Functional specialization, modularity and communication: Network models linking brain structure and function

Maria Grazia Puxeddu[a,1], **Caio Seguin**[a,1], **and Olaf Sporns**[a,b,c], [a] Department of Psychological and Brain Sciences, Indiana University, Bloomington, IN, United States; [b] Program in Neuroscience, Indiana University, Bloomington, IN, United States; and [c] Program in Cognitive Science, Indiana University, Bloomington, IN, United States

© 2024 Elsevier Inc. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

Key points

- Introducing the *connectome*: how we can model the brain as a network of interconnected brain regions.
- Describing organizational principles of the connectome by characterizing its topology in terms of functional specialization, modularity, and communication efficiency.
- Discussing the insight that the connectome topology can offer about brain function.

Abstract

Brain connectivity can be represented as a complex network, amenable to modeling and analysis using the tools of network science and graph theory. In this article we survey three approaches to characterize the topology of structural connectivity. We discuss families of graph metrics related to (i) specialized roles for individual network nodes (topological specialization), (ii) their clustering into modules, (iii) and models capturing network communication. We also clarify how these different network constructs relate to each other and inform brain function. In doing so, we discuss the insights that they can offer about brain functional connectivity and organization. Together with this article, we provide sample data and a set of analysis scripts as a starting point for practitioners in the field.

Introduction

The brain is a complex network, composed of billions of neurons organized into hundreds of cell types and regions whose dynamic activity underpins cognition and behavior (Sporns et al., 2005). The anatomical organization of brain networks develops and evolves into distinct architectures that define relations among neural elements across multiple scales. These relations enable functional specialization (Passingham et al., 2002), modular architecture (Sporns and Betzel, 2016), and communication processes (Seguin et al., 2023a) that unfold in time, in the course of spontaneous, stimulus-evoked and task-specific neural activations.

Network approaches have become integral components of data science, driven in part by the ubiquity and universality of networks in technology and engineering, as well as social and biological systems. Network science provides a theoretical foundation as well as well-defined analytic and modeling tools that enable the investigation of complex networked systems. The brain is a case in point (Bassett and Sporns, 2017). Over the last couple of decades an increasing number of studies have leveraged network science theories and tools to map the brain's structural and functional networks.

The distinction between structural and functional connectivity networks, here abbreviated as SC and FC, is fundamental, and somewhat unique to the brain (Bullmore and Sporns, 2009). While SC refers to anatomical connections between neural elements, FC measures statistical relationships between activity recorded from different locations in the brain. These two main domains of brain networks are mutually dependent. The structural architecture shapes neural activity and consequently functional connectivity.

[1]Contributed equally.

On the other side, functional connectivity also influences the structural backbone over longer periods of time, through mechanisms of neural plasticity and even on evolutionary time scales.

In this article we survey three sets of network neuroscience methods. First, we examine the structural basis of functional specialization. Second, we cover the extensive area of network modules and communities. Third, we review a set of tools that attempt to predict and capture communication processes. We then assemble these approaches and ask if they can be useful to predict functional connectivity. Finally, we discuss how these methods provide convergent and complementary insights into brain organization.

To illustrate the concepts discussed throughout the article, we perform simple analyses on a sample data set, obtained from the Human Connectome Project (HCP) (Van Essen et al., 2013). Both the code to reproduce the analyses and sample data are available on the following GitHub repository (https://github.com/mariagraziaP/chapter_DataNeuroscience).

Basic definitions

While network terminology has become widespread in neuroscience (Bassett and Sporns, 2017), it is useful to define some core terms at the outset. With the term *network*, we refer to a mathematical object used to model and analyze many complex systems, among which is the brain. The fundamental units of the system (neural elements in the case of the brain) and their mutual relations are formalized through networks as a set of nodes and edges (or links). Mathematically, we can summarize a network in the form of a square matrix A, called the *adjacency matrix*, of dimensions $N \times N$, with N being the number of nodes. A non-zero entry A_{ij} in the adjacency matrix denotes the existence of a connection between nodes i and j, and its value encodes the weight of that connection.

Once brain connectivity data have been organized in the form of a network, its topology, i.e. the relations between nodes and edges, can be investigated through a set of tools developed in the fields of graph theory and network science (Fornito et al., 2016). Of particular interest are the measures of segregation and integration, which document different aspects of the network's organization. A first peculiarity of brain network organization is that the distribution of the edges is far from uniform. Rather, they tend to cluster, forming highly interconnected groups of nodes (Sporns and Betzel, 2016). Segregation measures then describe the tendency of nodes to aggregate into *modules* (also named communities or clusters). Measures of integration, instead, are usually applied to capture how nodes are linked to each other through sequences of edges, also termed *paths*. These measures are important to describe how communication may occur in the network and how information is exchanged between nodes. A schematic of these measures is shown in Fig. 1.

Networks can be used to model structural and functional relationships between brain areas. Since the network interpretation changes with the modality, it is important to clarify the difference between the two. *Structural connectivity* (SC) refers to the anatomical (physical) connections linking distributed neural elements. *Functional connectivity* (FC) instead, encodes the statistical dependencies between the activity recorded from pairs of neural elements. The difference between the two types of connectivity is reflected in the topology of their networks and adjacency matrices. Structural brain networks are usually sparse. Because there is a metabolic cost associated with each anatomical connection, most pairs of brain regions are not directly connected and thus their interregional coupling is constrained (Betzel and Bassett, 2018). Between brain regions, structural connections are thought to be stable over short time periods, whereas some changes in density or efficacy have been observed across developmental phases

