Physics of Life Reviews 55 (2025) 41–45

Contents lists available at ScienceDirect

Physics of Life Reviews

journal homepage: www.elsevier.com/locate/plrev

Brain networkness: from dynamics to function and dysfunction reply to comments on: "Does the brain behave like a (complex) network? I. *Dynamics*"

D. Papo [a,b,*], J.M. Buldú [c]

[a] *Department of Neuroscience and Rehabilitation, Section of Physiology, University of Ferrara, Ferrara Italy*
[b] *Center for Translational Neurophysiology, Fondazione Istituto Italiano di Tecnologia, Ferrara Italy*
[c] *Complex Systems Group & G.I.S.C., Universidad Rey Juan Carlos, Madrid Spain*

ARTICLE INFO

Keywords:
Brain dynamics
Brain topology
Functional networks
Spatial networks
Structure-dynamics relationship

The question of whether the brain behaves like a network can be formulated in various ways, e.g. in terms of network relevance (is the network structure relevant, in some sense, to brain anatomy and activity?) or of observability and controllability (does the network structure retain sufficient information to adequately reconstruct the full system dynamics? Can brain activity be controlled by acting on its network structure?). In [1], we termed networkness the ways in which network structure explains brain anatomy and dynamics and ultimately its behaviour and set out to discuss how and to what extent the brain, particularly when thought of as a dynamical system, can genuinely be understood to behave as a network. Five commentaries to the target article addressed from different angles several key aspects of brain networkness, which we set out to discuss below.

1. What it means to be a network

Logically superseding the notion of brain networkness in the above sense is the understanding of what it means to be a complex network. At the most basic level, this involves understanding the extent to which a network structure carries more physiological meaning than bear connectivity and, as a result, whether there are genuine network-driven neural phenomena and network-based equivalents of *dys*connection syndromes [2].

Peron highlights disorder as a key property defining networkness. Indeed, complex networks are in essence a form of strong disorder [3,4], a typical feature of living matter in general. Such systems are associated with a lack long distance periodicity and by the presence of defects, impurities and heterogeneity, which in turn can be characterised in terms of symmetries and their break-down. If disorder is in some sense relevant at some scales, for instance if it determines the system's response function, it can effectively be

DOI of original article: https://doi.org/10.1016/j.plrev.2023.12.006.
E-mail address: david.papo@unife.it (D. Papo).
* Corresponding author.

https://doi.org/10.1016/j.plrev.2025.08.001
Received 1 August 2025; Accepted 1 August 2025
Available online 5 August 2025

thought to reflect the system's state of matter. States of matter differ in the way the component particles are arranged, and how they behave collectively, and transitions between such states can be described by an expansion of the free energy in powers of a quantity called *order parameter*, which distinguishes symmetry-broken and unbroken phases [5]. In this vein, task-dependent phase transitions [6] emerging from network structure reconfigurations may be understood as changing the system's mechanical response. In addition to a role in the system's dynamics and mechanical properties, network structure may also modulate the system's thermodynamics. For example, network structure may act as a control parameter for the system's temperature dependence [7].

2. Ontology vs. network reconstruction

Korhonen addresses the important (though typically not explicitly addressed) issue of whether a network representation genuinely reflects the way the brain carries out its function or merely constitutes a way to represent brain anatomy and activity.

There are two aspects worth highlighting. First, there is some degree of dependency between the ability to reconstruct network structure from data (or even at a theoretical level) and the ontology that can be derived from such a (re)construction. The issue of of brain activity's reducibility to a network representation is both a theoretical and an experimental one. The technical aspects of network reconstruction from experimental data have a profound impact on the observability of brain structure afforded by a network representation.

Second, in [1], we mainly discussed the extent to which a network representation explains the system's true *modus operandi*, rather than how such a structure allows investigating it theoretically or experimentally. These two aspects need not necessarily coincide. Nonetheless, the method used to investigate a system and the functions that the system actually implements are often equated, and so are a given structure's information content and the dynamical aspects that this structure supports. Furthermore, the operations allowed by a given extrinsic parametrisation may also not reflect the computations performed by the system. Likewise, that a given structure may be associated with a certain amount of information doesn't imply that such information is actually transferred, computed or functionally relevant.

