Fiber Demixing with the Tensor Distribution Function avoids errors in Fractional Anisotropy maps

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Introduction: DTI has been used to study white matter microstructure and fiber pathways by examining the 3D diffusion profile of water molecules in brain tissue. Even so, the single tensor model cannot resolve more complicated fiber configurations, e.g., tract crossings that occur in as many as 30-50% of white matter voxels. DTI-derived measures are incorrect where fibers cross or mix. High angular resolution diffusion imaging (HARDI) addresses this problem by applying more than 6 different diffusion-sensitized gradients [1]. In [2], we modeled the HARDI signal more generally as a unit-mass probability density on the 6D manifold of symmetric positive definite tensors, yielding a Tensor Distribution Function (TDF) at each point in the brain, to model fiber crossing and non-Gaussianity in diffusion MR images. From the TDF, one can derive simple analytic formulae for the water displacement probability function, fiber orientation distribution and their corresponding anisotropy measures.

Methods: Fractional anisotropy (FA) is a scalar value between zero and one, computed from the diffusion tensor, which describes the degree of anisotropy of a diffusion process. When FA=0, diffusion is isotropic (unrestricted in all directions), while FA=1 means that diffusion occurs only along one axis and is fully restricted along all other directions. Even so, fiber crossing or partial volume effects in DTI causes the calculation of FA to be incorrect. Here, we evaluated how DTI-derived FA and TDF-derived FA (see [3] for derivations) behave in different fiber crossing and different partial volume situations. We simulated two-compartment diffusion tensor (DT) models (with two dominant fiber tracts per voxel) to illustrate several situations. We considered three basic DTs [λ_1, λ_2, λ_3] (units: 10^{-3} mm^2/s) with representative eigenvalues for white matter (WM) [1.2, 0.2, 0.2], gray matter (GM) [0.2, 0.2, 0.2] and CSF [2, 2, 2], and 3 situations where these tissues were mixed in a voxel: 1) WM+WM, 2) WM+GM, 3) WM+CSF. We evaluated FA estimation in three simulations: 1) Compartments mixed with different weights: we vary the weighting of WM, the first compartment (*w1*) from 0 to 1 (at intervals of 0.2), and the other compartment's weighting to *w2=1-w1*, and assumed the two compartments crossed at 90 degrees; we set the number of diffusion-sensitized gradients (spherical samples) to N(g)=60 with b=1000 s/mm^2; 2) the crossing angle between two equally weighted compartments (w1=w2=0.5) was also varied to be 0, 30, 45, 60, and 90 degrees, with N(g)=60 and b=1000 s/mm^2; 3) the b-value was varied from 1000 to 6000 s/mm^2, for two equally-weighted compartments crossing at 90 degrees, with N(g)=60.

Results: All the above simulations were repeated 1000 times with artificially added Rician noise (SNR =10). TDF-FA was advantageous over DTI-FA in all simulations (**Figure 1**). TDF-FA was more stable as the crossing angle and b-value were varied, but the standard measure, DTI-FA, suffered more from the effects of fiber crossing and partial voluming.

Conclusions: FA, measured conventionally using the single-tensor DTI model, was less accurate in voxels with simulated fiber crossings and partial volume effects, which occur in 30-50% of the brain's white matter. Multi-fiber demixing (with the TDF method here) allowed us to correct the resulting FA values, which the single-tensor model of diffusion tends to underestimate.

References: [1]. Tuch DS. *Q*-ball Imaging. **MRM** 52(6):1358-1372 (2004).
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Table 1. Two compartments with variable weights. Compartment 1 is WM (FA=0.81), which has weighting coefficient w1; Compartment 2 can be WM, GM and CSF, with weighting coefficient (1-w1). The number of diffusion sensitized gradients is set to 60 with b=1000 s/mm^2; here the two compartments cross at 90 degrees (since GM and CSF are isotropic, the angle of crossing mainly applies to WM+WM). Rician noise was added with SNR=10. This table shows that DTI-FA is less accurate when affected by partial volume effects; TDF-FA corrects for this partial volume effect, giving higher values with mixing white matter tracts (w1=0.4 and 0.6 in the first row of table 1 as well as the first row of table 2), and lower values in isotropic cases (w1=0 in 2nd and 3rd rows).

W1	0		0.2		0.4		0.6		0.8		1	
	DTI-FA	TDF-FA	DTI-FA	TDF-FA	DTI-FA	TDF-FA	DTI-FA	TDF-FA	DTI-FA	TDF-FA	DTI-FA	TDF-FA
WM+WM	0.815	0.797	0.657	0.788	0.494	0.790	0.507	0.788	0.663	0.785	0.807	0.799
WM+GM	0.311	0.091	0.392	0.349	0.544	0.543	0.649	0.667	0.742	0.747	0.806	0.799
WM+CSF	0.161	0.101	0.239	0.303	0.359	0.550	0.506	0.750	0.662	0.843	0.817	0.800

Table 2. Simulated Two-compartment systems crossing at different angles. Two compartments are equally weighted; Compartment 1 is WM and Compartment 2 can be WM, GM and CSF (row 1, 2, and 3 respectively). The number of diffusion-sensitized gradients is 60 with b=1000 s/mm^2. Rician noise was added with SNR=10. This table shows that DTI-FA is incorrect, and generally underestimates the true FA of the component fibers, depending on the fiber crossing angle; TDF-FA can overcome this. Since GM and CSF are isotropic, fiber-crossing angle is redundant for rows 2 and 3.

Angle	0^0		30^0		45^0		60^0		90^0	
	DTI-FA	TDF-FA	DTI-FA	TDF-FA	DTI-FA	TDF-FA	DTI-FA	TDF-FA	DTI-FA	TDF-FA
WM+WM	0.815	0.800	0.770	0.789	0.702	0.782	0.617	0.778	0.480	0.781
WM+GM	0.595	0.622	0.610	0.608	0.596	0.617	0.605	0.606	0.601	0.626
WM+CSF	0.432	0.657	0.439	0.656	0.423	0.652	0.429	0.656	0.444	0.654

Table 3. The effect of varying b-values. Equally-weighted two-compartment systems,(with 90-degree crossing) are simulated. Compartment 1 is WM and Compartment 2 can be WM, GM and CSF. The number of diffusion-sensitized gradients is 60. Rician noise was added with SNR=10. TDF-FA is more stable as the b-value is varied, while DTI-FA decreases as b value increases.

b	1000 s/mm^2		2000 s/mm^2		3000 s/mm^2		4000 s/mm^2		5000 s/mm^2		6000s/mm^2	
	DTI-FA	TDF-FA	DTI-FA	TDF-FA	DTI-FA	TDF-FA	DTI-FA	TDF-FA	DTI-FA	TDF-FA	DTI-FA	TDF-FA
WM+WM	0.478	0.779	0.443	0.778	0.407	0.776	0.339	0.748	0.279	0.737	0.226	0.705
WM+GM	0.613	0.622	0.513	0.587	0.432	0.595	0.372	0.578	0.325	0.554	0.287	0.493
WM+CSF	0.447	0.655	0.455	0.756	0.359	0.824	0.271	0.826	0.217	0.802	0.188	0.752