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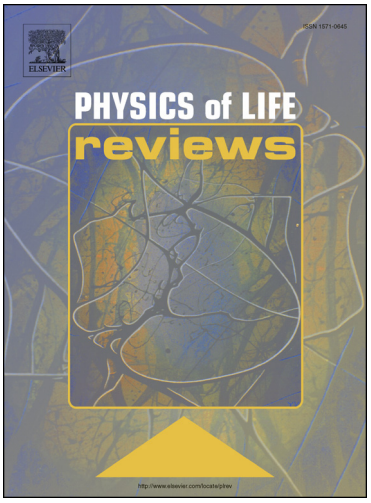

Network biology: Describing biological systems by complex networks

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Network Biology: Describing Biological Systems by Complex Networks, Comment on " Network Science of Biological Systems at Different Scales: A Review" by M Perc et al.

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I enjoyed reading Perc et al. review on analysing biological systems from network science perspective [1]. *Network science*, first started within Physics community, is now a mature multidisciplinary field of science with many applications ranging from Ecology to biology, medicine, social sciences, engineering and computer science. Perc et al. discussed how biological systems can be modelled and described by complex network theory which is an important application of network science. Although there has been considerable progress in network biology over the past two decades, this is just the beginning and network science has a great deal to offer to biology and medical sciences.

The first step in describing a biological system as a network is to extract the connectivity structure. One can use measures, such as cross-correlation or coherence to discover linear relation between individual entities (e.g. brain regions), or measures as synchronisation likelihood or phase synchronisation index to capture nonlinear relationships. This results in weighted connectivity matrices that can be analysed as weighted networks. A better approach is often to binarize to minimize the noise level and obtain more meaningful interpretation. This is a challenging task and it has been shown that different choices for binarization methods can lead to completely different results which may result in drawing misleading conclusions [2]. Although there is no consensus on the optimal method to binarize the weighted connectivity matrices, the one based on fixing network density is reasonable when two (or more) groups are compared in terms of network properties [3]. Various networks' statistical properties heavily depend on the number of connections existing in the network. Applying a uniform threshold for binarization will result in networks with varying densities, and the observed changes, e.g. between controls and patients, might be due to the different number of connections in the networks rather than the underlying mechanism. This problem can be fixed by keeping the density of the network the same for all subjects.

The examples that have been reviewed by Perc et al. are based on undirected networks. Indeed, most of the network biology research studies existing in the literature are based on undirected networks where bidirectional connections are considered between the individual nodes. However, connections in many biological systems are directed. Even in functional networks, there is always "effective connectivity" [4], where there is a flow of information in one of the directions between two connected nodes. Directed networks might show different properties than undirected ones. Afshari and Jalili showed that directed brain networks of Alzheimer's disease have characteristics that are not observed in undirected networks [5]. Figure 1 shows a methodology of obtaining directed brain functional networks based on electroencephalography recordings.

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