A NOVEL BIOPHYSICAL MODEL THAT CHARACTERIZES THE DISTRIBUTION OF ANISOTROPIC MICRO-STRUCTURAL ENVIRONMENTS WITH DWI (DIAMOND)

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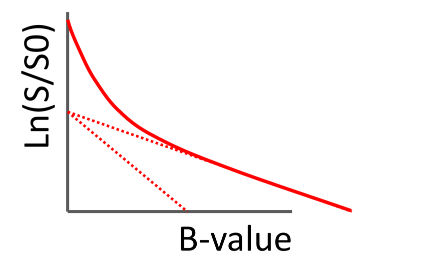
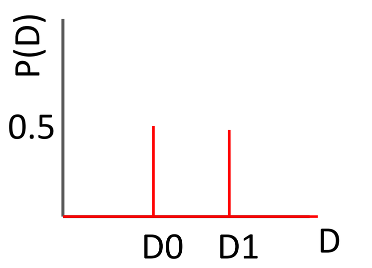
PURPOSE. A novel model that accounts for crossing fascicles and describes the tissue microstructure from diffusion-weighted images.

Free diffusion

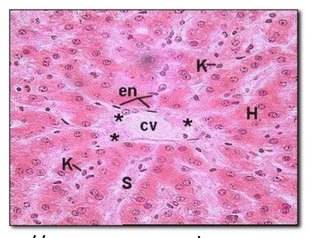


Traditional view : signal decay



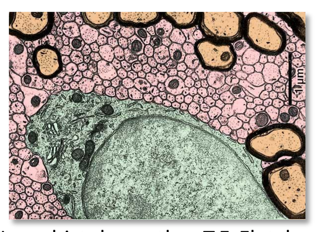
Dual representation : Density of probability

Living tissues



http://www.courseweb.uottawa.ca/

Liver:
Extra-cellular space
Different cells
...



Neurohistology atlas, T.F. Fletcher

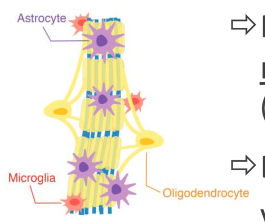
Brain:
Oriented cells (axons)
Myelinated axons
Unmyelinated axons
Glial cells
Extra-cellular space
...

I. Diffusion can be restricted/hindered

Interactions of water molecules with natural barriers

⇨ Measurement of the Apparent Diffusion Coefficient (ADC<D)

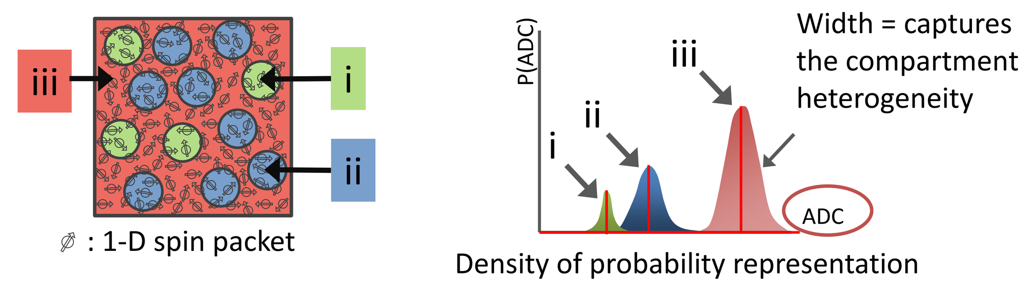
II. The spatial resolution is limited (≈ 6-27mm^3)



⇨ Mixing of the signal arising from a variety of large scale microstructural environments (LSME) (fascicles, extra-cellular space, …)

⇨ Each large scale microstructural environment can contain various microstructures (multiple cell types, sizes, geometries)

Yablonskiy, 2003: Statistical distribution model of the apparent diffusion coefficient (ADC)



