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Competing interests
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NETWORK NEUROSCIENCE

An 'edgy' new look

Network neuroscientists envision the brain as a network of nodes (regions) linked via edges (connections). A long-held assumption is that node-centric interactions are the primary phenomena of interest. Faskowitz et al. introduce a novel edge-centric framework with the potential to usher in a new era of discovery in connectomics research.

Lucina Q. Uddin

"...nature seems unaware of our intellectual need for convenience and unity, and very often takes delight in complication and diversity."
—Santiago Ramon y Cajal

Spanish neuroanatomist Santiago Ramon y Cajal introduced the 'neuron doctrine' to the scientific world, positing that the nervous system is made up of discrete individual cells, or neurons. This discovery set the stage for decades of research attempting to unravel the connectome, or complex wiring diagram, of the brain. As Ramon y Cajal presciently stated, this endeavor would be met with neither convenience nor simplicity.

The brain is a complex system, and the field of network neuroscience has emerged in recent years to meet the challenge of developing computational tools and theoretical frameworks to understand this complexity. Network measurement, construction and analyses form the foundation of contemporary human connectomics research and permit systems-level understanding of neurobiological phenomena at micro-, meso- and macroscales. Neuroscientists have recently adopted measurement tools from network science to uncover topological and dynamic properties of the human brain[1]. Among the most widely adopted are graph theoretical approaches that examine the properties of graphs (or networks) as sets of nodes (neurons or brain regions) and edges (anatomical or functional connections between neurons or brain regions) that represent system elements and their interrelations. These types of analyses have already provided insight into organizational features of the human brain including its hierarchical organization, community structure, and topological properties (for example, 'small worldness')[2].

In traditional graph theoretic analyses of brain networks, functional connectivity (FC) between brain regions—measured as correlation or coherence—is interpreted as an indicator of inter-regional communication[3]. Strong node FC is observed between two brain regions if they exhibit a high level of instantaneous co-fluctuation in their signals and reflects temporally correlated activity between brain regions. Faskowitz and colleagues[4] introduced a new metric they call edge FC (eFC) to capture a different aspect of inter-regional communication: the dynamics of edges themselves. If two sets of edges or connections co-fluctuate in concert, they exhibit strong eFC in this new framework. Importantly, as illustrated in Fig. 1, even pairs of brain regions with weak node FC can exhibit strong eFC. The added benefits of tracking eFC across the brain are that it permits analysis of how communication patterns evolve over time and can reveal whether similar patterns of communication are occurring across different parts of the brain simultaneously.

There were three main goals of the work aiming to introduce eFC to the network neuroscience community. The first was to develop a framework for analyzing eFC using three large, publicly available neuroimaging datasets, the Human Connectome Project[5], Midnight Scan Club[6] and Healthy Brain Network[7], to establish feasibility and evaluate the stability of the metric. The second was to partition eFC networks to explore community structures derived from this novel metric. The third was to assess how eFC can be modulated during brain states characterized by changes in sensory input during passive viewing of movies.

The authors first derived whole-brain 'edge time series' by calculating the product of time series for all pairs of brain regions to obtain estimates of their instantaneous co-fluctuation magnitudes. These values were used to construct edge-by-edge matrices, which were shown to be similar across the three tested datasets. In network neuroscience, brain regions are said to form 'communities' if their activity is highly coordinated or reflects shared functionality. Just like traditional analyses focused on nodes instead of edges, eFC was demonstrated to be significantly stronger for within-community edges than for between-community edges. The novelty of the approach introduced by Faskowitz and colleagues is that it overcomes limitations of previous methods that assign brain regions to only one community. Decades of evidence suggest that nodes can dynamically affiliate with multiple networks[8] and that the functional relevance of a brain area depends on the status of other connected areas, or the 'context' in which the region operates[9]. The eFC framework allows us to ask, "Which brain areas participate in multiple communities?" This permits modelling that can potentially capture nuanced patterns of brain dynamics and reveal the

