

# Genetic Analysis of Fibers in White Matter Pathways from HARDI Images

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## Introduction:

High angular resolution diffusion imaging (HARDI) reconstructs the local diffusion profile of water in the brain, which may be used to understand how genetic variation affects connectivity and fiber integrity. We can follow the major directions of diffusion to generate fibers using Tractography algorithms that can focus our analysis on vital points in the brain.

We generated fibers in HARDI images using a Hough based method and represented the fibers compactly in white matter pathways across the brain using paths. This representation allows us bring into correspondence a sample of subjects to complete an analysis of heritability on the fraction anisotropy (FA) across the paths.

## Methods:

We scanned 454 young adult twins with 105-gradient high-angular resolution diffusion imaging (HARDI) on a 4 T Bruker Medspec MRI Scanner. These 3D volumes were composed of 55 2-mm thick axial slices with a 1.79 mm isotropic in-plane resolution. 94 diffusion-weighted images ( $b = 1159 \text{ s/mm}^2$ ) were acquired with a uniform distribution of gradient directions on the hemisphere, in addition to 11 non-diffusion images. We corrected for motion and eddy current distortion using FSL.

A Hough transform based tractography method (Aganj 2011) voted on the best fibers from the image space using a fiber score function based on the fractional anisotropy (FA) and the orientation distribution functions (ODF) at each voxel. The resulting fibers were clustered into their respective white matter regions using their intersection with an atlas. We represented these bundles using paths that followed the highest density of fibers in the bundle (maximum density paths; MDP). These paths were computed in each subject and brought into correspondence using geodesic curve registration (Joshi 2007). We sampled fractional anisotropy along the path and computed Falconer's Heritability estimate (Falconer 1996). This compares correlations in pairs of monozygotic and dizygotic twins to estimate heritability for these white matter measures.

## Results:

The figures show the results of our analysis pipeline on the 454 subjects. We analyzed 66 different bundles in the brain and show the mean maximum density paths across the population. Curves are

colored by Falconer's heritability measure; red colors show where the fiber integrity (FA) is more heritable.

### Conclusions:

Our method compactly represents the white matter structure in the brain. It allows us to compute correspondences across a population and perform heritability analysis. These models dramatically reduce the dimension of the brain images and summarize the structure of neural pathways by focusing registration on smaller structures instead of the entire image or skeletonized versions of derived data.

### Imaging Methods:

Diffusion MRI

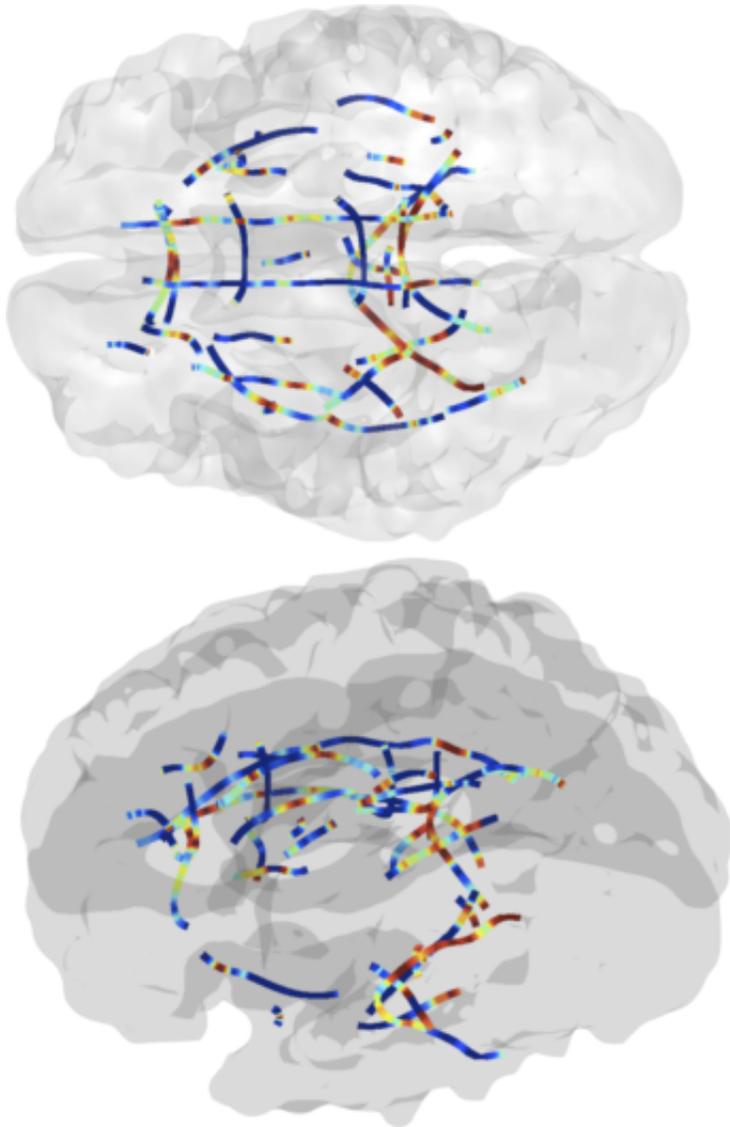


Figure 1. Axial and lateral views of MDPs color-coded with heritability. Fiber integrity is highly heritable (genetically influenced) in the regions highlighted in red colors.

### Abstract Information

## References

Aganj, I., et al. (2011) 'A Hough transform global probabilistic approach to multiple-subject diffusion MRI tractography', *Medical Image Analysis*, vol. 15, no. 4, pp. 414-425.

Falconer, D.S., MacKay T.F.C. (1996) 'Introduction to Quantitative Genetics', 4th Ed., Longmans Green, Harlow, Essex, UK.

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