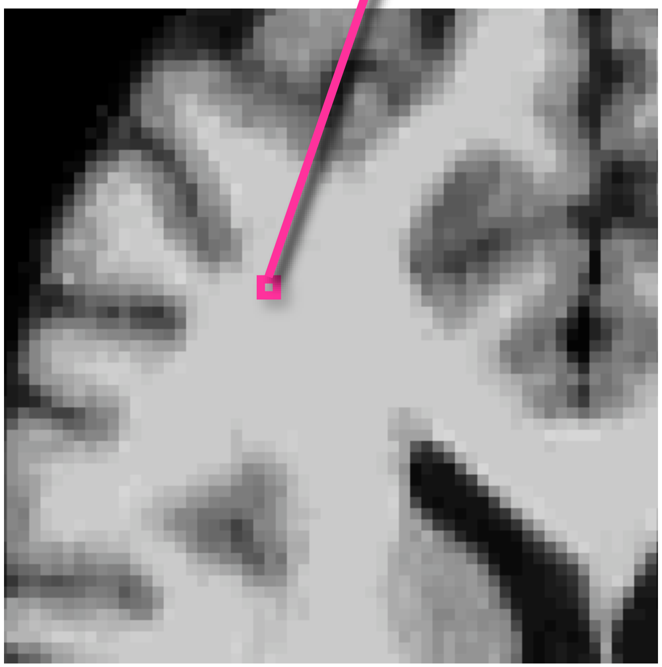


- One such ellipsoid at each voxel: Likelihood of water molecule displacements at that voxel

Diffusion tensor imaging

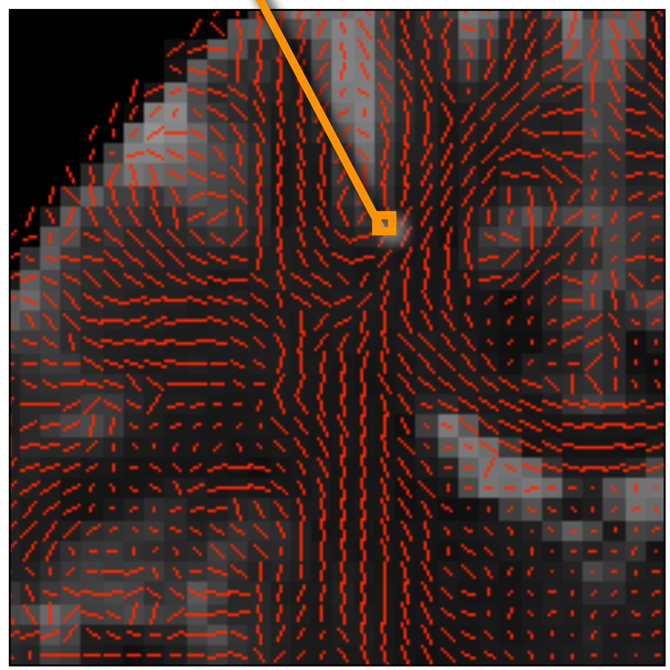
Image:

An **intensity value** at each voxel



Tensor map:

A **tensor** at each voxel

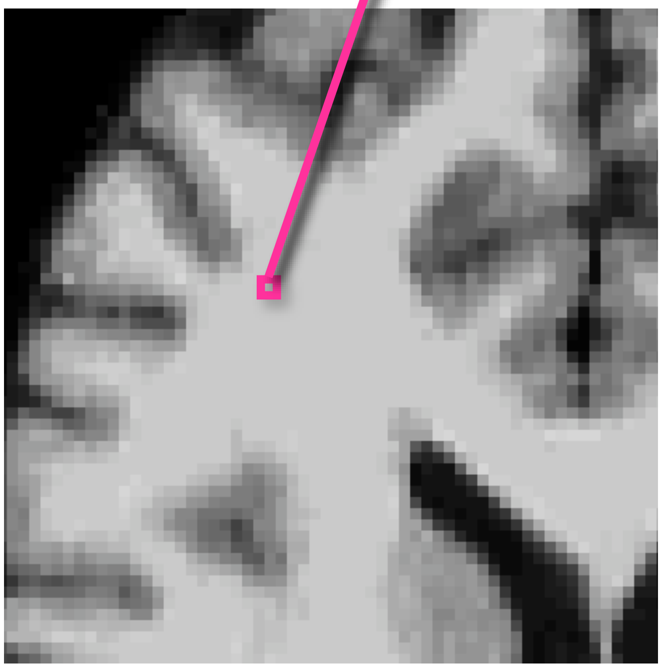


Direction of eigenvector corresponding to greatest eigenvalue

Diffusion tensor imaging

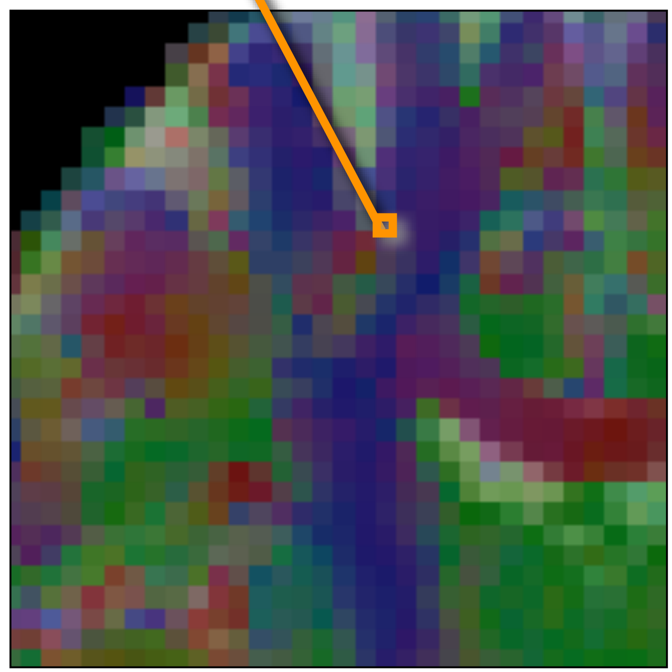
Image:

An **intensity value** at each voxel



Tensor map:

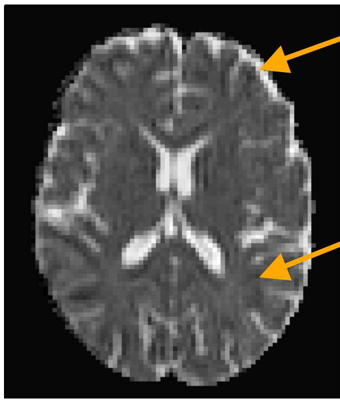
A **tensor** at each voxel



Direction of eigenvector corresponding to greatest eigenvalue

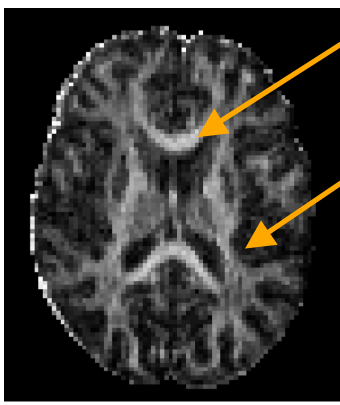
Red: L-R, Green: A-P, Blue: I-S

Scalar diffusion measures



Mean diffusivity (MD): Mean of the 3 eigenvalues

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



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

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

More summary measures

- **Axial diffusivity:** Greatest eigenvalue

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

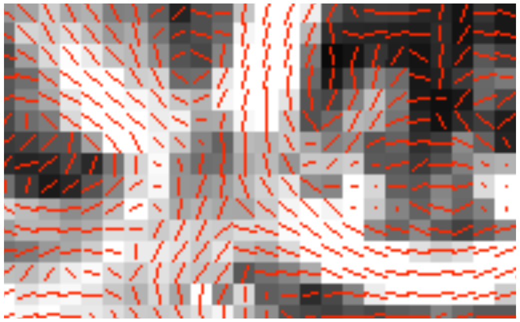
- **Radial diffusivity:** Average of 2 lesser eigenvalues

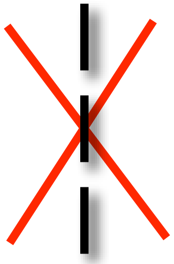
  $\mathrm{RD}(j) = [\lambda_2(j) + \lambda_3(j)]/2$

