How White Matter Tracts Cross Determines the DWI SIgnal

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Introduction:
Obtaining insight into the diffusion signature from different fiber crossing models is an essential step in disambiguation of the diffusion MRI signal, on the path to finding quantitative physiological biomarkers of disease. The MRI diffusion signal can help probe the microstructural characteristics of white matter (WM) fibers, knowledge of which is important for assistance in diagnosis/prognosis of neurological and psychiatric diseases. Most WM voxels contain more than one tract direction; so one of the main challenges in interpretation of diffusion MRI is to separate the contribution to the signal arising from the mixture of fiber directions in a voxel, from the contribution of fiber structural characteristics, e.g. myelin thickness or permeability, average axonal diameter, etc. High angular resolution diffusion imaging [1], at relatively high diffusion weightings, can provide significant information about the tract directions in a voxel (the orientation distribution function – ODF). And recent computationally intensive work attempts to differentiate crossing and "kissing" fibers and assessing both directional and microstructural information [2]. However, how the tracts cross has not been investigated – see Fig. 1 for two possible configurations. The Summation Model assumes that the signal is represented as the sum of signals from individual, non-exchanging, fiber bundles. In the case of crossing tracts that interleave, in addition to the partial voluming of different tract directions within a voxel, the signal may include contributions from water molecules that experience multiple directional environments during the diffusion measurement process. It's highly likely that the diffusion signature in these two cases will be different; investigations using analytical and Monte Carlo methods follow:

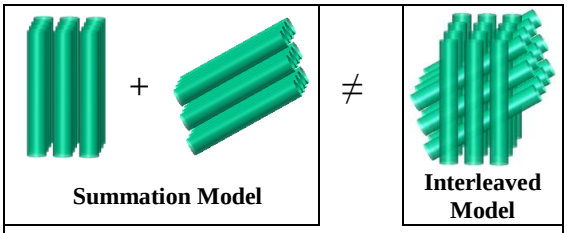

Fig. 1: Schematic description of Summation Model vs. Interleaved Model. The paths of water diffusion in two coherent and separated structures do not equal the paths in an interleaved structure.

Methods - 2D: A simple, narrow-pulse-approximation model of tracts crossing at an angle $\propto$ in **2D** space was implemented using tensor-based exchange equations. The exchange parameters, k_A and k_B, indicate the proximity of two populations of fibers having different directions, i.e., the "fineness" of the interleaving. The exchange rates ranged from $k_A=0$ (equivalent to the Summation Model) to $k_A=2/\Delta$, where Δ was the diffusing time. The exchange constants are related by detailed balancing, $P_A k_A = P_B k_B$ where $P_A+P_B=1$ are the population fractions.

$$\dot{M}_A = -\frac{b}{\Delta}\hat{\mathbf{g}}\mathbf{D_A}\hat{\mathbf{g}}^T M_A - k_A M_A + k_B M_B$$

$$\dot{M}_B = -\frac{b}{\Delta}\hat{\mathbf{g}}\mathbf{D_B}\hat{\mathbf{g}}^T M_B - k_B M_B + k_A M_A$$

with a diffusion tensor representing each tract. Diffusion in the direction perpendicular to the tract is given by $D_\perp$, and parallel to the tract is $D_\parallel$ (representative in-vivo WM values were used), giving:

$$\mathbf{D_A} = \begin{pmatrix} D_\parallel & \mathbf{0} \\ \mathbf{0} & D_\perp \end{pmatrix}, \mathbf{D_B} = \begin{pmatrix} D_\parallel - \xi\tan\alpha & \xi \\ \xi & D_\parallel - \xi/\tan\alpha \end{pmatrix} \text{ where } \xi = (D_\parallel - D_\perp)/(\tan\alpha + 1/\tan\alpha).$$

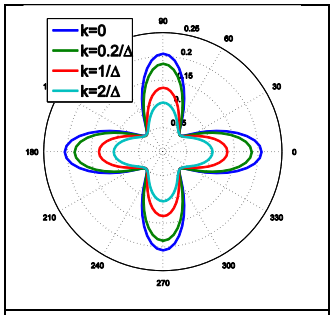

Fig. 2: Calculation of 2D ODF with different exchange rates.