3. When is the brain a network?

In a complex multiscale system, networkness may play a prominent role in some aspects or in some scale range but not in others. **Luppi et al.** and **Peron** address from different angles the question of defining *when* the brain can effectively be treated as a network, from both an ontological and a reconstruction-related viewpoint.

One important question is whether there exists a scale at which the set of nodes and their connections may start being a network. The onset of networkness can be marked by various conditions, one of which, i.e. the transition from continuous field to effective discrete structure, is discussed by **Peron**. Indeed, at global but also at mesoscopic scales, the brain can effectively be modelled as a continuous field [8–12]. Equipping the brain with a network structure requires mapping the underlying continuous field onto a discrete set of (not necessarily) point-wise nodes [13]. A network structure can be seen as a discretisation of the continuous field, i.e. a map from the space of continuous fields to the space of discrete ones, where the former can be recovered from the latter in the limit of infinitely dense nodes. The conditions under which the discretisation of the continuous field representation is non-singular and essentially without loss of information are poorly known. This is in part due to the fact that the discretisation steps, e.g. the parcellation step of complex spatially extended systems, are in general not intrinsic, for example they are typically not prescribed by the dynamics, indicating that the discretisation issue is both an ontological and a reconstruction-dependent issue. In practice, how much information is lost as a result of discretisation depends on the choice of the scales of description, observation, variations, and correlations [14]. On the other hand, the network structure becomes genuinely relevant when continuous and discrete representations become inequivalent, e.g. if the discrete structure constitutes a singular limit of the continuous field, inducing a qualitative change in the system behaviour with irreversible information loss.

4. Quest for the appropriate level of detail

Another important aspect of the target article addressed by **Luppi et al.**, **Korhonen**, and **Coombes et al.** is the extent to which brain representations are robust with respect to the level of neural detail accounted for in the neural space-to-network structure mapping and to the properties of the network structure itself.

On the one hand, at the neural nevel, network neuroscience models tend to filter out detail at all scales. Moreover, there is a lack of basic knowledge and stylized facts at computational, algorithmic and implementational levels of neural activity. For instance, exactly how information is transferred through dynamics and what computational tasks a given population is meant to solve are not always entirely clear. Depending on the space and on the scale at which nodes and links are defined, this may have a strong impact on the system's dynamics [15]. To understand the impact of this lack of knowledge it is useful to note that equipping a system with a network structure inherently involves coarse-graining and renormalisation at some scale and under some criterion [16,17]. A network node can be thought of as resulting from a renormalisation process at scales not considered in the model. The general dearth of neural stylised facts, particularly at computational and algorithmic levels, constitutes an intrinsic obstacle to the renormalisation stage of neural data implicit in network modelling's discretisation. This is because defining nodes and links at a given scale or, equivalently, renormalising a given scale, effectively defining community structure, require on the one hand a segmentation of the relevant space and, on the other hand, a criterion to define the relations among nodes. While more acute at mesoscopic than at microscopic neural scales, the problem exists at all scales. Consider for example the seemingly simplest case of neurons and their dynamical connectivity. Segmenting both anatomically and functionally a single neuron into compartments is by no means a trivial endeavour [18]. Similarly, there is no clear way of defining the relations between compartments at the computational and algorithmic levels. Thus, even at this scale, the space renormalisation that defining nodes involves is all but straightforward and so is the definition of the relationship among them.

On the other hand, in standard network neuroscience models, the network structure itself is often drastically simplified. At the most basic level, the structure would often be a static or, equivalently, steady state *simple graph*, i.e. a graph with no loops and no multiple edges between pairs of nodes. Thus, it is important to understand how literally should neural properties be incorporated into a network structure and what network structures better account for brain properties.

In [17] we specifically discussed the extent to which adding biological detail of various type and at various neural and network scales may qualitatively change network models of brain activity and conversely, the degree of network structure's universality (intended as robustness to changes in neurophysiological detail) or, somehow dually, the extent to which network models not explicitly incorporating important neural properties effectively approximate brain structure, dynamics and ultimately function or the extent to which observable brain behaviour strictly depends on the fine details of its neural components and of their interactions.