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

Beyond the tensor

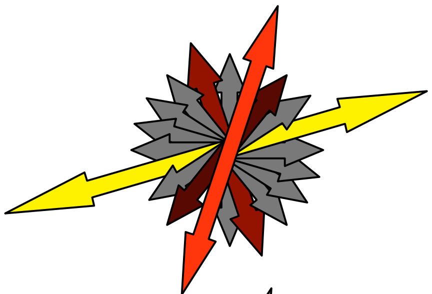
- The tensor is an imperfect model: What if more than one major diffusion direction in the same voxel?





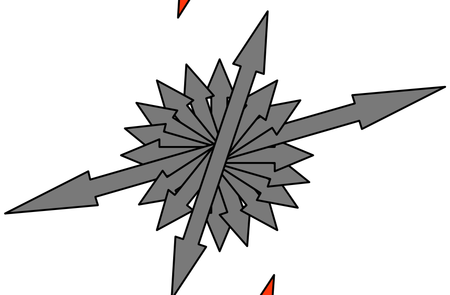
- High angular resolution diffusion imaging (HARDI)
  - A mixture of the usual ("rank-2") tensors [Tuch'02]
  - A tensor of rank > 2 [Frank'02, Özarslan'03]
  - An orientation distribution function [Tuch'04]
  - A diffusion spectrum (DSI) [Wedeen'05]
- More parameters at each voxel ⇒ More data needed

Models of diffusion



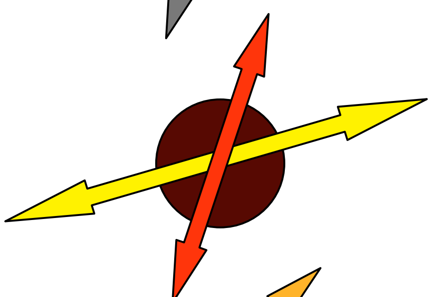
Diffusion spectrum (DSI):

Full distribution of orientation and magnitude



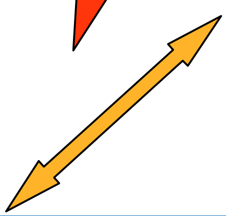
Orientation distribution function (Q-ball):

No magnitude info, only orientation



Ball-and-stick:

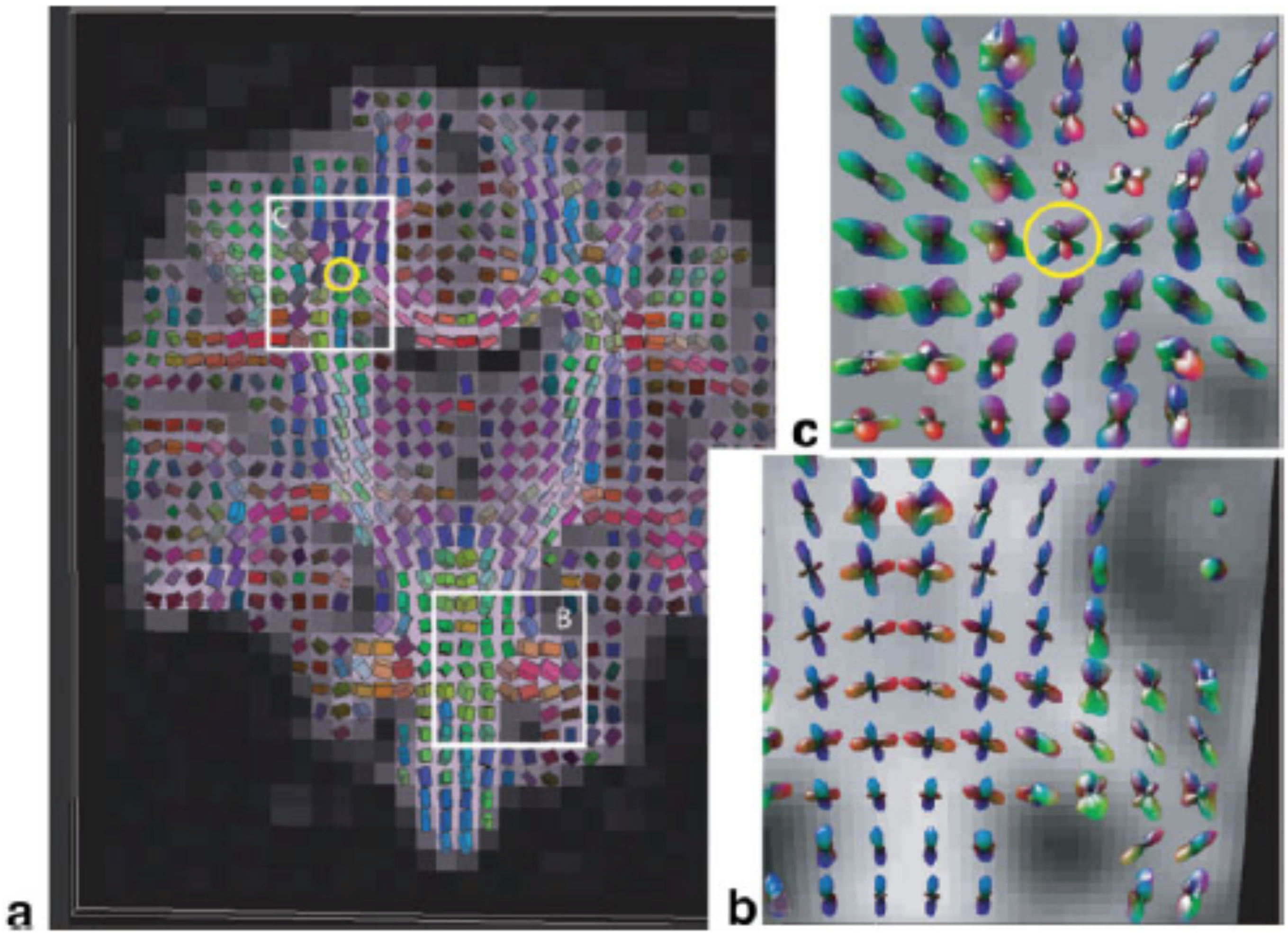
Orientation and magnitude for a small number of anisotropic compartments



