

# Accurate Estimation of Local Fiber Orientations for Groupwise Tractography

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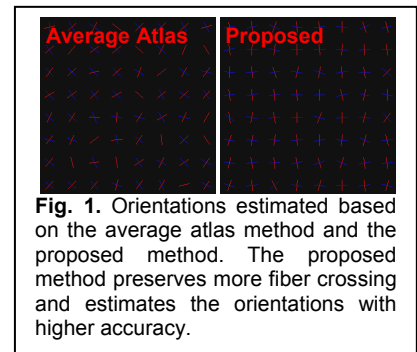
**INTRODUCTION:** White matter fiber tractography plays a key role in the understanding of brain circuitry *in vivo*. For tract based comparison of a population of images, a common approach is to first generate an atlas by averaging, after spatial normalization, all images in the population, and then perform tractography using the constructed atlas. The reconstructed fiber trajectories form a common geometry onto which diffusion properties of each individual subject can be projected based on the corresponding locations in the subject native space. We found, however, in the case of High Angular Resolution Diffusion Imaging (HARDI) where modeling fiber crossings is an important goal, the above-mentioned averaging method for generating an atlas results in significant error in the estimation of fiber pathway orientations and causes a major loss of fiber crossings. These limitations have significant impact on the accuracy of the reconstructed fiber trajectories and jeopardize subsequent tract analysis. As a remedy, we present in this paper a more effective means of performing tractography at a population level. A bipolar Watson distribution is determined for each voxel based on information given by all images in the population, giving us not only the principal orientations of the fiber pathways, but also confidence levels of how reliable these orientations are across subjects. These pieces of information are then fed into a probabilistic tractography framework which will reconstruct a set of fiber trajectories which are consistent across all images in the population. We will demonstrate that the proposed method, results in significantly better preservation of fiber crossings, and hence yields better trajectory reconstruction in the atlas space.

**METHODS: Spatial Normalization:** The computation of the transformation from subject to atlas space is not the focus of this work since our method is not limited to a particular registration method. Following the work described in [2], we utilize a hierarchical spherical harmonics based framework for registration of the High Angular Resolution Diffusion Imaging (HARDI) data. We then utilize the estimated transformation to map the orientation(s) at each voxel location (estimated by locating the local maxima of the orientation distribution function) to the atlas space. In addition, we rotate each orientation  $\mathbf{v}$  using  $\mathbf{v}' = \mathbf{F}\mathbf{v}/\|\mathbf{F}\mathbf{v}\|$ , where  $\mathbf{F}$  is a local affine transformation. **Orientation Distribution:** We model, at each voxel location, the distribution of orientations across subjects by employing the bipolar Watson distribution [1]:  $f(\mathbf{v}|\boldsymbol{\mu}, \kappa) \propto \exp[\kappa(\boldsymbol{\mu}^T \mathbf{v})^2]$ . It can be proven that the maximum likelihood estimator (MLE) of the mean orientation,  $\boldsymbol{\mu}$ , of the Watson distribution is given by the eigenvector corresponding to the largest eigenvalue  $\lambda_1$  of the dyadic tensor [3] defined as  $\mathbf{D} = \sum_i \mathbf{v}_i \mathbf{v}_i^T$  where  $i$  is an index indicating the subject. The MLE of the coherence parameter  $\kappa$  is given by  $1 - \lambda_1$ . For voxels containing  $n$  orientations,  $n$  mean orientations and coherence parameters are estimated for  $n$  Watson distributions. **Probabilistic Tractography:** Tractography is performed based on the field of Watson distributions, parameters of which are estimated as described above. When the track reaches a voxel with multiple orientations, one orientation is selected randomly based on a distribution which is determined by the similarity of the current orientation(s) with the prior orientation. The orientation which is more parallel to the prior orientation has a higher probability of being selected.

