Micro and Macro Structure from Diffusion Weighted MRI

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Outline

- Introduction
- Imaging diffusion using MRI
- Diffusion probability: Q-space
- Diffusion orientation: DTI
- Connecting voxels: Tractography
- Optimization: imaging and processing

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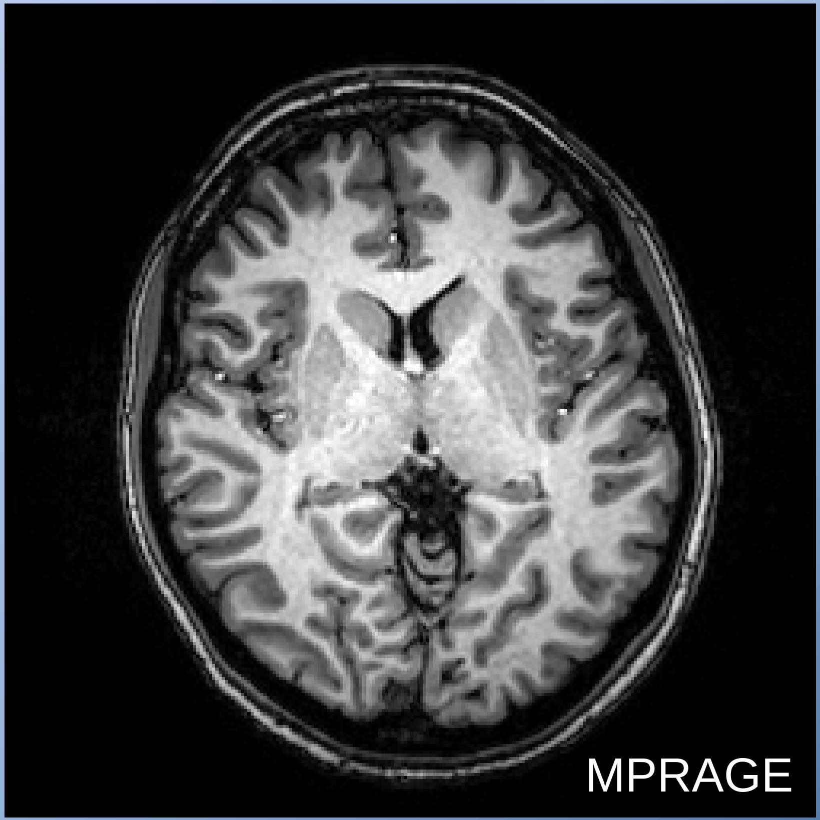
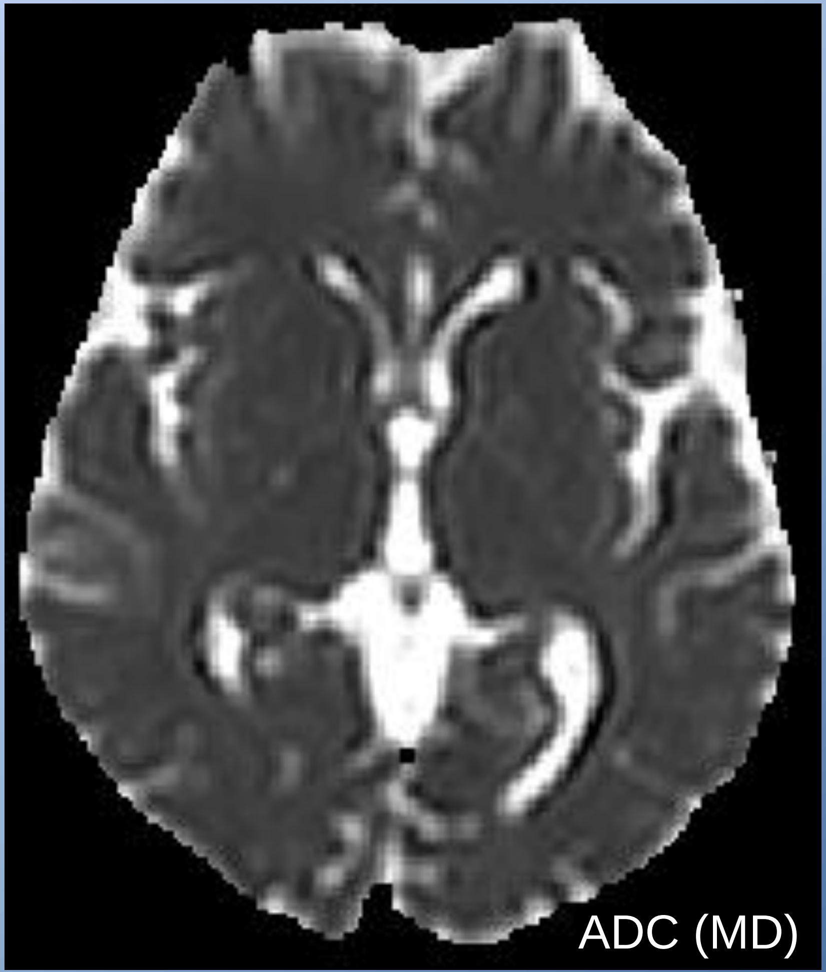
Structural MRI

- Conventional MRI
- Contrast dominated by
  - NMR properties: T1, T2, PD
  - MRI parameters: TR, TE, α
- White matter appears relatively homogeneous



Diffusion MRI

- How much does the water diffuse?
  - Depends on tissue
- Greatest diffusion in cerebrospinal fluid
- About the same overall diffusion in gray matter and white matter

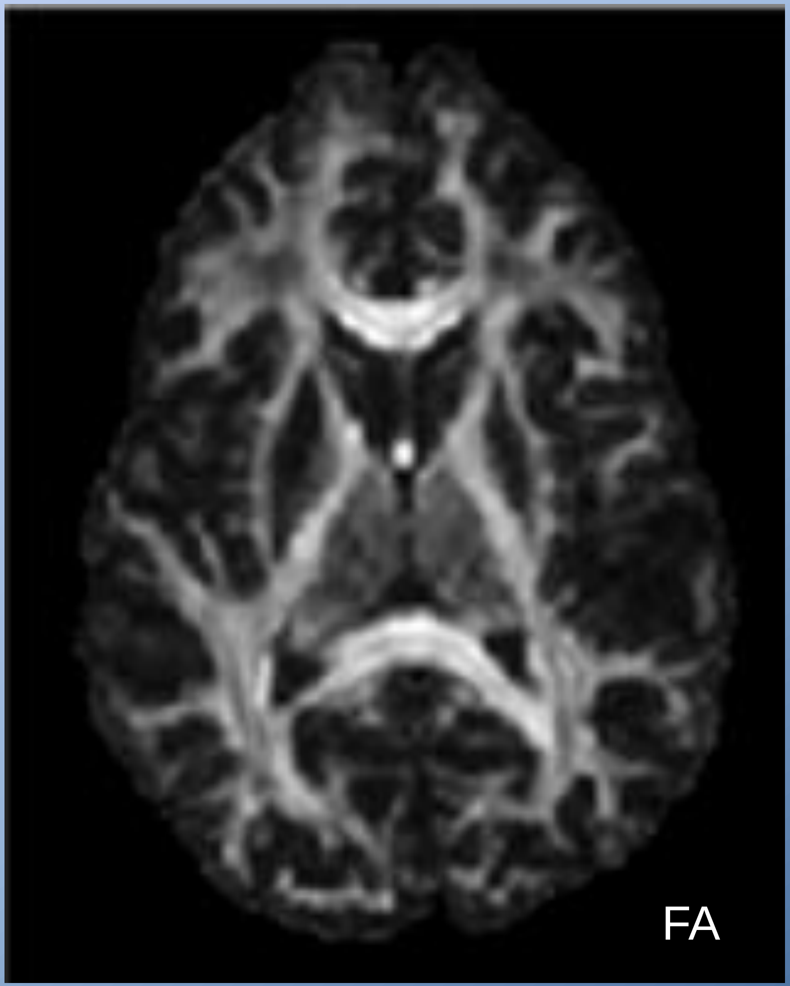


Is Diffusion Directional?

- Does the tissue have a preferred direction of diffusion?
  - Anisotropy
- Common measures:
  - Fractional anisotropy

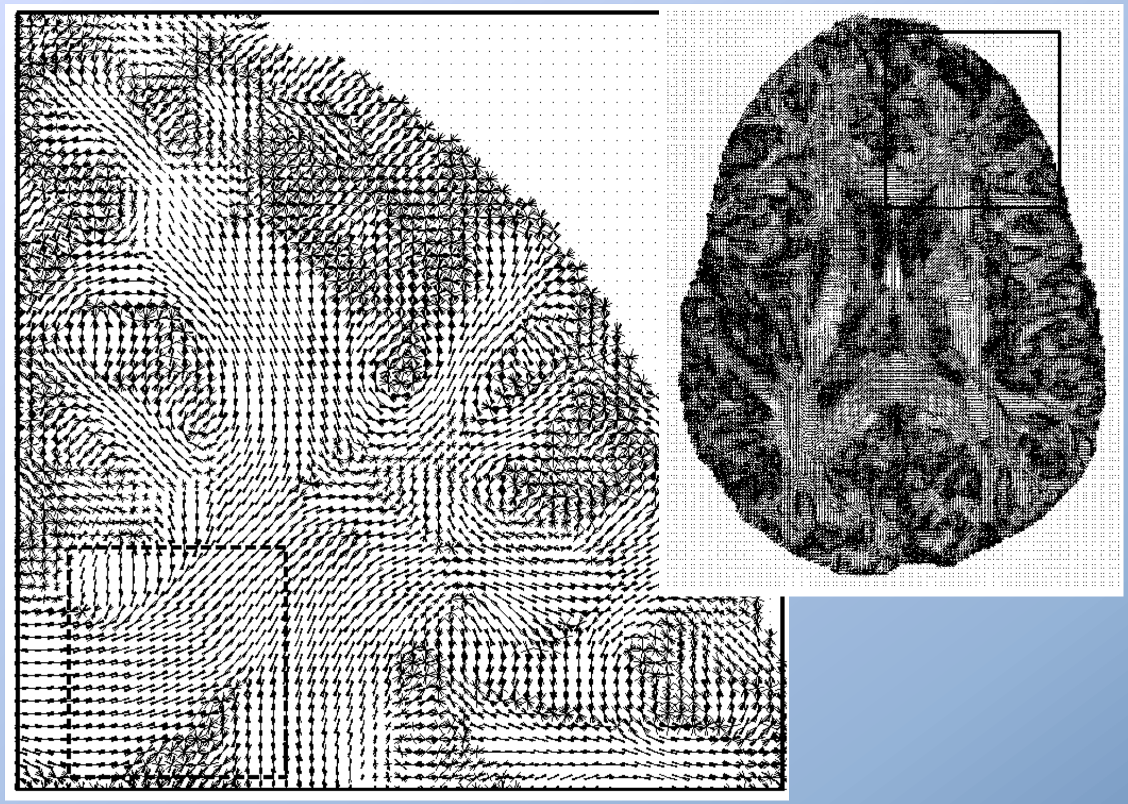
    FA
  - Relative anisotropy

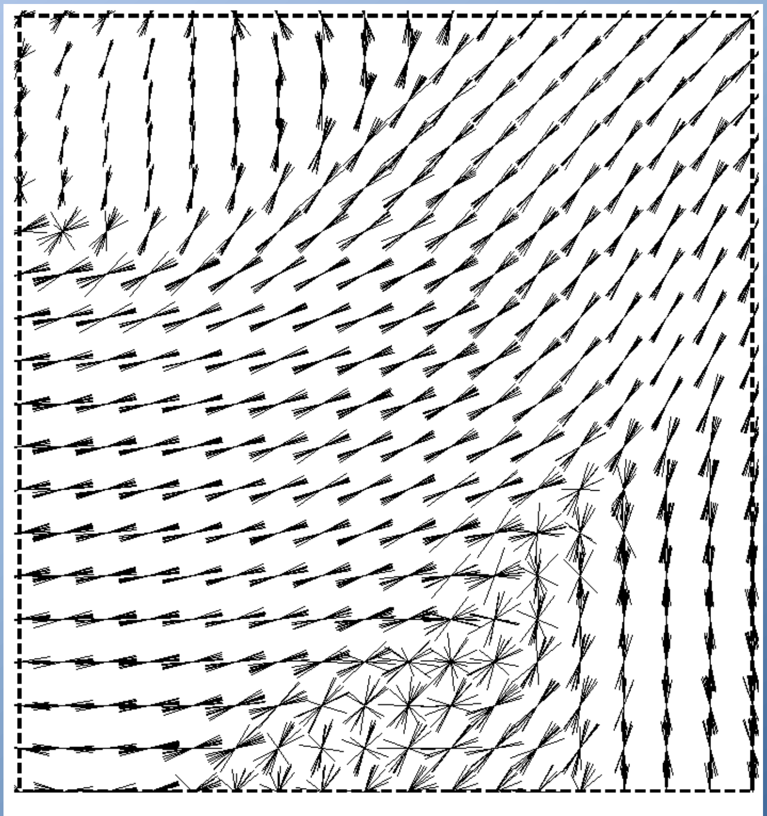
    RA



Orientation of Diffusion

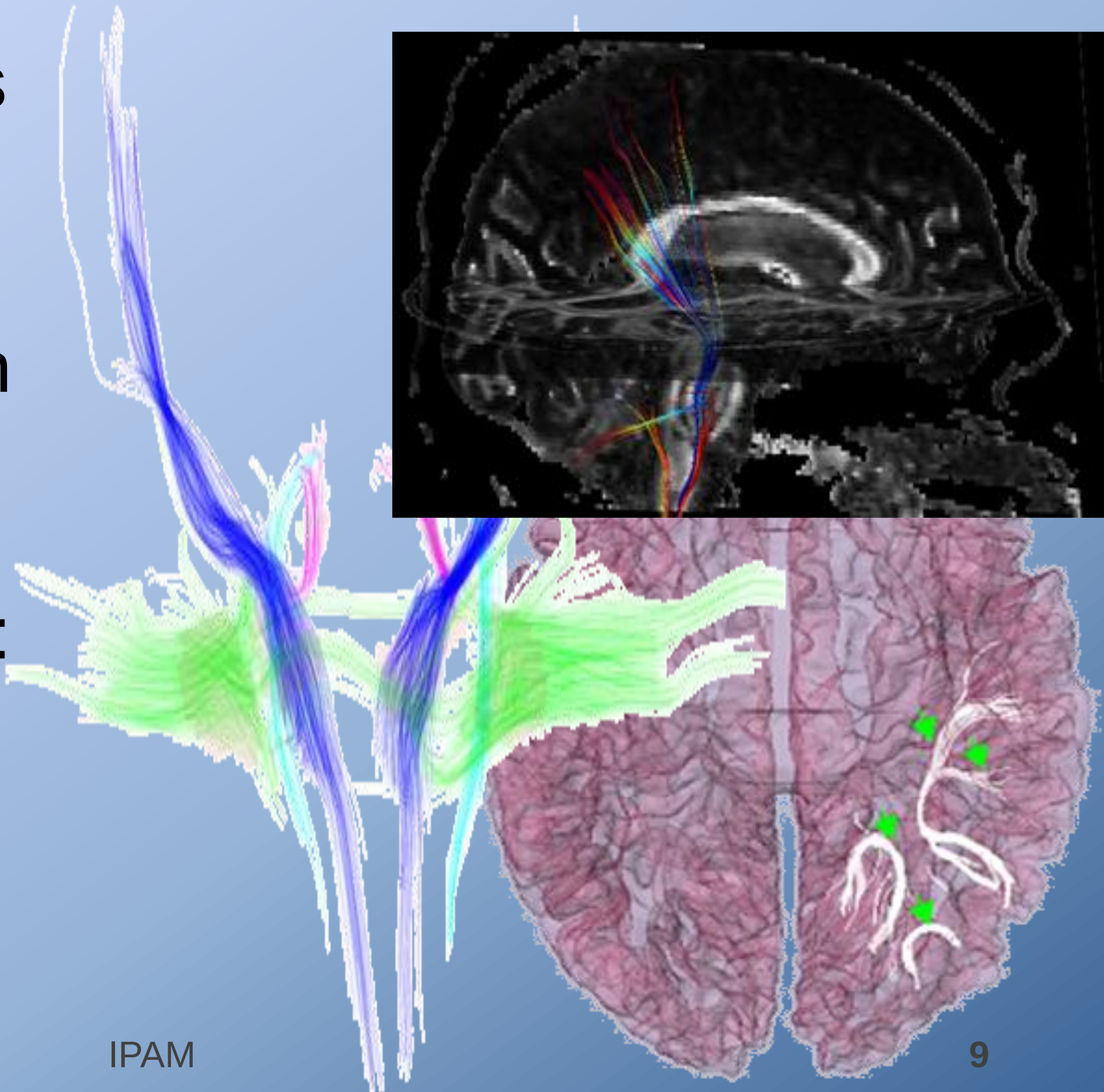
- What is the dominant orientation of diffusion?





Connecting Fibers

- White matter fibers define diffusion directionality
- “Pathlines” through the diffusion orientation field reconstructs fibers:
  - ➔ Tractography



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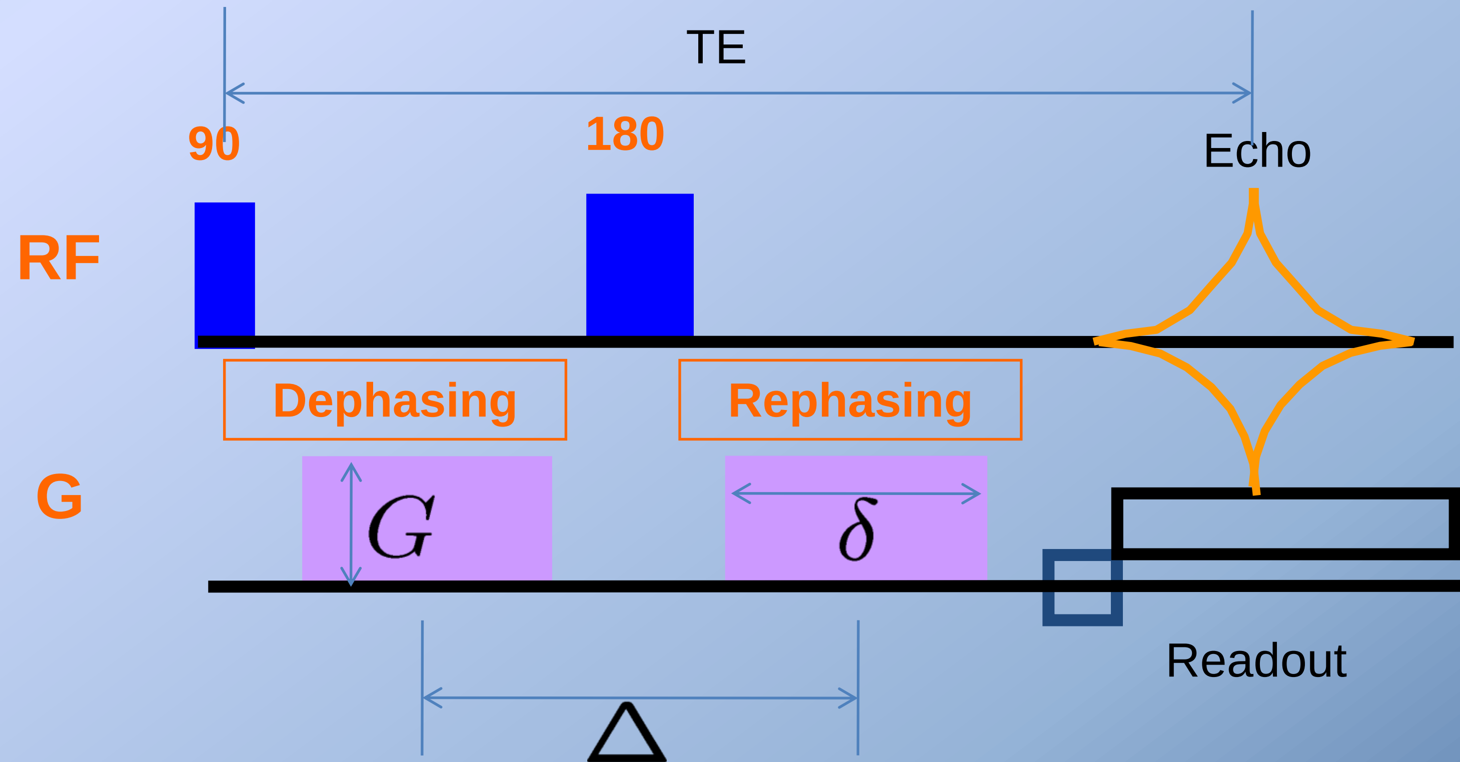
Magnetic Resonance Imaging