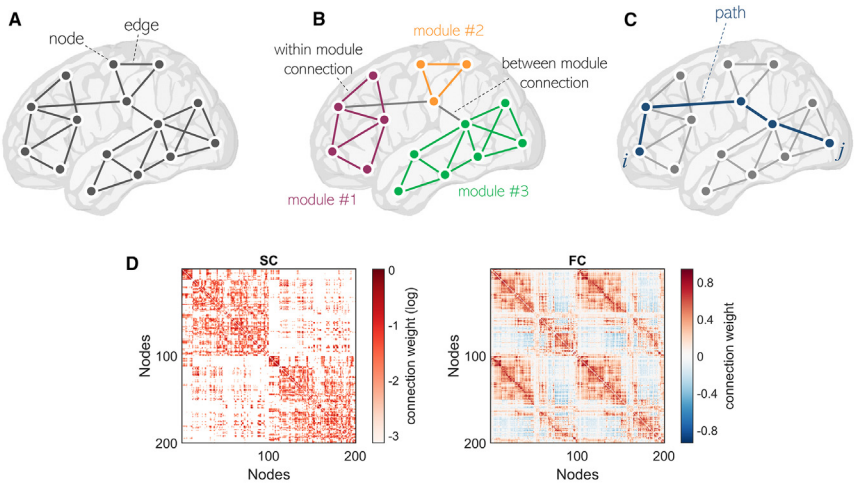

Fig. 1 Schematic representation of a brain network and its topological properties. (A) Nodes and edges represent different brain regions and their interconnections, respectively. (B) Brain networks can be partitioned into modules. In the example shown, the nodes are grouped into three modules identified by different colors. (C) Paths are sequences of edges that connect pairs of nodes in the network. In the illustration, the shortest path connecting node i to node j requires 4 edges. (D) Example of structural and functional connectivity matrices obtained from the HCP dataset. The SC matrix is sparse and made of only positive weights, while the FC matrix is fully connected and its entries can be either positive (red) or negative (blue).

and aging (Betzel et al., 2014; Puxeddu et al., 2020). On the other hand, functional networks are mathematical (statistical) constructs, so there are no direct physical or metabolic constraints limiting their density or interregional connectivity. Moreover, mounting evidence indicates that they exhibit significant fluctuations over short timescales, adapting to spontaneous and task-evoked neuronal activity (Cole et al., 2014; Gonzalez-Castillo and Bandettini, 2018).

To build brain networks, either structural or functional, there are multiple choices we can make to define nodes and edges, mainly related to the spatial and temporal resolution at which we observe the interactions between neural elements (Sejnowski et al., 2014). At a microscale level, structural networks can be reconstructed using electron microscopy, and the set of nodes and edges would be constituted by single neurons and their synaptic contacts and axonal projections (Schrö et al., 2017; Betzel et al., 2023; Winding et al., 2023). At mesoscale and macroscale levels instead, methods like tract-tracing or diffusion imaging have been used to build anatomical networks where the connectivity between neural populations or larger brain areas is investigated. Functional networks reflect neuroimaging modality and are usually estimated from fMRI, MEG, EEG, iEEG, or calcium imaging signals (Friston, 2011). Here nodes are gray matter regions and functional edge weights can be statistically determined from the signals originating from those regions in multiple ways, including zero-lag correlation, mutual information, coherence, or other bivariate metrics.

In this article we focus on MRI-derived brain networks, which are among the most widely used in network neuroscience. SC networks can be reconstructed from diffusion MRI and white-matter tractography (Zhang et al., 2022). Starting from a parcellation of the brain into large-scale areas (Eickhoff et al., 2018), which defines the nodes in the SC network, tractography algorithms estimate the putative trajectories and magnitudes of white matter tracts connecting these areas from diffusion MRI. Edge weights can be estimated in a variety of ways, commonly calculated as proportional to the number or density of tractography streamlines between two areas. Diffusion MRI cannot provide information on axonal directionality. Thus, structural connectivity will be formalized as a weighted, positive, sparse, and undirected network. Analogous parcellations of the brain into large-scale areas are used to identify the nodes of FC networks. Functional edges however are computed by determining statistical relationships between fMRI BOLD time-series recorded from those large-scale areas. Commonly, the Pearson correlation is used to infer such associations. As a result, fMRI-based FC networks are fully connected, undirected, and weighted matrices, with weights spanning the range $[-1, 1]$ (the same range as Pearson's correlation coefficients). An example of MRI-derived SC and FC networks is shown in **Fig. 1**.

Topological specialization

One of the most fundamental observations about neuronal and regional activity in the brain is that different neurons and regions are functionally specialized or segregated (Fornito et al., 2016). Functional specialization does not generally imply completely encapsulated function (as in phrenology) or extreme localization (one brain region, one cognitive task). Instead, it occupies a middle ground between localized and distributed function, with neural elements acquiring overlapping competencies that are enabled by network connectivity. In a seminal article, Passingham et al. linked anatomical inputs and outputs to physiological profiles of specialization (Passingham et al., 2002). Their concept of connectional fingerprint became one of the principal underpinnings of attempts to link brain structure to function.

In network terms, a fingerprint represents a row or column in an adjacency matrix. This simple construct encodes a node's connectivity profile and can be understood as the set of all inputs and outputs of a given neural element. The overlap between the topological fingerprint of two nodes is thought to reflect the similarity of their roles in processing information. Presumably, functional co-activation of two brain regions in part originates from their common structural connectivity pattern. The implication is that two neural elements with the exact same set of inputs and outputs are specialized to perform identical functional roles in the network. The greater the difference in fingerprints, the more distinct are their functional contributions.

A number of topological specialization measures have been proposed to quantify pairwise similarities in nodal fingerprints. Computed for all pairs of nodes, these measures yield an analytical transformation of the structural connectivity matrix that—beyond direct structural connections—also encode information on the topological similarity of unconnected nodes (**Fig. 2**). Here, we focus on the matching index and the cosine similarity, two widely used metrics that find utility in a range of network neuroscience applications, including the quantification of node homophily in generative models of brain networks (Betzel et al., 2016; Oldham et al., 2022) and the embedding of connectomics data into low-dimensional functional spaces (Rosenthal et al., 2018).

The matching index (Hilgetag et al., 2002) between nodes i and j is defined as

$$MI_{ij} = \frac{\left|\Gamma_{i\setminus j} \cap \Gamma_{j/i}\right|}{\left|\Gamma_{i\setminus j} \cup \Gamma_{j/i}\right|},$$

where $\Gamma_{i\setminus j}$ is the set of i's neighbors excluding j. Put simply, it is the number of common neighbors between i and j divided by their total number of neighbors, with a potential connection between i and j not taken into account in the calculation. As such, $MI_{ij} \in [0,1]$, with a value of 0 indicating that i and j do not share any neighbors and a value of 1 indicating a perfect overlap in their connectivity profiles. We note that this formulation of the matching index is closely related to the Jaccard similarity, and that alternative versions of this measure have been proposed to explicitly take into account connection weights.

