

Introduction to Diffusion Tensor Imaging

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Overview

Lecture in Two Parts

- Diffusion Tensor Imaging (DTI)
 - How do we image diffusion with MRI?
- Applications and Signal Processing
 - What is done with tensor information?

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Introduction

Structural MRI

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Introduction

Diffusion Weighted MRI

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Introduction

A Brief History of DTI

Stepkal & Tanner, et al	Le Bihan, et al	Käger, et al	Basser, et al	Pierpaoli and Basser	Mori, et al

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Diffusion

The Little Picture

Diffusion of Spins in MRI

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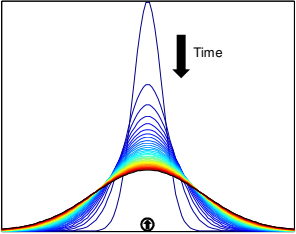
Diffusion

1-D Diffusion: Unrestricted

Diffusion of Spheres
 Location Probability

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

In a viscous medium:
 $D = \frac{kT}{6\pi\eta a}$
 k = Boltzmann's constant
 T = Temperature
 a = diameter of a sphere
 η = viscosity



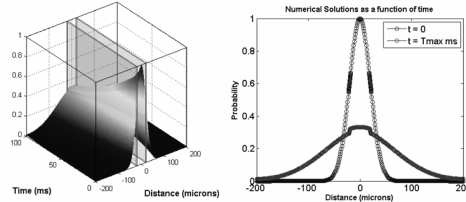
Note: Diffusivity of Free Water $\sim 2 \times 10^{-5} \text{ mm}^2/\text{s}$

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Diffusion

1-D Restricted Diffusion

High Permeability Membranes



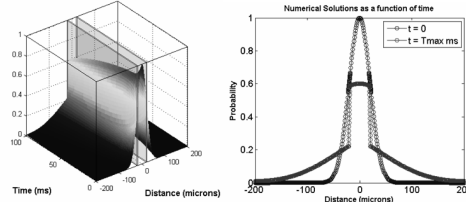
Numerical Solutions as a function of time

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Diffusion

1-D Restricted Diffusion

Low Permeability Membranes




Numerical Solutions as a function of time

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Diffusion

"Realistic" Diffusion

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



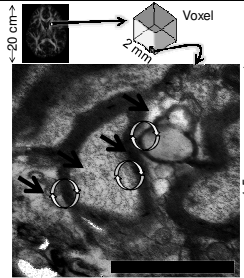
Restricted Diffusion in Cylindrical Geometry. Soderman O., Jonsson B., Journal of Magnetic Resonance, Series A, November 1995, vol. 117, no. 1, pp. 94-97(4)
 Orientational diffusion reflects fiber structure within a voxel - von dem H., Henkelman RM., Magn Reson Med. 2002 Sep;48(3):454-9.

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Diffusion

Which Protons Do We See?


- Multi-compartment sources of signal:
 - Intra-axonal \Rightarrow
 - Myelin \Rightarrow
 - Extra-cellular \Rightarrow
 - Intra-glia \Rightarrow
- All of the above!
 - And Exchange!



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MRI

Magnetic Resonance Imaging



Hopefully a review...

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MRI Spin Packets

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

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MRI Spin Dance: Spin Echo

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MRI Spin Dance: Diffusion Weighting without Motion

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MRI Spin Dance: Coherent (Bulk) Motion

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MRI Spin Dance: Incoherent Motion (Diffusion)

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Data Diffusion Weighted Imaging

In general, we don't know the fiber orientation to start with.
So acquire DWIs in many directions

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MRI Echo Attenuation: Short Pulse Approximation

$$E(\mathbf{q}, \Delta) = \underbrace{\int \int \int_{\mathbf{r}_0}^{\mathbf{r}} \rho(\mathbf{r}_0) p(\mathbf{r}_0 | \mathbf{r}, \Delta)}_{\text{Sum over Volume and Number of Spins}} \times \underbrace{\exp [i2\pi \mathbf{q} \cdot (\mathbf{r} - \mathbf{r}_0)]}_{\text{Phase Change Due to Motion from } \mathbf{r} \text{ to } \mathbf{r}_0}$$

Note (units: 1/length): $\mathbf{q} = \frac{1}{2\pi} \gamma \mathbf{g} \delta$

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MRI Echo Attenuation: Gaussian Diffusion