Density of probability representation

$$S_k = S_0 \int P(D) \exp(-b_k D)\, dD$$

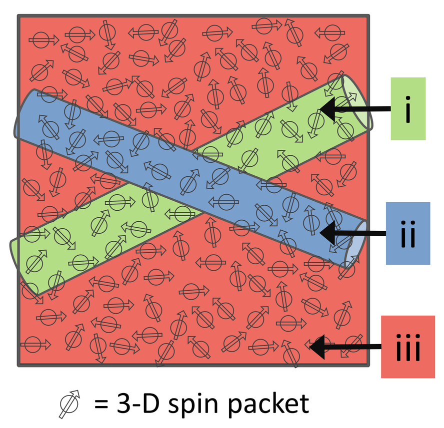
Integration over all ADCs

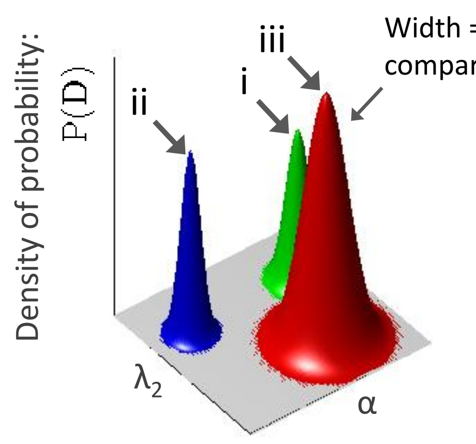
fraction of spin packets with a given ADC D in the voxel

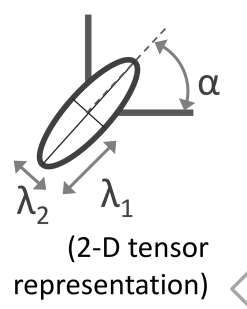
Contribution of a spin packet with ADC D

However : 1-D Model
Unable to characterize the 3-D diffusivity and heterogeneity of fascicles

DIAMOND : A STATISTICAL DISTRIBUTION MODEL OF THE 3-D DIFFUSIVITIES PRESENT IN EACH VOXEL



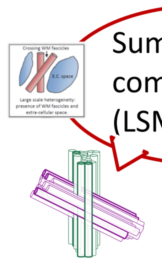




Tensor-variate density of probability

DW Signal: sum of the contribution of all the 3-D spin packets in the voxel:

$$(1)\qquad S_k = S_0 \sum_{j=0}^{N_c} f_j \int_{\mathbf{D}\in\mathcal{S}ym^+(3)} P_{\kappa^j,\boldsymbol{\Sigma}^j}(\mathbf{D}) \exp\left(-b_k \mathbf{g}_k^T \mathbf{D} \mathbf{g}_k\right) d\mathbf{D}$$



Sum over compartments (LSME)

Fraction of occupancy of the j[th] LSME

Composition of the j[th] LSME (=fraction of spin packets with **D**)

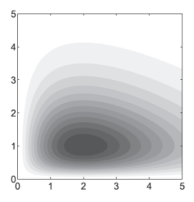
Contribution of the spin packets described by **D**

Integration over the set of symmetric positive definite matrices

Matrix-variate Gamma distribution of spin packets

Peak-shaped distribution defined over the space of symmetric positive definite matrices

$$P_{\kappa,\boldsymbol{\Sigma}}(\mathbf{D}) = \frac{|\mathbf{D}|^{\kappa-(p+1)/2}}{|\boldsymbol{\Sigma}|^{\kappa}\Gamma_p(\kappa)} \exp(-\mathrm{trace}(\boldsymbol{\Sigma}^{-1}\mathbf{D}))$$



κ : shape parameter **Σ** : scale parameter Expectation : $\mathbf{D}_0 = \kappa\,\boldsymbol{\Sigma}$ Mode: $\mathbf{D}_0(\kappa-1)/\kappa$

κ = concentration parameter. More concentrated around $\mathbf{D}_0$ as κ increases

Enables to compute an analytical solution for (1) (Guptar1999, Jian2007)

Generic expression of the signal arising from heterogeneous population of heterogeneous 3-D spin-packets

$$S_k = S_0 \sum_{j=0}^{N_c} f_j \left(1 + \frac{b_k \mathbf{g}_k^T \mathbf{D}_0^j \mathbf{g}_k}{\kappa_j}\right)^{-\kappa_j}$$