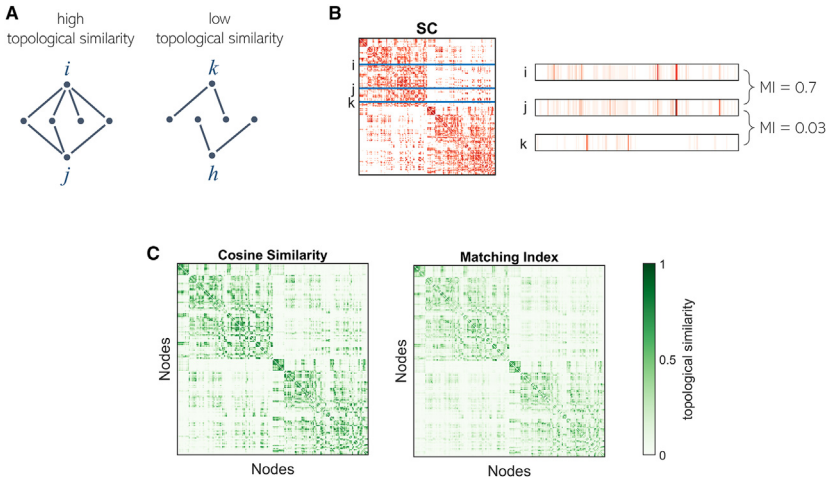

Fig. 2 Topological specialization analysis. (A) Toy model. Topological specialization is computed between pairs of nodes by observing their connectivity profiles. A key factor in determining topological similarity is the proportion of neighbors shared between two nodes, such that large (left) and small (right) overlap in connectivity fingerprints indicate distinct profiles of topological specialization. (B) Example of connectivity patterns of three nodes $\{i, j, k\}$ of the SC matrix. Nodes i and j present a similar connectivity pattern and therefore the Matching Index (MI) computed between their rows is high ($MI_{ij} = 0.7$). On the contrary, nodes j and k have highly diverse profiles of connectivity, causing a lower topological similarity ($MI_{jk} = 0.03$). (C) Cosine similarity and matching index matrices computed from structural connectivity (cf. **Fig. 1**). Matlab code to compute such metrics can be found in the GitHub repository (https://github.com/mariagraziaP/chapter_DataNeuroscience).

The cosine similarity between i and j is given by

$$CS_{ij} = \frac{A_i \cdot A_j}{\|A_i\| \times \|A_j\|},$$

where A_i is the i th row (or column) in the adjacency matrix. Here, the connectivity profiles of i and j are viewed as two vectors in N-dimensional space, and their similarity is computed as the cosine of the angle between them. In the formulation above, this is expressed as the dot product of the two vectors, divided by the product of their lengths. It follows that $CS_{ij} \in [-1, 1]$, with similarity values of -1, 0, and 1 denoting exactly opposite, orthogonal and proportional pairs of vectors, respectively.

Modularity

A major application of network science to the brain involves the data-driven discovery of network modules, also commonly called communities. The term module does not imply, as it does in some areas of cognitive science, complete separation or encapsulation of neural activity and behavioral competencies. Far from a Fodorian, cognitively encapsulated, view of modularity (Fodor, 1983), network modules are mathematically defined objects, corresponding to groups of nodes topologically *close* to each other (we will see different definitions of closeness later in this section) that can share connections and functions with other groups (Sporns, 2013). Evidence of network modularity has been observed in numerous neural systems, from model organisms, such as the *Caenorhabditis elegans* (Towlson et al., 2013) and the *Drosophila melanogaster* (Betzel et al., 2023), to mammals (Puxeddu et al., 2024) and humans (Hagmann et al., 2008). Intuitively, network modularity allows for balanced states of segregated and integrated information processing that support cognitive functioning. This definition of communities harmonizes with what Simon proposed as "near-decomposability" (Simon, 1962), a ubiquitous property of complex systems that confers a great advantage in terms of adaptability to evolutionary pressure, lifespan modifications, or focal dysfunction or damage.

Community detection is methodologically related to data clustering and segmentation, core topics of data science. Clustering is used to reduce the dimensionality of large systems or generate insights into the system's organization. In large and complex data, the detection of communities is notoriously hard and computationally demanding. While the majority of brain network data sets are modest in size (comprising hundreds to thousands of nodes), they do pose challenges mainly due to their spatio-temporal multi-scale organization (Betzel and Bassett, 2017). Not only do communities exist at multiple spatial scales, showing different levels of granularity, they also reconfigure at several temporal scales, from milliseconds during rapid reconfiguration (Puxeddu et al., 2021a), to learning (Bassett et al., 2011) and plasticity (Gallen and D'Esposito, 2019), and over development and the lifespan (Puxeddu et al., 2020). While we leave aside issues of network dynamics (time-changing edges and communities), often addressed through multi-layer modeling (Vaiana and Muldoon, 2020; Puxeddu et al., 2021b; Bassett et al., 2013), we will focus on the topic of spatial resolution of the communities. This is a central issue in network neuroscience that must be addressed in most neuroimaging datasets, as the topology of brain networks accommodates sets of modules that span multiple spatial scales and may be hierarchically nested (Ashourvan et al., 2019; Meunier et al., 2009).

There are dozens of definitions of modules and communities and numerous algorithms for detecting communities in network data (Fortunato, 2010). Typically, how nodes are grouped into modules depends on the research question. Communities can correspond to sets of neural elements that share dense mutual connectivity (assortative modules), similar connection patterns with the rest of the network (block modeling), or similar response profiles or time courses (as in functional connectivity). Frequently used methods for data-driven community detection in structural brain networks include spectral clustering, random walk models (Rosvall and Bergstrom, 2008), and stochastic block models (Peixoto, 2014). It is beyond the scope of this article to comprehensively illustrate and compare all the different approaches. Instead, we focus on one of the most commonly used and versatile, the *modularity optimization* (Newman and Girvan, 2004). Modularity optimization provides a partition of the network into modules whose connection density is maximally greater than the connection density that one would observe within the same modules imposed on a null connectivity model. Mathematically, these partitions are obtained by maximizing a quality metric, Q, called modularity, that in its original formulation is expressed as:

$$Q = \sum_{ij} \left[A_{ij} - P_{ij}\right] \delta\left(\sigma_i, \sigma_j\right).$$

Here, A_{ij} and P_{ij} are the weights of the connection between nodes i and j in the observed network and the null model, respectively, $\sigma_i \in [1, \ldots, K]$ indicates to which of the K communities nodes i and j belong, and δ is the Kronecker delta function, equal to 1 when the arguments assume the same value (nodes and are assigned to the same community) and 0 otherwise. By optimizing Q, we maximize the difference between A and P for co-assigned nodes, which leads to assortative communities whose internal density exceeds a null-case expectation.

