An Introduction to Network Neuroscience

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Educational Course - Full Day

Understanding brain connectivity is now a major focus of the human brain imaging community. The widespread use of data from the Human Connectome Project (HCP) and UK Biobank, combined with new releases from related projects, such as the developmental, lifespan, and disease-related HCPs, mean that researchers require training in sophisticated analytic techniques that are not typically part of standard training programs. Many of these approaches are not “off the shelf” and require deep understanding of their subtleties for valid application. Critically, connectivity analysis is no longer an exotic approach used only by expert practitioners; it is now a standard part of most brain imaging analyses. It is therefore critical to ensure that researchers completely understand the strengths and limitations of their analytic tools to promote rigorous, robust and reproducible science.

This workshop will provide attendees with the unique opportunity to learn the pros, cons, and practical considerations of network neuroscience from experts in the field. As the field transitions to a post-HCP era in which connectivity analysis is the norm, the concepts and methods covered by this workshop will be an essential part of any neuroimager’s training.

Objective

The core objective of the workshop is to provide attendees with practical knowledge to map, analyse and visualize structural and functional brain networks using current best practices, and provide interactive opportunities for attendees to seek advice from international experts.

At the end of this workshop, attendees will understand:
- the strengths and weaknesses of different methods for parcellating the brain and defining network nodes;
- how to quantify and interpret different measures of structural and functional connectivity;
- how to define network communities and hubs, characterize communication processes on networks, and respect limitations of current analytic methods;
- appropriate techniques for statistical inference on networks;
- how to use both graph theoretic and biophysical models of brain network dynamics; and
- how to conduct multimodal analyses to gain greater insight into network organization

Target Audience

Our target audience includes neuroscientists trained in biological or psychological sciences who have had little prior exposure to graph theory and brain network mapping, as well as individuals with a more quantitative background who have knowledge of the area and are interested in how graph theory can be applied to characterize neural networks. The breadth of topics covered in the workshop means that it is suitable for people with varying levels of experience.

Presentations

Basic Concepts of Network Neuroscience

Nervous systems are complex, interconnected networks showing elaborate organization over multiple spatial and temporal scales. A diverse array of imaging techniques is available for interrogating different aspects of neural structure and dynamics at each scale. Integrating information from these diverse datasets and measurement techniques is a major challenge for modern neuroscience and is an essential step towards developing coherent models of brain function. Network neuroscience provides a unified, common language for making sense of such diverse data because it renders the measured system in its most abstract form: a network of nodes connected by edges. Nodes represent processing elements of the system, and could correspond to cells, cell populations, or macroscale brain regions. Edges represent some measure of structural or functional interaction between nodes, regardless of the spatial or temporal scale at which that interaction occurs. Abstracting the system in this way not only provides a common way of representing different nervous systems, but it also offers a rich repertoire of tools and measures from graph theory and network science that can be used to understand different aspects of network organization and dynamics. In this talk, I will explain some of the fundamental concepts of network neuroscience, discuss different approaches to building graph models of brain networks, and outline some of the key considerations that must be made to ensure valid interpretation of analysis results. An understanding of these issues provides a necessary foundation for the use of more advanced topics covered throughout the workshop.

Presenter

Alex Fornito, Monash Biomedical Imaging Clayton, Victoria, Australia

Defining Network Nodes: How to best represent the brain?

At functional MRI measurement resolution, it is possible to apply network neuroscience methods to study functional connectivity patterns between every possible pair of voxels. However, the voxel unit does not map onto neuroanatomy, and the resulting 'dense connectomes' are computationally demanding and challenging to interpret. Therefore, functional connectivity methods are often applied using a lower-rank representation of the brain as a set of functional nodes. A node consists of a group of voxels that can together be considered as one functionally homogeneous unit and represented by a single timeseries. Many different representational approaches for node definition are available, and the choice of method has important implications for network neuroscience results and interpretation that are rarely explicitly stated or even considered. This talk provides a critical overview of different node definition methods such as hard parcellations (functional vs anatomical atlases), weighted parcellations, and gradients. A key focus of this talk is to clearly lay out the challenges and trade-offs involved in node definition. Considerations such as within-subject and between-subject variability, functional heterogeneity and multiplicity, representational ambiguity, and dimensionality will be discussed. Virtual polling and Q&A will be used to engage the audience in a discussion on what considerations to take into account when deciding the best representation of the brain for a specific research question.