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

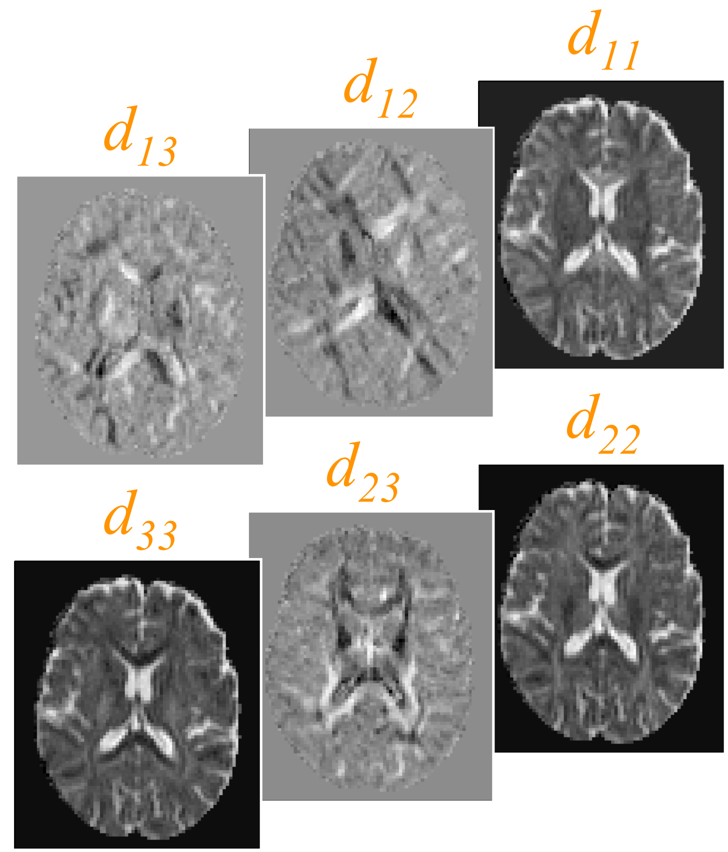
Data acquisition

- Remember: A tensor has six unique parameters

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

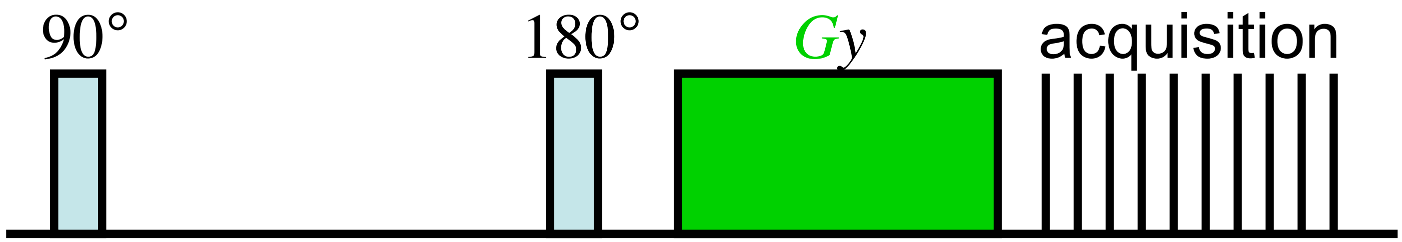
- To estimate six parameters at each voxel, must acquire at least six diffusion-weighted images

- HARDI models have more parameters per voxel, so more images must be acquired

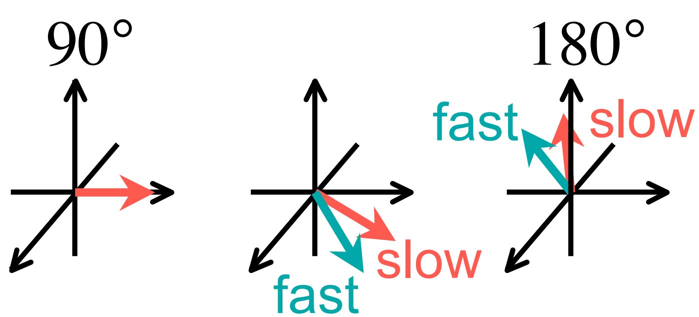


Spin-echo MRI

- Use a 180° pulse to refocus spins:



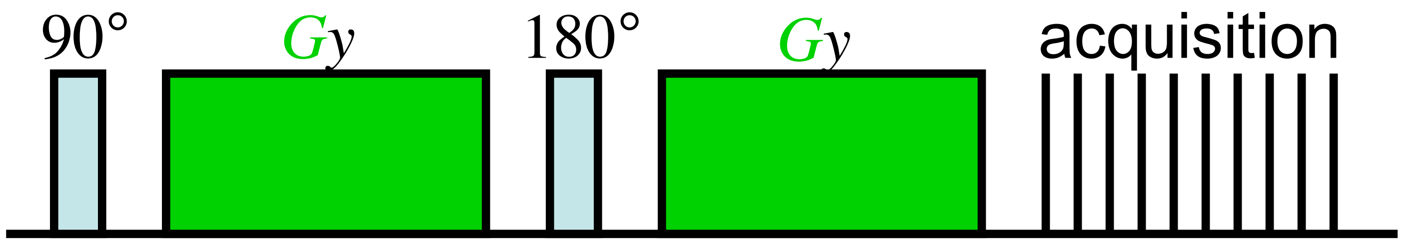
- Apply a field gradient *Gy* for location encoding



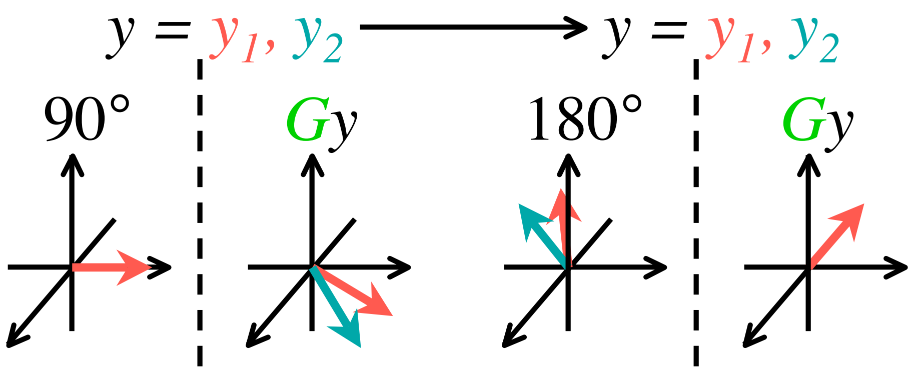
Measure transverse magnetization at each location -- depends on tissue properties (T_1,T_2)