But how do we build a null model for modularity optimization? An unequivocal answer to this question does not exist. Indeed, the many available choices of a null model make the approach versatile and able to address specific questions in neuroscience (Zamani Esfahlani et al., 2021). For instance, structural and functional networks present different topology and originate in different types of brain data, and thus we would assume they require different null models. Among the most appropriate for structural brain networks, there is the *configuration null model*, which assumes that the expected weight between two nodes P_{ij} is linked to their strength, k_i and k_j, through the expression $P_{ij} = \frac{k_i k_j}{2m}$, where $2m$ is the sum of the weights in the network. With this formulation, we build a null connectivity network model that preserves the degree sequence while randomizing the edges. More sophisticated null models also attempt to preserve spatial relationships. In fact, with the unrestrained randomization of the configuration model we generate null networks with links connecting nodes many times more distant and with a cost that far exceeds what is observed in anatomical networks. One way to preserve spatial relationships is using the binary structure of A as a mask and randomly assign weights to the edges (Roberts et al., 2016). The configuration model, as well as its modifications, are tailored for sparse positive networks, such as those in SC, but less suited for fully connected matrices with positive and negative weights like FC networks. In this second case, every node has an identical degree and edges are not independent (which is a necessary condition for the just described null model). A more appropriate null model for correlation networks then is the *uniform null model*, where every pair of nodes is connected with the same weight (Bazzi et al., 2016).

There are several optimization algorithms to maximize modularity, among which one of the most widely used is the so-called Louvain algorithm (Blondel et al., 2008). A computational issue is that the use of a global quality function requires the algorithm to identify the single partition that performs best. However, such a single solution does not exist. Instead, many near-optimal partitions of the same network will likely provide high and near-optimal Q-values. This issue is called near-degeneracy of modularity (Good et al., 2010) and is more and more evident as the size of the network increases. It is best practice then, to run the optimization algorithm many times, avoiding treating the first obtained partition as privileged. But how do we deal with the resulting set of partitions? While there exist many approaches, for instance selecting the most frequent partition or the partition most similar to all the others (a sort of centroid), Lancichinetti and Fortunato provided a method to identify a *consensus* partition out of an ensemble (Lancichinetti and Fortunato, 2012). The consensus is obtained by running the optimization algorithm on an *agreement matrix*, whose entries represent the frequency with which any two nodes have been assigned to the same module within the set of partitions. We can iterate the procedure by running many times the algorithm on such a matrix, obtaining a new set of partitions that can be co-classified again. It has been shown how a stable partition of the network is soon reached, after a few iterations.

Another issue in the optimization is that the Q-metric is biased and requires modification to detect modules at smaller or larger spatial scales (Fortunato and Barthélemy, 2007). For this reason, a more recent formulation includes a spatial resolution parameter γ that scales the importance of the null model P:

$$Q(\gamma) = \sum_{i,j} \left[A_{ij} - \gamma P_{ij}\right] \delta\left(\sigma_i, \sigma_j\right).$$

Low γ-values make it easier for the observed model to beat the null case so that more pairs of nodes would be likely assigned together forming big communities. As the γ-value increases, it becomes harder for two nodes to have an edge weight A_{ij} greater than γP_{ij}, making it unlikely for them to be assigned to the same modules. Thus, the number of detected modules is determined by the value of γ. Low-γ render coarse partitions made of few big clusters, while high-γ return fine partitions, made of many small communities. In this sense, the resolution parameter γ allows for a topological zoom-in and zoom-out of the meso-scale structures of the network. In **Fig. 3**A we report an example of SC partitions obtained at different settings of γ.

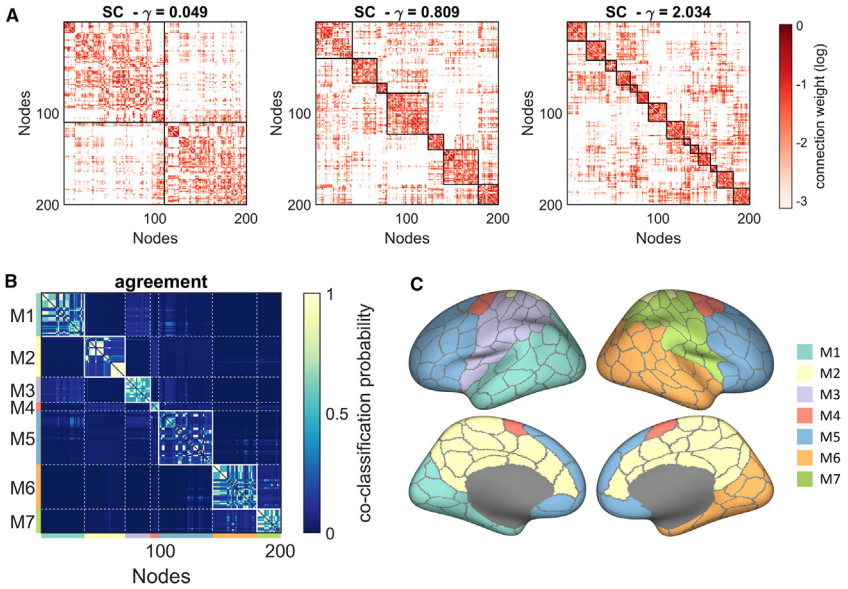

Fig. 3 Example of multi-resolution community detection. (A) Running the modularity optimization with different γ-values leads to differently resolved partitions of the brain network into modules of highly interconnected nodes. In the example, we show the SC matrix reordered according to the community affiliations resulting from three different γ. With this reordering the number of modules is given by the number of diagonal blocks and within-modules connections fall inside those blocks, highlighting an assortative modular organization. The three γ-values lead to partitions made of 2, 7 and 14 modules respectively. (B) Agreement (or co-classification) matrix computed on an ensemble of 1000 partitions obtained by sweeping γ over the range [0.001 10], with the number of modules ranging between 2 and 50. Nodes are reordered based on the consensus partitions computed on this matrix, which is made of 7 modules [M1, … , M7]. The Matlab code to compute MRCC and agreement matrix is available in the GitHub repository (https://github.com/mariagraziaP/chapter_DataNeuroscience). (C) Projection of the consensus partition onto the cortical surface. The allegiance of a node to one of the 7 communities is rendered through a color-code.