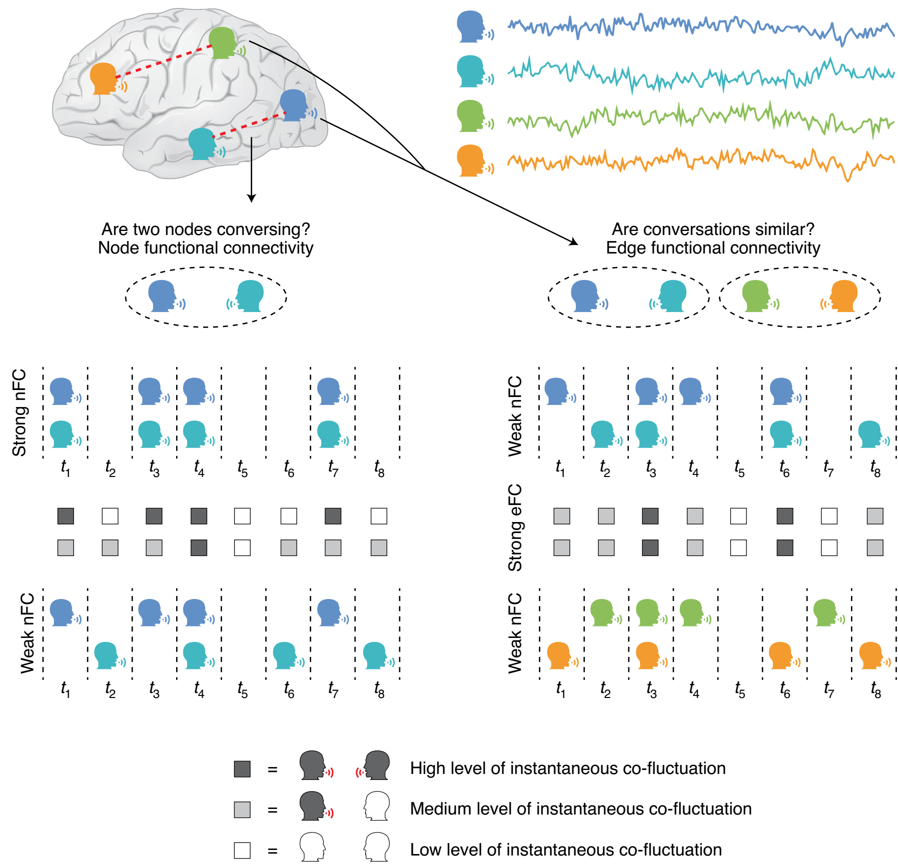

Fig. 1 | New metrics for network neuroscience. Traditional approaches for measuring brain networks focus on characterizing properties of brain regions using node functional connectivity (nFC, left). The new edge-centric approach introduced by Faskowitz and colleagues estimates the extent to which dynamic interactions across connections of the brain share similar patterns using edge functional connectivity (eFC, right). These two metrics provide complementary information, emphasizing different features of brain networks. As shown in the bottom right, two sets of nodes that each exhibit weak nFC can nevertheless exhibit strong eFC if the edges connecting them instantaneously co-fluctuate. Figure adapted from ref. [4], Springer Nature.

overlapping nature of communities. The authors found that sensorimotor and attention networks participate in disproportionately many communities compared with other brain systems.

Once eFC was demonstrated to be a reliable marker in task-free (resting state) functional MRI datasets, the authors explored how sensory input modulates this metric using passive movie-watching data from the Healthy Brain Network. An interesting finding from the comparison of resting state and task-related eFC was that brain entropy increased during movie-watching. Here, entropy serves as a measure of the uniformity of a node's community assignments, indexing overlap; higher entropy for a brain system indicates increasing overlap between communities.

Although it has long been appreciated that there is no direct one-to-one mapping between brain systems and cognitive functions, most cognitive and network neuroscience approaches still implicitly adopt this view[10]. It is increasingly acknowledged that our understanding of brain dynamics is incomplete and that this critical gap presents an obstacle to understanding how the brain flexibly functions[11]. The eFC approach introduced by Faskowitz and colleagues moves the field forward both by providing a new framework for quantifying and assessing patterns of dynamics and by explicitly modelling overlapping communities within the brain. These contributions will be particularly important in future efforts to delineate taxonomies of macroscale functional brain networks[12].

The framework introduced here will also pave the way for future breakthroughs in the nascent network neuroscience of psychiatry, where it is already evident that some key brain nodes and edges contribute disproportionately to pathologies emerging at different time points across the lifespan[13]. Metrics derived from the eFC approach may provide meaningful, previously unexplored biological features for pushing the boundaries of psychiatric neuroimaging[14]. The results from application of these novel methods will go a long way toward unraveling the complexity of the brain that Cajal so eloquently anticipated. ❐

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Competing interests

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