Captures the overall compartment diffusivity

Captures the compartment heterogeneity

Number of compartments = number of modes of P(D)

Estimation with an increasing number of compartments
Selection based on the generalization error

Introduction of a priori information

Unrestricted diffusion, isotropic restricted diffusion : isotropic modes

DIAMOND

For each fascicle: water molecules restricted and hindered by a fascicle represented by a single population of spin-packets

$$S_k = \mathcal{D}(\mathbf{D}_0^{\mathrm{iso,u}}, \kappa_{\mathrm{iso,u}}, f_{\mathrm{iso,u}}) + \mathcal{D}(\mathbf{D}_0^{\mathrm{iso,r}}, \kappa_{\mathrm{iso,r}}, f_{\mathrm{iso,r}}) + \sum_{j=1}^{N_f} \mathcal{D}(\mathbf{D}_0^j, \kappa_j, f_j)$$

$6N_f+5$ free parameters

$$\mathcal{D}(\mathbf{D}_0, \kappa, f) = S_0 f \left(1 + \frac{b_k \mathbf{g}_k^T \mathbf{D}_0 \mathbf{g}_k}{\kappa}\right)^{-\kappa}$$

DIAMOND^H

Water molecules restricted and water molecules hindered by a fascicle each represented by a population of spin-packets

$$S_k = \mathcal{D}(\mathbf{D}_0^{\mathrm{iso,u}}, \kappa_{\mathrm{iso,u}}, f_{\mathrm{iso,u}}) + \mathcal{D}(\mathbf{D}_0^{\mathrm{iso,r}}, \kappa_{\mathrm{iso,r}}, f_{\mathrm{iso,r}}) + \sum_{j=1}^{N_f} \left[\mathcal{D}(\mathbf{D}_0^{j,\mathrm{iax}}, \kappa_{j,\mathrm{iax}}, f_{j,\mathrm{iax}}) + \mathcal{D}(\mathbf{D}_0^{j,\mathrm{hin}}, \kappa_{j,\mathrm{hin}}, f_{j,\mathrm{hin}})\right]$$

Tortuosity model to link the eigenvalues of the intra-axonal and hindered terms

$$\lambda_2(\mathbf{M}_0^{j,\mathrm{hin}}) = \lambda_3(\mathbf{M}_0^{j,\mathrm{hin}}) = \lambda_1(\mathbf{M}_0^{j,\mathrm{hin}})(1-\nu^j) \qquad \nu^j = \frac{f_{j,\mathrm{iax}}}{f_{j,\mathrm{iax}}+f_{j,\mathrm{hin}}}$$

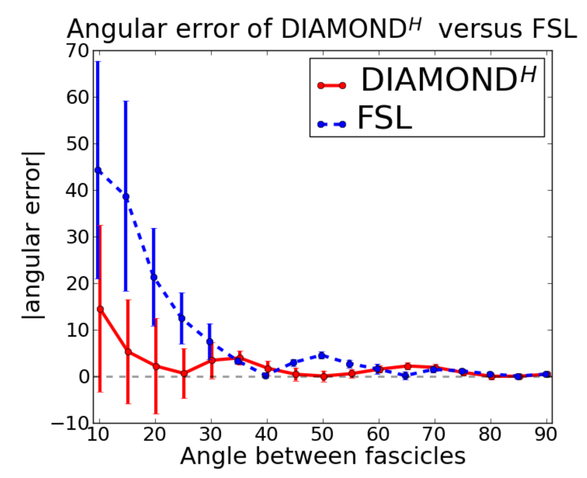
$8N_f+5$ free parameters

RESULTS

Simulations: angular reconstruction error

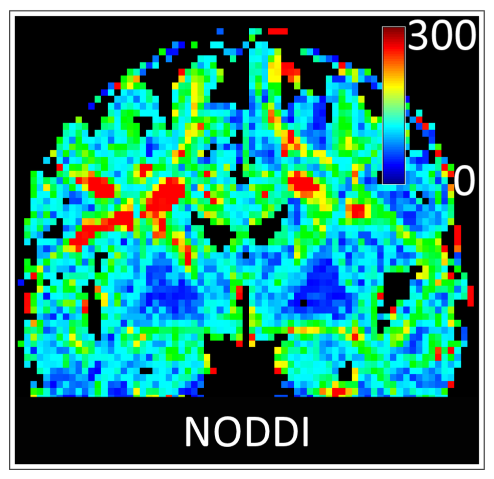
Two crossing fascicles (tensors FA=0.9), Rician noise 30dB, varying angles