While in many studies, the community structure of brain networks is investigated by imposing the default setting of $\gamma = 1$, it should be noticed that this represents only a specific scale of the network organization, that will generally not be privileged with respect to many, equally plausible, other partitions. Instead, the current best practice of community detection in brain networks suggests running the optimization systematically varying γ over a range of values that allow for a multiscale investigation of the modular structure.

Consensus and multiscale approaches can be combined by performing *multiresolution consensus clustering* (MRCC) (Jeub et al., 2018). This leads to a thorough analysis of the modular structure in brain networks, where both near-degeneracy and multiscale issues are addressed. The MRCC works by sweeping over a range of γ that gives good coverage of different scales. It then combines all the resulting partitions into an agreement matrix, also called *co-classification* matrix (CC) (**Fig. 3**B) of dimension $N \times N$, whose entries denote the frequency with which any pair of nodes is assigned to the same module across the γ spectrum. The CC can then be analyzed to study modularity in a γ-resolved way, without the need to settle for a specific resolution, or can be clustered again to find a consensus. In Jeub et al. (2018) the CC is clustered using a particular null model based on the ensemble of partitions, which allows for a statistical assessment of the significance of the co-classification. Hierarchical structures are then obtained by recursively iterating the procedure to modules obtained at the previous step, stopping when they do not split into any significant sub-modules. In the end, MRCC returns a set of hierarchical partitions that underlie the organization of the network at different spatial scales. The hierarchical aspect is of particular interest as it mirrors our understanding of the brain's modular organization, where brain areas are recursively aggregated in an attempt to balance information segregation within similar processing units at a single scale and integration between groups of units across multiple scales (Park and Friston, 2013).

Communication

Network communication processes are ubiquitous in nature. From the spread of infectious diseases in social networks, to failure cascades in power grids, to the routing of packages on the internet, the structure of complex networks shapes the flow of information between elements of a system (Estrada, 2011; Newman, 2003). In nervous systems, structural connectivity between neural elements enables exchange of neural signals, in the form of series of action potentials. The resulting signal traffic can be modeled as a communication process (Seguin et al., 2023a; Avena-Koenigsberger et al., 2018), exhibiting its own dynamics expressed as fluctuations in information flow. At the macroscale of the human connectome inferred from MRI, communication via white matter fibers facilitates interactions between gray matter regions, which in turn result in whole-brain patterns of functional connectivity.

Measures from graph theory and network science can be used to model communication in brain networks. Such models are most relevant for understanding functional interactions between anatomically unconnected neural elements, i.e., pairs of nodes for which communication is established via a sequence of one or more intermediate elements (Fig. 4A). Computed on structural connectivity, a network communication measure yields a communication matrix, which quantifies the difficulty (or ease, depending on the measure) of signal transmission between every pair of nodes. To achieve this, each measure assumes that communication takes place according to a certain policy to guide signal transmission through the network.

Traditionally, information flow in brain networks has been modeled via shortest topological paths (Fig. 4B, left). As such, communication between two nodes is considered to take place via the least costly path between them (e.g., via the fewest number of edges in an unweighted network). Many popular graph-theoretical measures used to describe brain networks are based on this conceptualization of neural communication, including the characteristic path length, network efficiency, betweenness centrality, and measures of small-world topology (Bullmore and Sporns, 2009; Rubinov and Sporns, 2010). Ultimately, all of these measures stem from the matrix of shortest path lengths. The first step in the computation of shortest paths is the monotonic transformation of strong connection weights into short connection lengths. This is necessary since the identification of shortest paths is a minimization problem, therefore requiring a measure of the cost associated with traversing each connection in the network. Connection lengths are typically computed as $L = 1/A$ or, assuming weights are defined between 0 and 1, $L = -log(A)$. The *shortest path length* between nodes i and j is then computed as

$$SPL_{ij} = L_{iu} + \ldots + L_{vj},$$

where $\{i, u, \ldots, v, j\}$ is the sequence of nodes visited along their shortest path.

In recent years, the assumption of neural communication via shortest paths has been increasingly called into question, owing to two notable shortcomings of this model. First, it presupposes that individual network elements have global knowledge of network topology, as the identification of shortest paths mandates information about the entire network. This requirement for a centralized, bird's-eye view of connectivity is unlikely to be met in nervous systems, where individual neural elements most likely do not possess knowledge of the network beyond their immediate vicinity (Goñ et al., 2013). Second, the heterogeneous distribution of edge weights characteristic of brain networks means that shortest paths traverse only a small fraction of all the edges in the connectome—the implication being that, if neural signals were transmitted *exclusively* via shortest paths, most white matter projections in the human brain would be inconsequential for inter-areal communication (Avena-Koenigsberger et al., 2017; Seguin et al., 2018).

In light of these drawbacks, multiple alternative measures have been recently proposed as candidate descriptors of connectome communication. In particular, attention has started to swift towards decentralized models that utilize local properties of network