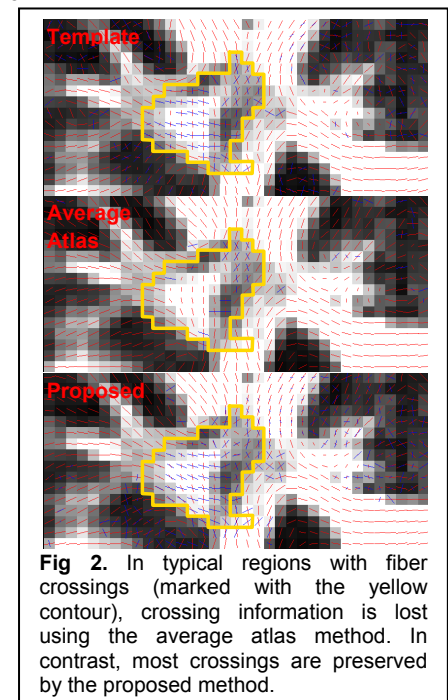
**MATERIALS:** Diffusion-weighted images were acquired for 14 adult subjects using a Siemens 3T TIM Trio MR Scanner with an EPI sequence. Diffusion gradients were applied in 120 non-collinear directions with diffusion weighting  $b = 2000\text{s/mm}^2$ , flip angle =  $90^\circ$ , repetition time (TR) = 12,400ms and echo time (TE) = 116ms. The imaging matrix was  $128 \times 128$  with a rectangular FOV of  $256 \times 256\text{mm}^2$ . 80 contiguous slices with a slice thickness of 2mm covered the whole brain. Data post-processing includes brain skull removal, motion correction and eddy current correction using algorithms developed and distributed as part of the FMRIB Software Library (FSL) package [4].

**RESULTS: Synthesized Dataset:** To evaluate the effectiveness of our method in preserving fiber crossings and in correctly estimating the local fiber orientations, we synthesized a  $8 \times 8$  image matrix (Camino [5]; two-tensor model) with each voxel containing a crossing with two orientations – one vertical and one horizontal. To simulate inter-subject variability, we perturbed the synthesized diffusion-weighted signal by applying a random rotation matrix (angle limited to  $45^\circ$ ) and adding isotropic complex Gaussian noise (SNR = 16) to each voxel. We applied these perturbations 10 times to the no-noise image and then used the resultant images to attempt to recover the 'true' orientations. As shown in Fig. 1, we found that the average atlas method, generated by averaging the diffusion-weighted signals, resulted in loss of fiber crossings and significant deviation of the estimated orientations (average orientation difference:  $37.34^\circ$ ). The proposed method gave a more consistent result (average orientation difference:  $15.72^\circ$ ). **Real Dataset:** Similar loss of fiber crossings was observed when real data were used (Fig. 2), again validating the effectiveness of our method. **Tractography:** The forceps minor is a fiber bundle which connects the lateral and medial surfaces of the frontal lobes and crosses the midline via the genu of the corpus callosum. To test whether this major fiber bundle is preserved by our method, we placed a small seed ROI at the point where the midline crosses the genu of the corpus callosum and performed tractography based on this seed. The results, shown in Fig. 3, indicate that the average atlas method results in premature termination of the fiber bundle. In contrast, the proposed method gives a more complete reconstruction of the fiber trajectories, which are more consistent with our anatomical knowledge of the bundle [6].

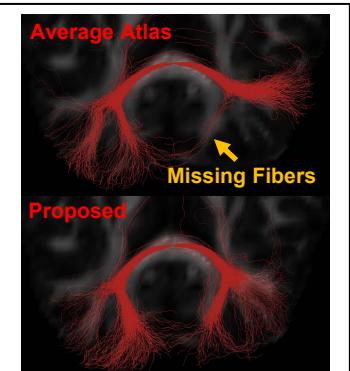
**REFERENCES:** [1] Watson, Biometrika, 1965. [2] Yap, MIAR, 2010. [3] Basser, MRM, 2000. [4] Smith, NeuroImage, 2004. [5] Cook, MRM, 2006. [6] Wakana, Radiology, 2004.



**Fig. 1.** Orientations estimated based on the average atlas method and the proposed method. The proposed method preserves more fiber crossing and estimates the orientations with higher accuracy.



**Fig 2.** In typical regions with fiber crossings (marked with the yellow contour), crossing information is lost using the average atlas method. In contrast, most crossings are preserved by the proposed method.



**Fig. 3.** The average atlas method results in premature termination of the forceps minor. The proposed method gives a more complete reconstruction of the bundle.