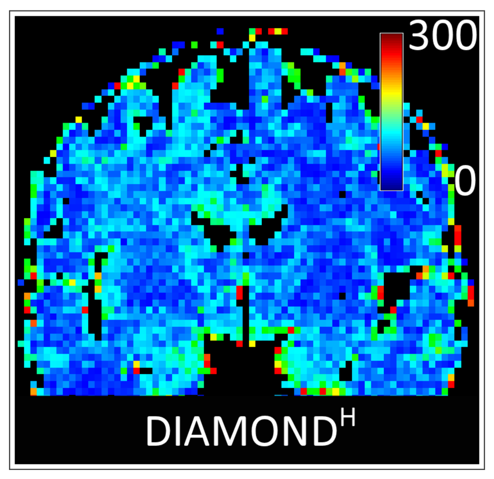
Low angular error reconstruction



Assessment of the generalization error

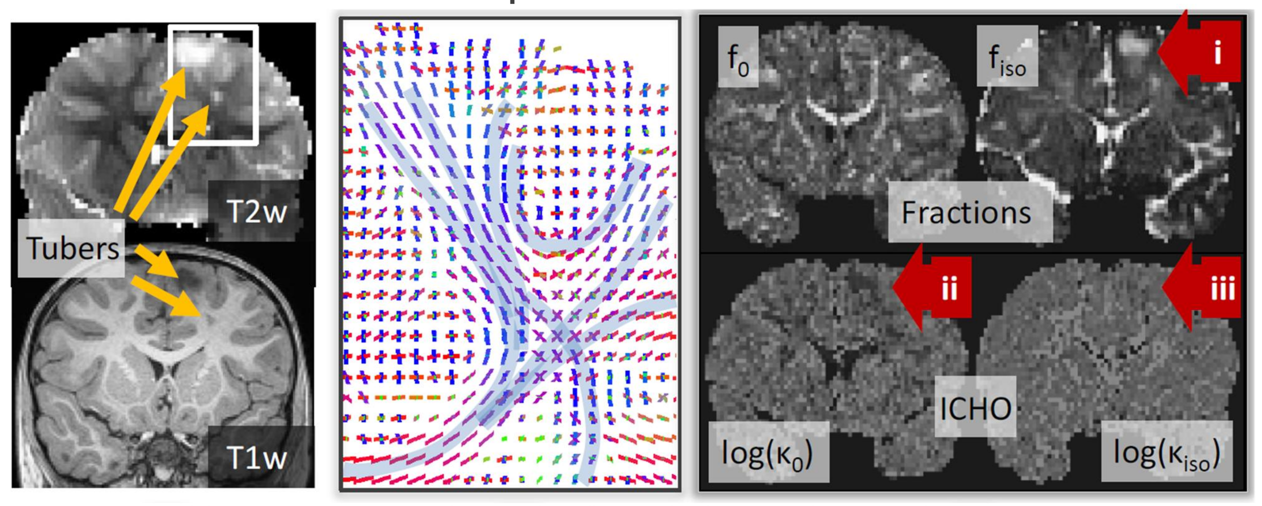
Acquisition (FOV=240mm, matrix-size=128x128, 68 slices, resolution=1.8x1.8x2mm3, TE=78ms, TR=10.1s, ~12min acquisition time) which provides a large number of different b-values between 1000s/mm2 and 3000s/mm2 with low TE and high SNR.





