

Graph theory for complex Networks-I

V.Yegnanarayanan¹ and G.K.Umamaheswari²

¹Senior Professor, Department of Mathematics,
Velammal Engineering College, Ambattur-Red Hills Road,
Chennai - 600 066, India. Email id: prof.yegna@gmail.com

²Research Scholar, Research and Development Centre,
Bharathiar University, Coimbatore-641046, India.

Abstract

A main goal of this paper is to highlight how graph theory and its carefully evolved network models help in the study of various complex networks in real-life situations, for instances, the human brain. We give a overview of the growth of complex network of brain and various type of brain connectivity. We also summarize a few open problems in this area.

Keywords: networks, graph theory, brain connectivity

AMS Subject Classification: 05C40, 05C82, 90BXX, 91D30

1. Introduction

Complex networks, in a range of disciplines from biology to physics, social sciences and informatics, have received significant attention in recent years [44,3,36]. What can an investigation of network structure and dynamics contribute to our understanding of brain and cognitive function? In our review, we address this question by highlighting a series of recent studies of complex brain networks and by attempting to identify promising areas and questions for future experimental and theoretical inquiry.

2. Graph theory and terminology

For the following definitions of graph theory terms used in this review we essentially follow the nomenclature (see also [40] for additional definitions and more detail). A Matlab toolbox allowing the calculation of these and other graph theory measures is available at <http://www.indiana.edu/cortex/connectivity.html>.

Adjacency (connection) matrix: The adjacency matrix of a graph is a $n \times n$ matrix with entries $a_{ij} = 1$ if node j connects to node i , and $a_{ij} = 0$ if there is no connection from node j to node i .

Characteristic path length: The characteristic path length L (also called 'path length' or 'average shortest path') is given by the global mean of the finite entries of the distance matrix. In some cases, the median or the harmonic mean can provide better estimates.[50]

Clustering coefficient: The clustering coefficient C_i of a node i is calculated as the number of existing connections between the node's neighbors divided by all their possible connections. The clustering coefficient ranges between 0 and 1 and is typically averaged over all nodes of a graph to yield the graph's clustering coefficient C . [50]

Connectedness: A connected graph has only one component, that is a set of nodes, for which every pair of nodes is joined by at least one path. A disconnected graph has at least two components.

Cycle: A cycle is a path that links a node to itself.

Degree: The degree of a node is the sum of its incoming (afferent) and outgoing (efferent) connections. The number of afferent and efferent connections is also called the 'in-degree' and 'out-degree', respectively.

Distance: The distance between a source node j and a target node i is equal to the length of the shortest path.

Distance matrix: The entries d of the distance matrix correspond to the distance between node j and i . If no path exists, $d_{ij} \rightarrow \infty$

Graph: Graphs are a set of n nodes (vertices, points, units) and k edges (connections, arcs). Graphs may be undirected (all connections are symmetrical) or directed. Because of the polarized nature of most neural connections, we focus on directed graphs, also called digraphs.

Path: A path is an ordered sequence of distinct connections and nodes, linking a source node j to a target node i . No connection or node is visited twice in a given path. The length of a path is equal to the number of distinct connections.

Random graph: A graph with uniform connection probabilities and a binomial degree distribution. All nodes have roughly the same degree ('single-scale'). **Scale-free graph:** Graph with a power-law degree distribution. 'Scale-free' means that degrees are not grouped around one characteristic average degree (scale), but can spread over a very wide range of values, often spanning several orders of magnitude.