Presenter

Janine Bijsterbosch, Washington University Washington, WA, United States

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Functional Connectivity Methods and Measures

This lecture will introduce the concept of functional connectivity to describe coordinated activity in different brain areas. There are a number of ways that functional connectivity can be measured, and each has advantages and disadvantages for a given research question. Metrics such as Pearson correlation, partial correlation independent component analysis, and coherence will be describe and demonstrated. The lecture will begin by focusing on average functional connectivity measurements, then expand to consider methods that capture time-varying aspects of functional connectivity. An overview of the decisions that must be made for whole-brain analysis of functional connectivity (parcellation, overlapping networks) will be presented as background for the remainder of the educational course. In addition to discussing the mechanics of measuring functional connectivity, this lecture will examine its interpretation. The role of external inputs (whether residing within the brain or arising from physiological processes or environmental stimuli) will be demonstrated, and mitigation of nuisance variables will be briefly described. An overview of the lingering controversy over global signal regression will be given, highlighting both advantages and disadvantages of the practice. Finally, some consideration for measuring functional connectivity at different scales (from layers to networks) will be presented as an illustration of these concepts.

Presenter

Shella Keilholz, Georgia Tech Atlanta, GA, United States

Quantifying Structural Connectivity

Estimation of the macroscopic structural connectome of the brain can be performed using diffusion MRI tractography. While the fundamental principles of this technology are relatively simple, there is a wide array of technical limitations of which any researcher must be aware, and state-of-the-art developments for which uptake is strongly advocated. This session will present a breakdown of the underlying requirements for the robust and quantitative reconstruction of brain structural connectomes. While attendees' attention will be drawn to relevant technologies, focus is instead placed on understanding of the complexities and challenges of structural connectome construction in their most general form, giving attendees the ability to critically assess the various technologies in the field and accurately contextualise them within the overall reconstruction and quantification framework. Firstly, the problem of structural connectome construction is decomposed to the challenge of quantifying some measure of white matter structural connectivity between two grey matter regions of interest: construction of the full structural connectome is simply the repetition of this process for all possible pairs of grey matter parcels. Following this, the four fundamental requirements for such measurement to be robust and meaningful are presented using the aptly-named acronym "TRAQ" (Trajectories; Reconstruction density; Attribution; Quantification). Each of these presents an opportunity for audience engagement to assess knowledge of existing software tools / models / methods and to challenge pre-conceptions or heuristics. Construction of brain networks using diffusion MRI tractography depends on a very large number of algorithmic processing steps, for little of which there is a consensus among experts in the field. This session aims to equip attendees with the requisite understanding to critically assess the various software methods utilised in the field and make informed decisions regarding their own experimental paradigms.

