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

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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 synchrotron-based x-ray microcomputed tomography data to validate FODs from dMRI over a whole mouse brain with isotropic resolution.

A perfusion-fixed mouse brain was scanned on a Bruker 9.4 T magnet with a 3D diffusion-weighted spin-echo sequence at 150 μm isotropic resolution. Data were acquired at a b-value of 3000 s/mm^2 over 30 uniformly distributed directions. The specimen was then stained with uranyl acetate, osmium tetroxide, and lead citrate in preparation for synchrotron x-ray imaging at the Advanced Photon Source at Argonne National Lab. The x-ray data were acquired using a mosaic sinogram stitching method, yielding a reconstructed image volume over the whole brain with 2.4 μm isotropic resolution.

Structure tensor analysis was performed on the x-ray data to estimate a primary orientation vector at each voxel. These orientations were then grouped into ROI the size of a single MRI voxel, and ground-truth FODs were computed by expanding the distribution of orientation vectors within each ROI onto spherical harmonic coefficients.

A sensitivity study was performed with simulated phantoms containing populations of fibers with various known crossing angles. Angular peaks in the FODs calculated using structure tensor analysis were within 2° of the true peaks for all fiber crossing angles.

This work introduces a ground truth dataset and methodology that will allow for whole-brain validation of dMRI FODs with natively isotropic resolution and no sectioning. Once the X-ray and dMRI data are registered, FODs can be reconstructed from the dMRI data using a number of available algorithms. Quantitative comparisons to the X-ray FODs across the whole brain will provide a wealth of information regarding the ability of these 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.