Adding neural detail, e.g. incorporating delays or considering glial cells, but also considering different models of neural activity from those that are standard in neuroscience and generalising network structures as suggested by **Coombes et al.** can in principle account for a larger phenomenological repertoire, providing new ways to conceive of brain anatomy, dynamics and function. However, it is also important to realise that the resulting structures face the same fundamental issues related to standard network models' intrinsicality, universality, and functional meaningfulness [17]: is structure a mere extrinsic description or can be thought of as part of its intrinsic *modus operandi*? If so, how does it allow function? What aspect of the neural system's network structure is functionally meaningful? To what extent is such a structure universal? Whether there exists an appropriate structure representing a given dynamical system may be context-dependent [19], but ultimately addressing these issues requires a better characterisation of basic neurophysiological facts and improved knowledge of the structure-dynamics-function relationship.

4.1. Network structure universality

In essence, a network representation constitutes an effective field theory for the underlying physical theory. Such a representation includes the appropriate degrees of freedom at a given length scale, while the information at shorter distances is treated as somehow residual. Suitable effective models result from the appropriate identification of a universal part complemented by detail-sensitive constants [20]. Finding the appropriate balance between these two aspects characterises the study of most complex biological systems.

In a statistical physics sense, universality expresses the fact that many systems show similar macroscopic properties even though they may profoundly differ in their microscopic ones. Such properties arise when the consequences of microscopic parameter modifications are effectively summarised by a small number of phenomenological parameters [20]. While the temporal structure of resting brain activity shows signs of universality [21], the role of network properties in its emergence is still unclear. However, how network structure may improve brain functioning representation as a function of neural detail and network structure is still an insufficiently understood matter.

An important issue picked up by **Coombes et al.**, i.e whether there may be a physics of the brain, and the associated one of how much of brain physics is related to network structure [1,22] turn out to be related to network universality [23]. This is because network theory is in essence a statistical mechanics approach to graph theory [3]. This approach implies that seemingly different physical systems can exhibit the same aggregate behaviour, which can be categorised into universality classes, whose large-scale behaviour can be explained by simple effective models defined in terms of an interaction network and few control parameters. Only symmetries, dimensions, and conservation laws prove to be significant, while microscopic details can be ignored. Ultimately, understanding the brain as behaving like a network boils down to determining whether a statistical mechanics approach makes sense and when scales details matter.

5. Role of network structure in function and dysfunction

Insofar as brain activity is designed to carry out some function, network relevance should ultimately be gauged in terms of a system's ability to perform given tasks. It is therefore natural to expect that network structure should be associated with some task-specific fitness. However, network neuroscience studies almost always equate the systems' bare dynamics and its function, i.e. its ability to perform a given task. This equivalence is misleading and dynamics should *prima facie* be distinguished from brain function [24]. This is why [1] dealt with the former while network structure's role in brain function will be treated in full in a companion paper [22]. **Rubinov** discussed some of the far-reaching implications of the gap between brain dynamics and function.

5.1. Separating dynamics from function

One important implication of considering genuine function pointed out by **Rubinov** is that such a differentiation between bare dynamics and function also fundamentally changes the way a networked system's overall behaviour is thought to arise. When equating function and dynamics, structure (including topology) and local dynamics may interact, and their respective scales are fundamental factors in determining the networked system's overall behaviour [15]. On the other hand, when differentiating between dynamics and function, this interaction pattern is greatly complexified by the additional highly non-trivial projection onto function.

Brain structure-dynamics-function relationships are likely governed by highly non-trivial maps [22,24]. Structure can arise in ways that are independent of the details of network structure [25], and structural complexity does not necessarily lead to functional complexity. Furthermore, a given network's function can vary in a context-dependent way [26,27], and different networks can give rise to similar function, although different structures tend to be optimal for different tasks. In general, there is no clear understanding of network structure's contribution to neural networks' dynamical and functional properties such as *sloppiness* and *degeneracy* [28,29]. Thus, which aspects and properties of network structure are necessary in a brain model and, as a result, which methods should be summoned to represent them [30,31] ultimately depend on the properties of such mapping.