Presenter

Robert Smith, The University of Melbourne, Victoria, Australia

Statistics for Brain Networks: Network thresholding, comparison, and models

Statistical inference on brain networks is an important application in connectomics. It is needed to identify connectome features that are impacted by disease, associated with cognitive performance or modulated by pharmacological interventions. Performing inference on brain networks is challenging due to the high dimensionality of connectomic data and the thousands of connections that are often examined for an effect. In this talk, connectomic inference at the connectional, nodal and global level will be considered. Connectional and nodal level inference involves testing the same hypothesis over many network elements. Network-specific methods to correct for the resulting multiple comparisons problem will be presented. Multivariate approaches for connectomic inference will also be introduced, including canonical correlation analysis and multivariate distance matrix regression. The second part of this lecture will focus on network thresholding. Given the importance of mapping connectomes with high specificity, thresholding is an important step to eliminate potentially spurious connections inferred from tractography, improve connectome specificity and emphasize certain topological properties. The difference between weight- and density-based thresholding will be explained in detail and the limitations of these two thresholding methods will be demonstrated with practical neuroimaging examples. Alternative network thresholding methods will also be introduced, including consensus thresholding, the disparity filter and thresholding approaches based on the minimum spanning tree. Publicly available software packages to implement the methods described in this lecture will be pointed out to attendees. Attendees will be provided with the knowledge to understand the basic principles of connectome inference and identify the most appropriate statistical methods and software for the inference task at hand. Attendees will also gain an understanding of the key considerations when thresholding brain networks.

Presenter

Andrew Zalesky, The University of Melbourne, Victoria, Australia

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Communication in Brain Networks

A central question in connectomics is how the topology of brain networks supports neural signalling and inter-regional communication. The efficiency and integrative capacity of brain networks is commonly estimated in terms of shortest path length, which assumes that optimally short paths are exclusively selected for communication. In contrast to shortest paths, alternative models consceptualize neural signaling as a structurally-guided diffusive process. Altogether, these models can be thought of as forming a spectrum, depending on how much knowledge or information is imparted on the system. When neural elements have perfect knowledge of the global topology, they may take advantage of the shortest path architecture, while the absence of such information potentiates random diffusion of neural signals. Interposed between these extremes are a rich set of communicability models that take advantage of path ensembles and allow near-optimal alternative routes. During this talk, I will present a conceptual framework for studying communication in structural and functional brain networks, as well as a set of guided examples of how these measures should be implemented and interpreted. I will also give an overview of how these models have recently been used to study cognition, development and neurological and psychiatric disorders.

Presenter

Misic Bratislav, University of Toronto Toronto, Ontario, Canada

Modules in Structural and Functional Brain Networks

The human brain can be modeled as a network of nodes and edges that represent brain regions and structural/functional connections, respectively. Computational tools from network science and graph theory can then be used to analyze brain network data, offering insight into the brain's organization and function. While network analysis has helped characterize local and global patterns of brain connectivity, it has proven especially conducive to our study of the brain's meso-scale structure. Meso-scale structure refers to divisions of a network's nodes and edges into meaningful clusters. Clusters highlight a system's functional units, circuits, or pathways, and offer a coarse-grained view of its organization. While there are many types of meso-scale structure, the most widely studied variety is so-called modular structure, in which clusters correspond to internally dense sub-networks referred to as "modules." Within the field of network neuroscience, modular structure has taken on particular significance. Modules are thought to engender specialized brain function, to support cost-efficient wiring, and to confer robustness to perturbations. Recent studies have reported links between variation of the brain's modular structure and cognitive load, disease state, and development. Despite its potential, the study of modular structure in empirical brain networks has proven challenging, due largely to the fact that the brain's ground truth modules are unknown. Instead, modules are detected algorithmically, an approach that introduces arbitrary processing decisions, free parameters, and algorithmic biases. In this talk, I will review brain network meso-scale structure, in general, and modular structure, in particular. I will describe the present state of research in this area and I will survey current methodologies for the detection and characterization of modules in brain networks, focusing on the popular method "modularity maximization" and its application to static brain connectivity. I will discuss common pitfalls associated with the use of modularity maximization and offer strategies for successfully mitigating these factors. These sub-topics including guidelines on how to fix the values of free parameters, the compatibility of modularity maximization with signed and weighted networks, and appropriate null models for comparison.

Presenter

Rick Betzel, Indiana University Bloomington, IN, United States

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Multilayer Networks in Neuroscience

The spread of graph theoretical approaches in neuroscience have empowered exciting research on, for example, either the structural or functional brain network. Why not both? In this presentation we introduce multilayer networks, a framework that allows us to incorporate both the structural and functional data into one mathematical object. Furthermore, multilayer networks provide a quantitative approach to examining complex multi-modal, multi-scale, and spatiotemporal data. Using examples from previous research, we will discuss the process of encoding data as a multilayer network, computations such as community detection one could use to analyze this object, and insights made possible by the framework. Finally, we will highlight visualization techniques and conclude the presentation with possibilities for multilayer networks in future neuroscience research.