Diffusion-weighted MRI

- Apply two gradient pulses:



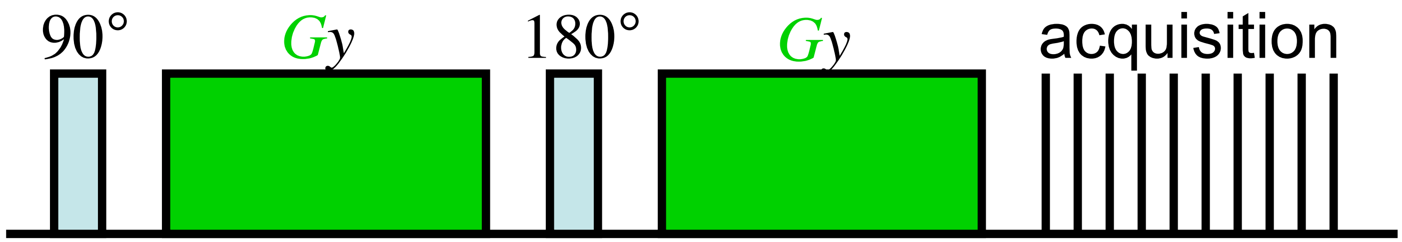
- **Case 1: If spins are not diffusing**



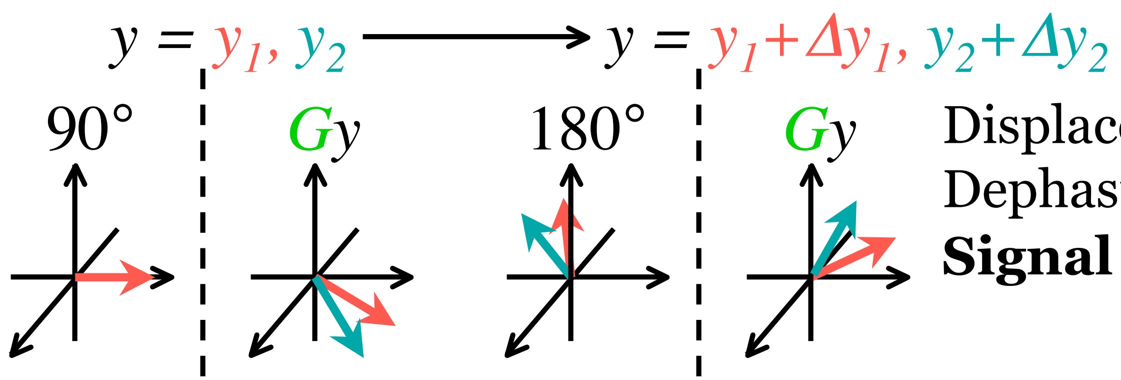
No displacement in $y \Rightarrow$
No dephasing $\Rightarrow$
No net signal change

Diffusion-weighted MRI

- Apply two gradient pulses:



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

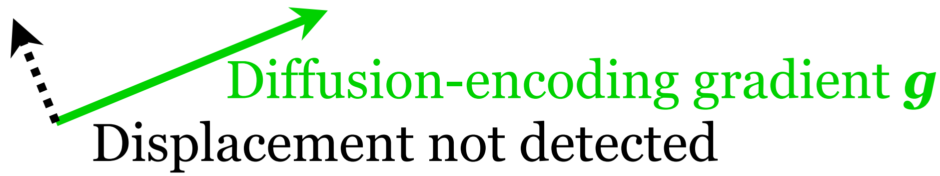


Displacement in $y \Rightarrow$
Dephasing $\Rightarrow$
Signal attenuation

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?