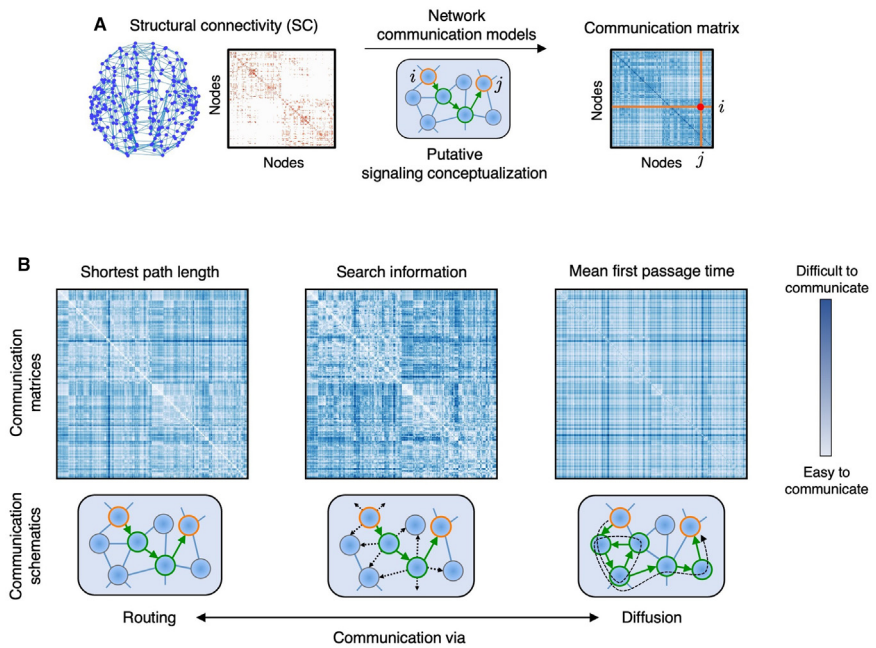

Fig. 4 Communication processes in brain networks. (A) A network communication measure quantifies the difficulty (or ease) of transmission between pairs of nodes, under the assumption that signals are transmitted according to a certain policy to guide network communication. Computed for every pair of nodes, the structural connectivity matrix (encoding only direct structural edges) is transformed into a communication matrix. (B) Examples of communication matrices obtained from different policies and conceptualizations of network communication, arranged on a spectrum from routing (efficient, selectively assessed paths) to diffusion (random walk dynamics). The Matlab code to compute such communication matrices can be found in the GitHub repository (https://github.com/mariagraziaP/chapter_DataNeuroscience).

topology to propagate signals, and may therefore provide more biologically plausible accounts of neural information flow (Seguin et al., 2023a; Avena-Koenigsberger et al., 2018). A quintessential measure of decentralized communication is the *mean first passage time*, which quantifies the average number of edges traversed by a random walker traveling from a source node to a target node (**Fig. 4**B, right).

Well-established mathematical operations can be used to describe the dynamics of random walks on networks, and the mean first passage time can be analytically computed from the transition probability matrix T, such that

$$T_{ij} = \frac{A_{ij}}{\sum_{k=1}^{N} A_{ik}}.$$

Importantly, modeling signal transmission as a random walk process does not mandate global knowledge of the network, as the behavior of the random walker is determined entirely by the out-degree of each node visited during the walk—a local property that could be conceivably accessed by elements of a nervous system (Goñ et al., 2013). However, while biologically plausible from an implementational standpoint, random walks are exceedingly inefficient policies to guide communication. Compared to the shortest path, random walks typically require orders-of-magnitude more steps through the network to establish a communication channel between two nodes (Avena-Koenigsberger et al., 2014).

Routing along shortest paths—efficient communication but strong knowledge assumptions—and diffusion via random walks—weak knowledge assumptions but inefficient communication—constitute opposite ends on a spectrum of signaling policies (Avena-Koenigsberger et al., 2019). Many other communication models have been proposed that negotiate different trade-offs between transmission efficiency and biological plausibility, and therefore occupy positions on the spectrum (Seguin et al., 2023a). Examples include navigation (Seguin et al., 2018), linear threshold models (Mišić et al., 2015), and communicability (Estrada and Hatano, 2008). Of particular interest are measures that explicitly combine aspects of shortest paths and random walks, such as the *search information* (Rosvall et al., 2005). This measure is related to the probability that a random walker will serendipitously travel between two nodes via their shortest path, and thus quantifies the accessibility of efficient paths to communication policies without centralized knowledge of the network (**Fig. 4**B, center). Search information can therefore be used to probe the extent to which the topology of the connectome naturally guides the flow of random walkers via efficient communication routes. Mathematically, the search information from nodes i to j is defined as

$$SI_{ij} = log_2\left(T_{iu} \times \ldots \times T_{vj}\right),$$

where $\{i, u, \ldots, v, j\}$ is the sequence of nodes visited along their shortest path and T is the transition probability matrix introduced above.

Accumulating evidence indicates that communication measures spanning the routing–diffusion spectrum offer utility in understanding various aspects of brain function. Network communication models have been reported to explain inter-individual differences in clinical, cognitive and behavioral scores (Seguin et al., 2020; Imms et al., 2021; de Lange et al., 2019), established patterns of cortical lateralization (Mišić et al., 2018), the propagation of electrophysiological activity following focal brain stimulation (Seguin et al., 2023b), and multiple aspects of spontaneous inter-regional co-activation inferred from fMRI time series (Goñi et al., 2014; Seguin et al., 2019; Zamani Esfahlani et al., 2022). Collectively, these studies indicate that augmenting structural connectivity matrices—encoding only direct anatomical connections—into communication matrices—describing polysynaptic interactions—improves the predictive utility of the structural connectome.

Despite this progress, it is important to note that network communication models provide only putative descriptions of neural signaling. It remains unclear which conceptualizations of network communication most accurately describe underlying biological processes. As such, efforts to systematically compare the utility of different measures to a wide range of neuroscientific research questions are necessary. Interestingly, to date, the few comparative studies evaluating the performance of communication models have highlighted the explanatory power of decentralized measures that deviate from the prevailing premise of routing along shortest paths (Mišić et al., 2018; Seguin et al., 2023b). Another emerging trend is the observation that model predictive utility may be context-dependent, with different communication measures providing better descriptions of neural signaling processes pertaining to different regions and systems, measured at different spatio-temporal scales, or related to different behavioral and cognitive demands (Seguin et al., 2020, 2022). Recent advancements in multi-policy communication models—allowing for the principled interpolation of distinct signaling strategies—provide a promising framework to systematically investigate the contribution of different models in varied contexts (Betzel et al., 2022), and may therefore facilitate insights into the mechanisms governing inter-areal connectome communication.

Links to brain function

The network metrics and constructs we introduced so far are all derived from the structural connectivity matrix. All of them deliver estimates of (dis)similarity or (dis)affiliation for pairs of nodes in the data, regardless of whether the node pair shares a direct structural connection. This way, the common thread among topological specialization, modularity and communication measures is that they augment the structural connectivity matrix—which is typically sparse, only containing information on direct anatomical connections—into denser matrices of putative functional associations. A number of studies have proposed to use these constructs for

predicting features of brain dynamics (Bullmore and Sporns, 2009; Suá et al., 2020), for example the brain's functional connectivity. Here, the ability of the surveyed network measures to estimate functional interactions between structurally unconnected nodes is critical, as it is well established that structurally unconnected neural elements can show robust patterns of functional connectivity (van den Heuvel et al., 2009; O'Reilly et al., 2013).

