Available online at www.sciencedirect.com

ScienceDirect

Physics of Life Reviews 11 (2014) 462–466

PHYSICS of LIFE reviews

www.elsevier.com/locate/plrev

Reply to comment

Brain networks: Moving beyond graphs
Reply to comments on "Understanding brain networks and brain organization"

Luiz Pessoa

University of Maryland, College Park, USA

Received 2 July 2014; accepted 7 July 2014

Available online 22 July 2014

Communicated by L. Perlovsky

Keywords: Brain; Networks; Dynamics; Ontology

I am very grateful for the insightful and thought-provoking commentaries, which raised several interesting issues. Importantly, the commentators identified important open questions. Here, I discuss some of the themes covered by Anderson [1], Bressler [2], Calhoun [3], Cauda and colleagues [4], Cisek [5], Hilgetag and von Luxburg [6], Horwitz [7], Laurienti [8], Muldoon and Bassett [9], Thompson [10], and Uddin [11].

Ontologies of mental functions and structure–function mapping

A network perspective, while necessary, also highlights formidable challenges to understanding the relationship between function and brain structure. For example, in the main article, I argue that from the standpoint of brain regions, the structure–function mapping is *many-to-many*. At the same time, I argue that the mapping will be many-to-many even when brain organization is conceptualized in terms of networks. Thus, the mapping problem is ameliorated, as it were, but not eliminated.

In contrast, Bressler [2] explicitly defends the possibility that structure–function mappings may be *one-to-one* when networks are employed: "If NCNs [neurocognitive networks] are uniquely composed of specific collections of brain areas, then each NCN has a unique function determined by that composition". But, Anderson [1] states that "the brain does not have *one stable unique* functional organization that can be discovered and described, but many dynamically interwoven ones". Here, I side with Anderson, because the function φ presumably implemented by network N is not invariant with respect to how the network is associated with other brain regions (Fig. 1). That is, because every region

DOI of original article: http://dx.doi.org/10.1016/j.plrev.2014.03.005.

DOIs of comments: http://dx.doi.org/10.1016/j.plrev.2014.05.001, http://dx.doi.org/10.1016/j.plrev.2014.05.003, http://dx.doi.org/10.1016/j.plrev.2014.06.004, http://dx.doi.org/10.1016/j.plrev.2014.06.005, http://dx.doi.org/10.1016/j.plrev.2014.06.006, http://dx.doi.org/10.1016/j.plrev.2014.06.014, http://dx.doi.org/10.1016/j.plrev.2014.06.017, http://dx.doi.org/10.1016/j.plrev.2014.06.018, http://dx.doi.org/10.1016/j.plrev.2014.06.019, http://dx.doi.org/10.1016/j.plrev.2014.06.022, http://dx.doi.org/10.1016/j.plrev.2014.07.002.

http://dx.doi.org/10.1016/j.plrev.2014.07.005

1571-0645/

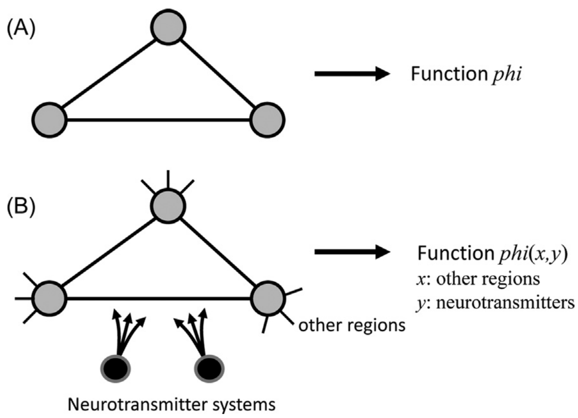

Fig. 1. Structure–function mapping for networks. (A) A network N composed of a set of regions is associated with a function φ. (B) Because the regions of network N are connected to other brain regions, the state of network N will depend on them as well. Moreover, the state of the network will depend on several neurotransmitter systems.

R in network N is connected not only to those regions belonging to N, but also to other brain regions, the state of network N depends on these other regions. Thus, the state of network N is not unique. In addition, the state of several major neurotransmitter systems is critical in determining function φ.

Laurienti [8] makes the more extreme proposal that the "notion of functional brain areas should be abandoned". This is a radical notion for mainstream neuroscience, but one that I agree with. In fact, that is the sense that I state that understanding the structure–function mapping at the level of brain regions is unproductive because regions are *not* meaningful units of function. The *network* is the unit, not the brain region.

This is not to say that the mapping between structure and function is arbitrary or random. On the contrary, though complex, and highly context-based, the mapping has a number of important *regularities*. For convenience, we may call these regularities the *dominant modes* of network N – as in the case of dorsal parietal and frontal regions being important for goal-driven attention and control [12]. More generally, as we have suggested [13], network regularities can be profitably characterized by functional fingerprints.

In the context of structure–function mappings, Anderson [1] suggests that one way to move forward is to develop *an* ontology that incorporates both neuroscience and psychology information (see Poldrack et al. [14]). Echoing his own comment cited above, I would suggest, however, that the mind does not have *one stable unique* functional organization that can be discovered and described in terms of an ontology, but many dynamically interwoven ones. But in a sense, this question should be settled pragmatically, that is, if useful ontologies are described that help understand and characterize the mind-brain, then they will serve their use. And perhaps *one* specific ontology may emerge the winner – though I side with the notion that we should seek multiple families of ontologies.

Becoming lost in "Big Data"

In the target article, the network approach was illustrated by drawing on methods that have modeled networks in terms of graph theory [15]. Cisek [5] notes that these methods, while interesting, also may lead us to "becoming helplessly lost in Big Data". I agree. Indeed, without linking network properties to behavior, they lose much of their appeal. For example, in one study, my group reported that a cue stimulus signaling reward was associated with greater integration of signals across two "networks", one more closely tied to stimulus valuation, another more closely tied to attentional control [16,17]. This was interpreted as greater cognitive-motivation integration during reward (vs. no reward) trials. While interesting, this type of result is fairly abstract (in addition, it does not pertain to interactions at the neuronal level per se). What would a stronger result look like? For example, one showing a close link between the amount of integration and behavioral performance, such that, say, the greater the integration, the better the task performance (Fig. 2).

More broadly, both Cisek [5] and Hilgetag and von Luxburg [6] challenge the network approach to brain function to become more *hypothesis driven*. It is true that much of the current research on brain networks – and especially research employing graph-theoretic approaches – is largely exploratory. To some extent, this was the case of our