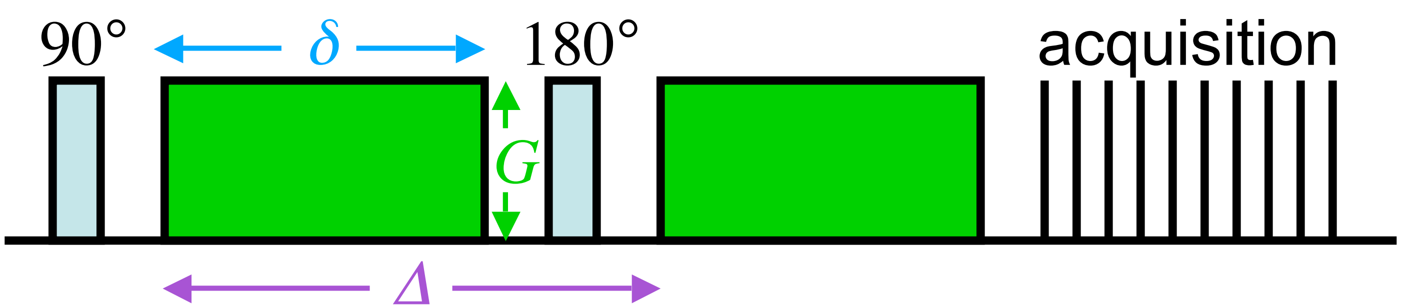
- Acquiring more directions leads to:
  - + More reliable estimation of tensors
  - – Increased imaging time ⇒ Subject discomfort, more susceptible to artifacts due to motion, respiration, etc.
- DTI:
  - Six directions is the minimum
  - Usually a few 10's of directions
  - Diminishing returns after 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 tensors in practice

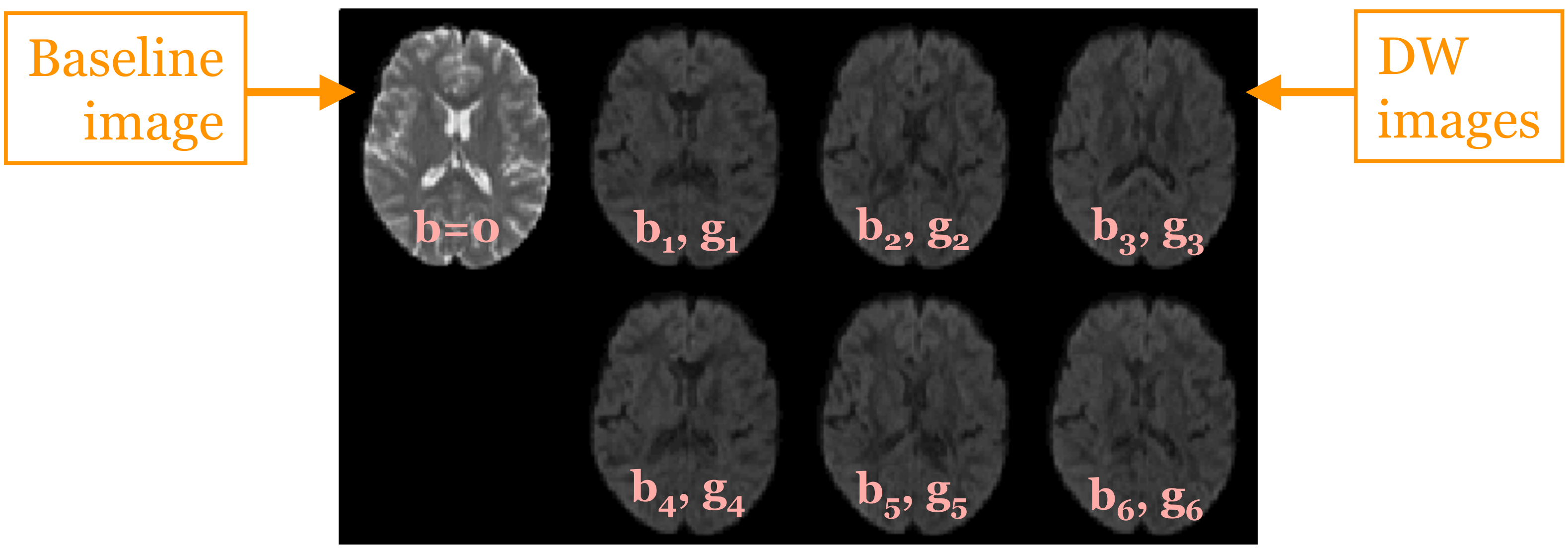
- DTI: b ~ 1000 sec/mm^2
- HARDI/DSI: b ~ 10,000 sec/mm^2