5.2. Renormalisation and emergence of function

Renormalisation is usually thought of as a powerful method to analyse complex multiscale systems and how their properties change in scale-dependent manner, but it can also be understood as a genuinely functional neural process. Along this line, function emerges from one particular coarse-graining procedure (which may not necessarily correspond to real space renormalisation) [32]. For instance, in the sensory domain, nodes and links are emergent properties induced by neuronal populations' receptor fields [31]. Note however that since it is not clear under what conditions renormalisation leads to functionally meaningful units, network structure emergence should not be equated with the emergence of function. Functional heterogeneity is in general a genuine emergent property which cannot be deduced from the system's structural properties e.g. structural heterogeneity or dynamical properties [33], and which can give rise to rather non-trivial phase space configurations [34].

5.3. Resilience and vulnerability

The general issue of neural functional equivalence, i.e. of whether two structures or dynamical trajectories can be considered identical up to some property, is in essence the same as that of network structure resilience with respect to biological detail and network specification.

From a functional viewpoint, an important question is the extent to which function, rather than bare dynamics, is robust to changes in network structure. A nested question is related to the scale-dependence of such relationship, i.e. the scales at which the structure-function map induces qualitative changes. Brain vulnerability to pathology could also be understood in terms of functional inertia with respect to network structure changes [2].

Resilience may refer to a system's structure, dynamics, or function [35]. In network neuroscience, studies refer to either *structural resilience*, i.e. the degree to which network properties are resilient to such sequences of such perturbations, typically of the anatomical network [36–38] or *dynamical resilience* i.e. a system's ability to conserve its asymptotic dynamics [35,39]. Structural and dynamical robustness do not necessarily imply *functional resilience* [40,41]. This again is a consequence of the non-trivial structure-dynamics-function map. Functional robustness is instead determined by the nature of the transitions realisable in the neighbourhood of underlying neuronal configurations, and the presence of large neutral regions in the system's configuration space or parameters which result in equivalent behaviour, wherein changes have no functional consequences [24,34,42].

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Javier M. Buldu reports financial support was provided by Spain Ministry of Science and Innovation. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Papo D, Buldú JM. Does the brain behave like a (complex) network? I. Dynamics. Phys Life Rev 2024;48:47–98.
[2] Papo, D., and Buldú, J.M. (2025). A complex network perspective on brain disease. arXiv:2507.23678.
[3] Barabási AL, Albert R. Emergence of scaling in random networks. Science 1999;286:509–12.
[4] Dorogovtsev SN, Goltsev AV, Mendes JFF. Critical phenomena in complex networks. Rev Mod Phys 2008;80:1275.
[5] Landau, L.D. (1965). On the theory of phase transitions, in *Collected Papers of LD. Landau*, (Pergamon, New York), pp. 193–216.
[6] Kozma, R., and Freeman, W.J. (2016). *Cognitive phase transitions in the cerebral cortex-enhancing the neuron doctrine by modeling neural fields*. Switzerland: Springer International Publishing.
[7] Papo, D. (2013). Brain temperature: what it means and what it can do for (cognitive) neuroscientists. *arXiv:1310.2906*.
[8] Ermentrout B. Neural networks as spatio-temporal pattern-forming systems. Rep Prog Phys 1998;61:353.
[9] Nunez PL. Toward a quantitative description of large-scale neocortical dynamic function and EEG. Behav Brain Sci 2000;23:371–98.
[10] Coombes S. Large-scale neural dynamics: simple and complex. Neuroimage 2010;52:731–9.
[11] Coombes S, Beim Graben P, Potthast R, Wright J, editors. Neural fields: theory and applications. Springer; 2014.
[12] Bressloff PC, Ermentrout B, Faugeras O, Thomas PJ. Stochastic network models in neuroscience: a Festschrift for Jack Cowan. Introduction to the Special issue. J Math Neurosci 2016;6:4.
[13] Korhonen O, Zanin M, Papo D. Principles and open questions in functional brain network reconstruction. Hum Brain Mapp 2021;42:3680–711.
[14] Lesne A. The discrete versus continuous controversy in physics. Math Struct Comput Sci 2007;17:185–224.
[15] Curto C, Morrison K. Relating network connectivity to dynamics: opportunities and challenges for theoretical neuroscience. Curr Opin Neurobiol 2019;58:11–20.
[16] Papo D, Zanin M, Pineda JA, Boccaletti S, Buldú JM. Brain networks: great expectations, hard times, and the big leap forward. Philos Trans R Soc B 2014;369:20130525.
[17] Papo, D., and Buldú, J.M. (2025). Biological detail and graph structure in network neuroscience. arXiv:2507.15789.
[18] Häusser M, Mel B. Dendrites: bug or feature? Curr Opin Neurobiol 2003;13:372–83.
[19] Bick C, Gross E, Harrington HA, Schaub MT. What are higher-order networks? SIAM Rev 2023;65:686–731.