Pulsed Gradient Spin Echo (PGSE) Sequence

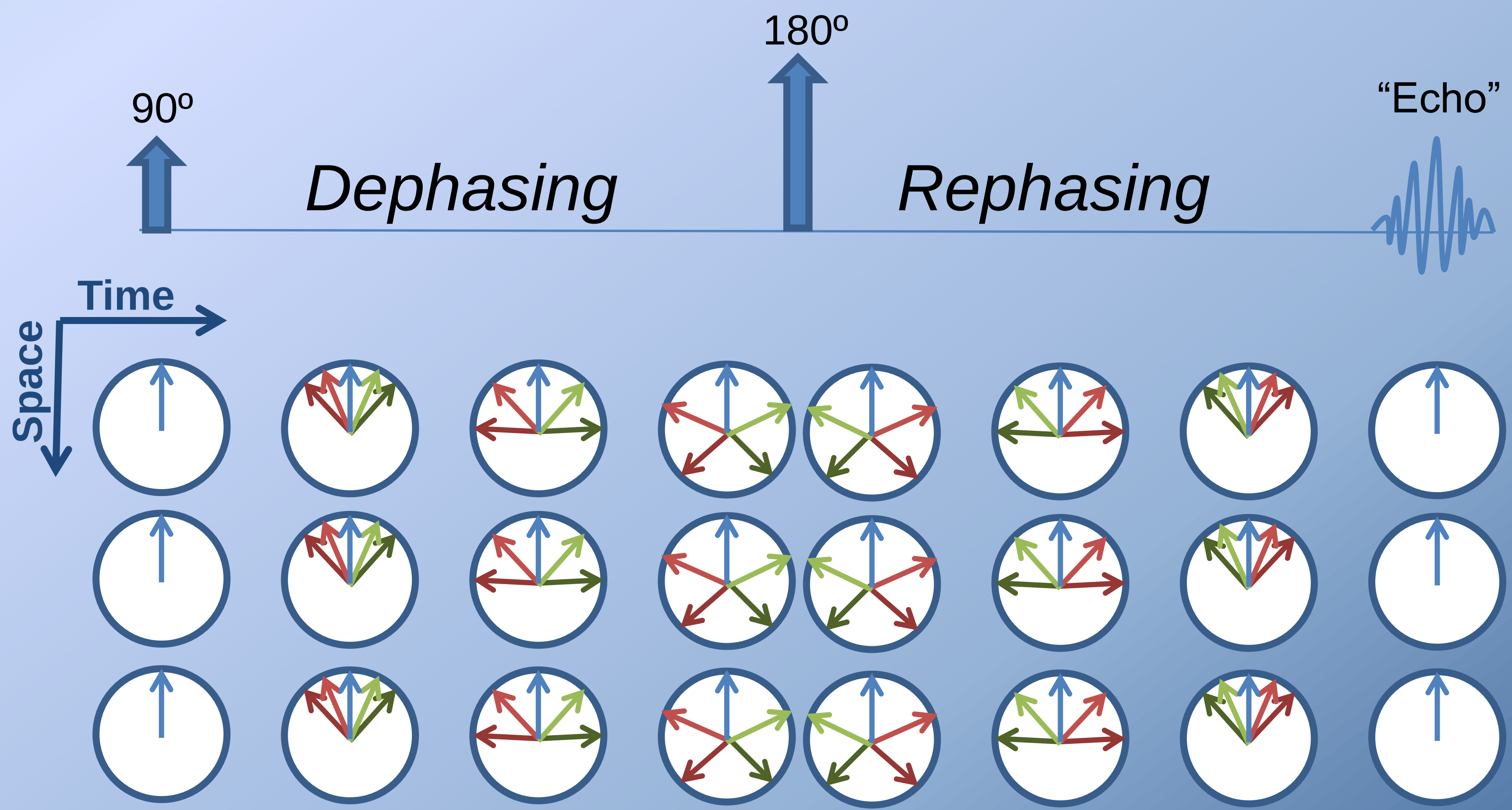


$$b = \gamma^2 G^2 \delta^2 (\Delta - \delta/3)$$

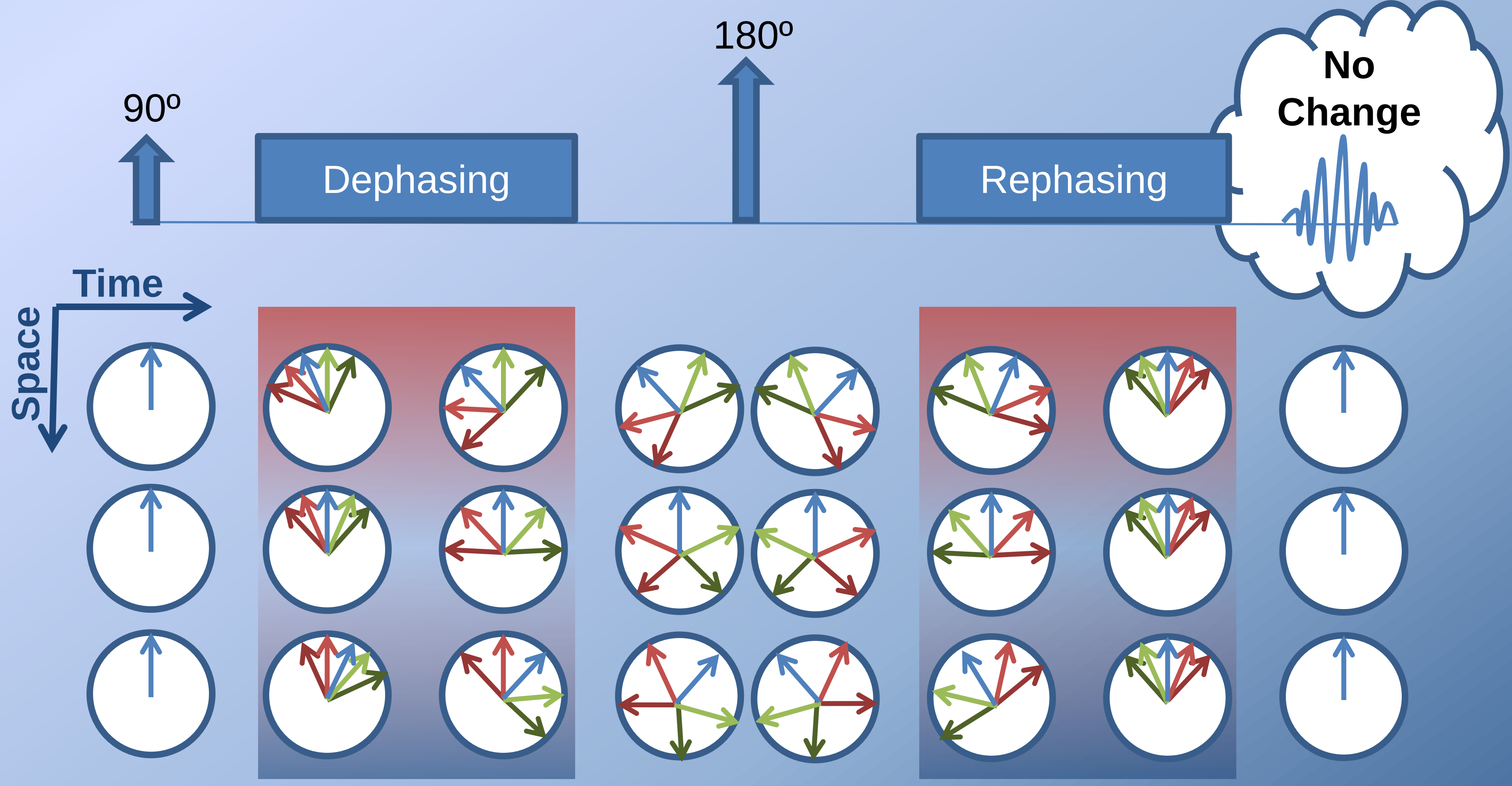
Dephasing Spins (no gradient)

- Transverse magnetization shown in a rotating frame of reference
  – Precession at the mean Larmor frequency ($\omega = \gamma B_0$) (vertical)
- Local effective fields are non-uniform: $T2^*$ effects
  – Slow spins rotate counter-clockwise
  – Fast spins rotate clock-wise

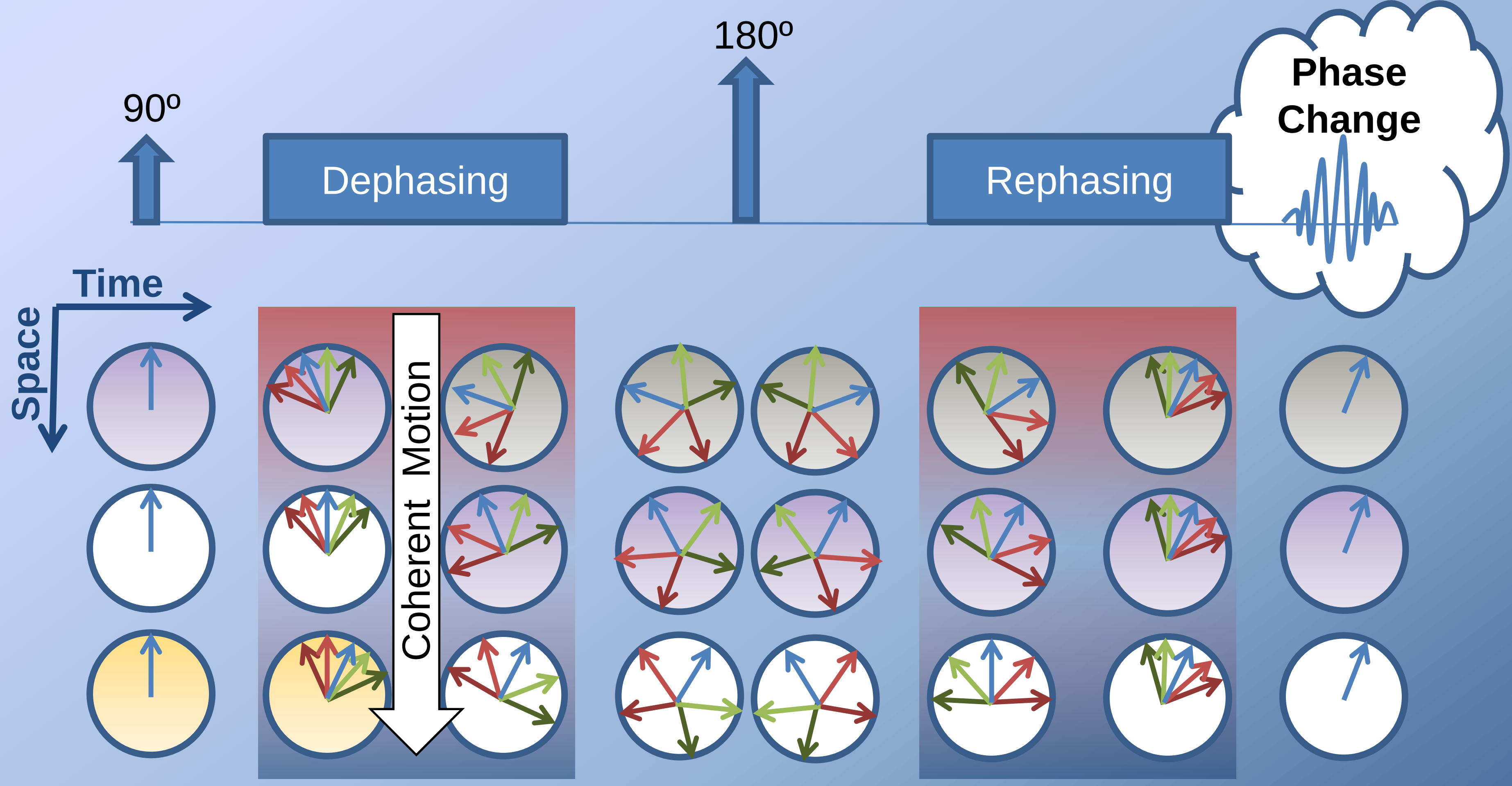
Rephasing Spins (no gradient)



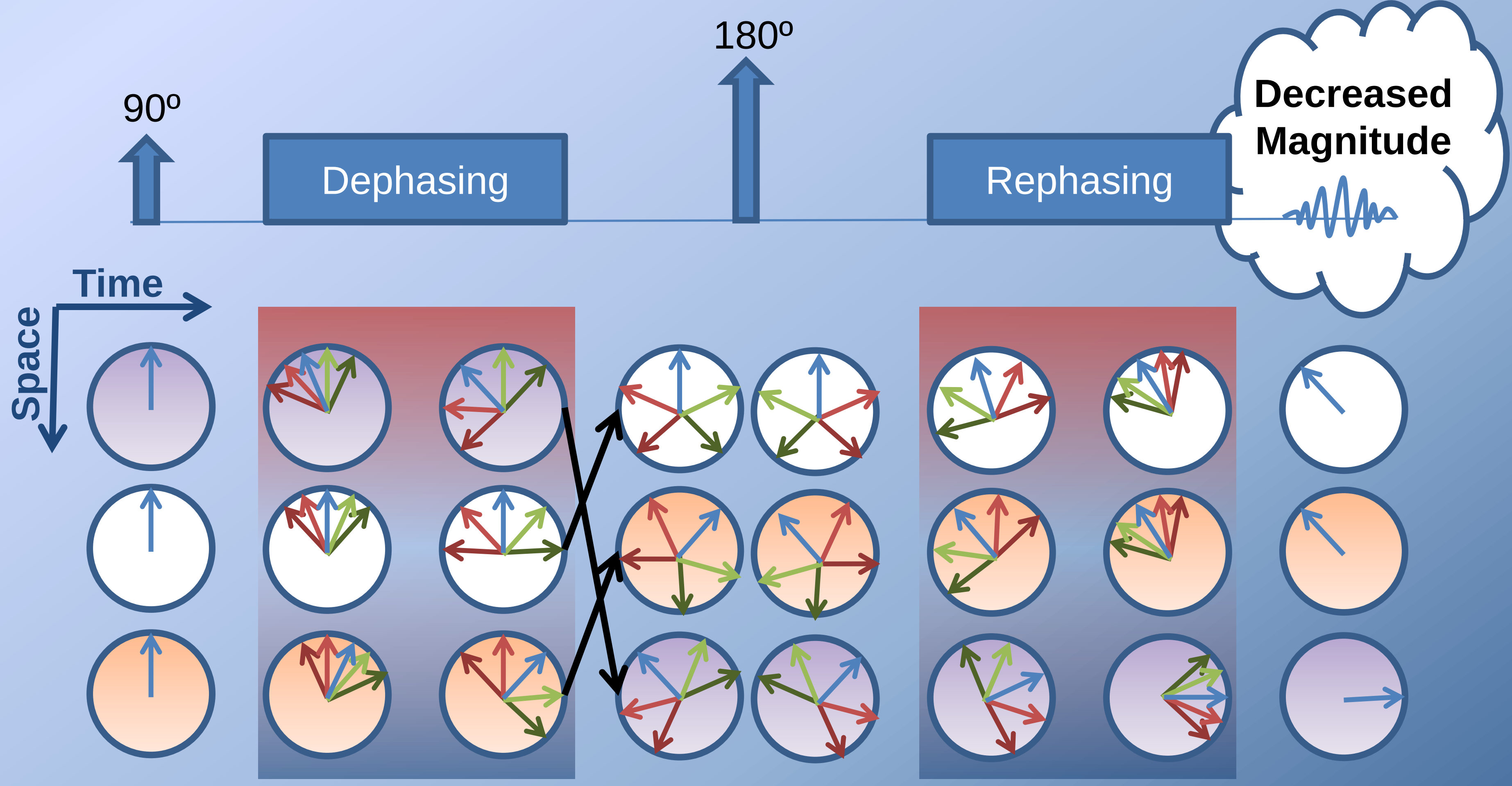
Effect of Applied Gradients (no motion or diffusion)



Effect of Applied Gradients (bulk motion, no diffusion)



Effect of Applied Gradients (with diffusion, no motion)



Stejskal-Tanner Formula

- Signal attenuation factor in PGSE:

$$S = S_0 e^{-bD}$$

- Where the b-value is:

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

- Two unknowns ➔ two observations to estimate D, apparent diffusion coefficient

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1-D Diffusion: Unrestricted

Diffusion of Spheres

Location Probability:

$$p(x,t) = \frac{1}{\sqrt{4\pi D t}} e^{-\frac{x^2}{4Dt}}$$
$$= \mathcal{N}(0, 2Dt)$$

In a viscous medium:

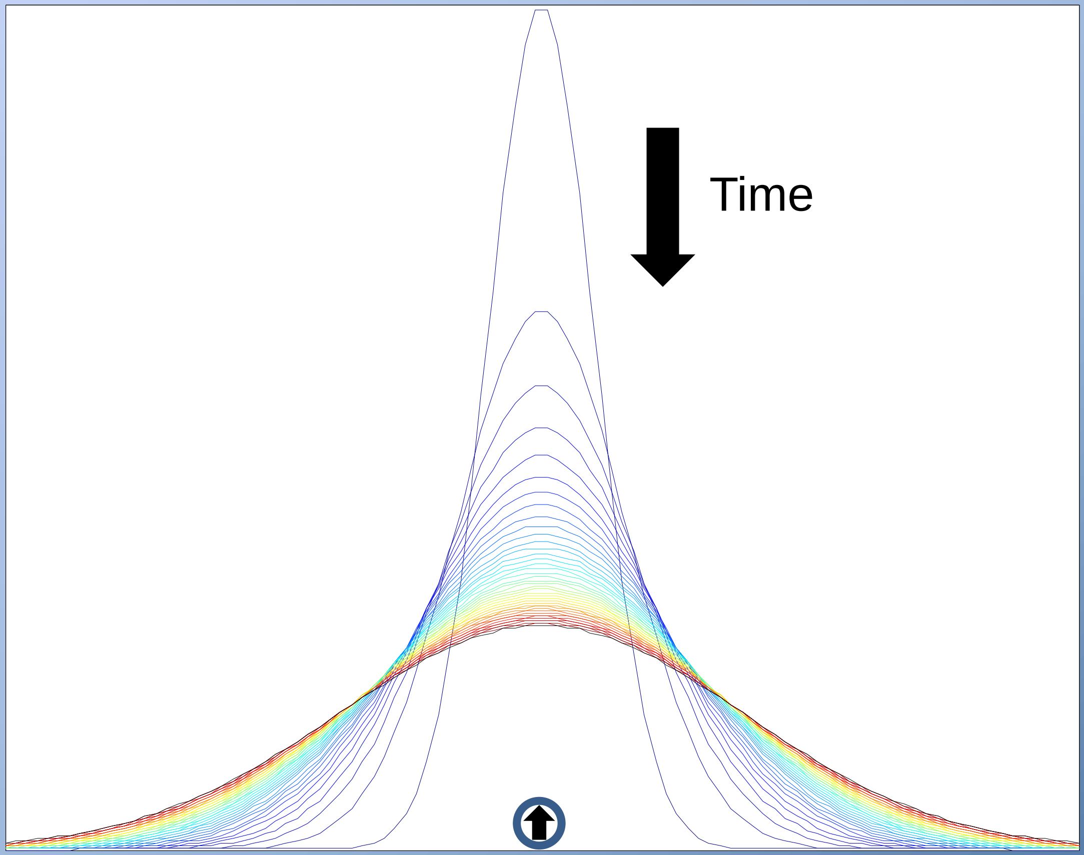
$$D = \frac{kT}{6\pi a \eta}$$

$k =$ Boltzman's constant

$T =$ Temperature

$a =$ diameter of a sphere

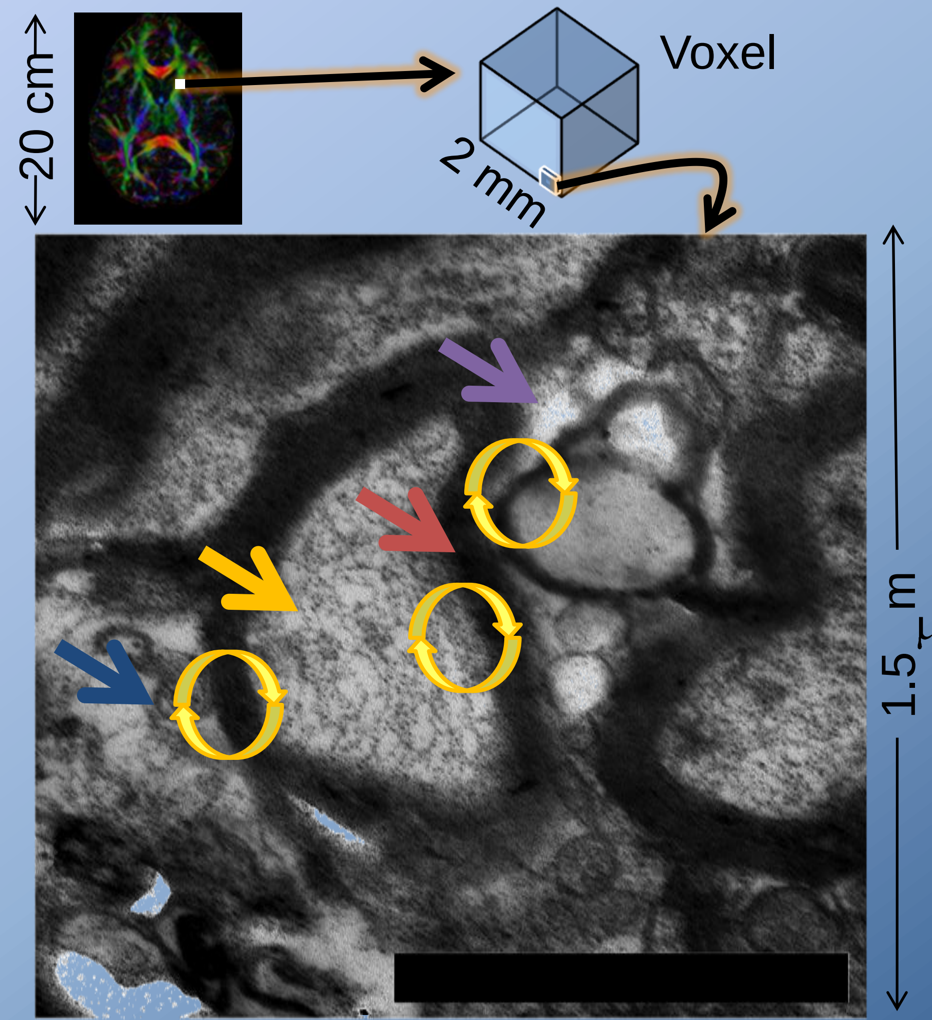
$\eta =$ viscosity



Note: Diffusivity of Free Water ~2 x 10^{-3} mm^2/s

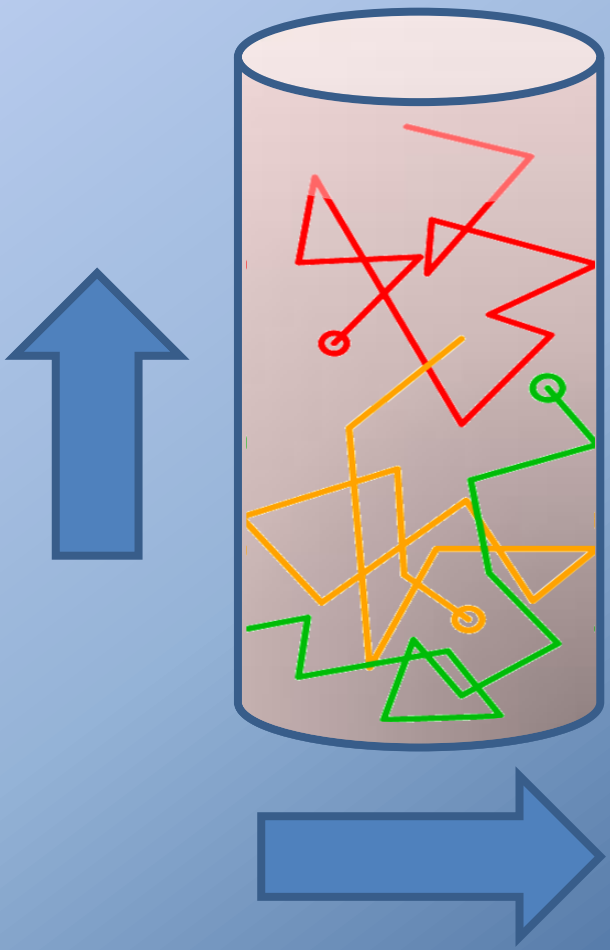
Which Protons Do We See?

- Multi-compartment sources of signal:
  - Intra-axonal =>
  - Myelin =>
  - Extra-cellular =>
  - Intra-glia =>
- All of the above!
  - And **Exchange**!



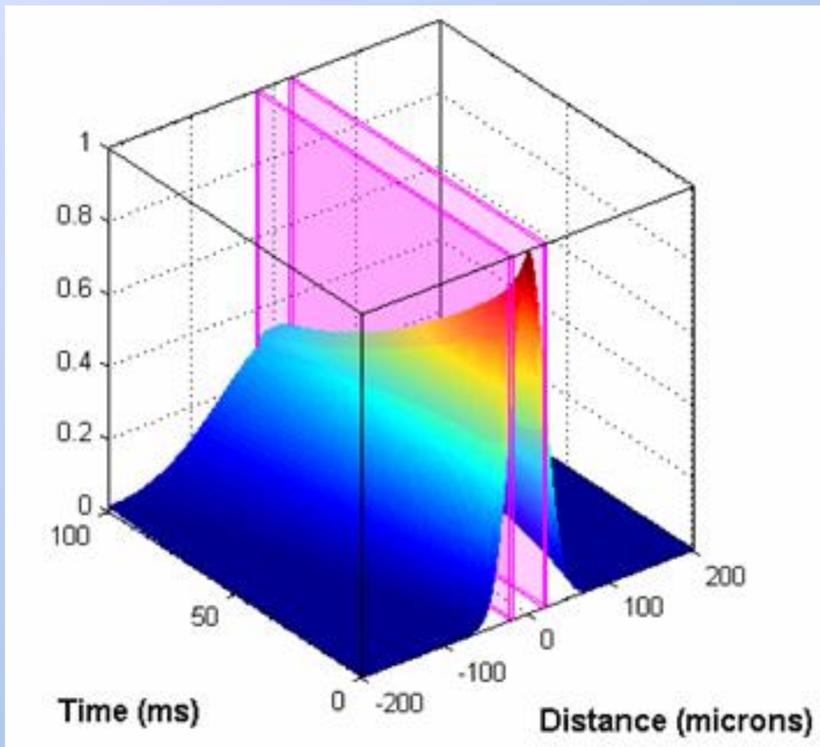
Restricted Diffusion

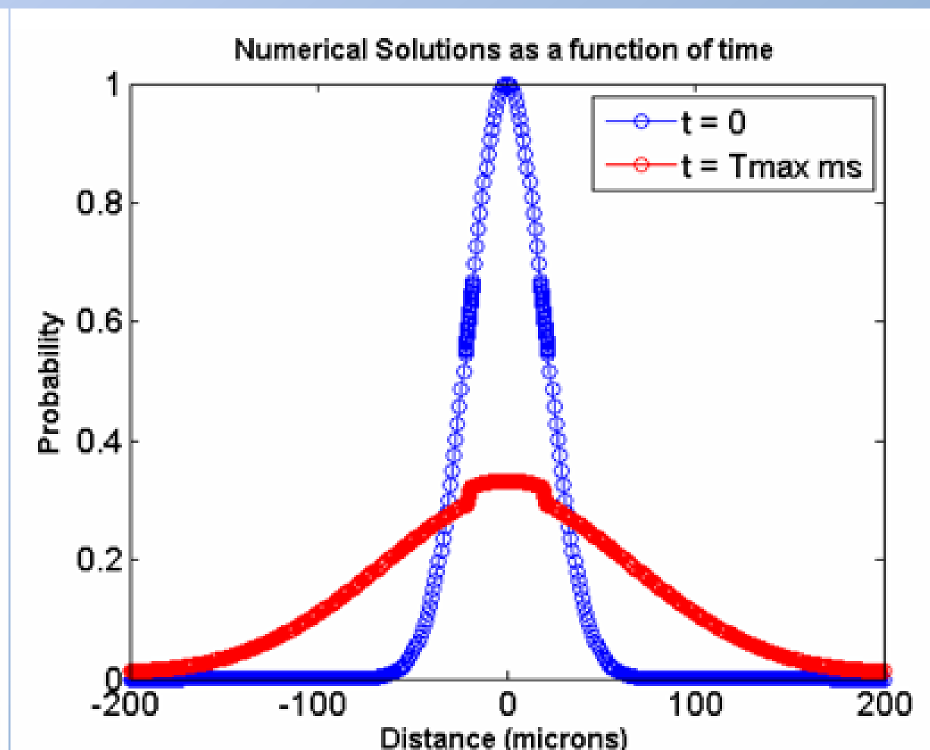
- Approximate a biological fiber as a impermeable cylindrical diffusion barrier
  - Unrestricted diffusion along the fiber axis
  - Symmetrically restricted diffusion perpendicular to the fiber axis



1-D Diffusion: Restricted

High Permeability Membranes

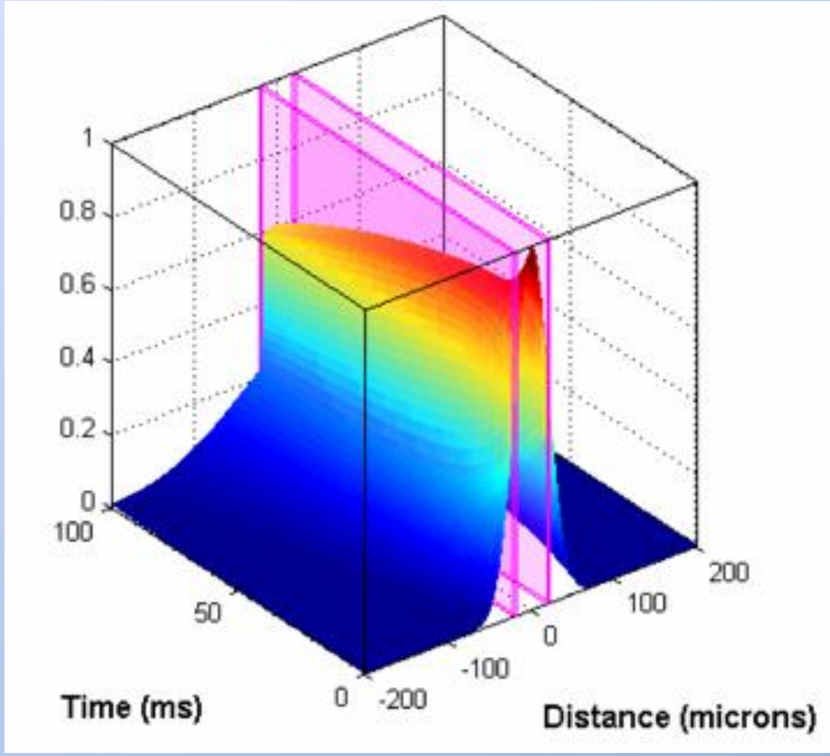


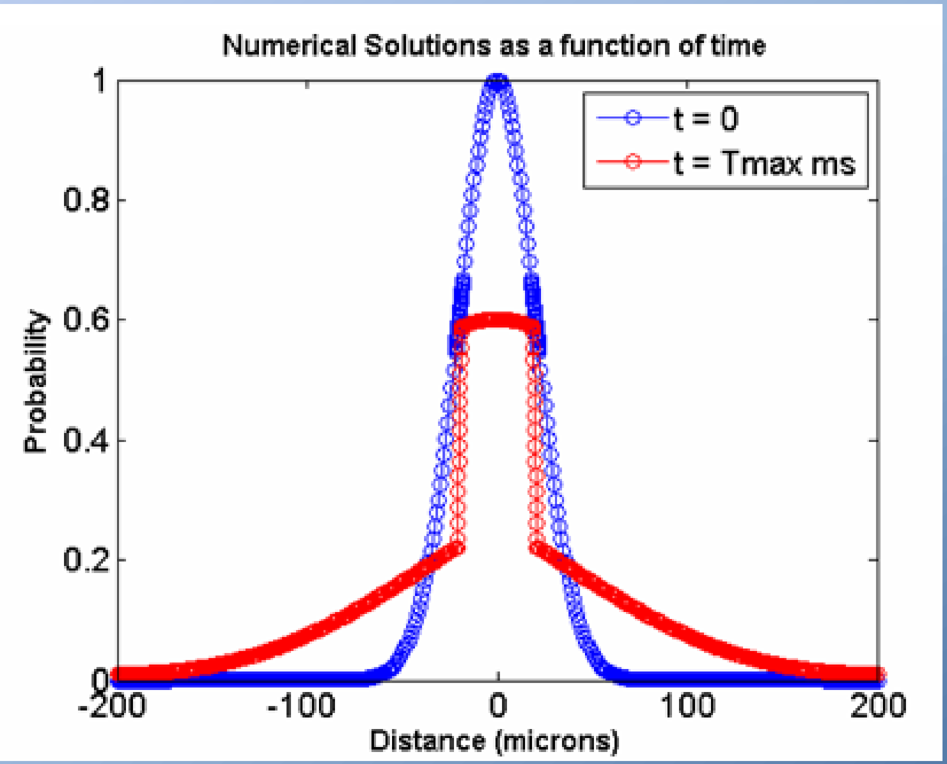


Jonathan Farrell

1-D Restricted Diffusion

Low Permeability Membranes





Jonathan Farrell

Diffusion Propagation: q-space

- Probability of spin diffusing distance r in time τ: $P(r,\tau)$ (diffusion propagator)
- PGSE signal: $S(q,\tau) = S_0 \int P(r,\tau)e^{i2\pi qr}dr$

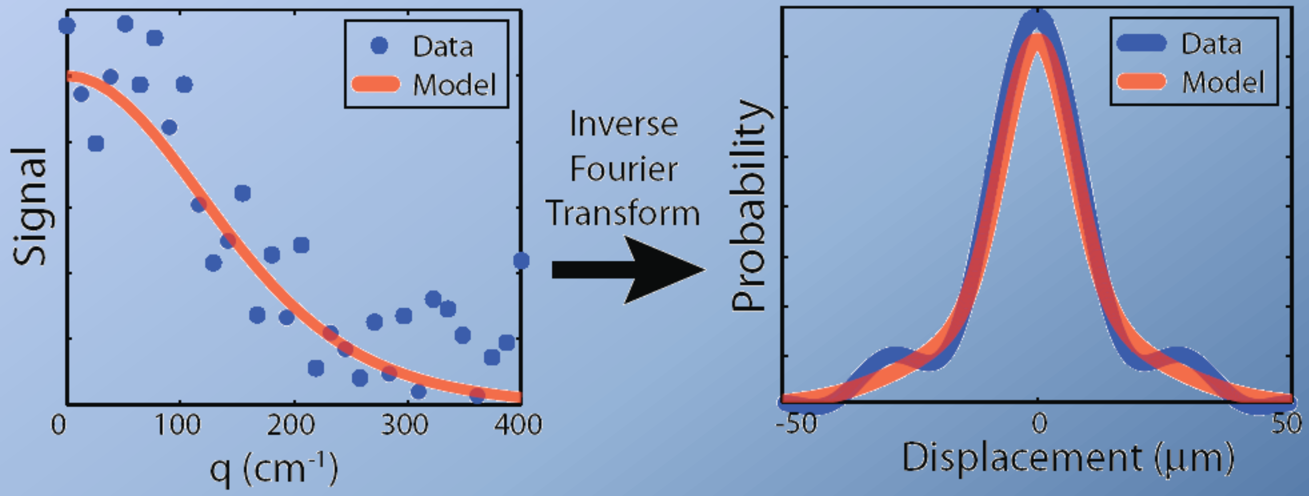
where $b = q^2(\Delta - \delta/3)$

- Estimate $p(r,\tau)$ by observing many $S(q,\tau)$'s and taking the inverse Fourier transform

$$P(r,\tau) = S_0^{-1} \int S(q,\tau)e^{-i2\pi qr}dr$$

1-D Q-space Experiment

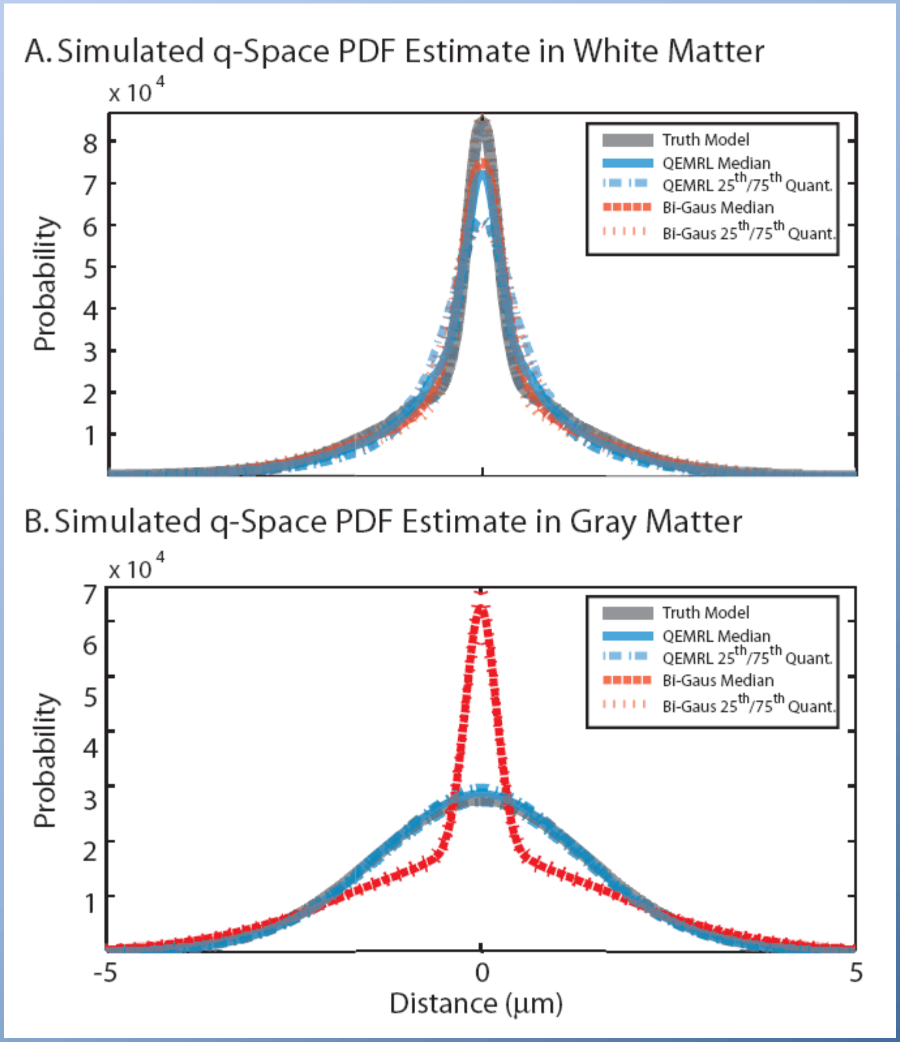
- In practice, we image S(q,τ) at many values of q, i.e. many b-values
- Then fit a smooth curve to the noisy data
- Then take inverse Fourier transform



QEMRL

Landman et al. 2008

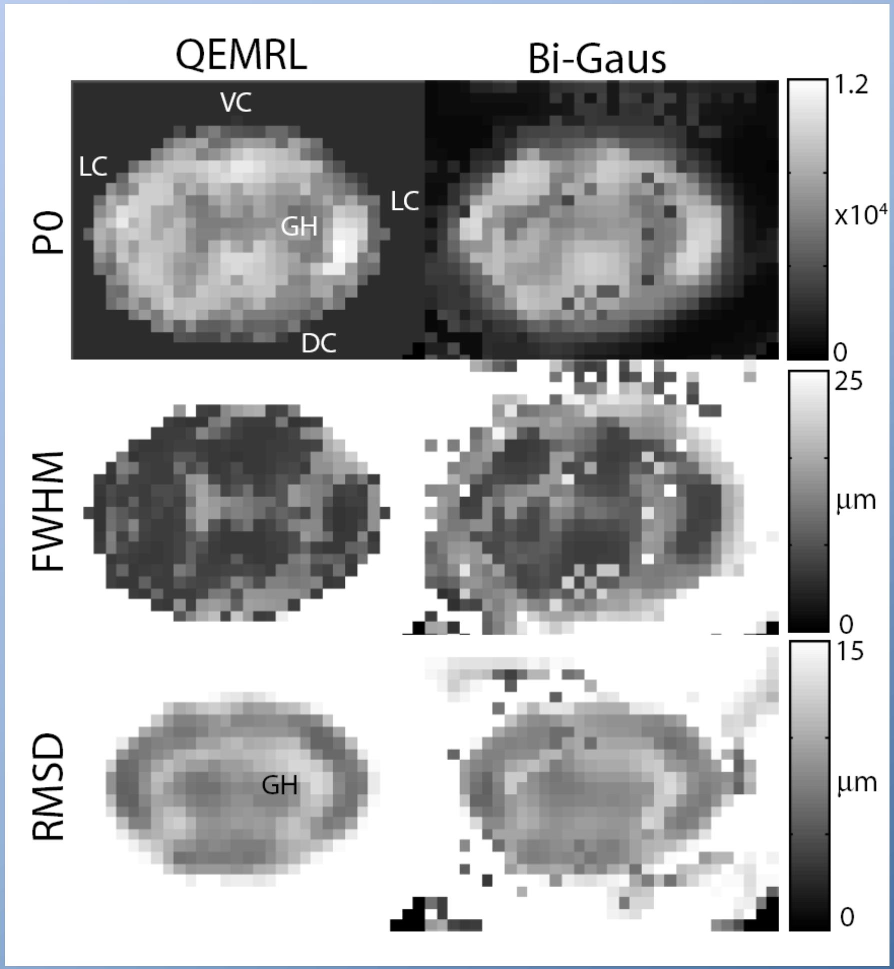
- Q-space Estimation by Maximizing Rician Likelihood (QEMRL)
- Positive mixture of Gaussian functions
- Number determined by L-curve criterion
- Positions and variances estimated



