Emerging methods for dynamic multidimensional brain functional connectivity analysis

Olaf Hauk Organizer
University of Cambridge
Cambridge, Cambridgeshire

Richard Henson, Professor Co-Organizer
University of Cambridge
Cambridge, East of England

Alexandra Woolgar Co-Organizer
MRC Cognition and Brain Sciences Unit, University of Cambridge
Cambridge, Cambridgeshire

Overview

Cognitive brain processes rely on the interaction of multiple brain regions. A full neuroscientific understanding of these processes therefore requires an accurate and complete description of connectivity among those regions including how information is transformed and exchanged between them. However, most current neuroimaging studies do not make use of the full multidimensional information that is potentially available from their data. While methods to analyse multivariate brain activation patterns within regions of interest have become standard in the neuroimaging community (such as MVPA and RSA, e.g. (Karimi-Rouzbahani, Woolgar, Henson, & Nili, 2021)), approaches for the investigation of interactions among those patterns across regions – i.e. multidimensional brain connectivity – have only recently begun to emerge (Anzellotti, Caramazza, & Saxe, 2017; Basti, Nili, Hauk, Marzetti, & Henson, 2020; Geerligs, Henson, & Cam-CAN, 2016; Goddard, Carlson, Dermody, & Woolgar, 2016; Shahbazi, Shirali, Aghajan, & Nili, 2021). Moreover, these novel methods have so far mainly been developed for and applied to fMRI data (Anzellotti et al., 2017; Basti, Mur, et al., 2019; Geerligs et al., 2016), and very few studies have begun to leverage the temporal information available from dynamic EEG/MEG imaging (Basti, Chella, Snyder, Pizzella, & Marzetti, 2019; Basti et al., 2020) which are ideally suited to study connectivity.
This symposium would be an important stepping stone towards the full characterisation of brain connectivity from dynamic neuroimaging data. Our speakers would describe and compare recently proposed approaches for multidimensional brain connectivity, as well as present novel approaches that are still under development and yet unpublished. The talks would cover the theoretical background of novel methods (Basti, Rahimi, Nili), their evaluation in simulation studies (Basti, Rahimi, Nili), as well as applications to neuroimaging studies on the mechanisms of cognitive processes (Goddard, Basti, Rahimi).
Researchers would therefore 1) learn about cutting edge approaches to estimate brain connectivity that will take neuroimaging to the next level, 2) become familiar with the main theoretical concepts behind these methods, and 3) obtain a realistic view on the opportunities and practical limitations of these methods. Methods and software developers would be inspired to implement and improve novel brain connectivity methods in openly available software packages.

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Lecture 1: *Understanding brain function through measurements of information exchange between regions*
Erin Goddard Presenter

Rich interconnectivity is a defining characteristic of the brain, and understanding what is communicated through these interactions is central to any complete account of brain functional networks. Methods for measuring connectivity between brain regions still predominantly rely on correlations in overall activity or synchrony between areas, without specifically measuring what information is being passed between brain regions. Here I will present two recent studies using a Granger-causal measure of the stimulus-related information exchanged between pairs of brain regions. The first was an investigation of the effects of spatial and feature-selective attention: information flow showed that frontal regions were shaping stimulus representations in early sensory areas at the time that the effects of attentional selection emerged. In another study, on visuospatial short-term memory, we found that during memory retrieval, information flow from posteromedial cortex to both prefrontal and occipital cortices was predictive of task performance across individuals. This suggests that posteromedial cortex plays a key role in the comparison of external stimuli with the remembered material. These two studies demonstrate how measuring information flow between regions can offer new insights into brain function.

Lecture 2: *Multi-dimensional functional connectivity in EEG/MEG: old and novel methods*
Alessio Basti Presenter

Although the reconstructed EEG/MEG source activity may show a multi-dimensional nature, the commonly used functional connectivity methods only rely on pairs of one-dimensional time courses. To overcome this potential suboptimality, multi-dimensional connectivity methods have been introduced. In my talk, I will conceptually and mathematically describe these recent methods, with a focus on those based on frequency-specific phase-coupling of neuronal oscillations, one of the most functionally relevant neural coupling modes. Then, I will discuss on the main advantages and drawbacks of using these multi-dimensional approaches by relying on the results obtained in realistic simulated scenarios and in real MEG (resting state and working memory) experiments. I will also focus on a novel approach based on the third order polyspectral analysis of the data. As opposed to the other frequency-specific phase-coupling methods, the latter allows to investigate the presence of cross-frequency (and thus nonlinear) phase-interactions from multi-dimensional time courses. Finally, I will talk about the potential real-time setting applications of these methods.

Lecture 3: *Multidimensional Pattern Connectivity - a novel functional connectivity metric for EEG/MEG research*
Setareh Rahimi Presenter

Functional and effective brain connectivity methods are essential to study the complex information flow in brain networks underlying human cognition. Only recently have connectivity methods begun to emerge that make use of the full multi-dimensional information contained in patterns of brain activation, rather than univariate summary measures of these patterns. To date, these methods have mostly been applied to fMRI data. Here, we introduce multidimensional pattern connectivity (MDPC) as a novel functional connectivity metric for EEG/MEG research. MDPC estimates the vertex-to-vertex transformations among multiple brain regions and across different latency ranges. It determines how well patterns in ROI X at time point tx can predict patterns of ROI Y at time point ty. For the case of linear transformations we demonstrated in simulations that MDPC is more sensitive to multidimensional effects compared to a univariate approach for realistic choices of number of trials and SNR. These results were extended to nonlinear version using artificial neural networks. We applied linear MDPC as well as its univariate counterpart to an existing dataset using a visual word recognition paradigm, investigating differences between a semantic decision (SD) and lexical decision (LD) task. MDPC detected significant effects very early on, and showed stronger task modulations than the univariate approach, suggesting that it is capable of capturing more information. We also observed more consistent and richer connectivity within the semantic network for left anterior temporal lobe (lATL) compared to angular gyrus, with greater connectivity for SD than LD, confirming a central role of lATL in the semantic brain network.

Lecture 4: *Different levels of inference about pairwise regional interactions*
Hamed Nili Presenter

Classic approaches to functional connectivity of two brain regions consider the correlation between regional average time courses. This type of analysis makes it possible to infer whether two regions are co-active or not. Another level of inference is to test whether two regions have shared information. For that, multi-dimensional connectivity methods are suited. Those methods do not require averaging, that can lose information, and target the information content of high-dimensional activity patterns. In my presentation I will focus on a class of multi-dimensional connectivity methods, named representational connectivity analysis or RCA. I will talk about a novel conceptualisation of RCA in the context of all other methods. I will talk about different variants of RCA (model-free and model-based RCA) and the different types of inferences they support. I will explain how model-free RCA tests if two regions have shared information, and how model-based RCA can be adopted to test whether two regions have shared information about a specific aspect of task/stimuli or whether information in one region is being transferred to another. I would use simulations and applications to neuroimaging data to elaborate on the different methods and clarify their differences. Finally, I will talk about a novel geometric-aware extension of model-free RCA, distance between 2nd moment matrices on the Riemannian manifold, which makes it possible to test for co-activation and shared information simultaneously. This novel metric also captures nonlinear regional interactions with high sensitivity. Using simulations, I will show how it goes beyond all previous measures that do not consider the underlying manifold of matrices used in representational similarity analysis.