It is important to note that there is no single representation of functional connectivity, as FC is modality and acquisition-dependent. Among the simplest and most widely applied is the covariance matrix, which, in fMRI studies, is commonly computed as the Pearson correlation among regional time courses. In many cases, raw correlations are processed to remove effects of unwanted influences or biases in data acquisition, e.g. the effects of head motion and global brain-wide signal components, to yield residuals or partial correlations. Alternative methods for computing pairwise relations among regional time courses such as full partial correlations and mutual information have been proposed (Craddock et al., 2013). While there is much promise in these alternatives, they are not yet widely applied and will be left aside, in favor of considering FC as a Pearson correlation of resting-state fMRI time courses.

The most common approach to evaluate structure–function coupling is to correlate the upper-triangular entries of the functional connectivity matrix to those of matrices derived from network measures (**Fig. 5**). Through this simple analysis, multiple reports have shown that several of the metrics surveyed in this article can explain significant amounts of variance in functional connectivity (Seguin et al., 2020; Goñi et al., 2014; Zamani Esfahlani et al., 2022). Some studies have used multivariate statistical models to investigate how these network metrics, in addition to spatial and genetic factors, can be combined to build multifaceted prediction tools of brain function (Betzel et al., 2019; Liu et al., 2022; Vázquez-Rodríguez et al., 2019). More recently, researchers have started to investigate structure–function relations at the level of individual cortical regions (Baum et al., 2020). This is achieved by separately correlating single rows (or columns) of the functional connectivity and network measure matrices, a procedure that results in a cortical map showing the extent to which the functional profile of each region is predicted by network measures computed on structural connectivity (Vázquez-Rodríguez et al., 2019; Baum et al., 2020). The principal finding stemming from these studies is that the function of sensory, unimodal regions appears more tethered to structural underpinnings than that of higher-order, multimodal cortical are.

Importantly, beyond purely predictive tools, these network metrics also provide an interpretable framework to investigate the relationship between brain structure and function, which can be used to generate and evaluate hypotheses about how anatomical connectivity is related to brain dynamics. Topological specialization measures, for example, posit that functional co-activation is determined by shared profiles of input and output projections, such that the degree of overlap in the connectional fingerprint of two nodes predicts their involvement in similar functional roles (Hilgetag et al., 2002). Alternatively, modularity metrics postulate that functional connectivity and its modular organization are related to the propensity of nodes to cluster into tight-knit structural components (Puxeddu et al., 2022). Communication measures offer yet another hypothesis, in which node pairs linked by efficient structural paths should be more prone to synchronous activity (stronger functional connectivity) in comparison to node pairs separated by long sequences of intermediate edges (Goñi et al., 2014).

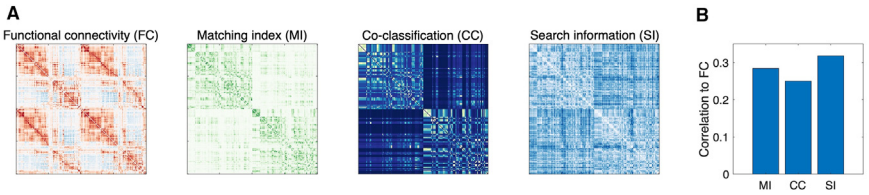

Fig. 5 (A) Functional connectivity matrix alongside examples of matrices derived from the application of network metrics to structural connectivity, including topological specialization (matching index), modularity (co-classification) and communication (search information) measures. (B) Correlation between functional connectivity and network measures. Bars show the absolute value of the Spearman rank correlation coefficient between the intra-hemispheric upper-triangular entries of the functional connectivity and network measure matrices.

Conclusion

Together, the three classes of measures considered in this article can be understood as providing gradually higher-level characterizations of the relationship between structure and function, starting from local connectional fingerprints, to mesoscopic network organization into segregated clusters, to global integration of information via network communication. As researchers continue to explore these network measures in connectivity datasets spanning a range of species, spatiotemporal scales, and clinical contexts, further progress in linking brain structure and function is expected to shed light on how the architecture of brain networks contributes to the rich functional dynamics observed in nervous systems.

References

Ashourvan, A., Telesford, Q.K., Verstynen, T., Vettel, J.M., Bassett, D.S., May 2019. Multi-scale detection of hierarchical community architecture in structural and functional brain networks. PLoS One 14 (5), e0215520. https://doi.org/10.1371/journal.pone.0215520.

Avena-Koenigsberger, A., et al., Oct. 2014. Using Pareto optimality to explore the topology and dynamics of the human connectome. Philos. Trans. R. Soc. B Biol. Sci. 369 (1653), 20130530. https://doi.org/10.1098/rstb.2013.0530.

Avena-Koenigsberger, A., et al., Jan. 2017. Path ensembles and a tradeoff between communication efficiency and resilience in the human connectome. Brain Struct. Funct. 222 (1), 603—618. https://doi.org/10.1007/s00429-016-1238-5.

Avena-Koenigsberger, A., Misic, B., Sporns, O., Jan. 2018. Communication dynamics in complex brain networks. Nat. Rev. Neurosci. 19 (1). https://doi.org/10.1038/nrn.2017.149.

Avena-Koenigsberger, A., Yan, X., Kolchinsky, A., van den Heuvel, M.P., Hagmann, P., Sporns, O., Mar. 2019. A spectrum of routing strategies for brain networks. PLoS Comput. Biol. 15 (3), e1006833. https://doi.org/10.1371/journal.pcbi.1006833.

Bassett, D.S., Sporns, O., Mar. 2017. Network neuroscience. Nat. Neurosci. 20 (3). https://doi.org/10.1038/nn.4502.

Bassett, D.S., Wymbs, N.F., Porter, M.A., Mucha, P.J., Carlson, J.M., Grafton, S.T., May 2011. Dynamic reconfiguration of human brain networks during learning. Proc. Natl. Acad. Sci. U. S. A. 108 (18), 7641—7646. https://doi.org/10.1073/pnas.1018985108.

