

# Communication in Brain Networks: Models, mechanisms, and applications

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## Symposium

Neuroimaging has extensively characterized structural and functional brain networks, but the processes linking these two descriptions of nervous systems remain poorly understood and a hot area of research. In recent years, network communication models have gained substantial attention as a framework to bridge the structure-function gap---communication unfolding on top of structural connectivity facilitates functional interactions between neural elements. As our understanding of neural information flow advances, the number of brain network communication models is quickly growing, with current conceptualizations of neural signalling ranging from routing protocols akin to engineered systems to diffusive spreading dynamics. In parallel, the number neuroscientific applications in which these models have found utility is also increasing. Examples of recent advances include functional and effective connectivity prediction, tracking of the spread of neurodegenerative pathogens, and modelling the impact of lesions on brain function and cognition.

This symposium will provide attendees with a diverse picture of the latest developments in brain network communication research. Speakers will cover graph-theoretical models of network propagation (Caio Seguin), structure-function coupling (Bertha Vázquez-Rodríguez), dynamic models of functional connectivity and theoretical mechanisms of information routing (Demain Battaglia), and clinical modelling of disrupted neural communication and regional functional interactions (Amy Kuceyeski). Attendees will gain an appreciation of the state-of-the-art methods and models available to investigate brain network communication, how these techniques can be used to study structure-function coupling in health and disease, and how connectome signalling relates to the dynamics of coupled neural populations. More broadly, the symposium will promote a dialogue between different communities within the OHBM membership that approach brain network communication through complementary angles of investigation.

## Objective

Attendees will be provided with the knowledge to:

- Understand the most prominent methods and model of brain network communication in the literature, including their pros, cons, and interpretation.
- Understand how brain network communication models can be applied to explore a range of cognitive, clinical, and systems neuroscience research questions.
- Promote further research on brain network communication models that brings together expertise from complementary neuroimaging sub-domains.

## Target Audience

Our symposium appeals to a wide range of researchers, including neuroscientists interested in understanding network modelling, methodologists wanting an update on advances in brain network communication, and clinicians seeking new avenues to characterize abnormal neural information processing.

# Presentations

## An Introduction to Brain Network Communication Models and Their Applications

Understanding how signals are communicated through the complex topology of structural brain networks is one of the most important challenges in neuroscience. Brain network communication models use concepts from graph theory and network science to explain how information is propagated through the connectome. Traditionally, integration in brain networks has been quantified using measures related to shortest path routing (e.g., characteristic path length and global efficiency). However, algorithmically, the identification of shortest paths demands individual regions to possess global knowledge of structural connectivity, a requirement unlikely to be met in decentralized systems such as the brain. Recent years have seen a sharp increase in the number of alternative brain network communication models, with particular emphasis to decentralized schemes---ones that rely on local knowledge of connectivity to propagate signals. This talk will provide an overview of the main models, measures and methods used to describe communication in brain networks. We organize current conceptualizations of neural signaling into a taxonomy that highlights the pros and cons of different network modelling approaches, and discuss the interpretations that can be drawn from the application of communication measures to brain connectivity data. Brain network communication models can be organized into three main categories: 1) routing protocols, 2) parametric models, and 3) diffusion processes. Routing protocols propose that signaling takes place via a small number of well-defined paths, while diffusion processes consider that neural information is stochastically diffused through the connectome along multiple walks. Parametric models are conceptually in between routing and diffusion models, contributing hybrid strategies that tend towards signaling via paths or walks, depending on how parameters of the model are tuned. Each of these broad categories are populated by several models. A brain network communication model formalizes a conceptualization of neural signaling into a concrete algorithm to integrate information across the connectome. While a model describes a strategy or algorithm, a network communication measure quantifies properties of the communication process such as signaling cost, efficiency or resilience. Computed on the connectome, network communication measures augment structural connectivity by modeling interactions between both anatomically connected (direct communication) and unconnected (polysynaptic communication) region pairs. A growing body of evidence supports the neuroscientific utility of this higher-order form of connectivity---in particular when adopting decentralized communication schemes. We spotlight the most recent and compelling evidence for the utility of brain network communication models, including applications to basic, cognitive, and clinical neuroscience. Examples include the modelling of effective and functional connectivity, predicting human behavior, explaining patterns of cortical lateralization, and tracking the spread of neurodegenerative pathogens. Finally, we discuss the many future challenges and opportunities in the rapidly growing topic of connectome communication. We cover emerging applications of communication models in brain stimulation research and highlight recent efforts in model validation---i.e., the difficult task of determining which of the many network communication models in the literature most accurately reflects underlying biological processes.

## Presenter

**Caio Seguin**, University of Melbourne Melbourne, VIC, Australia

## Structure and Function: Coupling, and impact on signal propagation

The physical connections between neural elements promote synchrony between brain regions, producing patterns of activity. Although function and structure are correlated, there is a considerable amount of functional connectivity that cannot be explained by structure alone. This coupling needs to take into account higher-order interactions, and the heterogeneous microstructural variations of the brain. We find that structure-function relationships vary across a macroscale unimodal-transmodal gradient, with a high coupling in primary sensory areas that decreases as the functional hierarchy of the region increases. We find that the shape of the path on which a signal travels depends on the functional hierarchy of the source and target of the message, which suggests that the unimodal-transmodal gradient could also be shaping the communication paths between neuronal populations. Altogether, these results promote the idea that the architecture of the structural network promotes communication patterns and that the functional properties of brain regions are related to their anatomical network embedding.