[20] Goldenfeld N, Martin O, Oono Y. Intermediate asymptotics and renormalization group theory. J Sci Comput 1989;4:355–72.
[21] Friedman N, Ito S, Brinkman BA, Shimono M, DeVille RL, Dahmen KA, Beggs JM, Butler TC. Universal critical dynamics in high resolution neuronal avalanche data. Phys Rev Lett 2012;108:208102.
[22] Papo, D., and Buldú, J.M. (2025). Does the brain behave like a (complex) network? I. Function. *In preparation*.
[23] Barzel B, Barabási AL. Universality in network dynamics. Nat Phys 2013;9:673–81.
[24] Papo D. Gauging functional brain activity: from distinguishability to accessibility. Front Physiol 2019;10:509.
[25] Advani M, Lahiri S, Ganguli S. Statistical mechanics of complex neural systems and high dimensional data. J Stat Mech Theory Exp 2013;2013(03):P03014.
[26] Biswas T, Fitzgerald JE. Geometric framework to predict structure from function in neural networks. Phys Rev Res 2022;4:023255.
[27] Ghavasieh A, De Domenico M. Diversity of information pathways drives sparsity in real-world networks. Nat Phys 2024;20:512–9.
[28] Gutenkunst RN, Waterfall JJ, Casey FP, Brown KS, Myers CR, Sethna JP. Universally sloppy parameter sensitivities in systems biology models. PLoS Comput Biol 2007;3:e189.
[29] Machta BB, Chachra R, Transtrum MK, Sethna JP. Parameter space compression underlies emergent theories and predictive models. Science 2013;342:604–7.
[30] Giusti C, Pastalkova E, Curto C, Itskov V. Clique topology reveals intrinsic geometric structure in neural correlations. Proc Natl Acad Sci U.S.A 2015;112:13455–60.
[31] Curto C. What can topology tell us about the neural code? Bull New Ser Am Math Soc 2017;54:63–78.
[32] Bradde S, Bialek W. PCA meets RG. J Stat Phys 2017;167:462–75.
[33] Ghavasieh A, De Domenico M. Statistical physics of network structure and information dynamics. J Phys Complex 2022;3:011001.
[34] Stadler PF, Stadler BM. Genotype-phenotype maps. Biol Theory 2006;1:268–79.
[35] Lesne A. Robustness: confronting lessons from physics and biology. Biol Rev 2008;83:509–32.
[36] Alstott J, Breakspear M, Hagmann P, Cammoun L, Sporns O. Modeling the impact of lesions in the human brain. PLoS Comput Biol 2009;5:e1000408.
[37] Warren DE, Power JD, Bruss J, Denburg NL, Waldron EJ, Sun H, Petersen SE, Tranel D. Network measures predict neuropsychological outcome after brain injury. Proc Natl Acad Sci U.S.A 2014;111:14247–52.
[38] Aerts H, Fias W, Caeyenberghs K, Marinazzo D. Brain networks under attack: robustness properties and the impact of lesions. Brain 2016;139:3063–83.
[39] Demongeot J, Goles E, Morvan M, Noual M, Sené S. Attraction basins as gauges of robustness against boundary conditions in biological complex systems. PloS One 2010;5:e11793.
[40] Kitano H. Towards a theory of biological robustness. Mol Syst Biol 2007;3:137.
[41] Schwarze, A.C., Jiang, J., Wray, J., and Porter, M.A. (2024). Structural robustness and vulnerability of networks. *arXiv:2409.07498*.
[42] Doyle JC, Csete M. Architecture, constraints, and behavior. Proc Natl Acad Sci U.S.A 2011;108:15624–30.