MINISYMPOSIUM

BRAIN NETWORKS: A WINDOW ON BRAIN FUNCTION AND DYSFUNCTION

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The brain can be thought of as a complex, multiscale network[1]. At the macro-scale, structural brain networks correspond to brain regions connected by fiber pathways [1, 2], which can be inferred from diffusion magnetic resonance imaging (MRI). Networks can also be formulated from large-scale brain dynamics; functional MRI, and electro- or magnetoencephalography (EEG/MEG) are used to measure brain signals, and functional networks are constructed based on the correlations or coherence between the recorded signals at different brain regions [1, 2]. Graph theory enables us to study these networks and consequently characterize healthy and pathological brain states [3]. Furthermore, the mathematical field of dynamics on networks allows a mechanistic understanding of brain networks [4], thereby informing the development of biomarkers and personalized treatments for neurological and neuropsychiatric disorders.

This minisymposium aims to bring together pertinent current research on the use of graph theory and dynamical systems theory to characterize and understand brain networks in health and disease. Speakers will address the most pressing directions of current research, namely whole-brain network models to investigate neurological diseases and clinical interventions. It will also be discussed the relation between functional and structural connectivity, and the use of graph theory to explore brain connectomes derived from data of people with a range of neurological disorders such as Alzheimer's disease, Parkinson's disease, and epilepsy. This research has the potential to be translated into useful clinical tools to better characterize and treat neurological disorders.

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WHOLE-BRAIN NETWORK DYNAMICS: MATHEMATICAL MODELS AND MECHANISTIC SCENARIOS

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Keywords: Network, Brain, Connectome, Neuroscience, Computational model.

Brain Connectomics is tracing an exciting new path in neuroscience research, where the brain is perceived as an elaborate network system with a complex wiring structure. Importantly, understanding how neural energy propagates through this network structure appears crucial for deciphering the still-puzzling brain signals recorded multi-modally over the last hundred years.

This talk will focus on models of macroscopic brain interactions, i.e. how segregated brain areas interact with each other via an organized highway system of white matter fibers. Assuming a reductionist approach, these mathematical models of whole-brain network dynamics consist in a system of coupled differential equations, where each equation represents a brain area and the area-to-area coupling is weighed by realistic neuroanatomical connectivity. These bottom-up inductive models appear in contrast with deductive data-driven approaches such as dynamic causal modeling where the coupling weighs are inferred from brain activity.

Generative models are generally explored via numerical methods and the resulting simulation results are subsequently compared with real human brain activity. Interestingly, the complex signals emerging from these synthetic brain network models share multiple features with empirical brain activity. Yet, the main advantage of these reduced computational models is not to serve as predictive models, but rather to serve as phenomenological models helping to depict fundamental network mechanisms at the genesis of the spatiotemporal patterns observed in brain activity [5].

Moreover, synthetic whole-brain network models can be artificially damaged, perturbed, or even re-wired, in order to explore the pathophysiology of neurologic and psychiatric diseases [6]. Such models have the potential of becoming increasingly helpful in the preparation of clinical interventions, including brain stimulation techniques such as transcranial magnetic/electrical stimulation or deep brain stimulation.

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MULTIPLEX NETWORK FINGERPRINTS OF THE RISK OF EVOLUTION FROM EARLY STAGES OF ALZHEIMER'S DISEASE

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Keywords: Graph theory, Functional connectivity, Alzheimer's disease.

Complex graph theory has been extensively used to investigate functional brain networks across the different stages of Alzheimer's disease (AD) (the so-called AD spectrum). Yet, little is known about what are the features of these networks, if any, that are the best predictors of the likelihood to progress from the earliest clinical stage (namely, mild cognitive impairment, MCI) to AD. Here, we apply phase synchronization measures to build MEG frequency-resolved functional brain networks in the source domain and assess the structure of the corresponding multiplex network (with as many layers as frequency bands analyzed) in a group of MCI patients half of whom converted to AD after a three year follow up. The results show that the converters present distinct single and multilayer differences in brain areas involved in the early stages of the disease. This outcome paves the way to use advanced graph-theoretic measures to predict the probability of MCI subjects to convert to AD.

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SPATIOTEMPORAL MODELING OF SEIZURE PROPAGATION AND TERMINATION IN HUMAN FOCAL EPILEPSY

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Keywords: Epilepsy, Neural fields, Connectomes, Large-scale modeling.

Epileptic seizures are one of the most common neurological disorders affecting about 65 million people worldwide. For patients with partial refractory epilepsy, the success of therapeutical interventions such as resective surgery or closed-loop electrical stimulation would benefit from a better understanding of seizure dynamical mechanisms. Yet, little is known about how seizures initiate, spread and terminate. Recent studies have shown a large diversity in the spatiotemporal patterns during seizure spread and termination, suggesting also a diversity in the underlying mechanisms.

In this talk, we propose a unifying perspective on epileptic seizure spatiotemporal dynamics. We spatially extended a model of local field potential dynamics for epileptic seizures, by adding homogeneous local and heterogeneous large-scale connectivity. The local connectivity kernel was informed by statistical analyses of anatomical data and was derived from first- and second-order expansions of exponentially decaying functions of distance. The heterogeneous connectivity was reconstructed from patient-specific diffusion MRI data (connectomes). Our field model exhibits robust dynamics for a large range of parameters of the coupling non-linear (firing-rate) functions.

Our field model accounts for contradictory reports of either moving or stationary source of traveling (2-3 Hz) spike-and-wave ictal discharges described in previous studies. Additionally, interaction of multiple time scales in our model explains how seizures can propagate slowly from the seizure onset area, but terminate synchronously across large brain areas. Our findings were confirmed by analyses of seizures recorded from patients with pharmacologically resistant epilepsy. Our results contribute towards a more accurate modeling of patient-specific epileptic brains, and the development of new methods for controlling seizures.

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UNDERSTANDING THE RELATION BETWEEN STRUCTURAL AND FUNCTIONAL BRAIN CONNECTOMES

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Keywords: Brain connectomes, Structural connectivity, Functional connectivity, Complex networks.

The quest to understand how structure shapes function lies at the heart of a broad spectrum of disciplines, ranging from molecular biology to network science. In the recent decades, it has been found that the bundles of axonal fibers of which white matter is made of, form a vast and complex network of intercommunications between the regions of the brain and also internally within the cortex. This finding complements the traditional perception of the brain, in which brain structures and regions are responsible for a given function, by exposing the vast potential of brain regions to communicate with each other. The functional implications of such interconnectivity is being largely debated. For example, the discovery that brain connectomes are modular while a few hub regions form a rich-club gathering multisensory information has led to the hypothesis of how this structure serves the capacity of the brain to segregate and to integrate information. On the other hand, EEG and fMRI allow us to measure brain activity and identify statistical relations across brain regions. It has been widely discussed in the literature how the underlying structural connectivity determines the emerging patterns of correlation (functional connectivity) observed in subjects at rest. Here, we will try to clarify some misconceptions to this respect. First, we will show that the structural connectivity is only one of the several factors influencing the empirically observed functional connectivity. Thus, structural connectivity shapes, but does neither determine nor predict the resting-state functional connectivity. Second, we will introduce novel tools we have recently developed to better understand the specific contribution of the structural connectomes on the propagation of external inputs over the network and their influence on the functional connectivity.

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