Modeling Structural Brain Connectivity

The human brain consists of a gigantic complex network of interconnected neurons. Together all these connections determine who we are, how we react and how we interpret the world. Knowledge about how the brain is connected can further our understanding of the brain’s structural organization, help improve diagnosis, and potentially allow better treatment of a wide range of neurological disorders.

Tractography based on diffusion magnetic resonance imaging is a unique tool to estimate this “structural connectivity” of the brain non-invasively and in vivo. During the last decade, brain connectivity has increasingly been analyzed using graph theoretic measures adopted from network science and this characterization of the brain’s structural connectivity has been shown to be useful for the classification of populations, such as healthy and diseased subjects. The structural connectivity of the brain estimated using tractography is, however, derived by integrating noisy estimates of the local fiber orientation in each voxel, entailing biases and limitations in the estimated connections and resulting in noisy graphs.

In this thesis, the ability of stochastic block models to extract the latent organization of structural brain connectivity graphs is investigated. It is found that both the stochastic block model and its non-parametric extension, the infinite relational model, are able to reliably extract a clustering that better accounts for structural connectivity than cortical atlases based solely upon surface morphology. Furthermore, a statistical prediction framework to quantify the ability of a cortical parcellation to account for structural connectivity is proposed. It is tested on two commonly used cortical atlases that are both based on surface morphology, as well as on a recently proposed cortical parcellation by Glasser et al. (2016) that is based on both task and resting-state functional magnetic resonance imaging, cortical thickness and myelin. It is found that all three atlases capture the structural connectivity much better than random, but also that the parcellation based on multiple modalities is superior to those solely based on surface morphology.

The generation of structural brain connectivity graphs comprises a comprehensive processing pipeline, with various experimenter-defined parameters. The settings of these parameters are, however, unclear and this subjective aspect complicates the cross-comparison of studies investigating structural brain connectivity derived from tractography. Even though scan acquisition parameters, i.e. spatial resolution, angular resolution and b-value, are often discussed as possible factors influencing the final result, the impact of these factors on the derived structural connectivity graph has not yet been investigated. Herein, structural connectivity graphs, generated using different combinations of the three aforementioned acquisition parameters, are validated by comparison to a connectivity graph derived using invasive tracer injections in monkeys. It is found that the choice of acquisition parameters influences the derived structural connectivity graph and that higher angular resolution is always beneficial. Surprisingly, it is also found that higher spatial resolution does not improve the derived graph, but further investigation is needed to confirm this result.
Whole-brain functional connectivity predicted by indirect structural connections

Modern functional and diffusion magnetic resonance imaging (fMRI and dMRI) provide data from which macro-scale networks of functional and structural whole brain connectivity can be estimated. Although networks derived from these two modalities describe different properties of the human brain, they emerge from the same underlying brain organization, and functional communication is presumably mediated by structural connections. In this paper, we assess the structure-function relationship by evaluating how well functional connectivity can be predicted from structural graphs. Using high-resolution whole brain networks generated with varying density, we contrast the performance of several non-parametric link predictors that measure structural communication flow. While functional connectivity is not well predicted directly by structural connections, we show that superior predictions can be achieved by taking indirect structural pathways into account. In particular, we find that the length of the shortest structural path between brain regions is a good predictor of functional connectivity in sparse networks (density less than one percent), and that this improvement comes from integrating indirect pathways comprising up to three steps. Our results support the existence of important indirect relationships between structure and function, extending beyond the immediate direct structural connections that are typically investigated.

Nonparametric Bayesian Clustering of Structural Whole Brain Connectivity in Full Image Resolution

Diffusion magnetic resonance imaging enables measuring the structural connectivity of the human brain at a high spatial resolution. Local noisy connectivity estimates can be derived using tractography approaches and statistical models are necessary to quantify the brain’s salient structural organization. However, statistically modeling these massive structural connectivity datasets is a computational challenging task. We develop a high-performance inference procedure for the infinite relational model (a prominent non-parametric Bayesian model for clustering networks into structurally similar groups) that defines structural units at the resolution of statistical support. We apply the model to a network of structural brain connectivity in full image resolution with more than one hundred thousand regions (voxels in the gray-white matter boundary) and around one hundred million connections. The derived clustering identifies in the order of one thousand
salient structural units and we find that the identified units provide better predictive performance than predicting using the full graph or two commonly used atlases. Extracting structural units of brain connectivity at the full image resolution can aid in understanding the underlying connectivity patterns, and the proposed method for large scale data driven generation of structural units provides a promising framework that can exploit the increasing spatial resolution of neuro-imaging technologies.

Comparing Structural Brain Connectivity by the Infinite Relational Model

The growing focus in neuroimaging on analyzing brain connectivity calls for powerful and reliable statistical modeling tools. We examine the Infinite Relational Model (IRM) as a tool to identify and compare structure in brain connectivity graphs by contrasting its performance on graphs from the same subject versus graphs from different subjects. The inferred structure is most consistent between graphs from the same subject, however, the model is able to predict links in graphs from different subjects on par with results within a subject. The framework proposed can be used as a statistical modeling tool for the identification of structure and quantification of similarity in graphs of brain connectivity in general.
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