3. Networks

Networks are sets of nodes linked by connections, mathematically described as graphs [20,7,12]. The nodes and connections may represent persons and their social relations [49], molecules and their interactions [31], or web pages and hyperlinks [1], often numbering in

the thousands or millions. What makes such networks complex is not only their size but also the interaction of architecture (the network's connection topology) and dynamics (the behavior of the individual network nodes), which gives rise to global states and 'emergent' behaviors. Recent work across a broad spectrum of complex networks has revealed common organizational principles. In many complex networks, the non-linear dynamics of individual network components unfolds within network topologies that are strikingly irregular, yet non-random. In many networks, clusters of nodes segregate into tightly coupled neighborhoods, but maintain very short distances among nodes across the entire network, giving rise to a small world within the network [50]. The degree to which individual nodes are connected forms a distribution that, for many but not all networks, decays as a power law, producing a scale-free architecture characterized by the existence of highly connected nodes (hubs) [5].

4. Complex Networks of a Brain

What about the brain? Nervous systems are complex networks par excellence, capable of generating and integrating information from multiple external and internal sources in real time. Within the neuroanatomical substrate (structural connectivity), the non-linear dynamics of neurons and neuronal populations result in patterns of statistical dependencies (functional connectivity) and causal interactions (effective connectivity), defining three major modalities of complex brain networks. Human cognition is associated with rapidly changing and widely distributed neural activation patterns, which involve numerous cortical and sub-cortical regions activated in different combinations and contexts [8,48,33,10]. Two major organizational principles of the cerebral cortex are functional segregation and functional integration [46,53,19], enabling the rapid extraction of information and the generation of coherent brain states. Which structural and functional principles of complex networks promote functional segregation and functional Integration, or, in general, support the broad range and flexibility of cognitive processes?

5. Types of Brain Connectivity

Anatomical connectivity is the set of physical or structural (synaptic) connections linking neuronal units at a given time. Anatomical connectivity data can range over multiple spatial scales, from local circuits to large-scale networks of inter-regional pathways. Anatomical connection patterns are relatively static at shorter time scales (seconds to minutes), but can be dynamic at longer time scales (hours to days); for example, during learning or development. Functional connectivity [18] captures patterns of deviations from statistical independence between distributed and often spatially remote neuronal units, measuring their correlation/covariance, spectral coherence or phase-locking. Functional connectivity is time-dependent (hundreds of milliseconds) and 'model-free', that is, it measures statistical interdependence (mutual information) without explicit reference to causal effects. Different methodologies for measuring brain activity will generally result in different statistical estimates of functional connectivity [25]. Effective connectivity describes the set of causal effects of one neural system over another [18]. Thus, unlike functional connectivity, effective connectivity is not 'model-free', but requires the specification of a causal model including structural parameters. Experimentally, effective connectivity can be inferred through perturbations, or through the observation of the temporal ordering of neural events. Other measures, estimating causal interactions can also be used (e.g. [16]). Functional and effective connectivity are time-dependent. Statistical interactions between brain regions change rapidly reflecting the participation of varying subsets of brain regions and pathways in different cognitive tasks

[8,48,33,10], behavioral or attentional states [11], awareness [33], and changes within the structural substrate related to learning [9]. Importantly, structural, functional and effective connectivity are mutually interrelated. Clearly, structural connectivity is a major constraint on the kinds of patterns of functional or effective connectivity that can be generated in a network. Structural inputs and outputs of a given cortical region, its connectional fingerprint [37], are major determinants of its functional properties. Conversely, functional interactions can contribute to the shaping of the underlying anatomical substrate, either directly through activity (covariance)-dependent synaptic modification, or, over longer time scales, through affecting an organism's perceptual, cognitive or behavioral capabilities, and thus its adaptation and survival.