Presenter

Ann Belvin-Sizemore, University of Pennsylvania Philadelphia, PA, United States

Multi-modal Connectomics: Combining micro- and macro- connectome data

The human brain comprises a complex network organized across several scales of organization: At the microscale level, the protein fingerprint of a region describes the local molecular architecture, with neurons and their axons, dendrites and synapses forming the fabric for local circuitry. In turn, at the macroscale level, these brain regions are interconnected by long-range white matter connections and functional interconnections forming large-scale anatomical and functional networks. Recent advances have made it possible to combine and integrate these different sources and scales of information at the connectome level. In this talk, we will discuss the field of 'multimodal connectomics', the multidisciplinary field that brings together data from different levels of nervous system organization together to form a better understanding of multi-scale relationships of brain structure, function, and behavior in health and disease. We will talk about the combination and integration of several fields of 'omics' with connectomics, discussing exemplary multiscale neuroscience studies that illustrate the importance of studying cross-scale interactions among the genetic, molecular, cellular, and macroscale levels of brain circuitry and connectivity and behavior. We will discuss in detail available multi-modal datasets and how to combine them with structural and functional MRI connectomics in practice. We will discuss the availability of these datasets, how to use them in the context of MRI, and discuss examples of online platforms to make a quick start in the field of multi-modal connectomics. We will discuss the practical challenges, current limitations and future directions of multimodal connectomics.

Presenter

Martijn van den Heuvel, Amsterdam University Amsterdam, Netherlands

The Virtual Brain Simulation Platform: Inferring principles of network interactions underlying cognition

The challenge in studying the brain as a complex adaptive system is that complexity arises from the interactions of structure and function at different spatiotemporal scales (Deco et al. 2017). Modern neuroimaging can provide exquisite measures of structure and function separately, but misses the fact that the brain complexity emerges from the intersection of the two. Here is where computational modelling of brain networks can help. Models that simulate different combinations of subordinate features of behaviour of a complex system that often can only be measured invasively (e.g. local population dynamics and long-range interactions) identify the combination of features that most likely give rise to emergent behaviour that often is observable noninvasively (e.g. EEG, MEG, fMRI) - and importantly those that are less likely. We can exploit the power of large-scale network models to integrate disparate neuroimaging data sources and evaluate the potential underlying biophysical network mechanisms. This approach is now feasible because of the developments in a whole-brain simulation platform, TheVirtualBrain (TVB). TVB integrates empirical neuroimaging data from different modalities to construct biologically plausible computational models of brain network dynamics. TVB is a generative model wherein biophysical parameters for the level of cell population activity and anatomical connectivity are optimized/fitted so that they generate an individual's observed data in humans (Ritter et al 2013), macaques (Shen et al 2019) or rodents. The inferences about brain dynamics, complexity, and the relation to cognition are thus made at the level of the biophysical features (e.g., balance of excitation and inhibition in a cell population) that generated the observed data (Schirner 2018), rather than particular features of the data (e.g. FC). Through extended simulation, the TVB modeling platform allows for a complete exploration of dynamics that are consistent with a particular empirically-derived neural architecture. This exploration can span the dynamics that have been observed empirically and those that are not observed but are plausible potentials. This potentiality is directly related to complexity, in that complex systems will engender more options in the production of similar behavior, which also imparts more resilience (Tononi et al 1999). Potential configurations, or hidden repertoires (Ritter et al 2013), may also underlie broader concepts of "cognitive reserve" (Stern 2003), which has been used to describe the ability of some persons to maintain high levels of cognitive function in aging and also in the face of damage or disease.

Presenter

Petra Ritter, Charite University Berlin, Germany