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

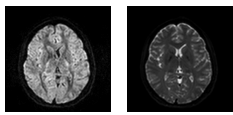
Note (units: time/length²): $\mathbf{b} = |\mathbf{q}|^2 \Delta$

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MRI The Tensor Model

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

Observe: S_g/S_0



Estimate \mathbf{D}

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MRI Diffusion Weighting: Summary

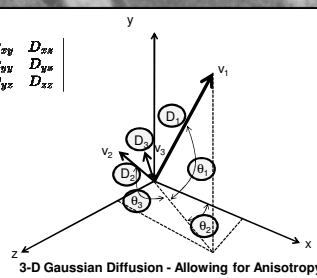
- Diffusion weighting gradients sensitize spin-echo MRI to motion
- Coherent motion results in phase changes (not magnitude changes)
- Incoherent motion (diffusion) results in decreased magnitude
- Estimate diffusion properties from observed signal attenuation

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Tensors The Tensor Model

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

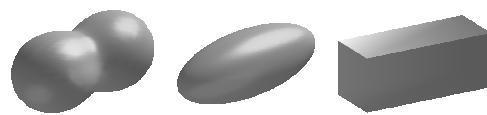
Notation: $D_1 = \lambda_1$, $D_2 = \lambda_2$, $D_3 = \lambda_3$



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

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Tensors 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

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

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Tensors **Tensors are usually a reasonable model**

- Observed signal is averaged over MANY cells and compartments.
- Average of many measurements from fixed distributions tends to a Gaussian.
- Empirically, Gaussians tends to fit well.

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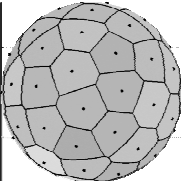
Tensors **Limitations**

- “Crossing fibers”
 - Intra-voxel “diffusion compartments” show strong structure
- Multi-level experiments (e.g., time)
 - Multiple compartments with different T2
 - Exchange between compartments
 - Very long or very short diffusion times
- **Tradeoff: Specificity versus Sensitivity**


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Data **Actual DTI Data**

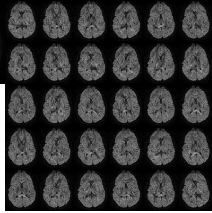
Set of Diffusion Weighting Directions (“scheme”)



Reference



Diffusion Weighted



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Data **“Computing” Estimating Diffusivity**

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

$$\frac{S_g + \eta_g}{S_0 + \eta_0} = e^{-b\mathbf{g}^T \mathbf{D} \mathbf{g}}$$

$$\ln |S_g/S_0| + \hat{\eta} = -b\text{ADC}_{\mathbf{g}}$$

$$-b \ln |S_g/S_0| - \hat{\eta}/b = \text{ADC}_{\mathbf{g}}$$

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Data **Estimating Tensors II**

$$\text{ADC}_{\mathbf{g}} = \mathbf{g}^T \mathbf{D} \mathbf{g}$$

$$= \begin{bmatrix} g_x^2 & g_x g_y & g_x g_z & g_y^2 & g_y g_z & g_z^2 \end{bmatrix} \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} & D_{yy} & D_{yz} & D_{zz} \end{bmatrix}^T$$

$$= \mathbf{G}_{\mathbf{g}} \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} & D_{yy} & D_{yz} & D_{zz} \end{bmatrix}^T$$

$$[\text{ADC}_{\mathbf{g}}] = [\mathbf{G}_{\mathbf{g}}] \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} & D_{yy} & D_{yz} & D_{zz} \end{bmatrix}^T$$

$$[\widehat{\text{ADC}}_{\mathbf{g}}] = [\mathbf{G}_{\mathbf{g}}] \begin{bmatrix} \hat{D}_{xx} & \hat{D}_{xy} & \hat{D}_{xz} & \hat{D}_{yy} & \hat{D}_{yz} & \hat{D}_{zz} \end{bmatrix}^T$$

$$[\mathbf{G}_{\mathbf{g}}]^{-1} [\widehat{\text{ADC}}_{\mathbf{g}}] = \begin{bmatrix} \hat{D}_{xx} & \hat{D}_{xy} & \hat{D}_{xz} & \hat{D}_{yy} & \hat{D}_{yz} & \hat{D}_{zz} \end{bmatrix}^T$$

Regression (Linear!?)

