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Mapping the Connectome in Multiple Sclerosis, Innovations in MRI Imaging

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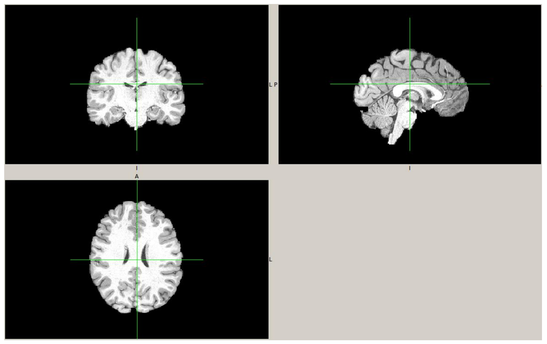
Introduction

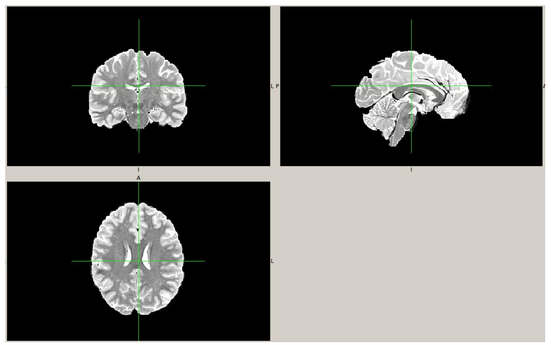
In neuroscience research, living human brains may be assessed with magnetic resonance imaging (MRI). MRI scanners use magnetic fields, radio waves, and field gradients to form images.

The MRI machine's electromagnet generates a magnetic field. The spin of protons in the matter of a brain align with or against the field. Pulses of radio frequency (RF) waves are emitted by antennas that excite these aligned protons, misaligning their spin. As the spins return to alignment, they emit RF waves, and these are received by antennas. The frequency is dependent on the magnetic field.

Applying a known gradient in the field, protons at different positions have different frequency emissions. Their contribution can be extracted through a Fourier transform. The signal from a particular location has a particular frequency and from this information the three dimensional image can be formed. The base unit is the voxel whose value is the relative intensity.



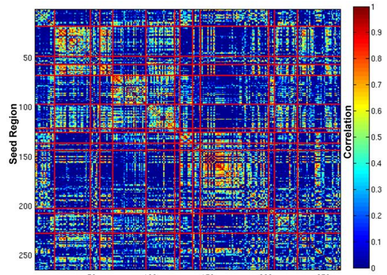
T1 weighted image demonstrating anatomy



T2 weighted image demonstrating pathology through water content

Background

The connectome is the inter-connectivity of brain regions according to white matter tracts and the functional relationships of activity between structures. For statistical analysis purposes, the connectome is often illustrated as a matrix whose axes are brain regions and whose entries are the relative connectivity between regions.



Functional connectome matrix (NIH Blueprint for Neuroscience Research)

Connectome visualization (Human Connectome Project)

Multiple Sclerosis (MS) is a neurodegenerative, demyelination disease. Myelin is the fatty material which sheathes the axons of nerve cells. White matter is brain matter with high lipid content and few cell bodies, comprised mostly of myelinated axon tracts. Grey matter is brain matter which contains many cells and few myelinated axons.

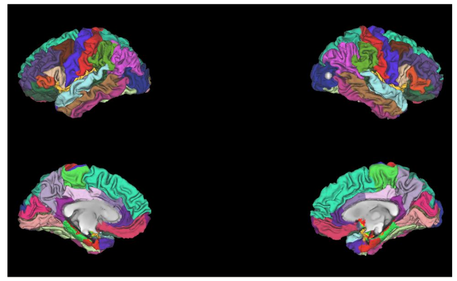
Lesions in the brain caused by MS may disrupt the healthy natural function of underlying white matter tracts and the relationship of activity between brain regions.

Complex protocols to process and analyze connectome data in healthy controls have been developed by the Human Connectome Project (HCP) research consortium fostered by the National Institutes of Health. However, these protocols require adaptation so that they may be applied to connectome data collected from persons with MS. We are designing protocols according to HCP guidelines to accurately reconstruct images of structural and functional connectivity in brains of people with MS.

Methods

Following the HCP Pipelines we begin structural preprocessing by averaging image repeats. Brain extraction is then performed, bias field is corrected for, and image is registered in the Montreal Neurologic Institute standard space.

FreeSurfer reconstruction is performed alongside manual interventions and checks beginning with control point (intensity normalization) correction, edits to the brain-mask volume and white matter volume, topological defect correction, skull strip correction, talaraich transform correction, and segmentation and cortical parcellation corrections.

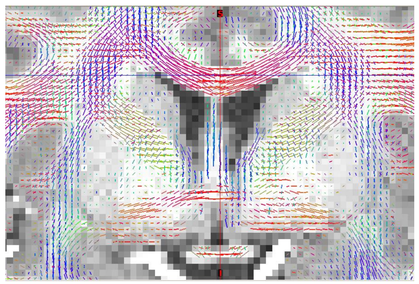


Cortical parcellation

Diffusion preprocessing begins with correction for differences in the magnetic susceptibilities of brain matter. Then eddy currents are corrected for. The corrected data may then be registered to the T1-space in a diffusion tensor model. However, this model allows only for one fiber orientation to be estimated per voxel.

FSL's Bedpostx, developed by the Oxford Centre for Functional MRI of the Brain, may be employed to account for instances where multiple fibers cross within a voxel.

As well, FSL's Probtrackx may be used to map seed region connectivity and generate our desired seed by seed functional connectome matrices.



Fiber orientation visualization

Methods (continued)

Knowing fiber orientations, we may connect fibers to form tracts (deterministic tractography). However, probabalistic tractography, rather than deterministic tractography, estimates the most likely fiber orientations in tracing tracts which is more sensitive to pathological abnormalities and uncertainty. The entirety of our processing is cortical surface reconstruction based for greater anatomical accuracy and sensitivity than volumetric analysis.

Conclusions

Currently, use of Probtrackx without parallelization capabilities is not a viable option as we estimate that processing of 40 to 50 sets of data would take on the order of hundreds of hours.

We anticipate the release of Probtrackx with graphics processing unit support while we are exploring other parallelized options to perform probabilistic tractography including MRtrix3. MRtrix3, developed by researchers at the Florey Institute, the University of Melbourne, King's College London, and others, provides another set of tools to exact tractography and produce our desired functional connectivity matrices.

Acknowledgements

- Dr. Michael Dwyer, Assistant Professor, Neurology, University at Buffalo, and Director, Neurology, Buffalo Neuroimaging Analysis Center
- Tom Fuchs, MD-PhD MSTP student, University at Buffalo
- The Buffalo Neuroimaging Analysis Center
- The University at Buffalo Center for Research and Creative Activities
- The Human Connectome Project
- The Freesurfer developers at the Martinos Center for Biomedical Imaging in the Laboratory for Computational Neuroimaging
- The FSL developers at the Oxford Center for Functional MRI of the Brain

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