Opportunities and Challenges in Brain Mapping with Diffusion MRI

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***Abstract*—Diffusion MRI provides new contrasts with which to image and map features of human brain microstructure and architecture *in vivo*. As powerful as this method currently is, it still has great potential to provide high-dimensional quantitative data with which to segment and cluster different brain regions, probe tissue microstructure and compartmental features, and provide clinicians with new quantitative imaging biomarkers with greater specificity and sensitivity.**

I. Introduction

It has long been a dream of neuroscientists to discover the basis of thoughts and feelings, and of clinicians to understand and cure complex disorders of the brain. A common presumption in both communities is that if one elucidates the "wiring diagram" and the purpose of each cell type, one can understand brain function in its entirety. Until 1990, the primary *ex vivo* techniques to assess brain wiring via white matter pathways were post-mortem cell, histological and whole-brain slice analysis. *In vitro* methods primarily consisted of analyzing electrical activity of groups of cells, syncytia in cell cultures, and recordings from brain slices.

The advent and development of macroscopic-scale *in vivo* MRI methods created new opportunities to study structure, architectural organization, and function in the living brain. Functional MRI (fMRI) [1] was proposed to follow brain activation in gray matter through changes in blood oxygenation. Various structural MRI methods, like T_1-imaging showed white matter regions with new definition. Diffusion Tensor MRI (DTI) [2] revealed new microstructural features, particularly diffusion anisotropy in white matter, which provided a means to reconstruct brain white matter pathways *in vivo*.

II. Discussion

One largely unrealized application of diffusion MRI data is to be able to study second and higher-order *field* properties inferred from a dense set of 10^7x1 mm^3 isotropic voxels. These data could be used to segment and cluster the brain into distinct anatomical regions, e.g., identifying Brodmann-like areas in the cortex, and virtually dissecting and elucidating all of the white matter pathways connecting them. This is inherently a statistical task [3], but to date, no comprehensive, robust and reliable imaging sciences toolbox has been developed for hypothesis testing of second and higher-order tensor data.

Another challenge is to be able to "drill down into the voxel"—to be able to estimate or measure microstructural cell and tissue-scale features from macroscopic, voxel-averaged MRI measurements. Our approach is to use single [4] and multiple [5, 6] Pulsed-Field Gradient (PFG) MRI methods to be able to probe water displacements and their correlations in different intra- and extra-cellular compartments owing to the different MR signature diffusing water molecules produce in different restricted domains.

Imaging and mapping the entire net displacement distribution of water molecules, to which the diffusion tensor can be shown to be the lowest order Gaussian approximation, allows one to identify and resolve different populations of white matter fibers in complex brain regions. However, no comprehensive imaging sciences framework exists for statistically testing features of these net displacement distributions within the imaging volume.

An additional complexity is the multi-scale organization of the brain. White matter, gray matter and glia are all hierarchically organized, having a fractal-like character. Diffusion MRI captures net water displacements over a micron-length scale and a millisecond time scale. Needed are new ways to probe a larger range of length and time scales in a systematic and integrated way to be able to achieve a more comprehensive description of the structure and organization of the brain.

New approaches to assess exchange among diffusing molecules in different compartments will help us estimate their proximity and the permeability of boundaries separating them.

III. Summary

Diffusion MRI is a powerful method that allows us to probe tissue microstructure by being able to measure the net displacement distribution of water molecules in different tissue compartments. While widely used clinically and in a myriad of neuroscience studies, Diffusion MRI continues to have potential to extract new and important tissue features. Opportunities exist to develop new imaging sciences methods and pipelines to analyze Diffusion MRI data for these ends.

References

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