# Assessment of bundle-specific axon diameter distributions using diffusion MRI tractography

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## 1 Introduction

The main limitation of diffusion tractography for connectivity studies is that the reconstructed tractograms are not truly quantitative. Microstructure imaging allows the estimation of more quantitative features of the neuronal tissue, such as the axon diameter distribution, but this analysis can only be performed voxelwise. Here, we extend a framework that we recently proposed for evaluating the plausibility of tractograms (COMMIT) with the aim of assessing bundle-specific axon diameter distributions as well. This possibility may have implications in connectomics, as it opens new perspectives for investigating brain connectivity at different scales.

## 2 Methods

The COMMIT framework (Convex Optimization Modeling for Microstructure Informed Tractography) enables expressing efficiently tractography and tissue microstructure estimation in a combined formulation.[1,2] COMMIT models the entire diffusion MRI (dMRI) image as a linear combination of the diffusion signal arising from all the fibers of an input tractogram, possibly in addition to local contributions from other tissue compartments, and allows expressing Microstructure Informed Tractography.

Inspired by the AMICO formulation[3,4] for mapping the mean axon diameter in a voxel using the linearized ActiveAx model,[5] we propose to extend the same principles to the space of streamlines and evaluate the feasibility of resolving fascicles composed of different axon calibers. The dictionary was build according to the CylinderZeppelinBall model.[6]

We tested our approach with data acquired on a perfusion-fixed Vervet monkey brain using an experimental 4.7T Varian system, according to the following protocol: 0.5 mm isotropic resolution, 44 b0, 239 q-space samples over 3 shells with $b = \{2320, 2970, 8800\}$ s/mm$^2$, Gmax $= \{300\}$ mT/m. All images were denoised and motion corrected.

# 3 Results

Figure 1 illustrates the aim of this work: given a tractogram that has no information about the caliber of the fibers (left), our method attempts to recover their actual axon diameter distributions (ADD). The tractogram on the right is colored according to the estimated mean diameter of each individual pathway and, indeed, the fibers in the mid-body of the corpus callosum (CC) appear composed of larger axons, as known from previous voxelwise studies.[5,7,8] This visualization, however, does not allow one to appreciate the actual axon composition of the bundles.

For this reason, in figure 2 we report the bundle-specific ADDs extracted from all the fibers in the tractogram that intersect the 4 different regions of interest (ROI) of the CC. For each ROI, we took all the fibers passing through it, computed their mean diameter and finally plotted their distribution to show the axon composition of each bundle. Figure 3 directly compares the ADDs recovered in the four CC ROIs with our method to appreciate the differences in the composition of the axon population in the four ROIs. Indeed, the bundles passing through the genu (red ROI) and the splenium (green ROI) contain more small-axons than fibers through the mid-body, especially in the blue ROI which seems characterized by a rather higher number of large axons. Our findings about the "ADD of fiber bundles" are compatible with the "voxelwise ADD" described in previous studies[7,8] and histological analyses[9] in the midsagittal slice of CC. Reassuringly, despite difference in species, our bundle-specific ADDs estimated on monkey resemble closely the voxelwise ADDs estimated on rat by;[8] in particular, compare their figures 1 and 4 with our results.

# 4 Conclusion

Our findings provide evidence of the feasibility to resolve fascicles composed of axons with different calibers using Microstructure Informed Tractography. The possibility of obtaining a description of brain connectivity at different scales, i.e. networks of axons with different calibers, may open new perspective for future connectomics analyses. This work only represents a proof of concept for extending local techniques for ADD estimation from a single voxel to entire fiber bundles, and results need to be validated with future studies.

# References


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# Figures

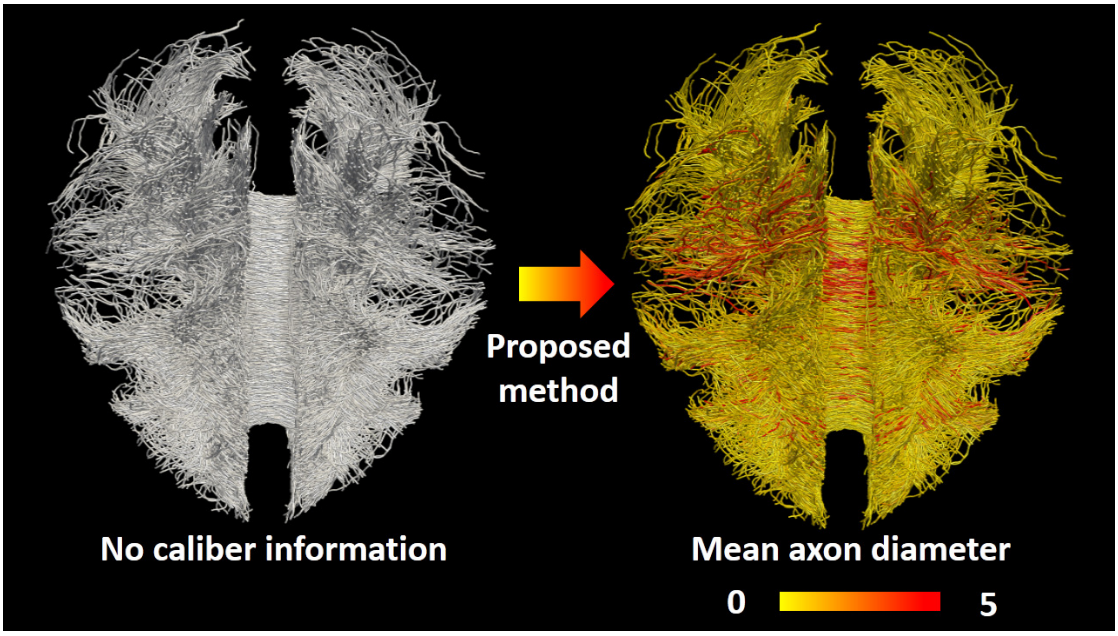


Figure 1: Comparison of the fibers traversing the CC before (left) and after (right) estimating the mean axon diameter with the proposed method.

