Two Tensor Analysis for White Matter Tractography - Methodological Evaluation

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Introduction: Many diseases that are known to affect the white matter of the brain, or are hypothesized to do so, are currently under investigation using DTI. Clinical DTI scans assume only one tensor per voxel, causing potential errors in tractography and in anisotropy quantification. Since high angular resolution imaging remains so far untenable for routine clinical use due to long acquisition times, the single tensor field should be augmented with additional information however possible. A method for two-tensor analysis based on the method proposed in Ref [1] increases the information yield from a conventional short DTI acquisition. It is based on physically reasonable assumptions leading to a constrained, two tensor model which, after the single tensor fit, has only **4** free parameters: ϕ_α and ϕ_β - the angles subtended by the two tract directions in the plane defined by the 3rd eigenvector, f – the fraction of the first tract $\in[0,1]$, and λ_1 – the apparent diffusion constant along the tract, which is assumed to be the same in both tracts. The model is fundamentally an empirical one, albeit with physical underpinnings (as is the single tensor description). In Ref. [1] the initial application of the method to *in-vivo* brain DTI was described. The current work focuses on **A.** evaluation of the sensitivity of the model to the tract configuration, **B.** evaluation of the sensitivity of the model to parameters related to data acquisition, and **C.** recognition of the voxels in which this model is applicable.

Simulations and Conclusions: Diffusion weighted signals originating from a voxel containing two tracts were simulated for each of 15, 30 & 60 directions for a b-value of 1000 s/mm². The angle between the tracts was varied from 0 to 90 degrees; the fraction of the 2nd tensor was varied from 0 to 0.5. Values for the apparent diffusion constants were extracted from the average of 134 midline corpus callosum voxels from *in-vivo* brain DW-EPI described in Ref. [1]. Each configuration had varying amounts of random noise added 100 times. The simulated signals were analyzed using the 4 parameter two-tensor model.

A. The angle between fibers & the fractional proportions of the respective tracts determine the accuracy of the fit – examples are shown in Fig. 1. Generally, as the separation angle grows and each tract's fractional volume approaches 50%, the accuracy of the estimate improves

B. The sensitivity to acquisition parameters was determined by comparing simulated data that would have equal acquisition times, i.e. if the number of gradient directions is doubled, the SNR is divided by $\sqrt{2}$. Fig. 1 shows that the optimal number of gradient directions out of the set [15,30,60] is 30.

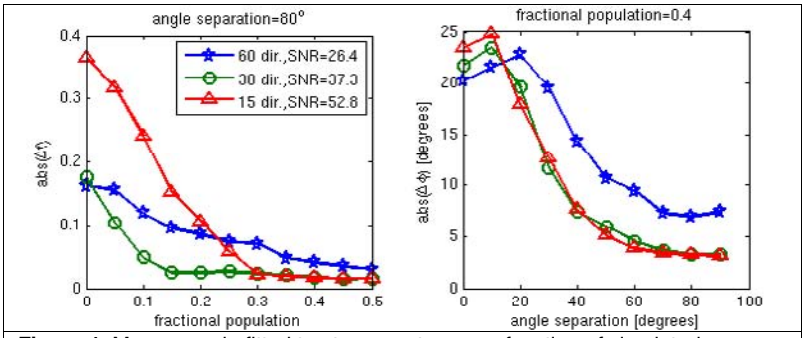

Figure 1. Mean error in fitted tract parameters as a function of simulated parameters. The two-tensor fitting accuracy is compared between simulations of comparable data acquisition times. *Left*: Error in fractional population as a function of simulated fractional population, for simulated angle separation of 80°. *Right*: Error in angle separation as a function of simulated angle separation for a tract population ratio of 0.4:0.6.

C. When to apply the model is an essential step in two-tensor analysis. The magnitude of the smallest eigenvector is an indicator of whether a voxel contains no more than two tracts. Although more than 2 tracts in a voxel could also yield a small value for λ_3 - they would all have to be lying in the same plane. It can be shown that even in this case 2-tract analysis is better than single tensor analysis. After this initial classification, the geometric shape of the single fitted diffusion tensor is determined, specifically the index of planar anisotropy, C_p (see the review in Ref. [2] for the definition of C_p) – only planar voxels are amenable to 2-tensor fitting. In Fig. 2 lower values of C_p can be visually correlated with higher errors associated with the two-tensor fit. Thus the value of C_p in each voxel can provide error assessment input to tractography, or provide a cutoff value for two-tensor analysis dependent on user-determined acceptable error values of angular separation and tract fraction.

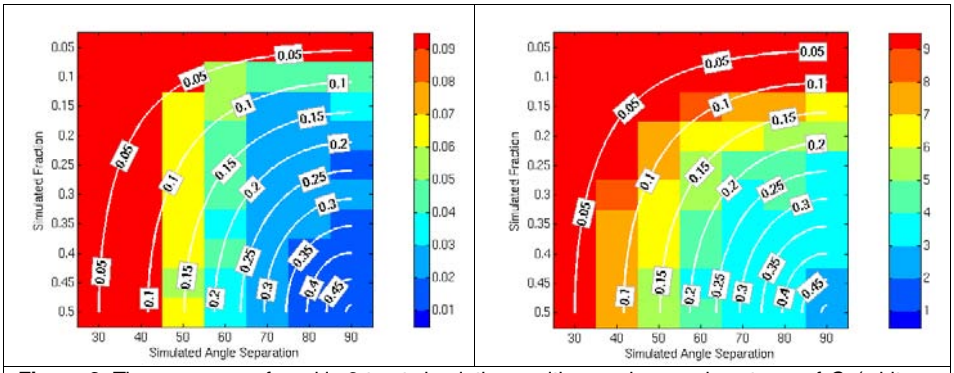

Figure 2. The mean error found in 2-tract simulations, with superimposed contours of C_p (white lines), shown as a function of the angle between two tracts, and the fractional populations. These plots can be used to determine the relationship between error values and C_p.
Left: Error in fitted tract fraction *Right*: Error in angle separation (degrees).

Summary: Our experience indicates that *in-vivo* many voxels exist that satisfy the criteria outlined above for two-tensor analysis. This method could elucidate tract directions at critical points of uncertainty, using conventionally acquired DTI data. This technique should significantly improve the ability to track smaller fibers in the brain, and to measure subtle changes in white matter fiber tract integrity. The next challenges in two-tensor applications are visualization and suitable tractography algorithms.

References: [1] S. Peled & C-F. Westin. Geometric Extraction of Crossing Tracts. *Proc. ISMRM* Miami 2005 p.1340. [2] C-F. Westin et al. Processing and visualization for diffusion tensor MRI. *Med Image Anal.* 2002 Jun;6(2):93-108.