QEMRL in the Spine

Landman et al. 2008

- Cervical spine
- QEMRL vs. Bi-Gaus
- Measure P0, FWHM, RMSD at each pixel
- Increased contrast in
  - GM horns (GH)
  - WM lateral column (LC)
  - WM dorsal column (DC)
  - WM ventral colum (VC)



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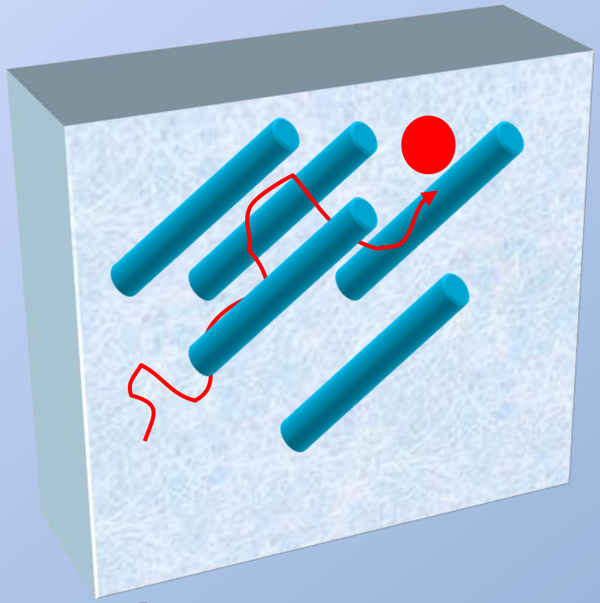
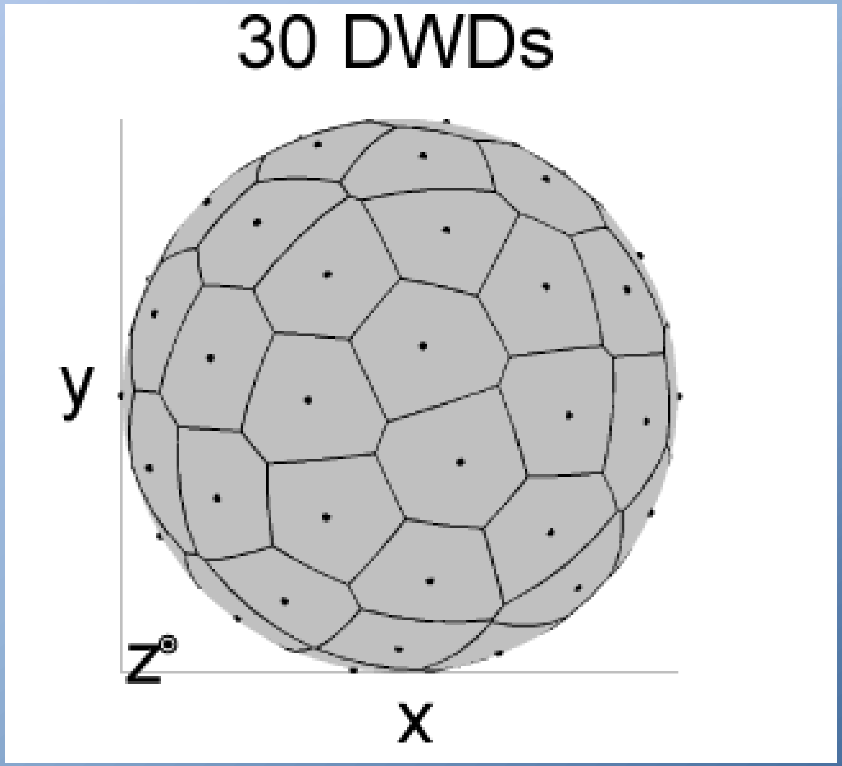
Diffusion Weighted Imaging

- Orientation of anatomy is not known a priori

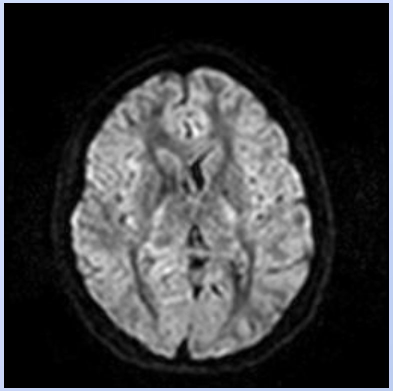


Anatomy

- Acquire DWI's in many directions



PGSE Imaging Equation (Gaussian diffusion)



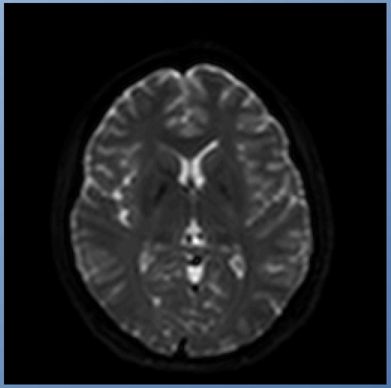
b-value

Diffusion Tensor

$$S(b, \mathbf{g}) = S_0 e^{-b\mathbf{g}^T \mathbf{D} \mathbf{g}}$$

Gradient Orientation

Signal without diffusion weighting



Note (units: time/length^2) :

$$b = |\mathbf{q}|^2 \Delta$$

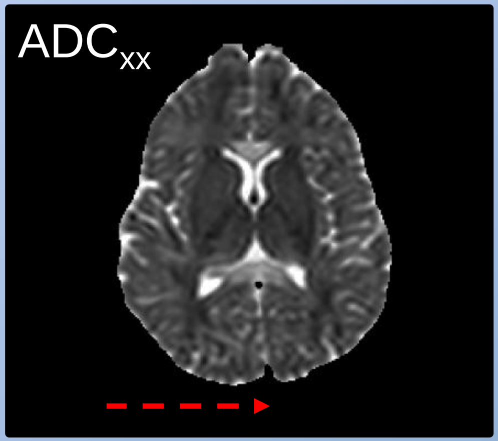
Estimating Diffusivity

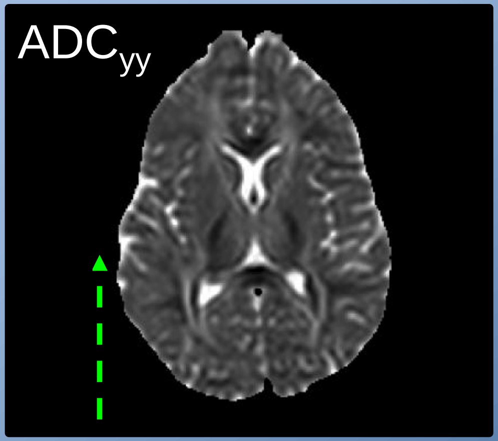
Signal attenuation

$$S(b, \mathbf{g})/S_0 = E(b, \mathbf{g}) = e^{-b\mathbf{g}^T\mathbf{D}\mathbf{g}}$$

$$\ln E(b, \mathbf{g}) = -b\mathrm{ADC}_{\mathbf{g}}$$

$$-(b^{-1}) \ln E(b, \mathbf{g}) = \mathrm{ADC}_{\mathbf{g}}$$





Estimating Tensors

- Relation of ADC to tensor elements

$$\begin{aligned}\mathrm{ADC}_{\mathbf{g}} &= \mathbf{g}^T \mathbf{D} \mathbf{g} \\ &= [g_x^2\, g_x g_y\, g_x g_z\, g_y^2\, g_y g_z\, g_z^2][D_{xx}\, D_{xy}\, D_{xz}\, D_{yy}\, D_{yz}\, D_{zz}]^T \\ &= \mathbf{G}_g [D_{xx}\, D_{xy}\, D_{xz}\, D_{yy}\, D_{yz}\, D_{zz}]^T\end{aligned}$$

- Least squares estimate:

$$[\hat{D}_{xx}\, \hat{D}_{xy}\, \hat{D}_{xz}\, D_{yy}\, \hat{D}_{yz}\, \hat{D}_{zz}]^T = [\mathbf{G}^T \mathbf{G}]^{-1} \mathbf{G}^T [\mathrm{ADC}]$$

- LMMSE estimate:

$$[\hat{D}_{xx}\, \hat{D}_{xy}\, \hat{D}_{xz}\, D_{yy}\, \hat{D}_{yz}\, \hat{D}_{zz}]^T = [\mathbf{G}^T \Sigma^{-1} \mathbf{G}]^{-1} \mathbf{G}^T \Sigma^{-1} [\mathrm{ADC}]$$

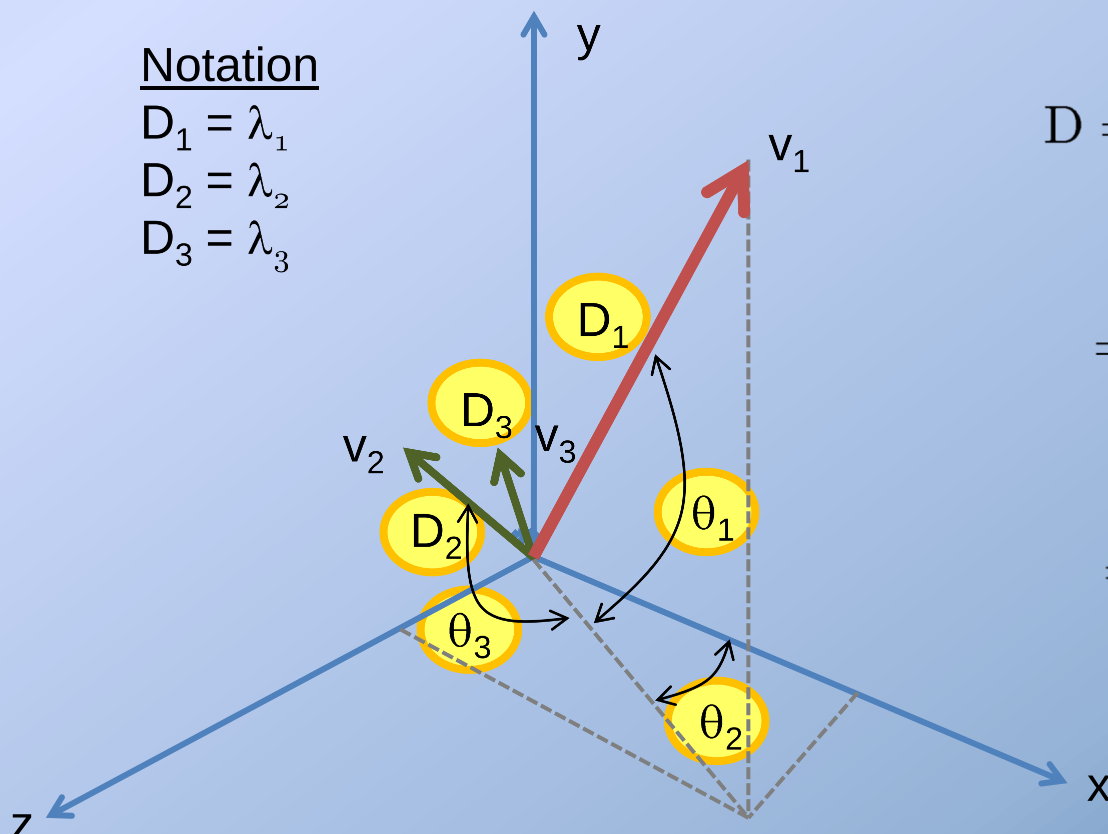
The Tensor Model

Notation

$D_1 = \lambda_1$

$D_2 = \lambda_2$

$D_3 = \lambda_3$



$$\mathrm{D} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{bmatrix}$$

$$= V \begin{bmatrix} \lambda_1 & & \\ & \lambda_2 & \\ & & \lambda_3 \end{bmatrix} V^T$$

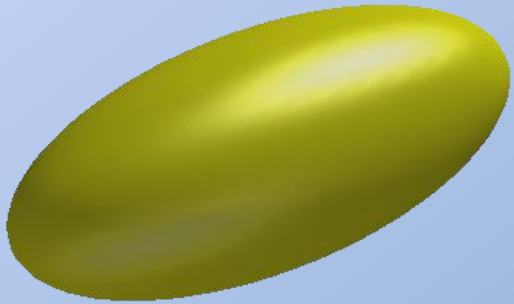
$$= \begin{bmatrix} v_1 & v_2 & v_3 \end{bmatrix} \begin{bmatrix} \lambda_1 & & \\ & \lambda_2 & \\ & & \lambda_3 \end{bmatrix} \begin{bmatrix} v_1 & v_2 & v_3 \end{bmatrix}^T$$

Eigenvalues = Diffusivities
Eigenvectors = Orientation

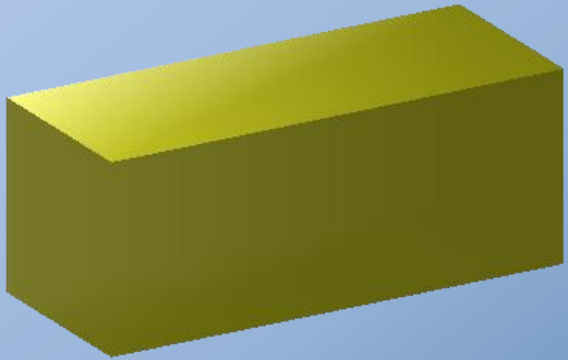
3-D Gaussian Diffusion - Allowing for Anisotropy
6 Degrees of Freedom

Common Tensor Glyphs

Diffusion Peanut
Distance from the origin represents apparent diffusivity in each orientation



Diffusion Ellipsoid
Surface is an isosurface of the probability of diffusion



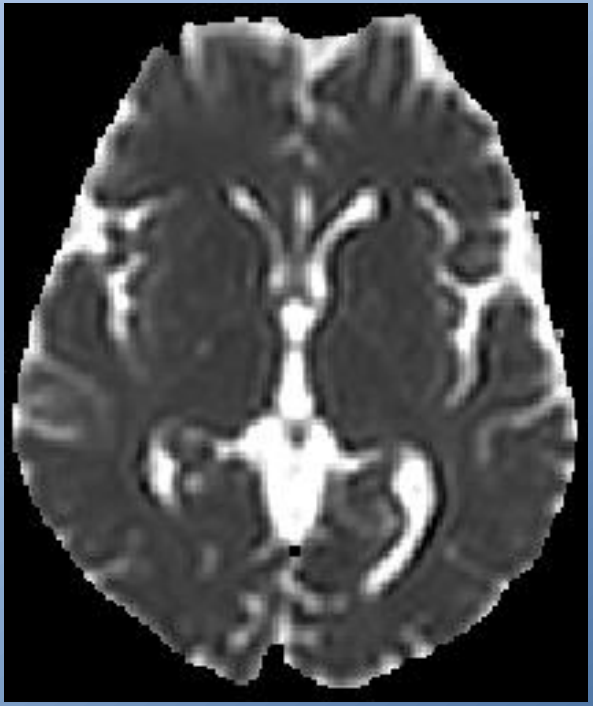
Diffusion Box
Length of edges represents the diffusivity along the principle axes

$$\lambda_1 = 2.5, \lambda_2 = \lambda_3 = 1$$

Mean Diffusivity

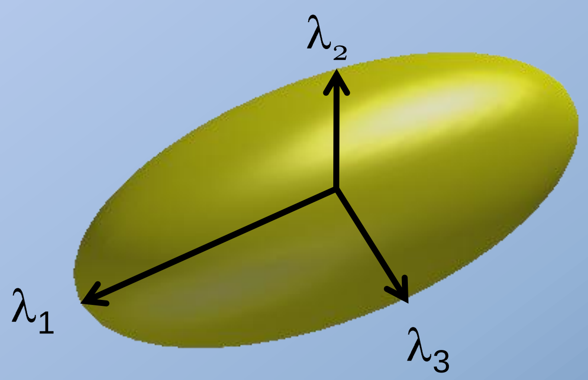
- “Apparent diffusion coefficient” varies by direction: ADC_g
- Need an “invariant” metric
- Solution:
  - Mean Diffusivity
  - Apparent Diffusion Coefficient
  - Tensor Trace

$$\mathrm{ADC} = \mathrm{MD} = \frac{\mathrm{tr}\mathbf{D}}{3} = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3}$$



Anisotropy

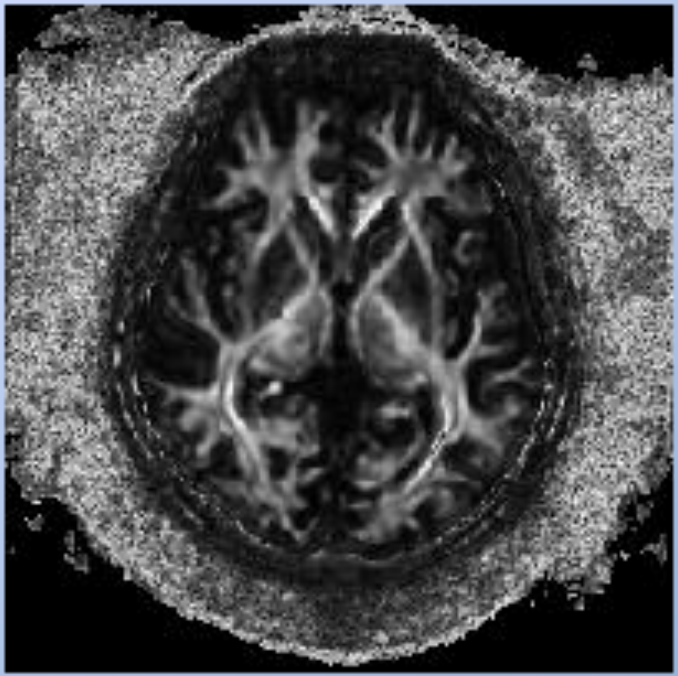
- First Metrics
  - "Ratios" of Eigenvalues
  - Sorting Problem
- Invariant Metrics
  - Fractional Anisotropy
  - Relative Anisotropy
  - Lattice Index



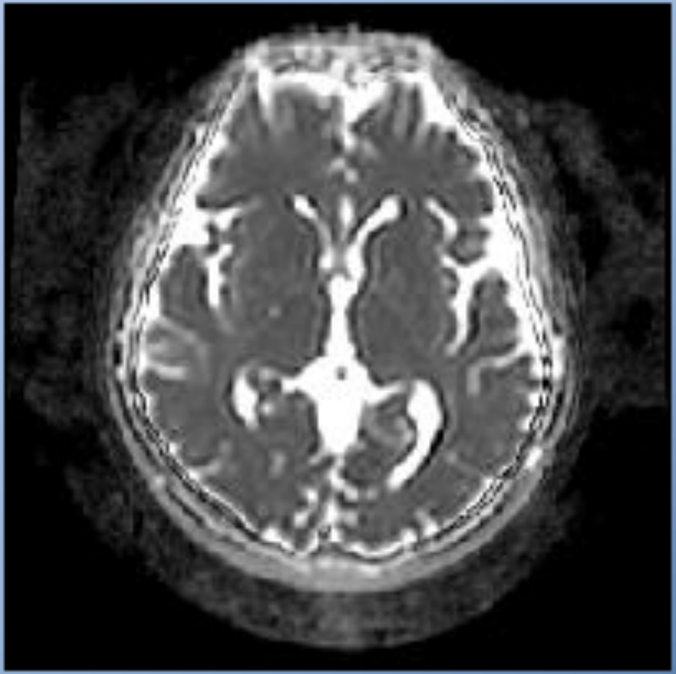
$$\mathrm{FA} = \sqrt{\frac{3}{2}\frac{(\lambda_1-\bar{\lambda})^2+(\lambda_2-\bar{\lambda})^2+(\lambda_3-\bar{\lambda})^2}{\lambda_1^2+\lambda_2^2+\lambda_3^2}}$$

