

# Resolve Fiber Orientation Ambiguity Using HARD Imaging

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## Introduction

Diffusion tensor imaging has become the primary imaging modality for non-invasive characterization of the micro-structure of living tissue particularly of the brain white matter (1). While interest in this technique is growing, its limitations have also been recognized (2). A fundamental limitation is that the tensor model, usually employed to describe the anisotropy of water diffusion, is unable to characterize diffusion with complex compartmentation such as fiber crossing, kissing or joining. In these cases, the apparent decrease in diffusion anisotropy creates ambiguity in fibers' orientation, making it hard to reveal the fibers' topological structure within the voxel. To address this problem, High Angular Resolution Diffusion (HARD) imaging (3) involves measurements with diffusion sensitizing gradient applied in many directions, thus fully capturing the directional dependence of water diffusion and providing more detail in tissue microstructure. A model for analyzing HARD data, called Fiber ORientation Estimated using Continuous Axially Symmetric Tensors (FORECAST) (4) provides a reliable way to estimate the fiber orientation distribution. The purpose of this study is to develop techniques to resolve the ambiguity of fiber orientation using HARD measurements and neighborhood analysis of FORECAST model results, aiming to establish a more useful tool for tissue micro-structural characterization.

## Methods

**1. Experiments with numerical simulation data** Four different kinds of fiber topology within a 3x3 voxel area were considered, with the central voxel containing crossing, kissing, joining and bending fibers, respectively, as showed in Fig1 top. The magnitude of the diffusion weighted signal was calculated for each case, with  $\text{tr}(b)=1000\text{s}/\text{mm}^2$  and diffusion gradients applied in 92 directions given by the third-order icosahedral tessellation of a sphere. For all fibers, mean diffusivity  $\bar{\lambda} = 0.9 \times 10^{-3} \text{mm}^2/\text{s}$  and perpendicular diffusivity  $\lambda_{\perp} = 0.5 \times \bar{\lambda}$ . The fiber angular distribution (FAD) of each voxel was estimated using the FORECAST model with a 4<sup>th</sup> order spherical harmonic expansion, then the angular correlation coefficient (ACC) of the FAD in each voxel with respect to the central voxel's FAD was calculated. The central voxel's FAD shape and the ACC gradient (a 2D vector) were compared.

**2. Experiments with in vivo human HARD data** HARD data from a healthy human subject were acquired on a Philips 3T scanner, generating a dataset of 96x96x55 voxels at spatial resolution of 2.5 mm<sup>3</sup>. Diffusion weighting ( $\text{tr}(b)=1000\text{s}/\text{mm}^2$ ) was applied as in the simulation. Four scans were acquired and averaged to yield a dataset with higher SNR (total scan time ~90min). Then the averaged data were used to calculate the FAD (4<sup>th</sup> order,  $\bar{\lambda} = 0.9 \times 10^{-3} \text{mm}^2/\text{s}$  for whole dataset and  $\lambda_{\perp}$  optimized for each voxel) and the ACC gradient vector (in 3D space). The fiber composition in each voxel was determined by its gradient magnitude and its angle  $\theta$  from the FAD maximum ( $0 < \theta < 75^\circ$  for joining,  $0 > \theta > 75^\circ$  for bending, ACC gradient  $< 0.25$  for kissing).

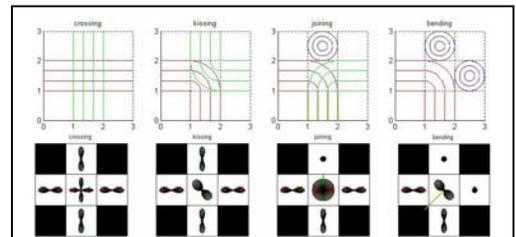


Figure1. Top: 2D fiber geometry for simulations, each color denotes one fiber bundle, the blue ones run perpendicular to the plane; Bottom: color-encoded FAD and ACC gradient vector.

## Results

As illustrated in Figure 1 bottom, the crossing fibers show a cross-shaped FAD, the joining fibers show a pancake-shaped FAD, while the other two FADs have single ambiguous "peanut" shapes. By comparing the ACC gradient vectors (their magnitudes and relation to the FAD maximum), the two cases can also be resolved. For the kissing case, the gradient is a zero vector, while the vector in the bending case points perpendicular to the FAD maximum. Figure 2 shows some examples from the in vivo human data, demonstrating the ability of this method to resolve the ambiguity. Note that due to image noise, some voxels near the threshold ( $0 \approx 75^\circ$ ) between bending and joining may be misclassified.

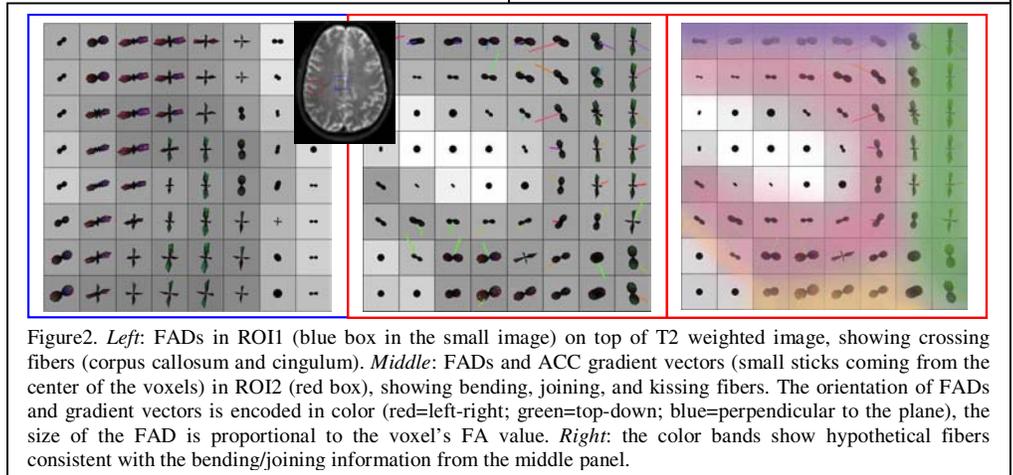


Figure2. Left: FADs in ROI1 (blue box in the small image) on top of T2 weighted image, showing crossing fibers (corpus callosum and cingulum). Middle: FADs and ACC gradient vectors (small sticks coming from the center of the voxels) in ROI2 (red box), showing bending, joining, and kissing fibers. The orientation of FADs and gradient vectors is encoded in color (red=left-right; green=top-down; blue=perpendicular to the plane), the size of the FAD is proportional to the voxel's FA value. Right: the color bands show hypothetical fibers consistent with the bending/joining information from the middle panel.

## Discussion and Conclusion

A limitation of this work comes from the assumptions of the FORECAST model, i.e., axially symmetric tensors and same mean diffusivity for all fibers. Also, image noise in the HARD data affects the accuracy of FAD estimation and therefore the final results. Future work will be extended to more complicated areas, and include de-noising techniques, optimizing the classification parameters, which should make this approach more robust and useful for fiber tractography and fiber bundle separation.

## Acknowledgements

This work was supported by NIH/NIBIB grant R01-EB02777

## References

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