Combining Tractography and Microstructure to Assess Bundle-Specific Axon Diameter Distributions

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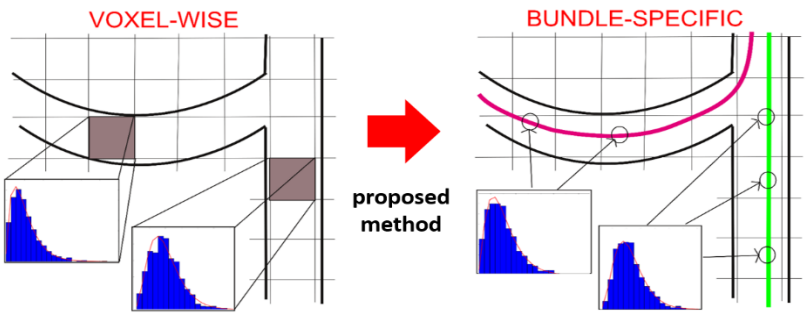
PURPOSE

Microstructure imaging allows the estimation of quantitative features of the neuronal tissue, such as the axon diameter distribution, but, to date, this analysis can only be performed voxel-wise[1] and not bundle-specific. In fact, the extracted features represent a superimposition of fiber tracts passing through the voxel, and thus are not suitable for connectivity analyses, top figure left. Here, we propose an extension of the Microstructure Informed Tractography[2, 3] framework that we recently developed for evaluating the plausibility of tractograms with the aim of extracting bundle-specific microstructure proprieties, like axon diameter distribution, top figure right. This possibility may have profound implications in connectomics, as it opens new perspectives for investigating brain connectivity on different scales.



METHODS

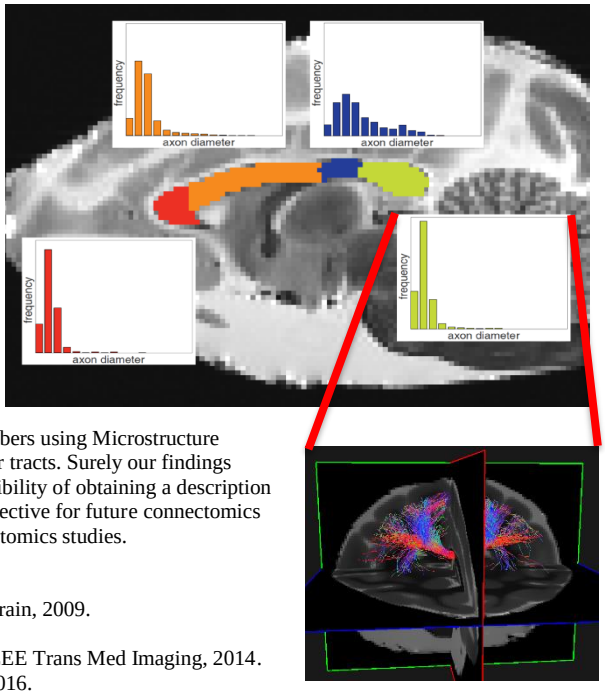
COMMIT (Convex Optimization Modeling for Microstructure Informed Tractography) is a framework we recently proposed [2, 3] to express efficiently both tractography and tissue microstructure estimation in a unified formulation. In a nutshell, COMMIT models the whole diffusion MRI (dMRI) image as a linear combination of the diffusion signal arising from all the fiber tracts in an input tractogram, possibly in addition to local contributions from other tissue compartments, and allows expressing microstructure informed tractography as a convenient linear system: $y = Ax + \eta$, where y contains all dMRI measurements, A is the linear operator (or dictionary) implementing a generic multi-compartment model for the signal contributions of the tracts in each voxel and η is the acquisition noise. The contributions x of all compartments can then be estimated solving a nonnegative least-squares problem: $argmin_{x \geq 0} \; ||Ax - y||_2^2$.

The dictionary A was build according to the CylinderZeppelinBall model: axons represented as cylinders with given radii and fixed longitudinal diffusivity $d_\parallel$, extra-axonal space modeled as anisotropic tensors with same $d_\parallel$, but different $d_\perp$, and also as isotropic diffusion. The proposed formulation considers each streamline as possibly consisting of distinct axon populations having different calibers and, thus, we allow multiple contributions to be defined per individual pathway. The estimated coefficients x that are associated with each fiber tract represent its axon diameter distributions (ADD).

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: $0.5mm$ isotropic resolution, 44 b0, 239 q-space samples over 3 shells with $b = \{2320, 2970, 8800\}\ \frac{s}{mm^2}$, $G = \{300, 220, 300\}\ \frac{mT}{m}$, $\Delta = \{12, 20, 17\}\ ms$, $\delta = \{6, 7, 10\}\ ms$, $TE = 36\ ms$. All images were denoised and motion corrected. Whole-brain tractography was performed using the probabilistic iFOD2 algorithm ($100K$ streamlines) and the tissue model was set as follows: 20 cylinders with radii equally-spaced in the range $0.01 - 8\ \mu m$, $d_\parallel = 0.6 \cdot 10^{-3}\ \frac{mm^2}{s}$, $d_{iso} = 2.0 \cdot 10^{-3}\ \frac{mm^2}{s}$ and 7 different values for $d_\perp$.

RESULTS

As the input tractogram has no information about the caliber of the fiber tracts, our method attempts to recover the tract's ADD by fitting the previous global model to the dMRI signal. Bottom figure reports the bundle-specific ADDs extracted from all the fiber tracts in the tractogram that intersect 4 different regions of interest (ROI) in the CC. For each ROI, we took all the fiber tracts passing through it and plotted their distribution to show the axon composition of each bundle. Indeed, the fiber tracts passing through the genu (red ROI) and the splenium (green ROI) contain more small-axons than the bundles going through the mid-body, especially in the blue ROI which seems characterized by a rather higher number of large axons.



DISCUSSION

Our results about the "bundle-specific ADD" are compatible with the "voxel-wise ADD" described in previous studies[1] and histological analyses[6] in the midsagittal slice of CC. Reassuringly, despite differences in species, our bundle-specific ADDs estimated on monkey resemble closely the voxel-wise ADDs estimated on rat by[1]; in particular, compare their figures 1 and 4 with our results.

CONCLUSION

Our results provide evidence of the feasibility to distinguish bundles composed of axons with different calibers using Microstructure Informed Tractography[4,5], thus extending local techniques for ADD estimation from the voxel level to fiber tracts. Surely our findings represent only a proof of concept and need to be confirmed with future experiments. Nonetheless, 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 and, hence, makes it possible to start performing truly quantitative and biologically driven connectomics studies.

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