DIAMOND^H: Lower generalization error. Better predicts unseen data

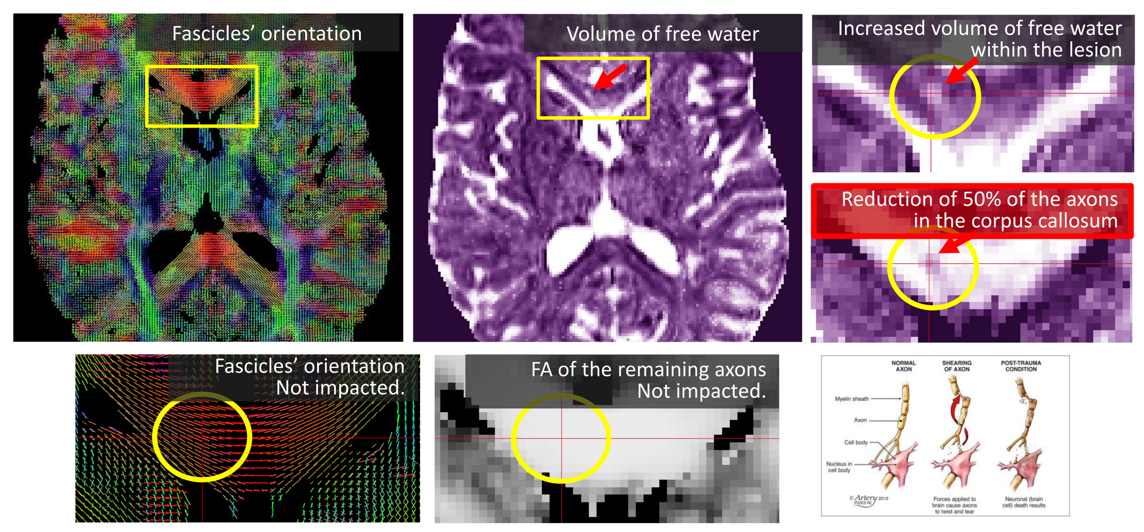
Tuberous Sclerosis Complex



○ Increased heterogeneity along the fascicle located in a tuber in a TSC patient (ii).
May reflect heterogeneous myelination or heterogeneous mixture of glial cells as observed in mice models of TSC.

○ Increased unrestricted diffusion in the region of the tuber (i)
May reflect increased extra-cellular space, the presence of perivascular spaces, or the presence of giant cells typically observed in TSC brain specimens.

Traumatic Brain Injury



⇨ Suggest diffuse axonal injury leading to axonal death, while the remaining axons remain unchanged

DISCUSSION

- 3-D statistical distribution model of the 3-D diffusivities in each voxel
- Characterizes the **DI**stribution of **A**nisotropic **M**icr**O**-structural e**N**vironments with **D**WI (DIAMOND)
- Provides both connectivity & WM microstructure information
  - Models each fascicle in each voxel (Unlike DTI, NODDI)
  - Low angular error
  - Characterizes each compartment diffusivity and heterogeneity
  - Characterizes the fraction of occupancy of each compartment
- Similarly to Kurtosis imaging, exhibits a positive b^2 term

$$S_0 \sum_{j=1}^{N_p} f_j \left(1 + \frac{b_k \mathbf{g}_k^T \mathbf{D}_0^j \mathbf{g}_k}{\kappa_j}\right)^{-\kappa_j} = S_0 \sum_{j=0}^{N_p} f_j \exp\left(-b_k \mathbf{g}_k^T \mathbf{D}_0^j \mathbf{g}_k + \frac{b_k^2}{2\kappa_j}\left(\mathbf{g}_k^T \mathbf{D}_0^j \mathbf{g}_k\right)^2 - \frac{b_k^3}{3\kappa_j^2}\left(\mathbf{g}_k^T \mathbf{D}_0^j \mathbf{g}_k\right)^3 + \dots\right)$$

  - But balanced by higher order terms (not valid only for small b)
  - Crucial difference : tissue model, not mathematical property
- Phenomenological model : captures the heterogeneity of diffusion that is consistent with an (oriented) tissue compartment.
- Better predicts diffusion measurements
- Provides novel imaging biomarkers