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Data **Estimating Tensors III**

$$\eta?$$

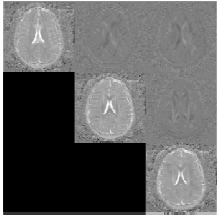
$$[\mathbf{G}_{\mathbf{g}}]^{-1} [\hat{S}_{\mathbf{g}}/\hat{S}_0] = \begin{bmatrix} \hat{D}_{xx} & \hat{D}_{xy} & \hat{D}_{xz} & \hat{D}_{yy} & \hat{D}_{yz} & \hat{D}_{zz} \end{bmatrix}^T$$

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Tensors

What do we do with tensors?

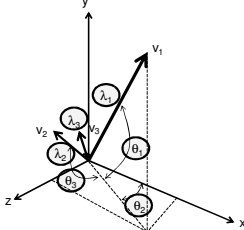
- Contrasts
- Fiber Tracking
- Interpolation
- Estimation: *Revisited*



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Contrasts

Eigen-Decomposition



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

$$= R^T \begin{vmatrix} \lambda_1 & & \\ & \lambda_2 & \\ & & \lambda_3 \end{vmatrix} R$$

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

Eigenvalues = Diffusivities
Eigenvectors = Orientation

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Contrasts

Diffusivity

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

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

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

$$ADC = \frac{\text{tr}D}{3}$$

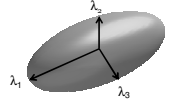
$$= \frac{\lambda_1 + \lambda_2 + \lambda_3}{3}$$

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Contrasts

Anisotropy

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



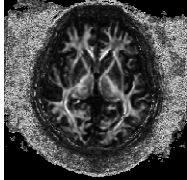
$$FA = \sqrt{\frac{3}{2} \frac{(\lambda_1 - \bar{\lambda})^2 + (\lambda_2 - \bar{\lambda})^2 + (\lambda_3 - \bar{\lambda})^2}{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}}$$

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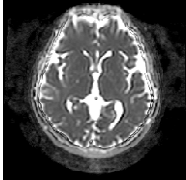
Contrasts

Clinical Contrasts

FA
Fractional Anisotropy



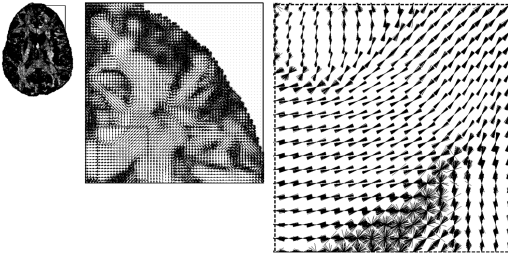
MD (ADC)
Mean Diffusivity



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Contrasts

Orientation



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Contrasts

DTI Colormap Images

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Contrasts

Question: Do we need the full tensor?

- Mean diffusivity?
- Fractional anisotropy?
- When can we get away with fewer than 6+1 observations? Would we want to?

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Tracking

Fiber Tracking

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

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Tracking

Advanced Fiber Tracking

- Probabilistic tracking
- Fiber "sampling"
- Wave front propagation
- Non-tensor tracking
- Connectivity strength assessment
- Cluster analysis

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Interpolation

Tensor Interpolation

Linear:
 $f T_1 + (1-f) T_2$

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

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

Geodesic-Loxodrome

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

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Interpolation

Emerging Methods

250x Faster than Geodesic-Loxodromes

(work in progress)

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Estimation: Revisited

Statistical Methods

$$[\mathbf{G}_g]^{-1}[\hat{\mathbf{S}}_g/\hat{\mathbf{S}}_0] + \hat{\eta}/b = [\hat{D}_{xx} \hat{D}_{xy} \hat{D}_{xz} \hat{D}_{yy} \hat{D}_{yz} \hat{D}_{zz}]^T$$

- Linear regression is a Maximum Likelihood (ML) method when the errors are i.i.d. Gaussian
- Weighted linear regression (WLS) is ML when the errors are Gaussian with unequal variance
- Do we know what how the errors are distributed?**

