## Multiple Kernel Spherical Deconvolution and Intrinsic FA of Crossing Fiber Populations

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## INTRODUCTION

Diffusion tensor imaging (DTI)<sup>[1]</sup> has become the most widely used tool to study brain white matter structures non-invasively. Parameters derived from DTI, such as fractional anisotropy (FA), have been demonstrated to provide valuable neurobiological information. As DTI suffers from fundamental limitations, high angular resolution diffusion imaging (HARDI) methods have been developed to reveal complex white matter structures. Spherical deconvolution (SD) is one of the most popular approaches to resolve crossing white matter fiber bundles by constructing a fiber orientation distribution (FOD) function. The FOD can be estimated through a spherical harmonic (SH) transformation directly<sup>[2, 3]</sup>, or obtained via a Richardson-Lucy like algorithm iteratively<sup>[4]</sup>. Both approaches require *a priori* knowledge of a response kernel, i.e., the diffusion weighted (DW) signal profile of a single-fiber population. Clearly, the response kernel contains information that is characteristic of the structural properties of nerve tissues and may provide important biomarkers in neurobiological studies. However, conventional SD approaches do not allow for an independent estimate of this property for each fiber in a voxel.

# PURPOSE

In previous work, we demonstrated how the multiple kernel spherical deconvolution (MKSD) method can resolve orientations of multiple crossing fiber populations and at the same time provide estimates of the diffusion properties intrinsic to each single-fiber population<sup>[5]</sup>. In this work, we aim to develop fiber tracking algorithms based on MKSD FODs and to study the stability of tract-specific intrinsic FA estimates. We expect MKSD would relax the "calibration" issues in SD FOD reconstruction<sup>[6]</sup>. **METHODS** 

Data acquisition and processing: HARDI images of a healthy volunteer were acquired on a 3T Philips scanner. Three DWI scans were acquired at  $b = 1000, 2000, 3000 \text{ s/mm}^2$  respectively, with isotropic voxel size (2.5 mm)<sup>3</sup>. Each scan consisted of 70 diffusion-sensitizing directions evenly distributed on a unit sphere (scanning time ~13 min). Eddy current correction and motion correction were done simultaneously by affine registration<sup>[7]</sup>, followed by voxel-wise whole brain MKSD analysis.

Fiber tracking: A deterministic fiber tracking algorithm was implemented in MATLAB. Seed points were evenly distributed in the seeded voxels. At each step, the local fiber orientation was trilinearly interpolated between surrounding orientations within 30 degrees of the current marching direction. For voxels containing multiple fiber orientations, only the one vielding lowest curvature is selected. Fiber components with volume fractions below threshold (<0.1) were not included in the interpolation. Stopping criteria include: stepping into CSF or gray matter, turning sharply  $(>45^{\circ})$ , or reaching the threshold of maximum length (15cm).

Stability analysis: To test the stability of the MKSD method, bootstrapping was performed on a voxel-wise basis. The initial run of MKSD with measured signal was used as putative "noisefree" data, and the fitting residuals were permuted and added onto the "noise-free" data to create a new dataset<sup>[8]</sup>. For each created dataset, a new run of MKSD was performed. 100 iterations of bootstrap were implemented for each voxel. RESULTS

Three crossing fiber bundles were identified (Fig 1a). The FA



Figure1. The estimated FA intrinsic to specific fiber bundles and its stability. In the left panel, three fiber bundles were identified (a), and the FA of each fiber bundle, estimated by MKSD, was rendered on the streamlines (b, c). Six consecutive voxels in the SLF (interdigitating with CF) demonstrate spatially smooth FA compared to the single tensor model (shown in blue) in the right panel. Across 100 iterations of permutation, the variation in FA estimates was shown in histograms. Real FA estimates are labeled with dashed lines. DTI tensors and FODs pertaining to CF and SLF respectively were also shown. Transparent gray was three times standard deviation in FODs.

value intrinsic to each fiber bundle was rendered on the streamlines (Fig 1b, c). Bootstrapping results demonstrated that the FA of an anatomically well-defined white matter fiber bundle shows a reasonable degree of continuity along the pathway. The intrinsic FAs pertaining to different single-fiber populations were differentiable even considering the fitting errors due to noise and both were well above the single tensor estimate, which suffers from partial volume averaging.

## CONCLUSIONS AND DISCUSSIONS

The MKSD approach is able to resolve crossing fibers, and distinguish changes in fiber coherence from changes in intrinsic fiber diffusion anisotropy. These may provide more accurate analysis of the properties of fiber pathways in the brain. Future work includes modeling of fanning fibers in MKSD, which may provide more precise intravoxel fiber structural estimates for probabilistic fiber tracking. REFERENCES [1] Basser et al., Biophys J 66:259 (1994). [2] Tournier et al., Neuroimage 23:1176 (2004). [3] Anderson, Magn Reson Med 54:1194 (2005). [4] Dell'Acqua et al., IEEE TBME 54:462 (2007). [5] Fan et al., Proc. ISMRM 1:4016 (2011). [6] Parker et al., Neuroimage 65:433 (2013). [7] Netsch and van Muiswinkel, IEEE TMI 23:789 (2004). [8] Jeurissen et al., HBM 32:461 (2011).