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

Looking at diffusion 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



From image to 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

- 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 $\mathbf{D}_j$

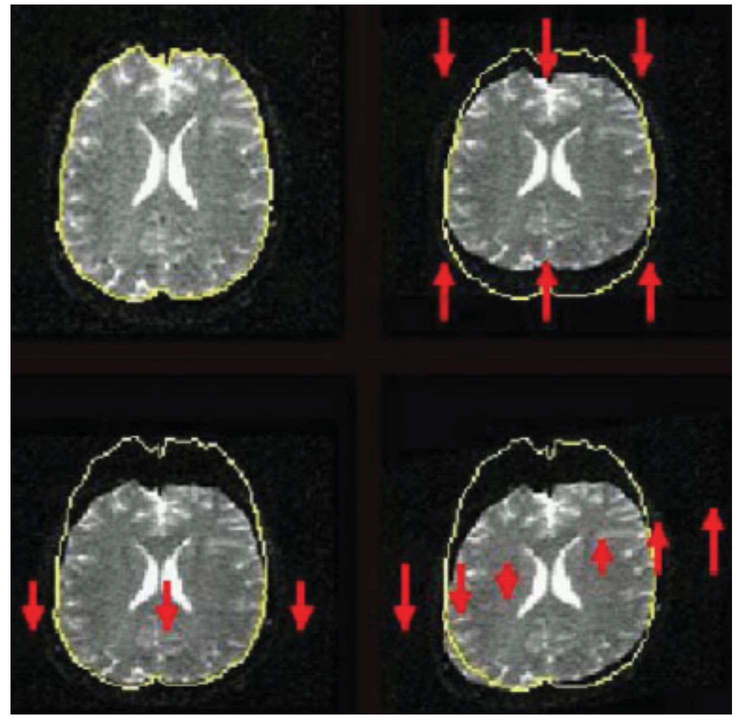
Field inhomogeneities

- 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

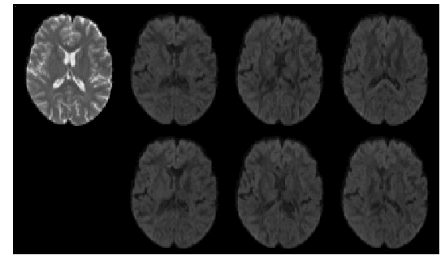
- Fast switching of diffusion-encoding gradients induces eddy currents in conducting components
- Eddy currents lead to residual gradients that shift the diffusion gradients
- The shifts are **direction-dependent,** *i.e.*, different for each DW image
- Results: geometric distortions

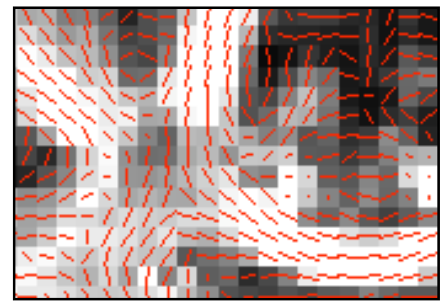


From Le Bihan *et al.*, Artifacts and pitfalls in diffusion MRI, JMRI 2006

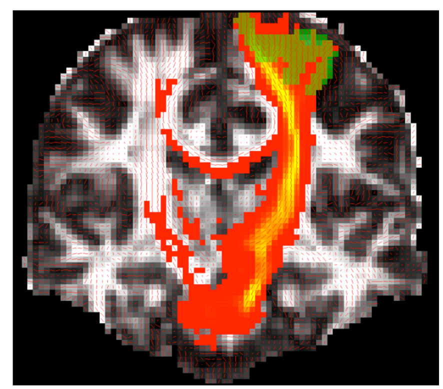
Data analysis steps

- 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