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 dMRI provides an accurate model 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 with dMRI (*waiting on MRI specs from Sean*) at 150 μm isotropic resolution. The specimen was then stained (*what are the stains? Other info on uCT sample preparation?*) and imaged at the Advanced Photon Source at Argonne National Lab using a mosaic stitching method, yielding an image volume over the whole brain with 1.2 μm isotropic resolution. N (*actual 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 from the dMRI data were evaluated based on overall agreement in FOD shape, correct assessment of the number of fiber populations, and angular accuracy in orientation (*criteria taken verbatim from Schilling*).

(*Results TBD. I think the goal should be to demonstrate comparable results to previous validation studies over a few ROI, to justify the use of this dataset/method for a future whole-brain study.*)

This study has demonstrated the feasibility of performing quantitative 3D validation of dMRI FODs with synchrotron x-ray data. Applying 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 (*It might be cool to one day have a spatial map over the whole brain of where the MRI is failing*). Ground truth FODs across the whole brain will allow for future large-scale validation studies in both dMRI and tractography.