5.1 Structural contributions of individual areas and motifs:

At the local level, simple statistical measures ('network participation indices', [30]) can be used to characterize inputs and outputs of individual areas. These measures include an area's in-degree and out-degree, and its 'transmission' coefficient, defined as the relative number of efferents to afferents. Such measures allow identification of highly connected nodes (hubs) and provide an initial functional characterization of areas as either (mainly sending) 'broadcasters' or (mainly receiving) 'integrators' of signals. For macaque visual cortex [17], the average efferent/afferent ratio is close to 1, with a standard error of 0.4 [24], indicating that brain regions tend to engage in cooperative ('give-and-take') information-processing. The 'matching index' captures the pairwise similarity of areas in terms of their specific afferents and efferents from other parts of the network [24,40]. One of the central assumptions of systems neuroscience is that the functional roles of brain regions are specified by their inputs and outputs. In agreement with this concept, one finds that pairs of areas with high matching index also share functional properties [24]. In general, the 'connectional fingerprint' of a cortical area can serve as an indicator of its functional contribution to the overall system [37]. On the next higher level of organization – neural circuits linking small sets of connected brain areas – the approach of motif analysis can be used to identify patterns of local interconnections that occur with a significantly higher frequency in real networks than in randomized networks of the same size [34,35,4]. Biological and technological networks contain several characteristic motifs, such as 'feed forward loops' and 'bi-parallel pathways'. A systematic analysis of motifs in brain networks revealed a small number of characteristic motifs shared among several examples of cortical networks (O. Sporns and R. Kotter), potentially indicating common modes of information processing.

5.2 Large-scale connection patterns

Graph theoretical analysis of large-scale connection patterns of cat and monkey has revealed characteristic properties, several of which are shared across neural systems and species. All large-scale cortical connection patterns (adjacency matrices) examined so far exhibit small-world attributes with short path lengths and high clustering coefficients [23,39,42,43]. These properties are also found in intermediate-scale connection patterns generated by probabilistic connection rules, taking into account metric distance between neuronal units [43,41]. This suggests that high clustering and short path lengths can be found across multiple spatial scales of cortical organization. The quantitative analysis of structural connection patterns using graph theory tools provides several insights into the functioning of neural architectures. In-degree and out-degree specify the amount of functional convergence and divergence of a given region (see above), whereas the clustering coefficient measures the degree to which the area is part of a local collective of functionally related regions. The path length between two brain regions captures their potential 'functional proximity'. If no path exists, no functional interaction can take place.

Various global connectivity features of cortical networks have been described and characterized with the help of multivariate analysis techniques, such as multidimensional scaling or hierarchical cluster analyses [24]. For example, streams of visual cortical areas have been identified that are segregated functionally [47] as well as in terms of their inputs, outputs and mutual interconnections [51]. Topological sequences of areas might provide the layout for signaling pathways across cortical networks [38]. Alternatively, hierarchies of cortices can be constructed, based on the laminar origin and termination patterns of interconnections [17,22]. To identify the clusters which are indicated by the high clustering coefficients of cortical networks, a computational approach based on evolutionary optimization was proposed [23]. This stochastic optimization method delineated a small number of distinctive clusters in global cortical networks of cat and macaque [23] as well as primate prefrontal cortex [29]. The algorithm could be steered to identify clusters that no longer contained any known absent connections, and thus produced maximally interconnected sets of areas. The identified clusters largely coincided with functional cortical subdivisions, consisting predominantly of visual, auditory, somatosensory-motor, or frontolimbic areas [23]. On a finer scale, the clusters identified in the primate visual system closely followed the previously proposed dorsal and ventral visual streams, revealing their basis in structural connectivity patterns. In networks composed of multiple distributed clusters, inter-cluster connections take on an important role. It can be demonstrated that these connections occur most frequently in

all shortest paths linking areas with one another [26]. Thus, inter-cluster connections can be of particular importance for the structural stability and efficient working of cortical networks. The degree of connectedness of neural structures can affect the functional impact of local and remote network lesions [52], and this property might also be an important factor for inferring the function of individual regions from lesion induced performance changes. Indeed, the cortical networks of cat and macaque are vulnerable to the damage of the few highly connected nodes [32] in a similar way that scale-free networks react to the elimination of hubs [2]. Random lesions of areas, however, have a much smaller impact on the characteristic path length.

6.How Complex Networks grow?

