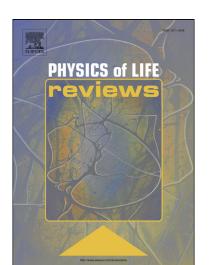
## Accepted Manuscript

Why network neuroscience? Compelling evidence and current frontiers

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## ACCEPTED MANUSCRIPT

## Why Network Neuroscience? Compelling Evidence and Current Frontiers

Comment on "Understanding brain networks and brain organization" by Luiz Pessoa

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The recent application of network theory to neuroscience has brought new insights into understanding the relationship between brain structure and function [1]. As Peossa describes in his extensive review [2], the organization of the brain can be viewed as a complex system of connected components that interact at many scales [3], both in the underlying structural architecture and through temporal functional relationships. Importantly, he emphasizes that we must shed the view that a specific brain region can be tied to a specific function and instead view the brain as a dynamic and evolving network in which overlapping sub-networks of brain regions work together to produce different functions. In fact, the complexity of these evolving interactions is now driving the future of network science [4], as efforts focus on developing novel metrics to capture the dynamic essence of these interconnected networks.

Networks are commonly characterized by their topological properties, such as the prevalence of hub nodes or community structure [5]. One topological property that many biological networks share is a "small-world" structure [6], that is, a high level of local clustering, yet short path length between any two nodes. This structure is thought to facilitate efficiency of information transfer and processing. While many studies suggest that the brain can be characterized as a small-world network [7], Peossa questions this observation, citing recent papers by Markov et al. [8,9] that use tracing techniques in macaque monkeys to reveal a high density of connections between brain areas. However, the claim that a high density of connections implies that the network cannot display a small-world structure is misleading, as it overlooks the very important fact that brain networks fall into a class of networks with weighted edges, where each connection has a strength and not all connections contribute equally to the overall structure. Indeed, many of the observed connections in these tracing studies were characterized as weak, and therefore the network of strong connections remained sparse. While there is currently no standard method for characterizing small-world structure in weighted networks, future efforts in network theory should focus on developing this important concept to determine its relevance for fundamental principles of brain network organization.

As Pessoa points out, the observation that brain networks display many weak connections has also spurred recent work examining the value of these weak ties and their impact on

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