Clinical Contrasts

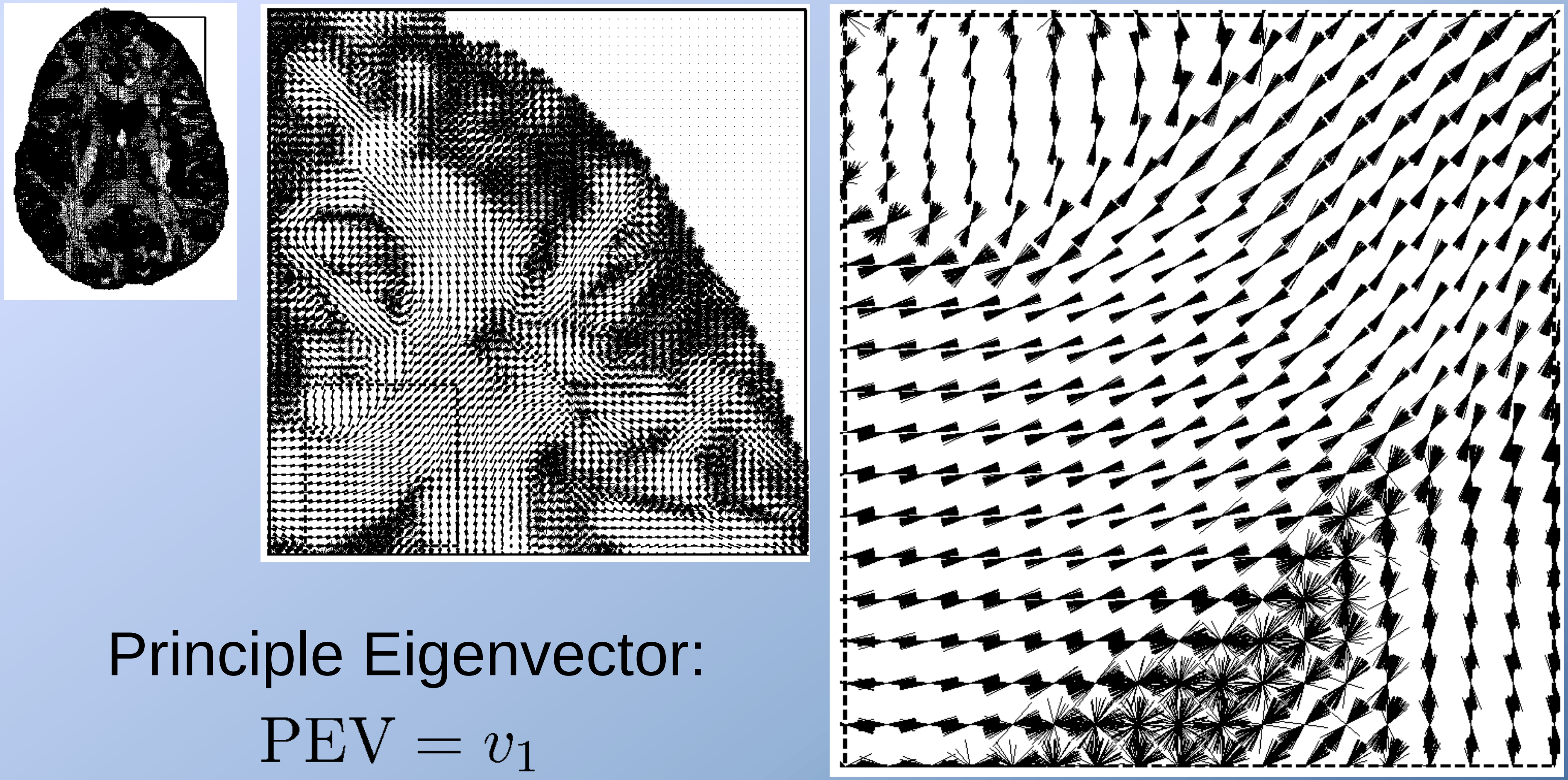
FA
Fractional Anisotropy



MD (ADC)
Mean Diffusivity



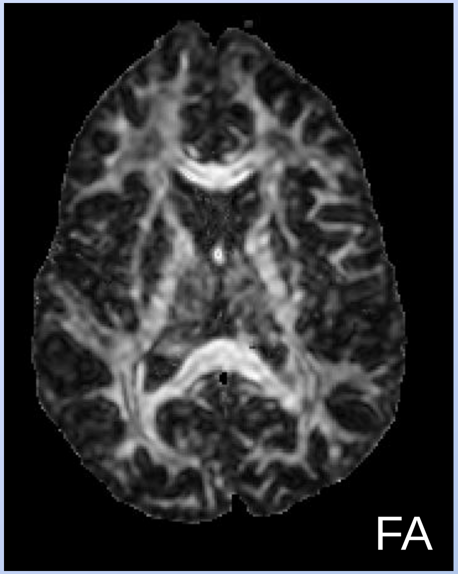
Orientation



Principle Eigenvector:

$$\mathrm{PEV} = v_1$$

DTI Colormap Images



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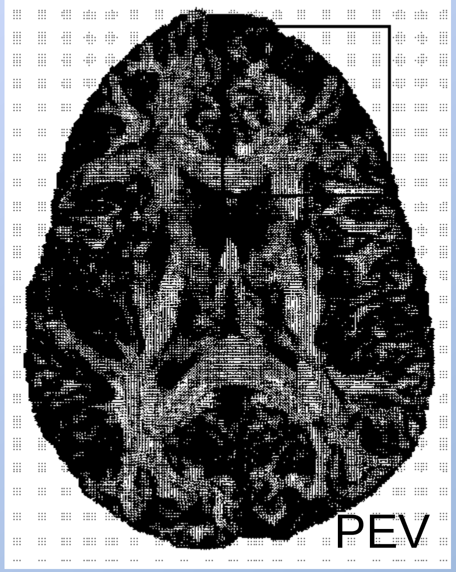

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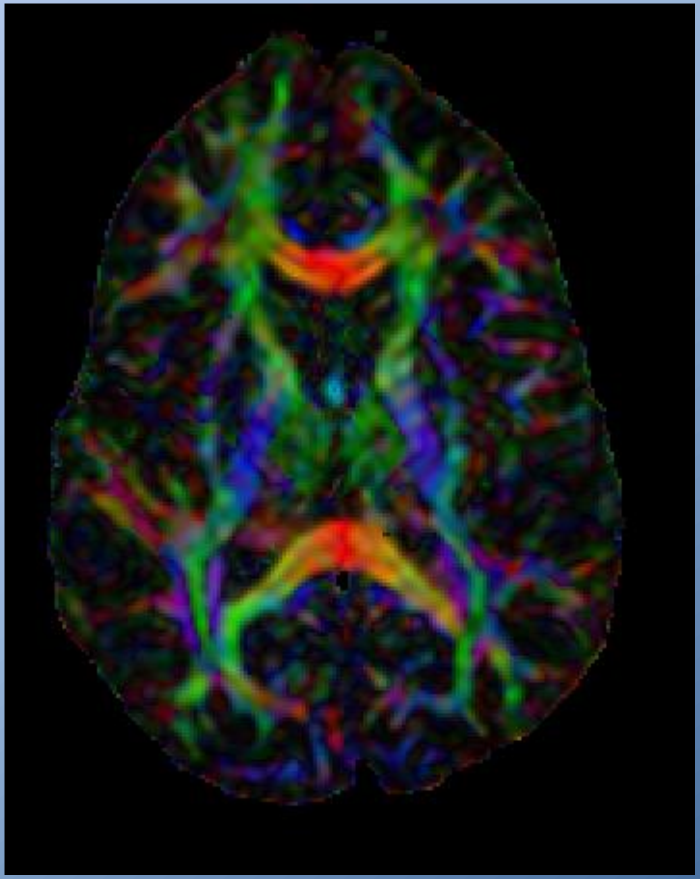


- Pure red: left to right
- Pure green: front to back
- Pure blue: head to foot
- Colors blended by direction
- Intensity multiplied by FA

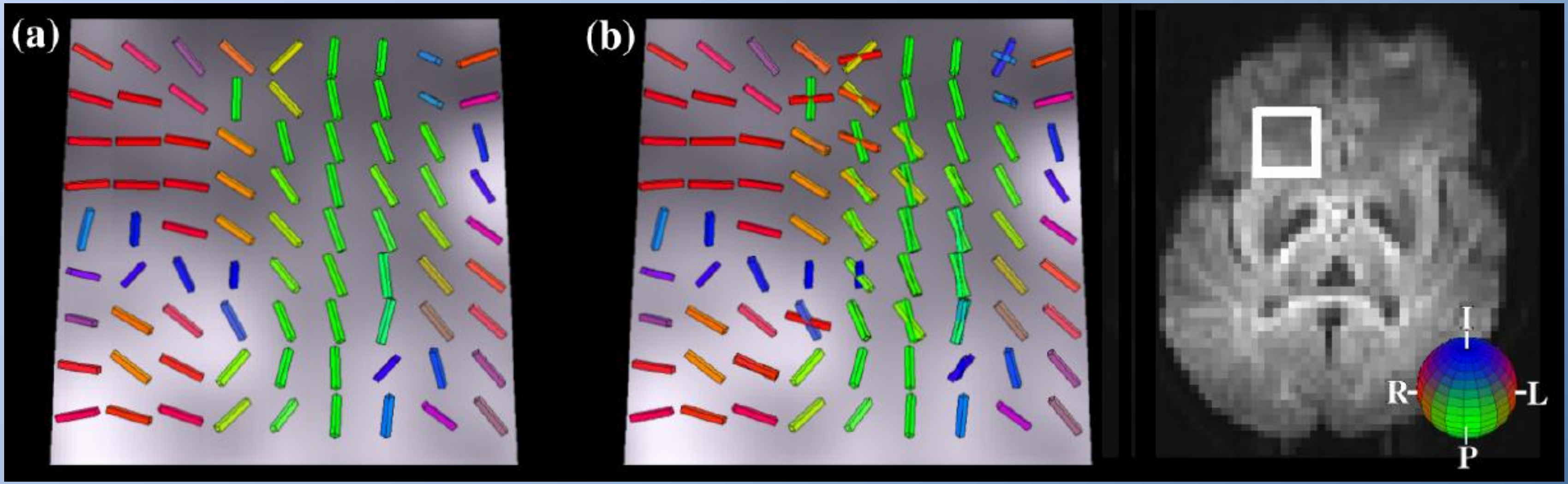
Multi-tensor Models

Tuch et al. 2002

- Observed signal ratio:

$$E(b) = \sum_j f_j e^{-b\mathbf{g}_j^T \mathbf{D}_j \mathbf{g}_j}$$

- Solve for tensor coefficients and partial fraction mixture coefficients



Diffusion Spectrum Imaging

Tuch et al. 2002

- Return to q-space

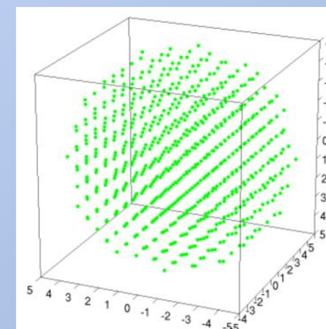
$$E(\mathbf{q},\tau) = \mathcal{F}\{P(\mathbf{R},\tau)\}$$

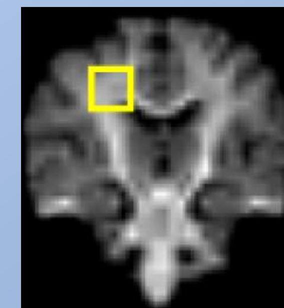
- Sample *many* q's and reconstruct

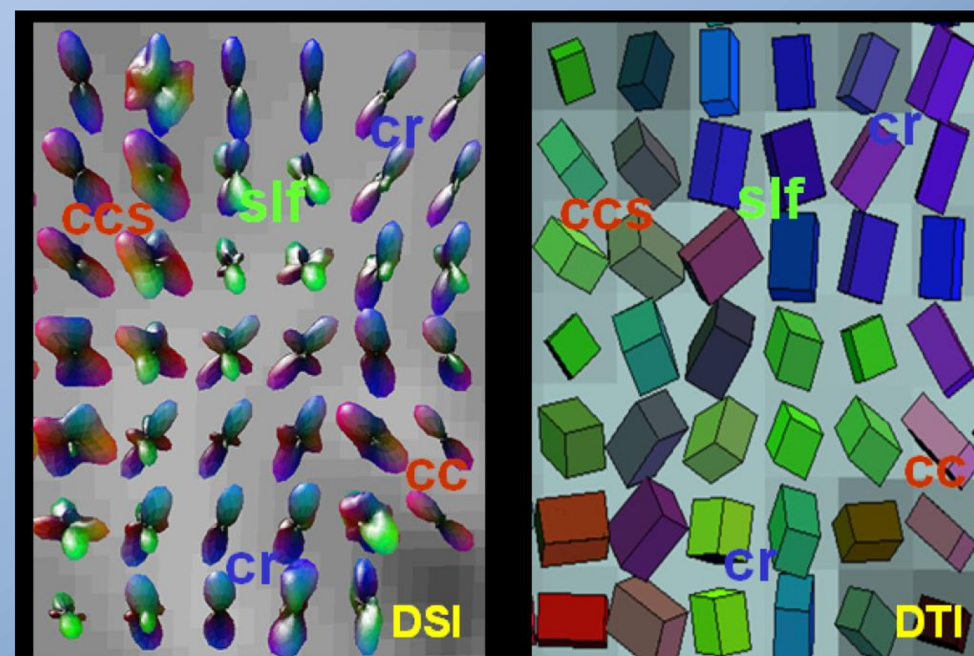
$$P(\mathbf{R},\tau) = \mathcal{F}^{-1}\{E(\mathbf{q},\tau)\}$$

- Project to the sphere yields orientation distribution function

$$\psi(\mathbf{u}) = \int_0^\infty P(\rho\mathbf{u},\tau)d\rho$$







Q-Ball Imaging

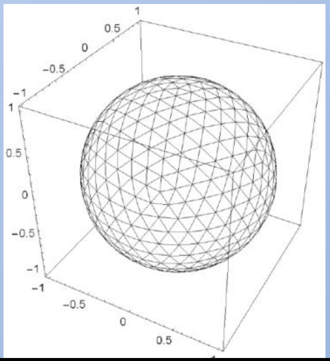
Tuch et al. 2002

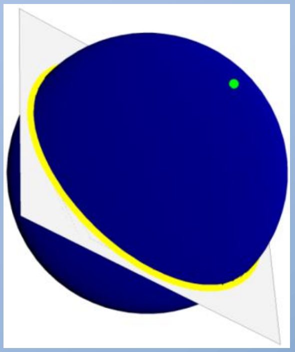
- Return to q-space

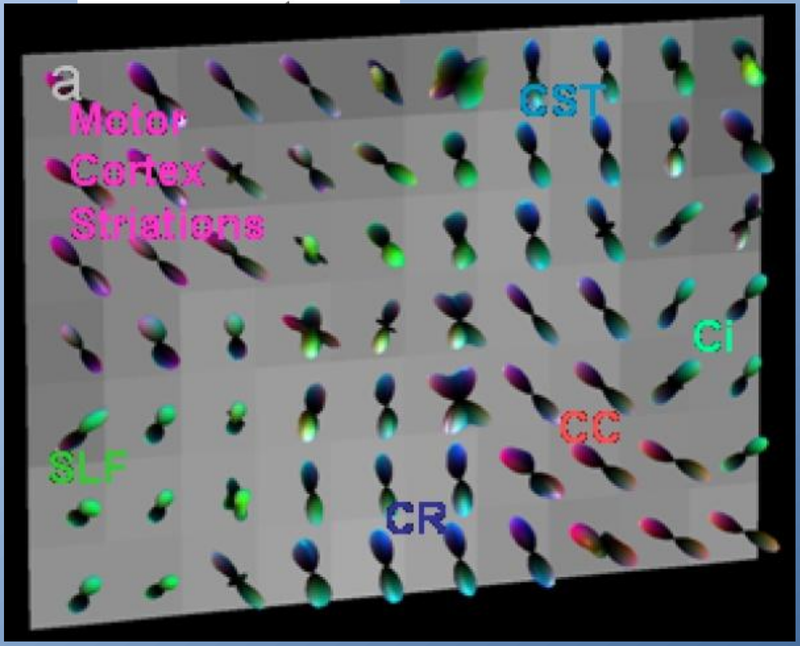
$$E(\mathbf{q},\tau) = \mathcal{F}\{P(\mathbf{R},\tau)\}$$

- Sample *many* q's on spherical shell
- Take the Funk transform; yields approximation of the ODF

$$\tilde{\psi}(\mathbf{u}) = \mathcal{G}[E(\mathbf{q},\tau)](\mathbf{u})$$



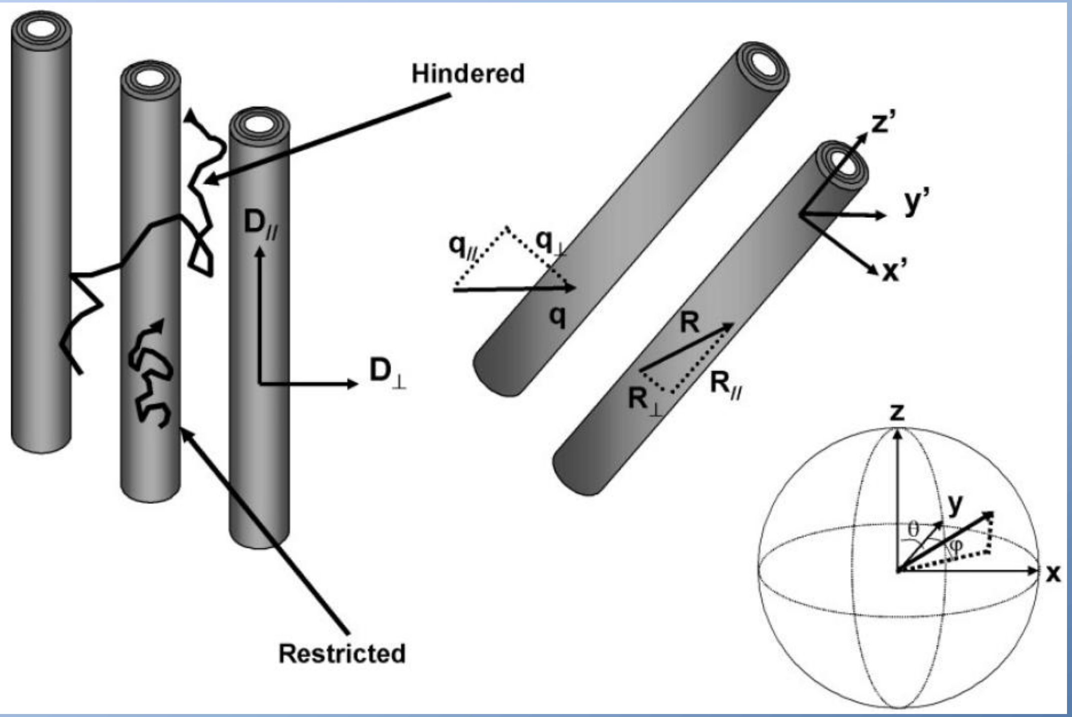




Hindered and Restricted Model of Diffusion

Assaf et al. 2004

- Q-space methods are model-free → do not relate explicitly to tissue parameters
- How to relate observed signal to actual tissue parameters?
- Signal attenuation model:



$$E(\mathbf{q},\tau) = \sum_{i=1}^{M} f_h^i E_h^i(\mathbf{q},\tau) + \sum_{j=1}^{N} f_r^j E_r^j(\mathbf{q},\tau)$$