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Estimation: Revisited

Tissue Orientation Matters

Variable Shape (FA)
Aligned **With** DW Direction
Blurry Poles

Variable Orientation (PEV)
Aligned **Against** DW Direction
Blurry All Over

200 Simulated Estimates Superimposed

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Estimation: Revisited

Variability Is Orientation Dependent

$\sigma_{FA}(PE_v)$

$\sigma_{FA}(PE_e) - \sigma_{FA}(\text{Jones } 30)$

$\sigma_{FA}(\text{Jones } 30)$

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Estimation: Revisited

Noise Modeling

	Acquired k-Space	Zero-padded k-Space	Reconstructed Images	Complex Image	Magnitude Image
Pencil Acquisition					
	i.i.d.	i.i.d. (central)	Spatially Correlated	Spatially Correlated	Spatially Correlated
	$\mathcal{N}(0, \sigma) + j\mathcal{N}(0, \sigma)$	$\mathcal{N}(0, \sigma) + j\mathcal{N}(0, \sigma)$	$\mathcal{N}(0, \sigma) + j\mathcal{N}(0, \sigma)$	$\mathcal{N}(0, \sigma_{xy}) + j\mathcal{N}(0, \sigma_{xy})$	$\mathcal{R}(S, \sigma_{xy})$
				Artifacts!	$\mathcal{R}(S, \sigma_{xy}) + F_{xy}$

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Estimation: Revisited

Noise Modeling II

Diffusion Images i.i.d. Spatially Correlated
 $\mathcal{R}(S, \sigma_{xy}) + F_{xy}$

Diffusion Images i.i.d. Spatially Correlated
 $\mathcal{R}(S, \sigma_{xy}) + \bar{F}_{xy}$

?

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Estimation: Revisited

Diffusion Tensor Estimation by Maximizing Rician Likelihood

$$\frac{S_{dw}}{S_{ref}} = e^{-b\mathbf{g}^T \mathbf{D} \mathbf{g}}$$

Stejskal-Tanner Model

Neglect Artifacts

$$S_{ref} \sim \mathcal{R}(S_{ref0}, \sigma_{xy})$$

$$S_{dw} \sim \mathcal{R}(S_{ref0} e^{-b\mathbf{g}^T \mathbf{D} \mathbf{g}}, \sigma_{xy})$$

$$\mathcal{L}(S_{dw1}, \dots, S_{dwn}, S_{ref}) = \mathcal{R}(S_{ref0}, \sigma_{xy}) \prod_{i=1}^N \mathcal{R}(S_{ref0} e^{-b\mathbf{g}_i^T \mathbf{D} \mathbf{g}_i}, \sigma_{xy})$$

$$\hat{\mathbf{D}} = \underset{\mathbf{D}, S_{ref0}, \sigma_{xy}}{\text{argmax}} \mathcal{L}(S_{dw1}, \dots, S_{dwn}, S_{ref})$$

8 Unknowns
Reference Signal (x 1)
Noise Level (x 1)
Tensor Coefficients (x 6)

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Results

ML Improves Tensor MSE

Correctly Initialized Noise		Incorrectly Initialized Noise ($\pm 20\%$)	
Bimodal behavior		Bimodal behavior	
Above 20:1 SNR:		Above 25:1 SNR:	
Tensor Type	Δ MSE	Tensor Type	Δ MSE
Isotropic (CSF)	4.4 \pm 1.7%	Isotropic (CSF)	-2.1 \pm 3.1%
Low FA (GM)	6.9 \pm 1.1%	Low FA (GM)	4.4 \pm 0.9%
Moderate FA (WM)	20.3 \pm 1.3%	Moderate FA (WM)	19.8 \pm 1.2%
High FA (WM)	33.3 \pm 1.7%	High FA (WM)	33.1 \pm 1.5%

Below 20:1 SNR: Degraded performance

Below 25:1 SNR: Degraded performance

SNR in clinical reference images is ~40:1 (2.5 mm isotropic – brain - 1.5T)

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Estimation: Revisited

ML Improves Tensor Coefficient Variability

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Thank you.

- My Research Interests
 - Design of diffusion weighting protocols for spinal cord, musculoskeletal and brain imaging
 - Statistical estimation in diffusion weighted MRI
 - non-Gaussian diffusion with protocols using many diffusion weighting directions

Seth Smith, Bennett Landman, Jonathan Farrell, Viser Belagu, Daniel Reich, Peter Calabresi, Peter van Zijl
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