Towards whole-brain validation of diffusion MRI fiber orientation distributions with x-ray microcomputed tomography

Scott Trinkle, Sean Foxley, Narayanan Kasthuri and Patrick La Rivière

Diffusion MRI (dMRI) is a powerful, non-invasive tool for characterizing three-dimensional (3D) tissue microstructure on a macroscopic scale, and is widely used in both research and clinical settings. New methods of reconstructing 3D fiber orientation distributions (FODs) from dMRI data are rapidly being developed, each based on the assumption that the diffusion contrast from dMRI provides an accurate representation of the underlying anatomical fiber structure. Previous efforts to validate these FODs have relied on ground truth histological data with non-isotropic resolution over small regions of interest (ROI). In this study, we demonstrate a pipeline for the use of natively isotropic, synchrotron-based x-ray microcomputed tomography data to validate FODs over a whole mouse brain.

A post-mortem brain was scanned on a Bruker 9.4 T magnet with a 3D diffusion-weighted spin-echo sequence at 150 μm isotropic resolution. Data was acquired at a b-value of 3000 s/mm^2 over 60 uniformly distributed directions. The specimen was then stained with uranyl acetate, osmium tetroxide and lead citrate in preparation for x-ray imaging at the Advanced Photon Source at Argonne National Lab. The x-ray data was acquired using a mosaic stitching method, yielding an image volume over the whole brain with 1.2 μm isotropic resolution. N (number TBD) sample ROIs were identified for validation based on anatomical locations with crossing fiber populations that are known to challenge dMRI algorithms. Structure tensor analysis was performed on the x-ray data to compute a ground truth FOD at each ROI. The corresponding FODs were reconstructed from the dMRI data using two high angular resolution diffusion imaging (HARDI) methods: constrained spherical deconvolution and Q-ball imaging. FODs from both HARDI methods were compared to the ground truth x-ray FODS and evaluated based on overall agreement in shape, correct assessment of the number of fiber populations, and angular accuracy in orientation.

(Quantitative results TBD)

This study has demonstrated the feasibility of performing quantitative 3D validation of dMRI FODs with synchrotron x-ray data. This marks the first available ground truth dataset and methodology to allow for whole-brain validation of dMRI FODs with natively isotropic resolution and no sectioning. The application of this analysis to a whole mouse brain will provide a wealth of information regarding the ability of different dMRI algorithms to represent microstructural regions of varying complexity, and will provide the means to perform future large-scale validation studies in dMRI, tractography, and connectomics.