CHARMED

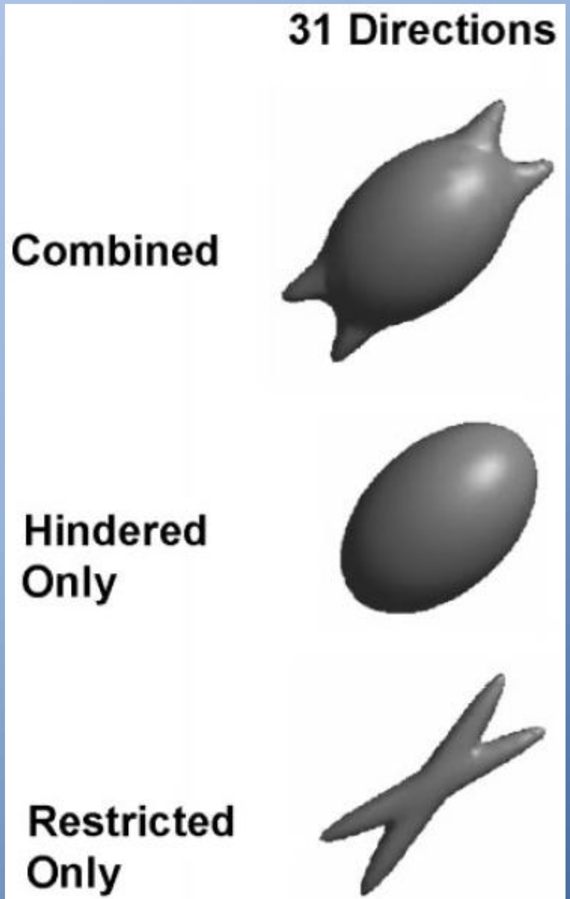
Assaf et al. 2004

- Given observed DWI fit a model to E(q,τ)
- Compute diffusion propagator

$$P(\mathbf{R},\tau) = \mathcal{F}^{-1}\{E(\mathbf{q},\tau)\}$$

- Plot isodiffusion surfaces

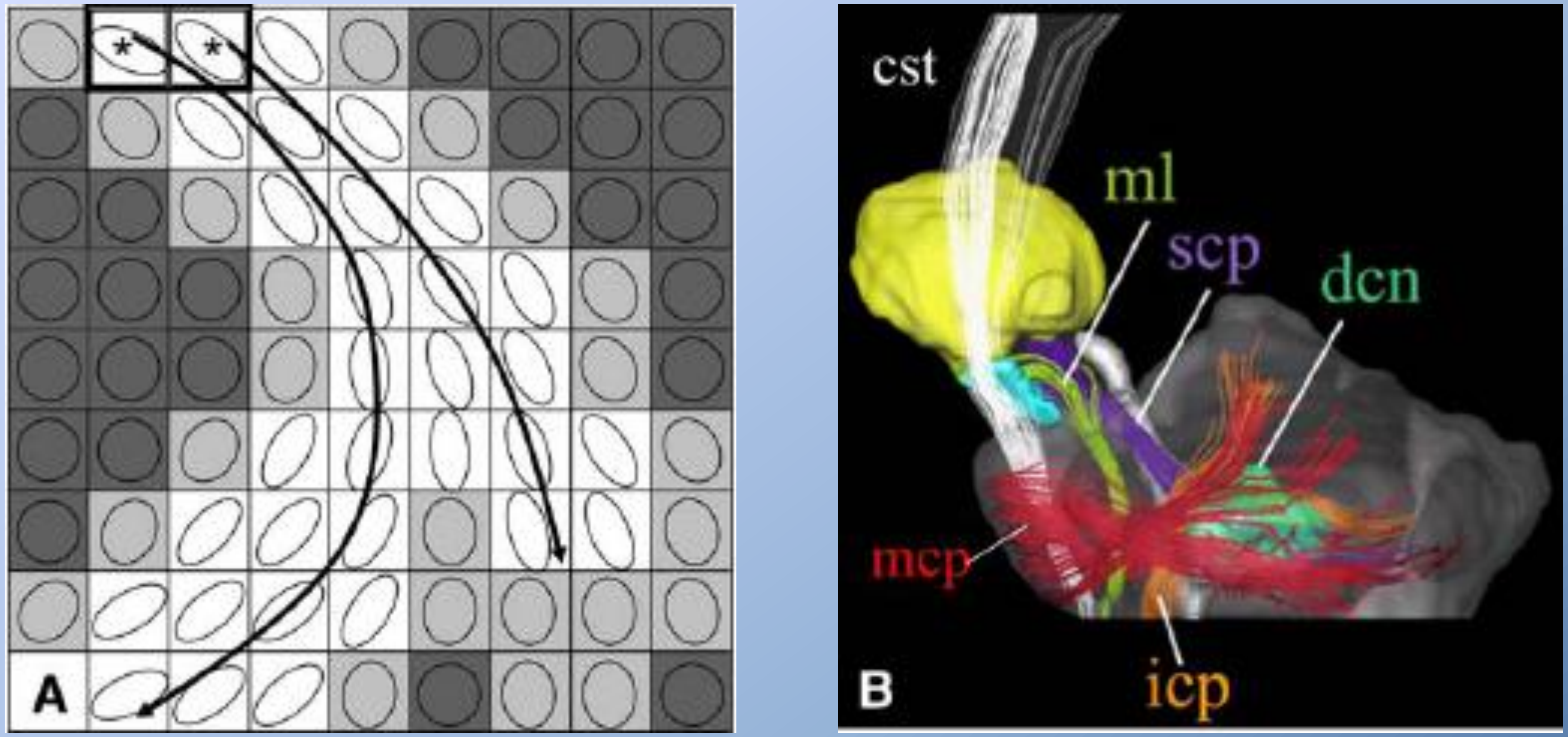
- Example: M=2,N=2; 15 parameters



Outline

- Introduction
- Imaging diffusion using MRI
- Diffusion probability: Q-space
- Diffusion orientation: DTI
- Connecting voxels: Tractography
- Optimization: imaging and processing

Fiber Tracking

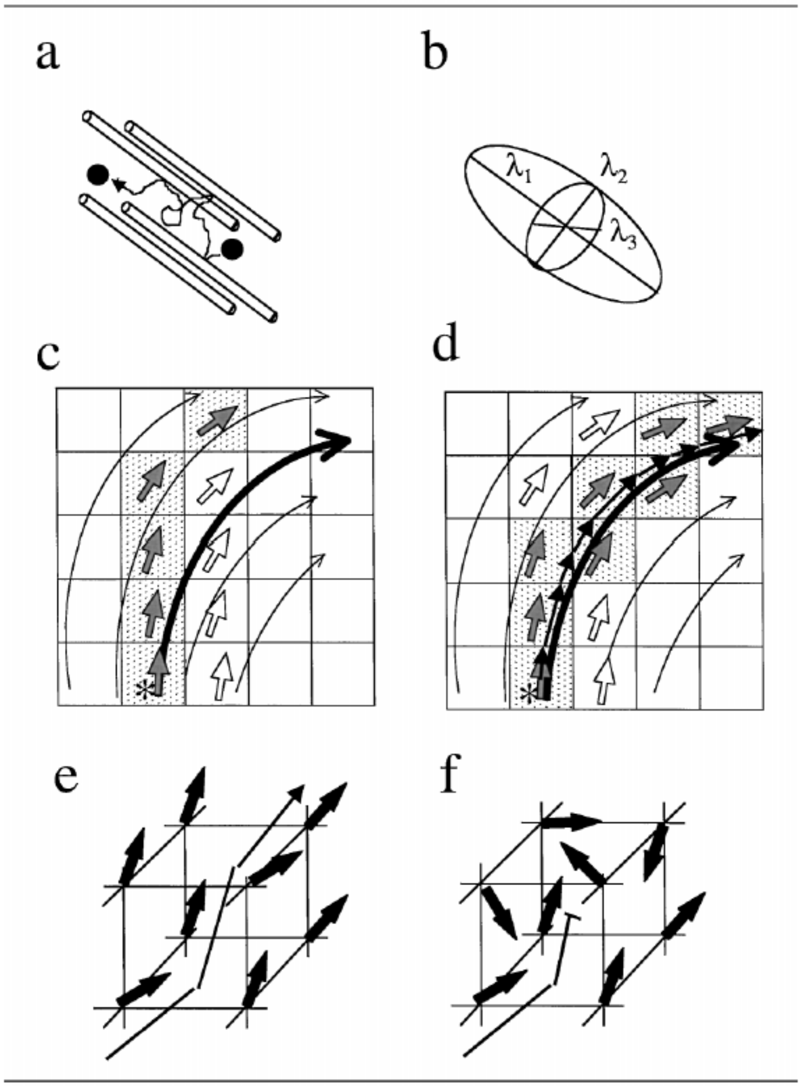


S. Mori and J. Zhang (2006) Principles of Diffusion Tensor Imaging and Its Applications to Basic Neuroscience Research. Neuron 51, 527–539

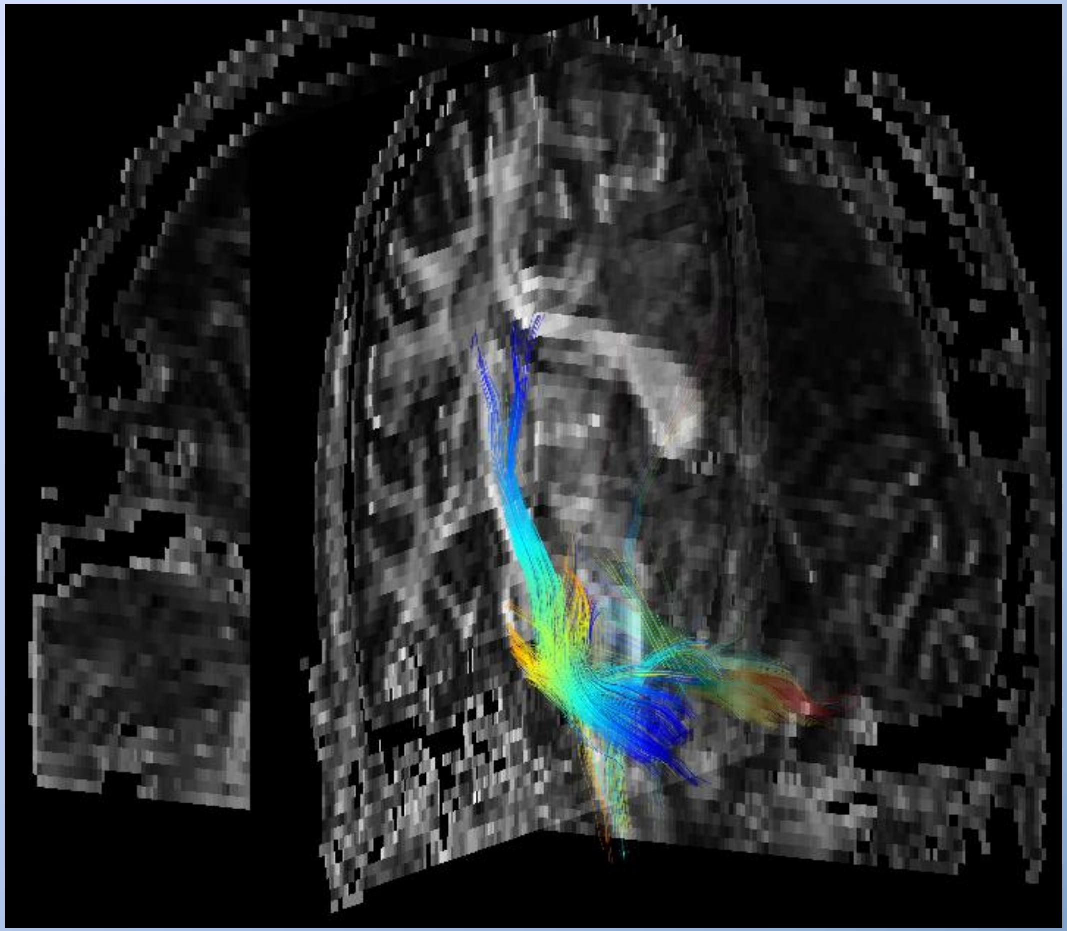
Line Propagation: FACT

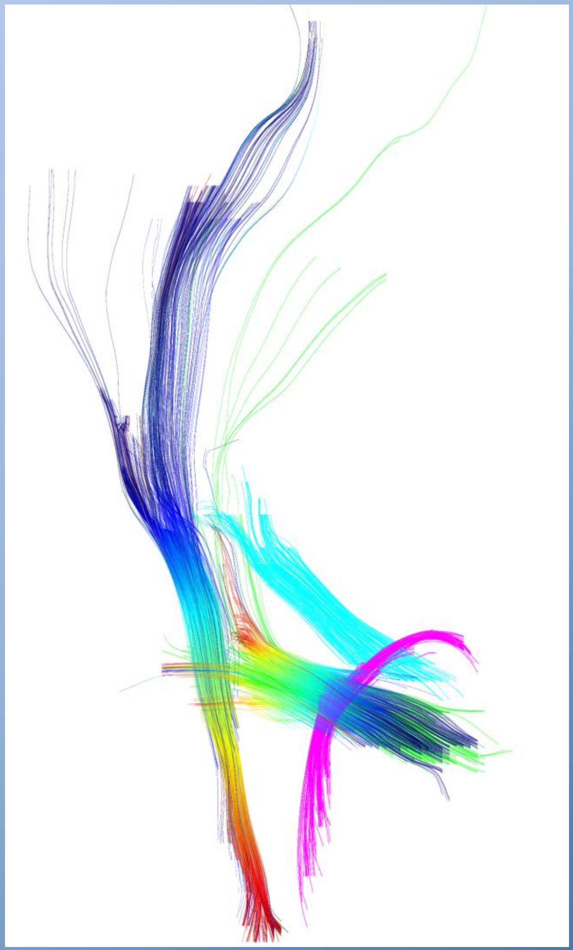
Mori et al., 1999

- Principle eigenvectors define voxel direction
- Seek streamlines through vector field
- Limits/principles:
  - Small steps
  - Tensors interpolated
  - FA > 0.2?
  - Fiber align?
  - Memory or no memory?



Tractography Examples





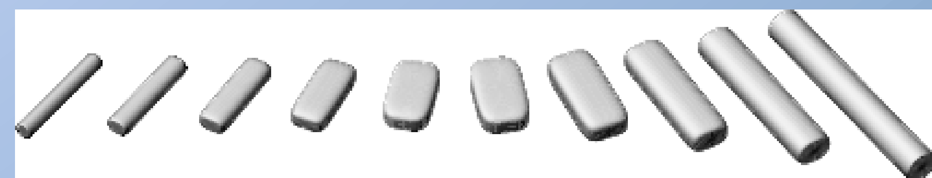
Tensor Interpolation

Linear:

$f\ T_1 + (1-f)\ T_2$

Riemannian:

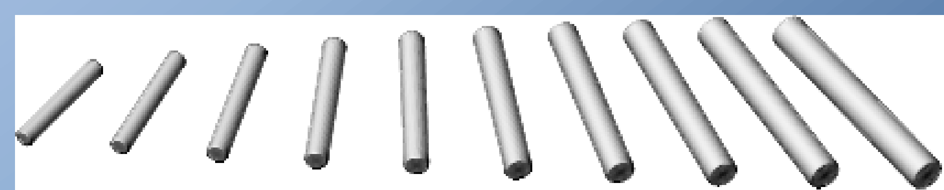
$T_1^{1/2} (T_1^{-1/2} T_2 T_1^{-1/2})^f T_1^{1/2}$



Log-Euclidean:

$\exp[\ f \log(T_1) + (1-f) \log(T_2)]$

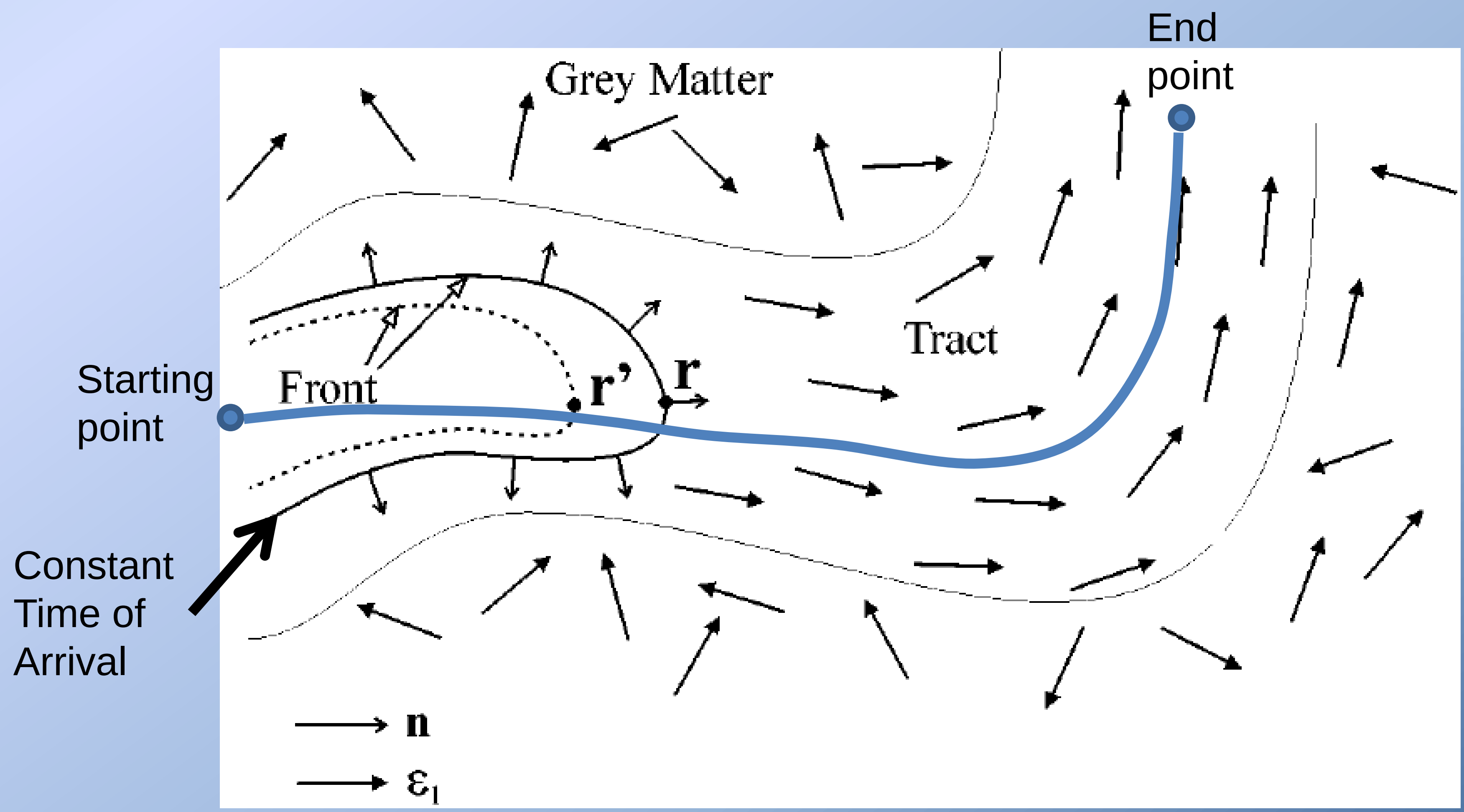
Geodesic-Loxodrome



G. Kindlmann, et. al., (2007) "Geodesic-Loxodromes for Diffusion Tensor Interpolation and Difference Measurement". MICCAI.