The physical structure of biological systems often reflect their assembly and function. Brain networks are exception, containing structures that are shaped by evolution, ontogenetic development, experience-dependent refinement, and finally degradation as a result of brain injury or disease. To understand how various developmental factors affect functional specializations of brain networks, it is helpful to consider biologically inspired models based on known constraints of neural development. Previous algorithms for the generation of random and scale-free networks constitute unlikely growth algorithms, as they ignore the fact that cortical networks develop in space. Preferential attachment [3], for instance, would establish links to hubs independent of their distance. In biological networks, however, long-distance connections are rare, in part because the concentration of diffusible signaling and growth factors decays with distance. Accounting for this constraint, a spatial growth model was presented [27] in which growth starts with two nodes, and a new node is added at each step. The establishment of connections from a new node u to one of the existing nodes v depends on the distance $d(u,v)$ between nodes, that is, $P(u, v) = \beta e^{-\alpha d(u,v)}$.

This spatial growth mechanism can lead to networks with similar clustering coefficients and characteristic path lengths as in cortical networks when growth limits are present, such as extrinsic limits imposed by volume constraints. Lower clustering results if the developing model network does not reach the spatial borders and path lengths among areas increase [28]. By comparison, a preferential attachment model might yield similar global properties, but fails to generate multiple clusters, as found in cortical networks.

Global Network Design

Can local spatial growth rules yield the known corticocortical topology? In addition to similar global properties, defined by clustering coefficient and characteristic path length, the generated networks also exhibit wiring properties similar to the macaque cortex, whose network and wiring distribution . This supports the idea that the likelihood of long-range connections among cortical areas of the macaque decreases with distance [28]. Total wiring length both in the cortical and spatially grown networks lies between benchmark networks in which connections are randomly chosen, and in which only the shortest-possible connections are established. The (few) long-range connections existing in the biological networks might constitute shortcuts, ensuring short average paths with only few intermediate nodes. Thus, the minimization of this property might compete with global wiring length minimization. As a by-product, the short-distance preference for inter-area connections during spatial growth can lead to optimal component placement [13] without the need of a posteriori optimization. Intuitively plausible growth mechanisms have been proposed for the large classes of small-world [50] and scale-free networks [5]. Such topological algorithms, however, are not biologically realistic and do not represent good models for the development of cortical networks. Alternative developmental algorithms were proposed recently that acknowledge spatial constraints in biological systems, while also yielding different types of scale-free and small-world networks [27,28]. It will be an important challenge to refine these computational models by drawing on the wealth of data available from studies in developmental neurobiology [45], to reproduce the specific organization of cortical networks. Especially intriguing is the role that experience might play in network growth. Although the same complement of connections appears to exist in different individuals of a species, the density of specific cortical fiber pathways can vary substantially between individual brains [21]. It is currently not clear whether this variability is partly attributable to activity-dependent processes. If so, it might be described by recent approaches that couple changes in connection topology to the dynamical evolution of connection weights [6].

7. Some open problems

- What are the best experimental approaches to generate large and comprehensive connectional datasets for neural systems, especially for the human brain?
- What is the time scale for changes in functional and effective connectivity that underlie perceptual and cognitive processes?

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- Are all cognitive processes carried out in distributed networks? Are some cognitive processes carried out in more restricted networks, whereas others recruit larger subsets?
- Does small-world connectivity reflect developmental and evolutionary processes designed to conserve or minimize physical wiring, or does it confer other unique advantages for information processing?
- What is the relationship between criticality, complexity and information transfer?
- Is the brain optimized for robustness towards lesions, or is such robustness the by-product of an efficient processing architecture?
- What is the role of hubs within scale-free functional brain networks?
- How can scale-free functional networks arise from the structural organization of cortical networks?

Conclusion

In this survey, we briefly outline the important aspects of the complex network with reference to brain and how graph theory techniques are adopted to model various interesting phenomenon addressing the growth of the complex networks. For more on this topic also see [14].

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