Characterizing white matter pathways of the living rat brain by *Tractometry*

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Introduction:

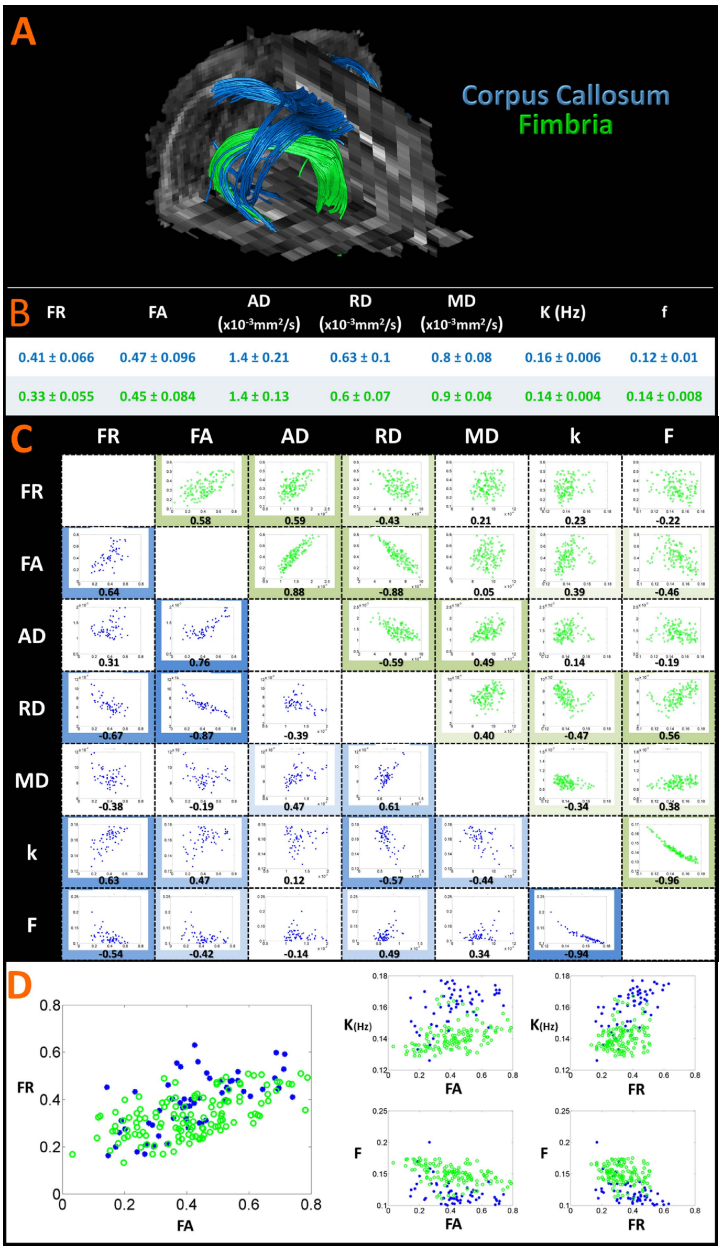
Diffusion tensor imaging (DT-MRI) [1] is a powerful tool that yields several widely used indices for white matter (WM) analysis such as fractional anisotropy (FA) and the principal eigenvector, which is used for estimation of fiber orientation and pathways reconstruction (i.e., tractography). However, DT-MRI uses a unimodal Gaussian to describe such complexity and thus lacks specificity to tissue sub-components. FA measurements can be modulated by various components of white matter microstructure (e.g., axonal membrane, degree of myelination [2]) and the pathway architecture (intra-voxel dispersion). Therefore, to have more accurate and informative descriptions of WM and to understand its structural organization through development and impairment, we exploit the *tractometry* [3] framework which uses more specific and sensitive indices to tissue subcomponents. Recent works [4,5] used *tractometry* to examine the variations of each parameter across different brain regions and fiber pathways, and how they differ between individuals. The *tractometry* framework incorporates different imaging modalities such as CHARMED [6] and qMT [7] which estimate the axonal density and myelination respectively. In this work, we aim to implement *tractometry* on different fasciculi of rats to compare intra- and inter-fasciculus variation with histological validation. We present here the preliminary results of *tractometry* measurements of Wistar rats on two representative well defined pathways, the corpus callosum (CC) and fimbria.

Methods:

3 Wistar rats (3 months old) were scanned on a 7T/30 Bruker Biospec system equipped with 400mT/m gradients. The protocol comprised: (1) qMT acquisitions using a 3D FLASH sequence, 2 flip angles of 1000 and 2800^{o} with 8 offsets (between 1000 to 30000Hz). (2) CHARMED acqusitions comprising 3 b values of 1000, 2000 and 4000 s/mm^2 with 30 non-collinear directions per shell.

DT-MRI was calculated from the first shell of CHARMED (b-value = 1000 s/mm^2). qMT and CHARMED analyses were performed using in-house MATLAB script to extract the exchange rate (k), the relative concentration of macromolecular protons (F) and the volume fraction of the restricted compartment (FR). DT-MRI data were analyzed by *ExploreDTI* [8] for tractography and visualization and to extract the fractional anisotropy (FA), mean diffusivity (MD), axial and radial diffusivities (AD and RD respectively) for the examined fiber systems.

Results: Fig. A shows the CC and fimbria pathways (through all results, the blue hue is related to CC and green to fimbria) superimposed on an FA image. The tractometry metrics across each fiber systems were highly variable; therefore sections that exhibit homogeneity were manually marked to evaluate the differences between properties of the two pathways. The mean and standard deviation of the tractometry metrics for the two pathways are given in Fig. B with similar colors to Fig. A. The higher specificity of CHARMED over DT-MRI is reflected in FA and FR indices, where FR differentiates between the two, and allocates higher axonal density to the CC over the fimbria, while FA finds no differences between them. Fig. C shows multiple scatter plots of the correlation between the microstructural metrics of the two fibers, where the p values (corrected for multiple comparisons) are reflected with the background opacity (white background – no significance, darker hue – more significant). The relations between FA, FR and qMT metrics are demonstrated in Fig. D. The FA/FR, k/FR, F/FR graphs show the sensitivity of qMT and CHARMED metrics to the fiber myelin content and microstructure, and estimate distinct values for each pathway.



Conclusions and Summary:

The *tractometry* framework exploits a combination of imaging methods that provide higher sensitivity to underlying tissue subcomponents. We demonstrate the ability of tractometry to provide microstructural characterization of different WM pathways in the living rat brain,. In the next steps, we will extend our measurements to large populations of rats from 3 different types, and validate our measurements with postmortem histology.

References:

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