Wavefront Tractography

Parker et al., 2002

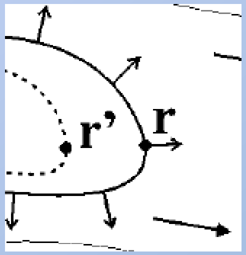


Fast Marching Tractography

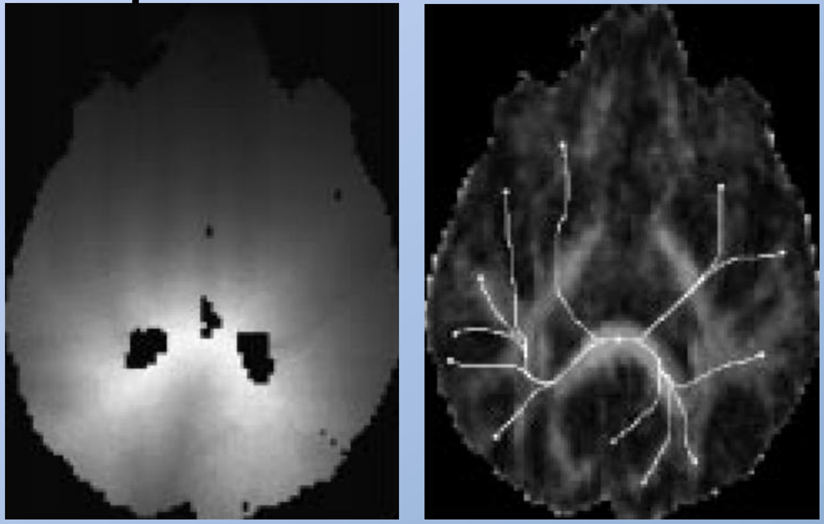
Parker et al., 2002

- Speed function

$$F_2(\mathbf{r}) = \min(F_2(\mathbf{r}'), |\mathbf{e}_1(\mathbf{r}' \cdot \mathbf{n}(\mathbf{r}))$$



- Gradient descent through T yields pathlines



- Connectivity metric

$$\phi_2 = \min_s \left| \frac{\mathbf{x}'(s)}{|\mathbf{x}'(s)|} \cdot \mathbf{e}_1(\mathbf{x}(s)) \right|$$

Optic radiation

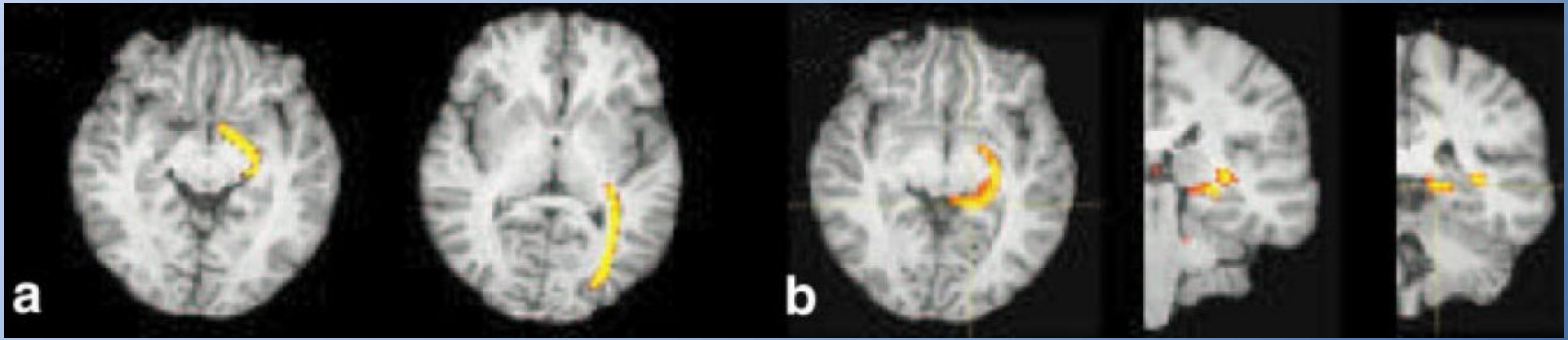
Plot top 1%

Visual cortex

Probabilistic Tractography

Behrens et al., 2003

- Model uncertainties in data and models
  - $(\theta, \phi, \psi, \lambda_1, \lambda_2, \lambda_3, S_0, \sigma)$
- Sample from the model to create fiber probabilities
- Can create connectivity probability matrix



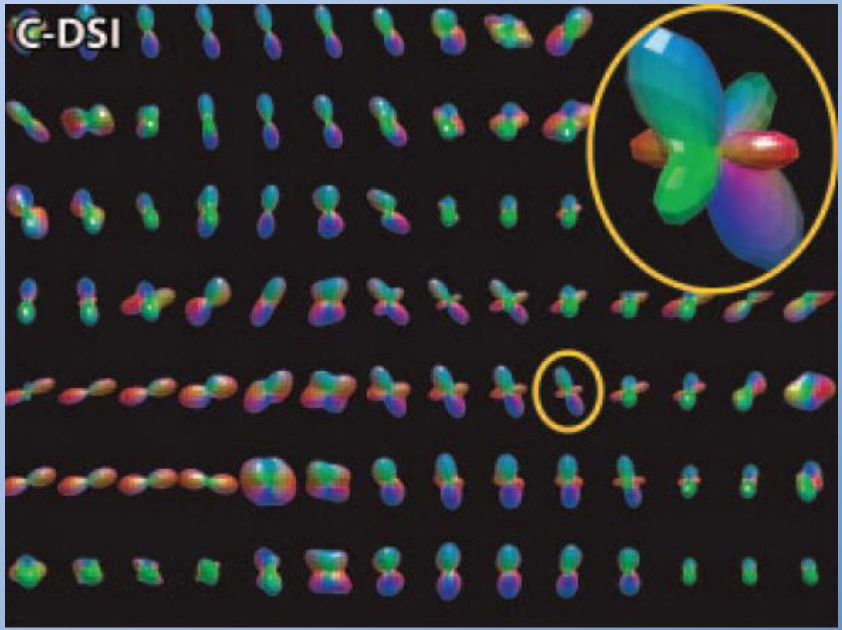
Tracking in DSI and Q-ball

Tuch, 2002

- Start with Orientation Distribution Function (ODF)

$$\psi(\mathbf{x}, \mathbf{u})$$

- Trace the local orientation of the ODF



$$\mathbf{x}(t) = \mathbf{x}(0) + \int_0^t \arg\max_{|\dot{\mathbf{x}}(s)|} \psi(\mathbf{x}(s), |\dot{\mathbf{x}}(s)|)\beta(|\ddot{\mathbf{x}}(s)|)ds$$

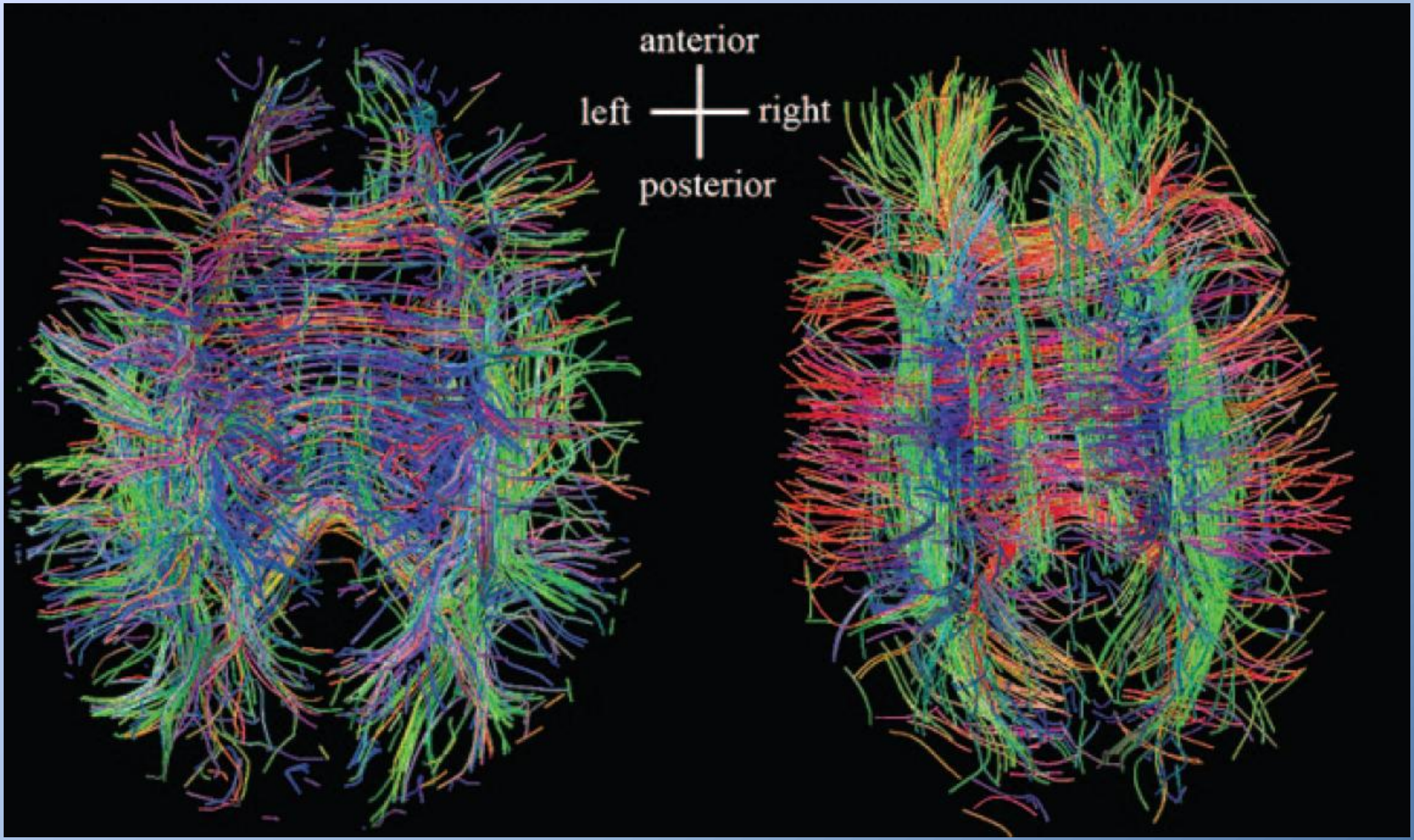
β is a stiffness function, e.g.,

$$\beta(\gamma) = \exp(-\kappa\gamma^2)$$

DTI Versus DSI

Hagmann et al., 2006

DTI DSI

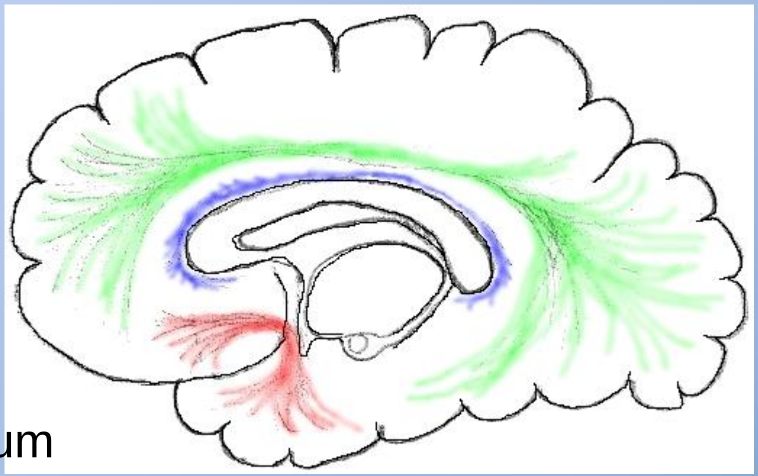


Automatic Tract Labeling

Bogovic et al, 2008

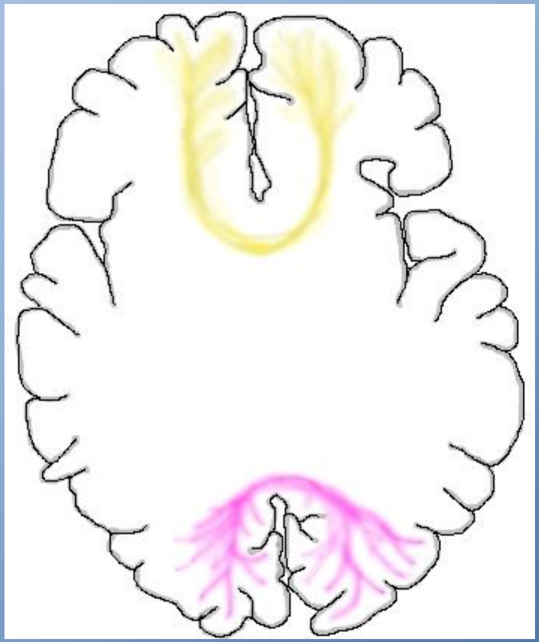
- Reconstruct and label cortex (CRUISE+)
- Find fibers connecting two gyri

Superior longitudinal fasciculus



cingulum

uncinate



Forceps minor

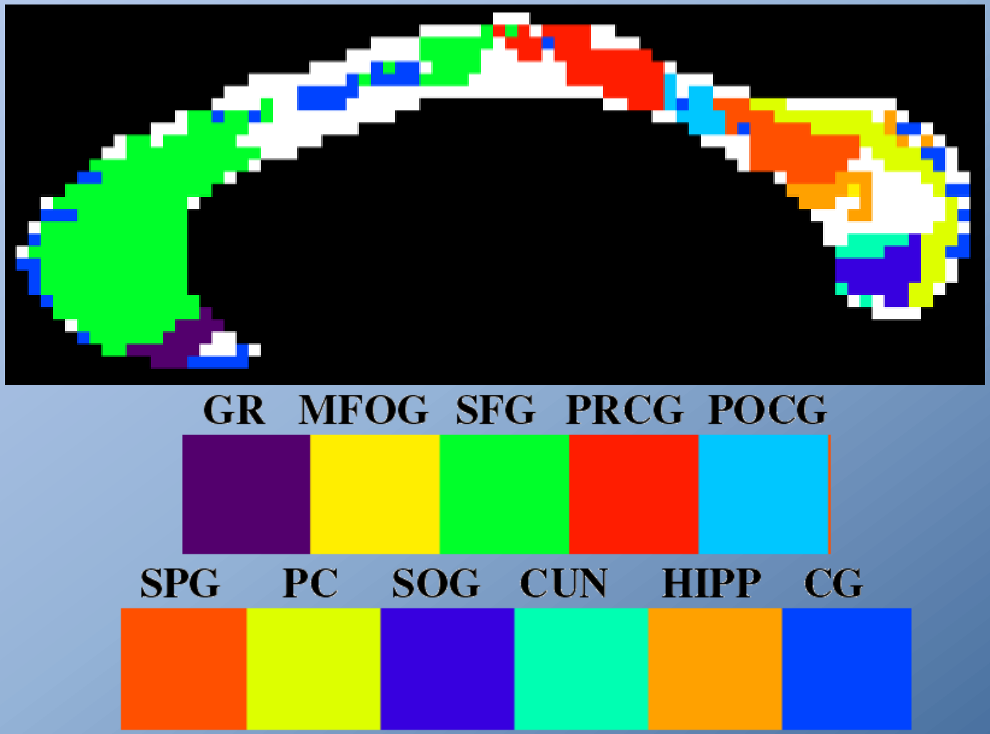
Forceps major

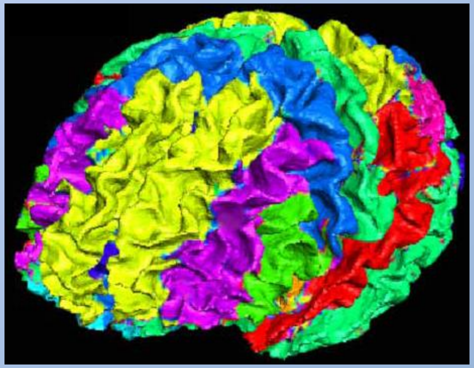
Segment Corpus Callosum

Huang et al., 2006

- Identify contralateral cortico-cortico fibers
- Label where they “hit” the corpus callosum

GR=gyrus rectus
SFG =superior frontal gyrus
PRCG=precentral gyrus
POCG=postcentral gyrus
SPG=superior parietal gyrus
PC=precuneous gyrus
SOG=superior occipital gyrus





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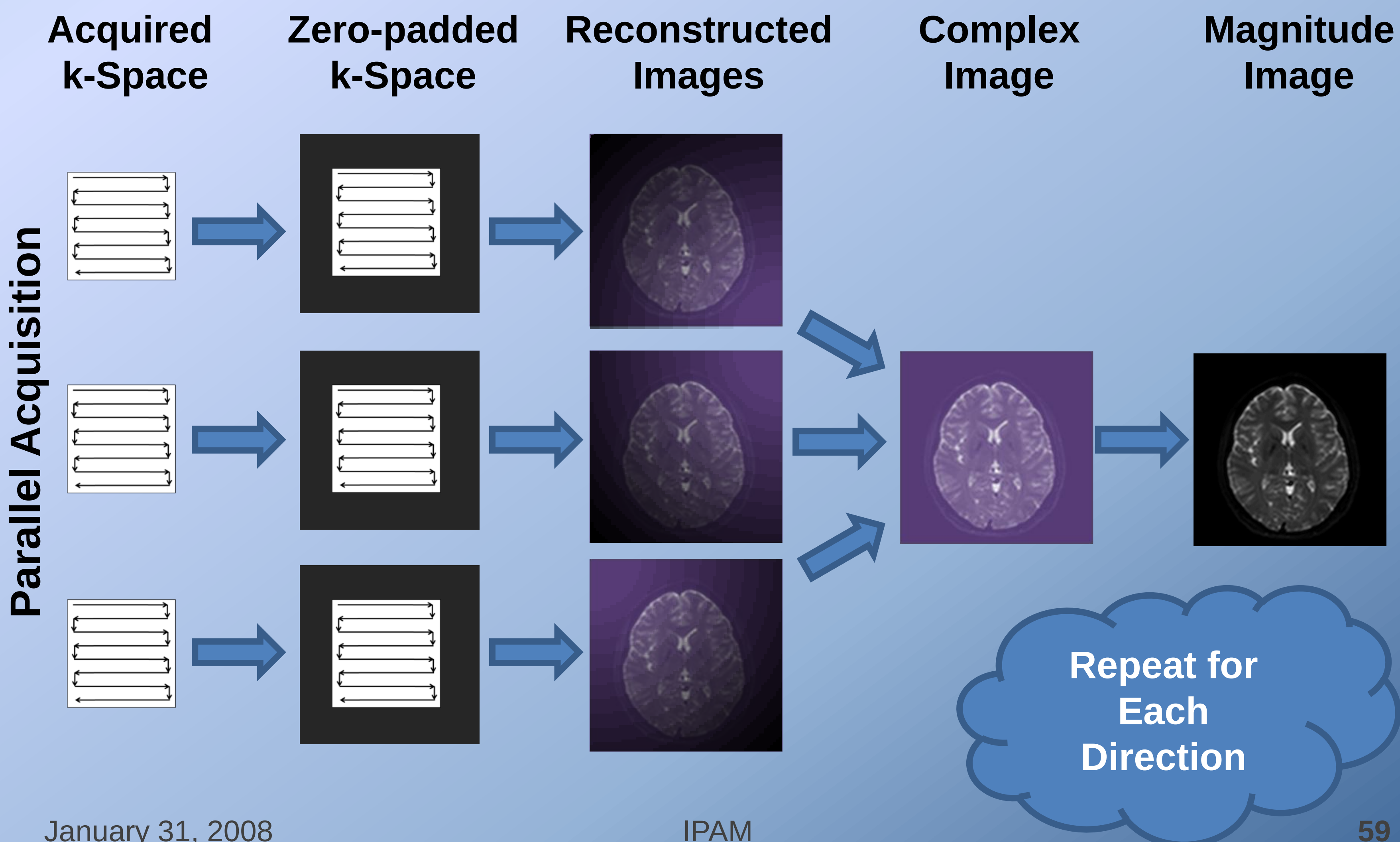
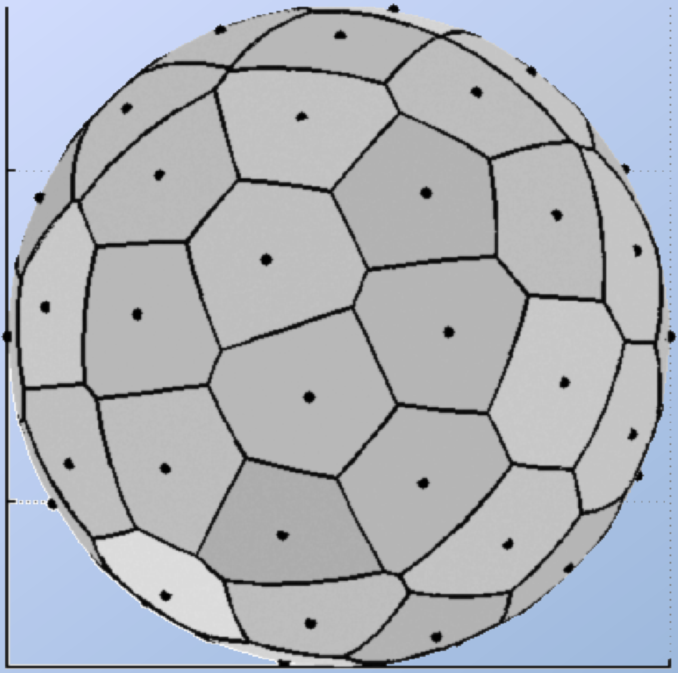
Inside the Scanner

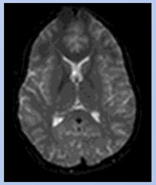


Actual DTI Data

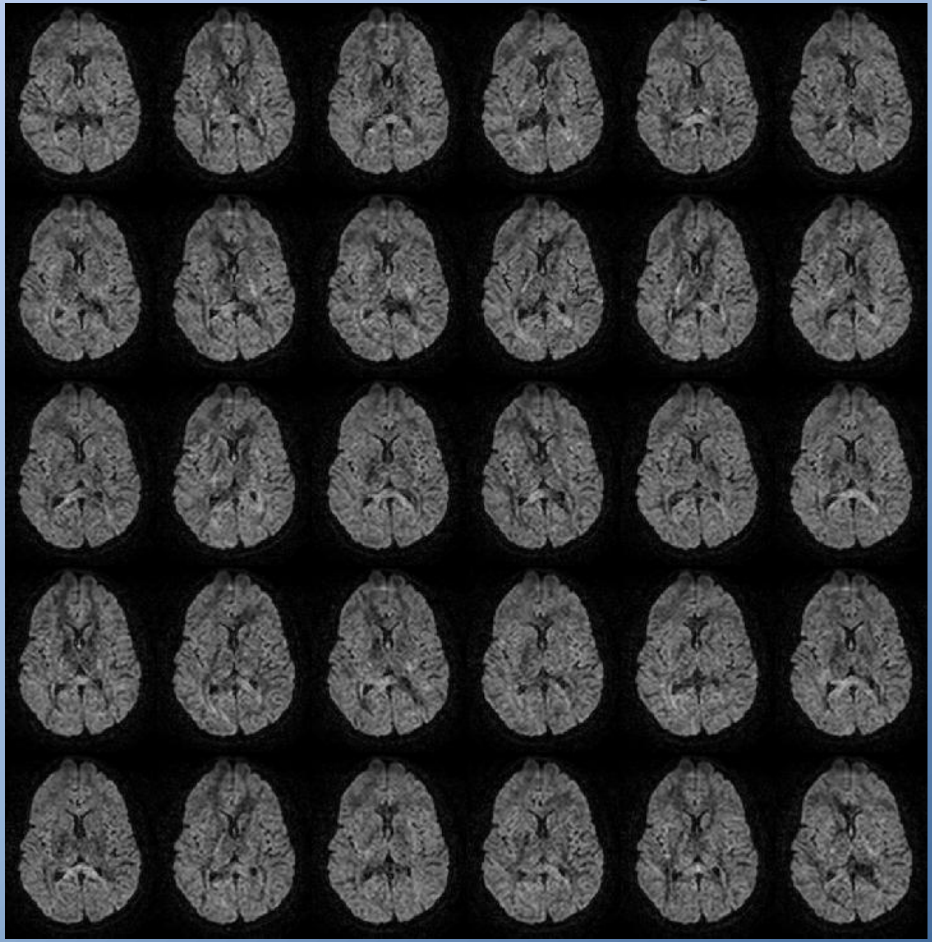
Set of Diffusion Weighting Directions ("scheme")