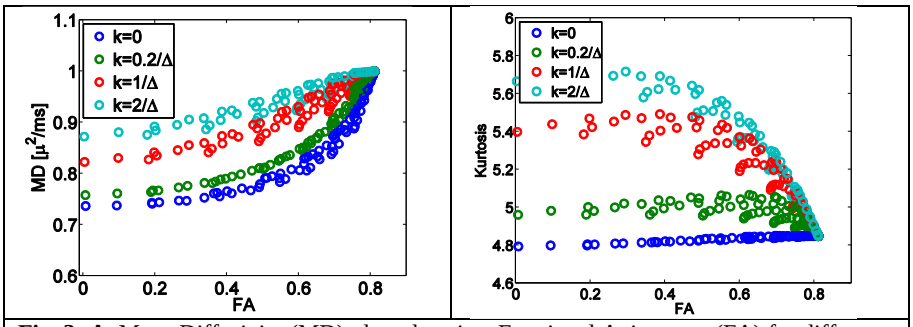

Fig. 3: A. Mean Diffusivity (MD) plotted against Fractional Anisotropy (FA) for different exchange rates. **B.** Diffusional Kurtosis is highly dependent on exchange.

Fig. 2 shows calculated 2D ODFs for different exchange rates for equally sized fibers crossing at 90°. Notice that the peaks of the ODF become significantly less pronounced when crossing tracts effectively share water (represented by higher values of the exchange parameter). The calculation was then performed for all crossing angles, $\propto$, and population fractions P_A and P_B, resulting in the plots in Fig. 3A,B. Notice here the significantly higher mean diffusivity calculated from interleaved tracts ($k\neq0$) vs. non-interleaved tracts ($k=0$). Fig. 3B shows the kurtosis calculated from the mean signal (averaged over all directions) at multiple b-values [3] exhibiting a clear dependence on exchange between tracts.

Methods – 3D: **3D** Monte Carlo simulations were performed - Fig. 4 shows the resulting ODF calculated via the spherical harmonics basis method proposed in [40]. The peaks of the ODF are considerably less pronounced in the Interleaved Model.

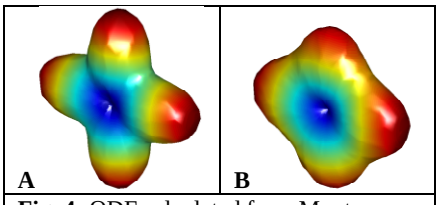

Fig. 4: ODF calculated from Monte Carlo simulations of crossing tracts. **A.** Summation Model; **B.** Interleaved Model. (b=8000 μ^2/ms).

Results and Conclusions: When crossing tracts interleave, the peaks of the ODF are less sharp. Moreover, models based on a multi-tensor fit may be less applicable. Calculations indicate that interleaving may be detectable since it would affect the mean diffusivity and the kurtosis.
Further Work: Extension of the Monte Carlo simulations to include intra- and extra-cellular compartments, T_2 information, and multiple b-values. Comparison of simulations to in-vivo data in order to find limits on the exchange between intra- and extra-cellular compartments.

References: [1] Tuch DS et al. *Proc ISMRM 1999* p.321 (1999). [2] Sherbondy AJ, Rowe MC, Alexander DC. MICCAI 2010, Part I LNCS 6361, p.183. [3] Kärger J et al *Adv. Magn. Reson.* 12:1, 1988; [4] Jensen JH et al *Magn Reson Med* 2005; 53:1432-1440. [5] Descoteaux M, et al. *Magn Reson Med*. 2006;56(2):395-410.