### Presenter

Bertha Vázquez-Rodríguez, McGill University Montreal, Quebec, Canada

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## Dynamics, Connectivity Dynamics, Functional Dynamics

Beyond structural connectivity, describing anatomical interconnections, functional connectivity analyses have attempted to characterise how interconnected brain regions interact and exchange information to give rise to flexible function on top of a relatively rigid connectome, at least on the fast time-scales relevant for behavior. More recently, there has been a shift of interest from "how functional networks are" to "how functional networks evolve", with a multitude of studies showing how the capability of functional networks to change along time correlates with performance in various cognitive tasks and alterations of this performance in pathological conditions, even when this capability for flexibility is estimated intrinsically from resting state measures, rather than during actual tasks. It is thus important to understand how such network flexibility can be generated and controlled. In our previous works we have shown that different states of the collective system's dynamics, such as, e.g. modes of phase-locked oscillations, translate into different ways to exchange information between coupled regions on top of a fixed structural circuit (Kirst et al., 2016). Via the degeneration of its "dynome", a given structural connectome can thus give rise to a multiplicity of possible functional connectomes, each associated to a different dynamical state in the accessible dynome. Sampling of this dynome along spontaneous noise-driven activity would thus give rise to a temporally structured variability of functional connectivity at rest, as suggested by large-scale computational models reproducing the richness of the empirically observed resting state functional connectivity dynamics at the working points in which dynamics is the most degenerate (Hansen et al., 2015). Various predictions of this theoretical proposal can be formulated. First of all, changes in different functional connections should not be independent between them, since the current functional networks reflect first of all a global system's state rather than specifically segregated processes. We find indeed that the fluctuations of different links of functional connectivity along the resting state are not random but different links fluctuate in correlated or anticorrelated manners, under the influence of a "connectivity between connections" or "meta-connectivity" and the joint control of localized "meta-hub" regions with global reach of influence (Battaglia et al., 2020; Lombardo et al., 2020). Second, we predict that the effects of localized perturbations to ongoing dynamics may result in brain-wide distributed changes of functional connectivity, including on connections remote from the stimulated site (Kirst et al., 2016). Once again through computational modelling, we predict that distinct components of the remote effects of a local stimulation may be mediated by the structural connectome, when the effects of perturbation are merely propagated to anatomically neighboring regions, and by the functional connectome, when the effects modify nonlinearly the ongoing collective dynamics. These effects should depend furthermore on the global brain dynamical state, with the same stimulation having different effects depending on the current working point of collective dynamics (Papadopoulos et al., 2020). Third, we predict that changes in parameters of local regional dynamics, such as local excitation/inhibition balance or the strength of recurrent inhibition, may affect the functional coupling between distant regions, in a way which would emulate effective changes of the properties of their structural coupling. In this way, for instance, strengthened local inhibition may affect phase-synchronization between regions in a way equivalent to a change of the inter-regional latency of propagation (Benitez-Stulz et al., in preparation; in cooperation with Boris Gutkin). Ultimately, we suggest that the dynamics of functional connectivity

may be in large part the visible "shadow" of the underlying self-organized collective dynamics of neural circuits, inaccessible to direct experimental observations but accessible in models, and that this dynamic is constrained, but only in part, by the structural connectome. Variations of network metrics would thus be the indirect signature of variations occurring at the level of hidden dynamical states, advocating for the design of new tools able to reverse engineer from activity time-series what the dynamical state of brain networks is and how this state evolves and morphs through time under the influence of exogenous or endogenous factors. 1. Papadopoulos et al. PLoS Comput Biol. 2020. 2. Battaglia et al. NeuroImage. 2020 3. Lombardo et al. NeuroImage. 2020. 4. Kirst et al. Nat Comms. 2016. 5. Hansen et al. NeuroImage. 2015.

#### Presenter

**Demian Battaglia**, Université Aix-Marseille Marseille, Provence-Alpes-Côte d'Azur, France

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#### Structure-function (Dis)connectome Coupling: Brain network modeling in disease

The question of how anatomy and physiology are related is one of the fundamental questions in biology, particularly in neuroscience where studies of form and function have led to fundamental discoveries. Studies analyzing the relationship between the brain's structural (white matter) connectome (SC) and functional (physiological co-activation) connectome (FC) have produced a consensus that SC-FC alignments do exist to some extent. Various approaches, including biophysical computational models, network diffusion models, graph theoretical, machine learning or statistical approaches have been used to capture the relationship between SC and FC. Of course, pathology from various neurological diseases and disorders like traumatic brain injury, disorders of consciousness, stroke, dementia and multiple sclerosis can disrupt both SC and FC and cause changes to their alignment. Recent investigations have focused on how pathology can alter SC-FC coupling, how these brain networks interact to propagate disease or how they may be reorganized to promote recovery. Specifically, increased alignment of SC and FC has been associated with worse cognition in people with mild traumatic brain injury, multiple sclerosis and aging-related cognitive impairment, as well as lower measures of awareness in people with disorders of consciousness. Understanding these fundamental, multi-modal network mechanisms of disease and recovery could allow personalized, targeted therapeutic approaches to promoting beneficial brain network reorganization to enhance recovery from neurological disease.

#### Presenter

**Amy Kuceyeski**, Weill Cornell Medicine, Ithaca, NY, United States