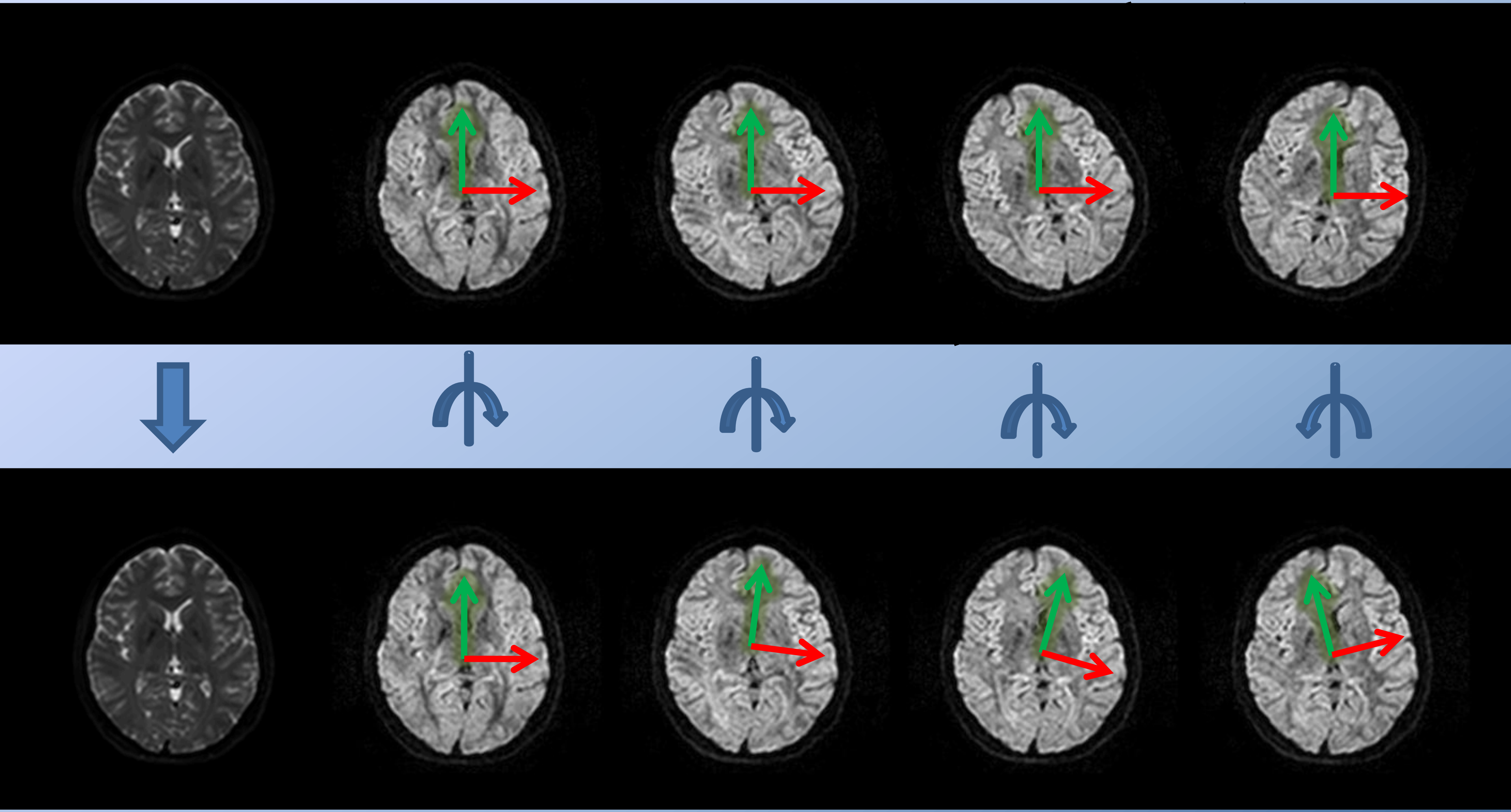
Reference



Diffusion Weighted



Motion Correction



Software: CATNAP

GOAL:

- To simplify and accelerate DTI & anatomical data processing

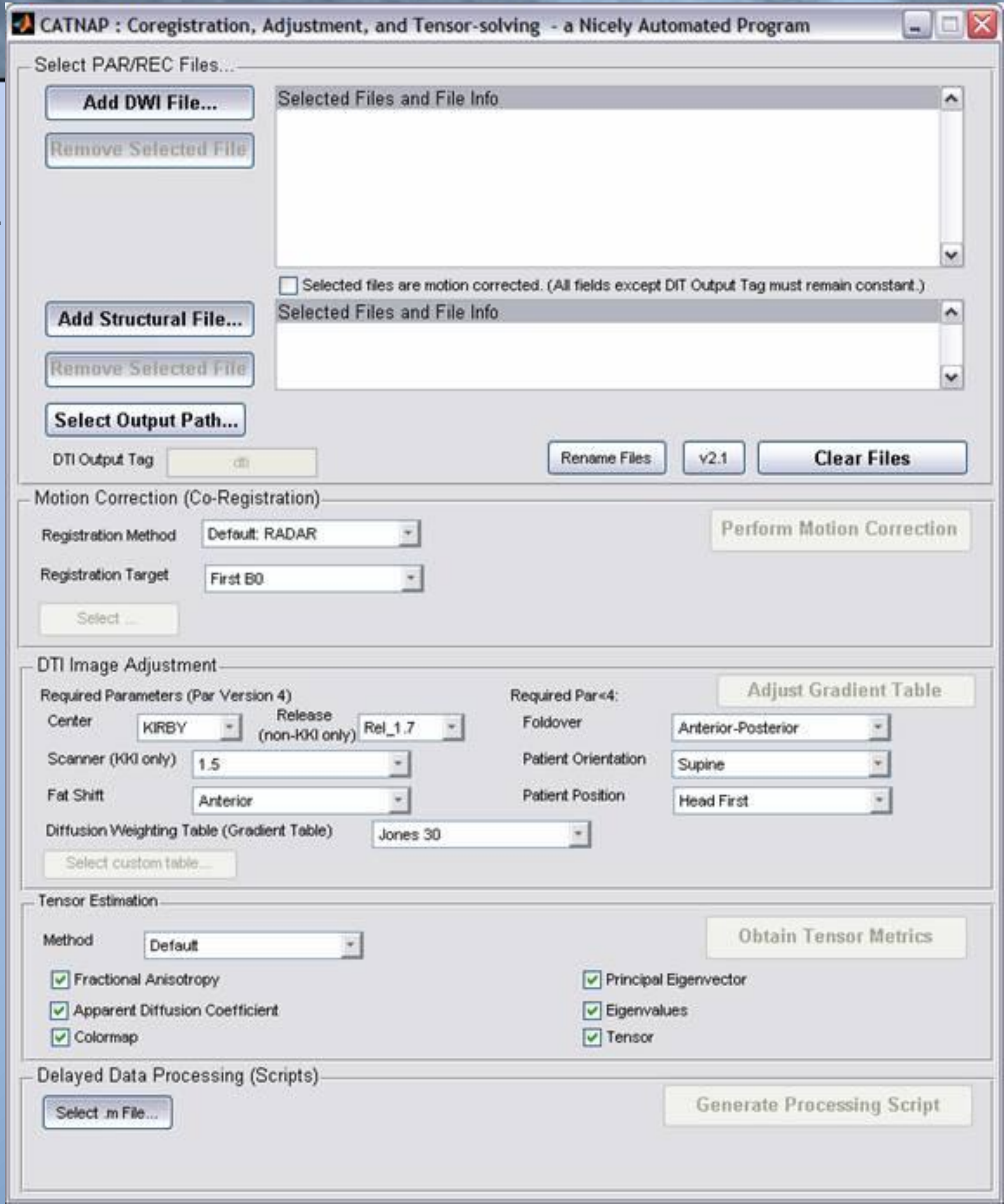
HOW IT WORKS:

- Coregistration with FSL FLIRT
- Computes DTI gradient table
- Computes diffusion tensor and DTI contrasts

DETIALS:

- Runs in MATLAB
- Philips data only (so far)

http://iacl.ece.jhu.edu/~bennett/catnap/



Rician Noise: DTEMRL

Landman et al. 2007

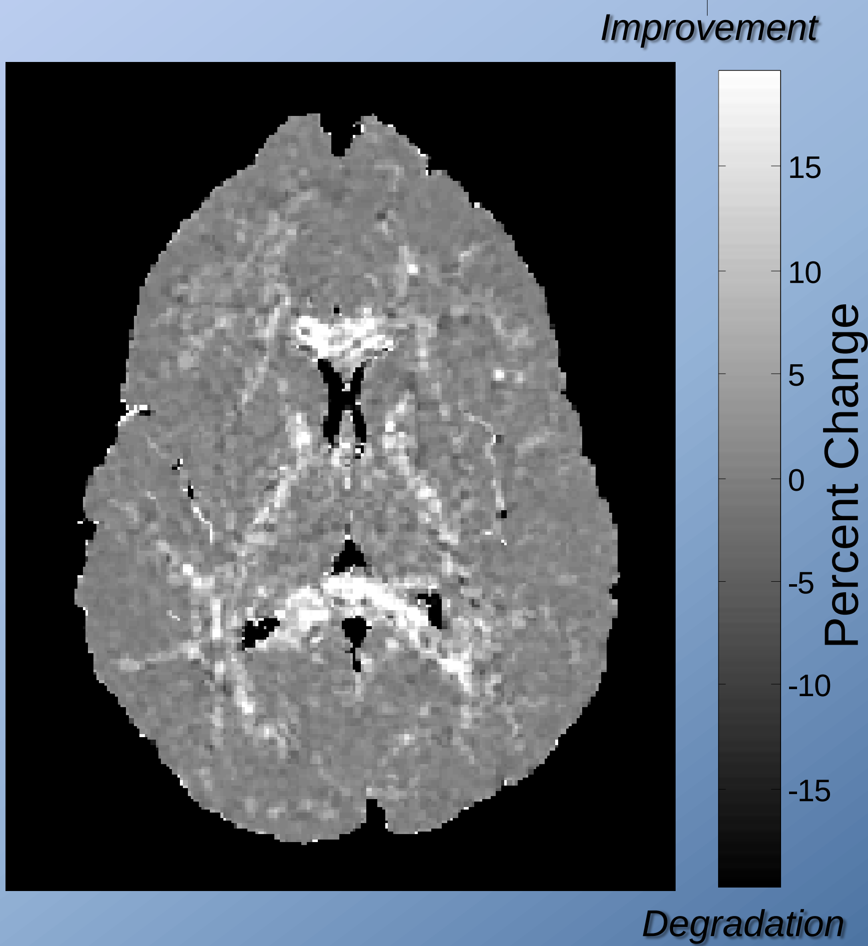
- Rician density:

$$p(x;\nu,\sigma) = \frac{x}{\sigma^2} e^{-\frac{x^2+\nu^2}{2\sigma^2}} I_0\left(\frac{x\nu}{\sigma^2}\right)$$

- Log likelihood:

$$L(\hat{\mathsf{D}}, \hat{S}_0, \hat{\sigma}_{0:N}; S_{0:N}) = \sum_{i=0}^{N} \ln p(S_i; \hat{S}_0 e^{-b g_i^T \hat{\mathsf{D}} g_i}, \hat{\sigma}_i)$$

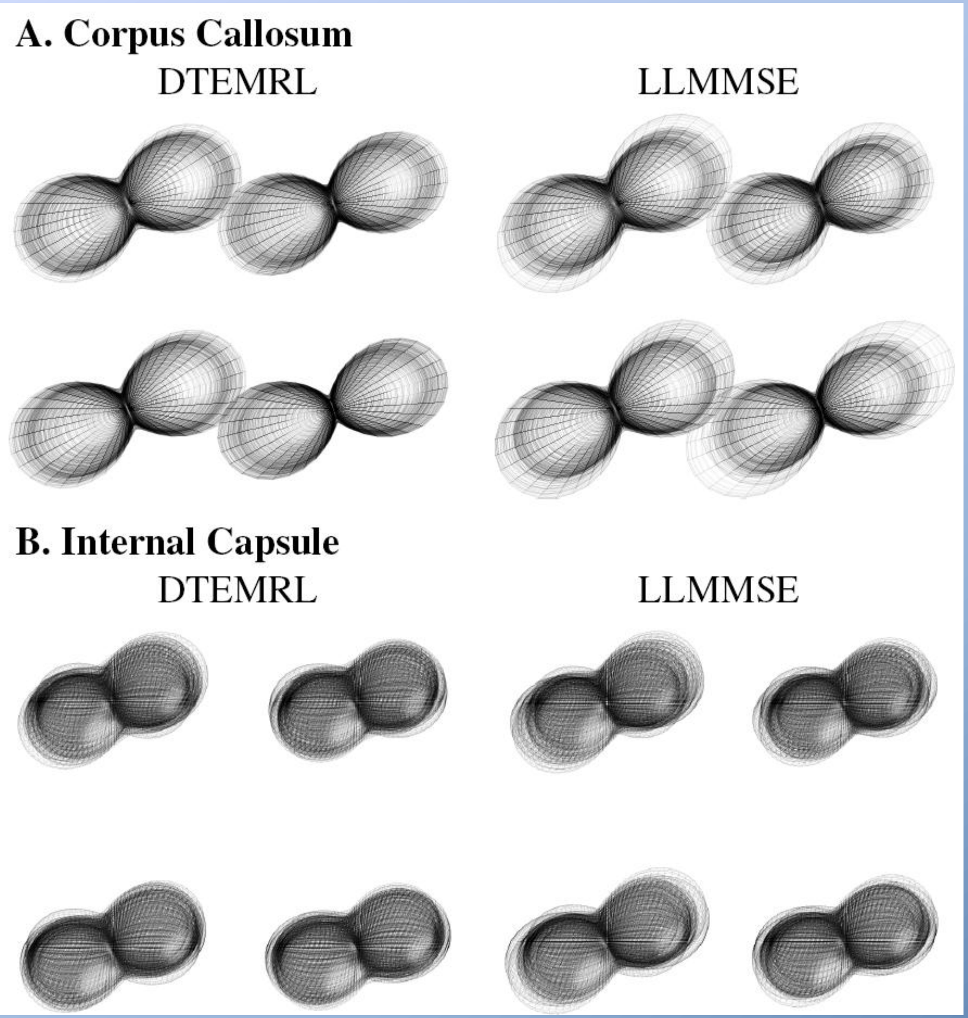
- Maximize over 8 parameters



Percent Improvement

DTEMRL Improves LLMMSE

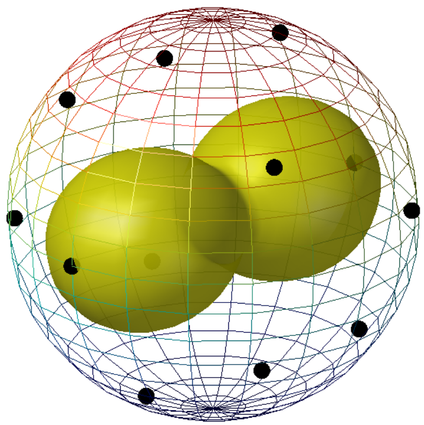
Landman et al. 2007



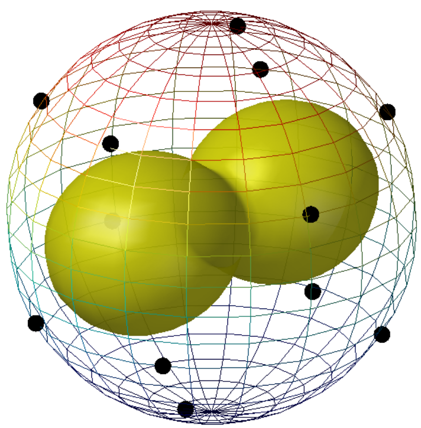
Tissue Orientation Matters

Landman et al. 2007

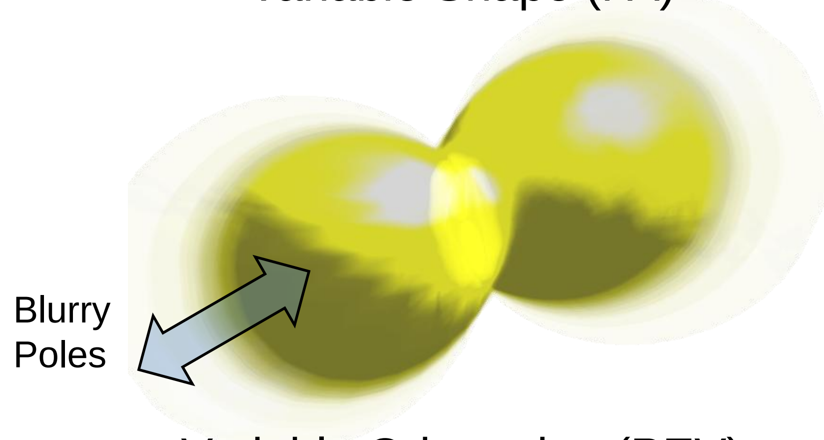
Aligned
With
DW Direction



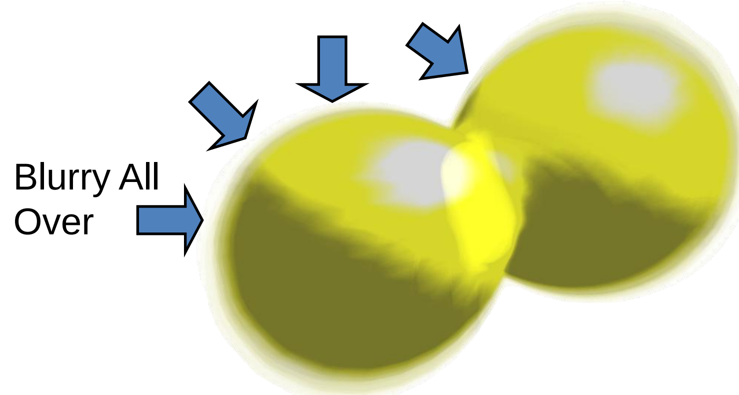
Aligned
Against
DW Direction



Variable Shape (FA)



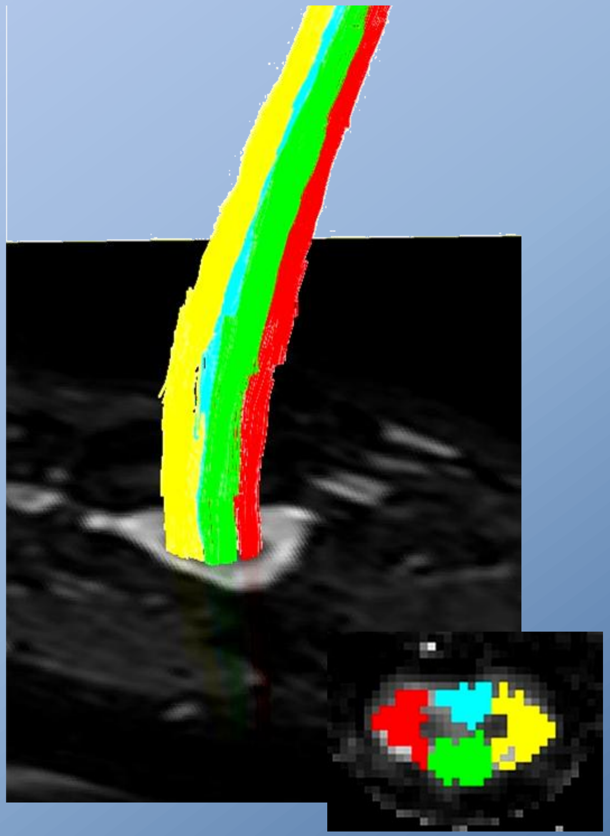
Variable Orientation (PEV)



200 Simulated Estimates Superimposed

Significant Questions

- Are reproducible tracts real?
- What is clinical feasibility of DSI, Q-ball?
- What is optimal tradeoff in spatial resolution versus q-space resolution?
- How do things change in long τ regimes?
- Can we resolve diverging, crossing, and “kissing” fibers?
- How to quantify WM contribution?
- How to interpolate DTI, ODF?



Seth Smith, Bennett Landman, et al.