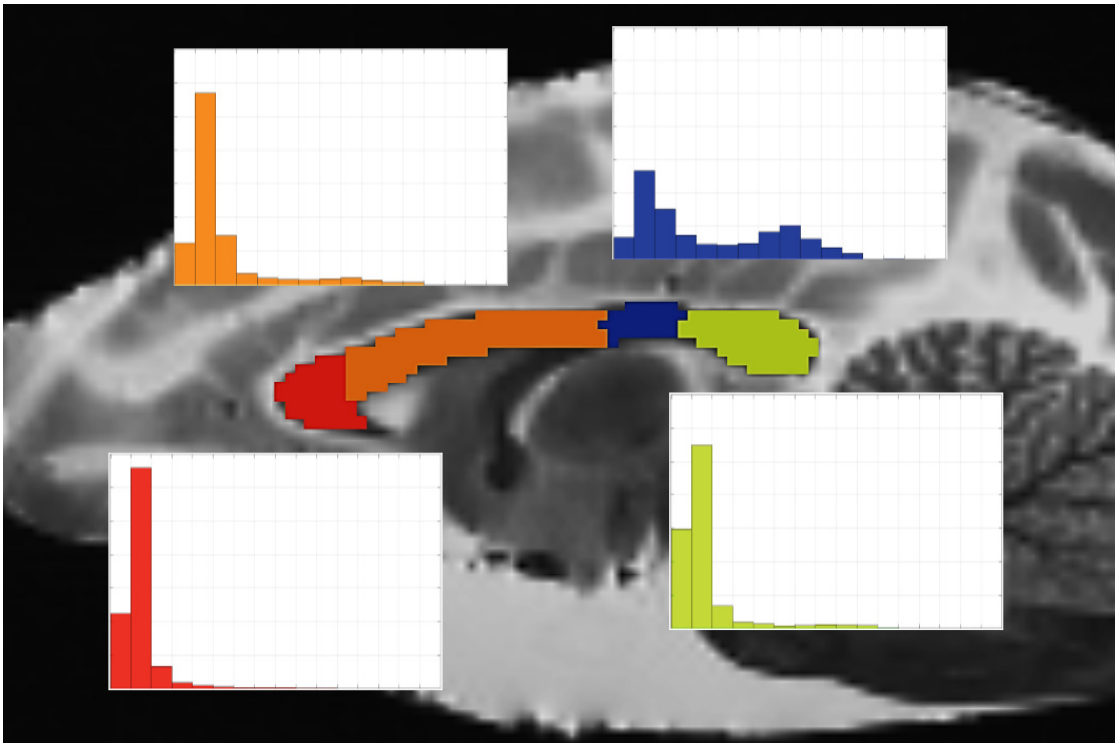

Figure 2: Sagittal section of the CC with superimposed the axon diameter distributions (ADD) estimated with our approach corresponding to the fiber bundles intersecting the 4 regions of interest.

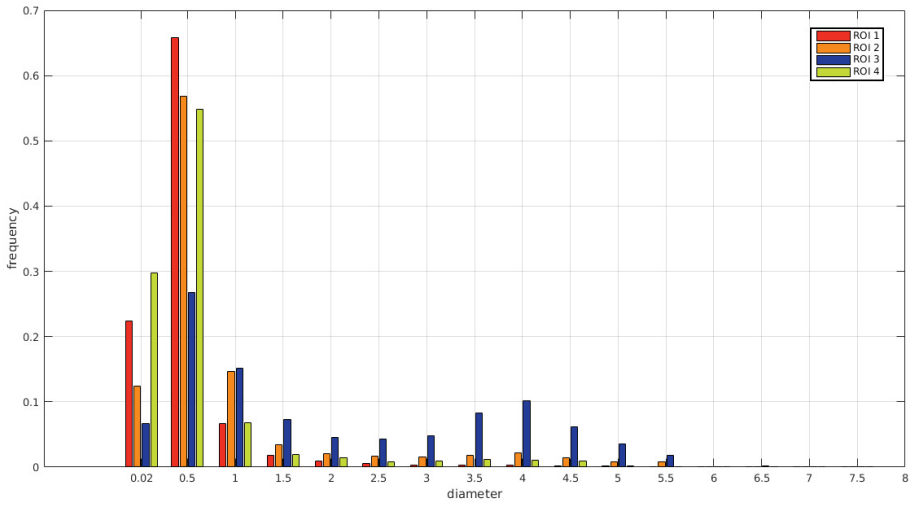


Figure 3: Direct comparison of the axon diameter distributions (ADD) estimated with our approach corresponding to the fiber bundles passing through the 4 regions of interest.