Identifying and Reducing Model Bias in Network Neuroscience

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Symposium

Network neuroscience is a nascent field that analyzes large-scale brain networks constructed from modern neuroimaging datasets. The field seeks to discover fundamental organizational principles of structural and functional brain networks. To this end, network neuroscience studies conducted in the last decade have adopted increasingly sophisticated models to explain and predict the organization of brain network structure, function, evolution, development and disease.

Network neuroscience has devoted considerable attention to data quality and analysis replicability. In contrast, the field has devoted little attention to the problem of model bias — the closeness with which network neuroscience models represent target neurobiological phenomena. This symposium brings together statistical, cognitive, computational and network neuroscientists to directly engage with this pressing but little explored problem. The symposium will broadly focus on the following questions:

1) What does it mean to understand the structure and function of brain networks?
2) How can we define and quantify model bias in network neuroscience?
3) How can we specify and select models with progressively smaller bias?

The symposium will comprise four complementary talks that span statistical perspectives on model bias, causal inference of brain connectivity, as well as strong interdependence of structural and functional brain-network models. The presentations will be followed by an interactive discussion between panel members and symposium attendees.

Overall, the presentations and discussion will emphasize diverse approaches to identifying and reducing model bias, and the importance of these approaches for genuine progress in network neuroscience. The speakers represent a diverse group of researchers from around the world and at various career stages.

Objectives

- Participants will develop an understanding of distinct types and sources of model bias.
- Participants will develop an understanding of the importance of model bias in network neuroscience.
- Participants will develop an understanding of diverse approaches to reducing model bias in network neuroscience.

Target Audience

This symposium is of interest to all neuroimaging researchers who seek to interpretably analyze the organization of brain networks. While the discussion will focus on network neuroscience, all insights will be equally applicable to other explanatory models of neuroimaging and neurophysiological datasets.

Presentations

Tackling Bias in Network Neuroscience From a Statistical Perspective

The inference of high dimensional phenomena from imperfect measurement is inherently biased. Work in statistics has identified and investigated distinct components of such bias, including estimation and approximation bias. Estimation bias denotes the systematic deviation between an estimate of model parameters from the true model parameters. In contrast, approximation bias denotes the systematic deviation between a simplifying model and a true but more complex model. In this talk, I will review the nature of these fundamental concepts in statistics and discuss how these concepts can be used to interrogate models in network neuroscience. I will emphasize that, in many instances, competing models in network neuroscience may be fundamentally indistinguishable with respect to the available data. I will discuss the implications of this problem of model identifiability to data acquisition and study design. I will also emphasize issues that can better inform our choices for investigation of brain network mechanisms through observational and perturbational approaches. In summary, my talk will provide a statistical overview of model bias and its relevance to studies in network neuroscience.

Presenter

Manjari Narayan, Stanford University Palo Alto, CA, United States

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Causal Inference of Human Brain Connectivity from Aggregate Population Activity

There are several major stumbling blocks for causal inference of human brain connectivity. On the one hand, whole-brain imaging has poor spatial and temporal resolution which impedes the ability to observe neuronal activity. On the other hand, single-neuron electrode recordings have extremely poor spatial coverage, and a consequent massive confounding problem. Some have proposed that this confounding makes causal inference intractable [1]. Finally, our ability to apply systematic, targeted manipulations in a way that can support mechanistic interpretations is limited to coarse-scale and non-invasive approaches. This leaves us with limited options. First, we can abandon the pursuit of causality altogether. Second, we can study causality in simple organisms such as C. elegans, for which we have complete neuronal wiring diagrams, and in which we can simultaneously observe and manipulate the activity of many neurons. Third, we can attempt to reduce dimensionality by inferring causality from aggregate activity of large neuronal populations. In this talk, I will focus on the third option. I will build on a recently proposed framework for redefining the term “functional connectivity” [2], to evaluate the extent with which we can infer mechanisms of brain function from aggregate signals, such as local field potentials, equivalent current dipoles, and even the BOLD response. I will emphasize organizational regularities that can make such inference tractable by reducing the confounding problem. Such regularities include the columnar organization of neocortex, the nonuniform intra- and interlaminar connectivity within cortical microcolumns, the exponential decay of local connectivity with distance, the separability of brain regions into subcortical nuclei and cortical areas, and hierarchically organized long-range projections. I will argue that this stereotypic and modular organization can support valid causal inferences from aggregate population activity. [1] Mehler DMA and Körding K (2020). The lure of misleading causal statements in functional connectivity research [preprint]. arXiv:1812.03363; [2] Reid AT et al. (2019). Advancing functional connectivity research from association to causation. Nature Neuroscience. 22, 1751–1760.

Presenter

Andrew Reid, University of Nottingham Nottingham, Nottinghamshire, United Kingdom

In Silico Analyses of Wiring Principles of Brain Connectomes

The wiring of mammalian brains exhibits a highly non-random pattern, with stereotypic connectivity between specific neuronal populations and with network topological features, such as modules. In this talk, I will present results from systematic computational modelling studies that explore principles of brain development and plasticity which may underlie these characteristic features. The talk will present analyses of a plethora of brain connectomes from human and non-human animals. It will show that many local and global features of brain connectivity can be explained by the presence of developmental gradients and stochastic connection growth. These results suggest that known spatial and temporal constraints can account for many higher order brain-network properties. For example, it will show that the ubiquitously observed feature of modularity can be explained by a simple biological plasticity rule, through formation of links between network nodes with a large topological overlap. The talk will argue that neurobiologically interpretable computational modeling allows to understand the principles of brain-network organization by sketching the latent space of developmental mechanisms. The presented results will illustrate that a very small set of wiring formation principles replicates much of the complexity of invertebrate and vertebrate (including human) brains. Importantly, the results demonstrate how the seemingly endless number of distinct network-science models can in practice be drastically reduced by grounding the modeling approach in neurobiological phenomena, rather than in phenomenological approaches based on models imported from other disciplines.

Presenter
Alexandros Goulas, University Medical Center Hamburg, Germany

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Discovery of Truer Models in Network Neuroscience

A basic aim of science is to find truer models of observed reality. But because the ground truth is unknown and inaccessible, models can only be truer relative to rival models. Science makes progress when it selects progressively truer models relative to progressively stronger rivals. Model comparison drives this important process. It does so, in large part, through reducing model specification bias, by guarding against the selection of overly complicated or overly simple models. In contrast to this scientific ideal, most current analyses in network neuroscience confirm overly complicated models through rejection of overly simple null models. Such analyses are circular insofar as they repackage existing knowledge as novel insight. In practice, this circularity leads to conceptual confusion, and wastes valuable time, effort and funding. It is a problem in need of an urgent solution. One solution to this problem involves the specification of rival models constrained by competing explanatory features. Each of these models defines a data distribution. Unbiased sampling from these distributions generates surrogate data, and in this way allows to select between competing models. In this talk, I will discuss results that use this approach to evaluate fundamental architectural principles of human neuroimaging networks. I will present several interpretable models of whole-brain voxel-resolution activity that account for much of the structure of the default network, dynamic functional connectivity, architectural gradients and other higher-order phenomena. These results illustrate how rigorous model comparisons can reduce redundant explanations, clarify explanatory gaps and drive progress in network neuroscience.

Presenter
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