Bassett, D.S., Porter, M.A., Wymbs, N.F., Grafton, S.T., Carlson, J.M., Mucha, P.J., Mar. 2013. Robust detection of dynamic community structure in networks. Chaos Interdiscip. J. Nonlinear Sci. 23 (1), 013142. https://doi.org/10.1063/1.4790830.

Baum, G.L., et al., Jan. 2020. Development of structure—function coupling in human brain networks during youth. Proc. Natl. Acad. Sci. U. S. A. 117 (1), 771—778. https://doi.org/10.1073/pnas.1912034117.

Bazzi, M., Porter, M.A., Williams, S., McDonald, M., Fenn, D.J., Howison, S.D., Jan. 2016. Community detection in temporal multilayer networks, with an application to correlation networks. Multiscale Model. Simul. 14 (1), 1—41. https://doi.org/10.1137/15M1009615.

Betzel, R.F., Bassett, D.S., Oct. 2017. Multi-scale brain networks. Neuroimage 160, 73—83. https://doi.org/10.1016/j.neuroimage.2016.11.006.

Betzel, R.F., Bassett, D.S., May 2018. Specificity and robustness of long-distance connections in weighted, interareal connectomes. Proc. Natl. Acad. Sci. U. S. A. 115 (21), E4880—E4889. https://doi.org/10.1073/pnas.1720186115.

Betzel, R.F., Byrge, L., He, Y., Goñi, J., Zuo, X.-N., Sporns, O., Nov. 2014. Changes in structural and functional connectivity among resting-state networks across the human lifespan. Neuroimage 102, 345—357. https://doi.org/10.1016/j.neuroimage.2014.07.067.

Betzel, R.F., et al., Jan. 2016. Generative models of the human connectome. Neuroimage 124, 1054—1064. https://doi.org/10.1016/j.neuroimage.2015.09.041.

Betzel, R.F., Medaglia, J.D., Kahn, A.E., Soffer, J., Schonhaut, D.R., Bassett, D.S., Nov. 2019. Structural, geometric and genetic factors predict interregional brain connectivity patterns probed by electrocorticography. Nat. Biomed. Eng. 3 (11). https://doi.org/10.1038/s41551-019-0404-5.

Betzel, R.F., Faskowitz, J., Mišić, B., Sporns, O., Seguin, C., May 09, 2022. Multi-policy models of interregional communication in the human connectome. bioRxiv. https://doi.org/10.1101/2022.05.08.490752.

Betzel, R., Puxeddu, M.G., Seguin, C., Oct. 29, 2023. Hierarchical communities in the larval Drosophila connectome: links to cellular annotations and network topology. bioRxiv. https://doi.org/10.1101/2023.10.25.562730.

Blondel, V.D., Guillaume, J.-L., Lambiotte, R., Lefebvre, E., Oct. 2008. Fast unfolding of communities in large networks. J. Stat. Mech. Theor. Exp. 2008 (10), P10008. https://doi.org/10.1088/1742-5468/2008/10/P10008.

Bullmore, E., Sporns, O., Mar. 2009. Complex brain networks: graph theoretical analysis of structural and functional systems. Nat. Rev. Neurosci. 10 (3). https://doi.org/10.1038/nrn2575.

Cole, M.W., Bassett, D.S., Power, J.D., Braver, T.S., Petersen, S.E., Jul. 2014. Intrinsic and task-evoked network architectures of the human brain. Neuron 83 (1), 238—251. https://doi.org/10.1016/j.neuron.2014.05.014.

Craddock, R.C., et al., Jun. 2013. Imaging human connectomes at the macroscale. Nat. Methods 10 (6). https://doi.org/10.1038/nmeth.2482.

de Lange, S.C., et al., Sep. 2019. Shared vulnerability for connectome alterations across psychiatric and neurological brain disorders. Nat. Human Behav. 3 (9). https://doi.org/10.1038/s41562-019-0659-6.

Eickhoff, S.B., Yeo, B.T.T., Genon, S., Nov. 2018. Imaging-based parcellations of the human brain. Nat. Rev. Neurosci. 19 (11). https://doi.org/10.1038/s41583-018-0071-7.

Estrada, E., 2011. The Structure of Complex Networks: Theory and Applications. Oxford University Press. https://doi.org/10.1093/acprof:oso/9780199591756.001.0001.

Estrada, E., Hatano, N., Mar. 2008. Communicability in complex networks. Phys. Rev. E 77 (3), 036111. https://doi.org/10.1103/PhysRevE.77.036111.

Fodor, J.A., 1983. The Modularity of Mind. A Bradford Book, Cambridge, MA, USA.

Fornito, A., Zalesky, A., Bullmore, E., 2016. Fundamentals of Brain Network Analysis. Academic Press.

Fortunato, S., Feb. 2010. Community detection in graphs. Phys. Rep. 486 (3), 75—174. https://doi.org/10.1016/j.physrep.2009.11.002.

Fortunato, S., Barthélemy, M., Jan. 2007. Resolution limit in community detection. Proc. Natl. Acad. Sci. U. S. A. 104 (1), 36—41. https://doi.org/10.1073/pnas.0605965104.

Friston, K.J., Jan. 2011. Functional and effective connectivity: a review. Brain Connect. 1 (1), 13—36. https://doi.org/10.1089/brain.2011.0008.

Gallen, C.L., D'Esposito, M., Apr. 2019. Brain modularity: a biomarker of intervention-related plasticity. Trends Cognit. Sci. 23 (4), 293—304. https://doi.org/10.1016/j.tics.2019.01.014.

Goñi, J., Avena-Koenigsberger, A., de Mendizabal, N.V., van den Heuvel, M.P., Betzel, R.F., Sporns, O., Mar. 2013. Exploring the morphospace of communication efficiency in complex networks. PLoS One 8 (3), e58070. https://doi.org/10.1371/journal.pone.0058070.

Goñi, J., et al., Jan. 2014. Resting-brain functional connectivity predicted by analytic measures of network communication. Proc. Natl. Acad. Sci. U. S. A. 111 (2), 833—838. https://doi.org/10.1073/pnas.1315529111.

Gonzalez-Castillo, J., Bandettini, P.A., Oct. 2018. Task-based dynamic functional connectivity: recent findings and open questions. Neuroimage 180, 526—533. https://doi.org/10.1016/j.neuroimage.2017.08.006.

Good, B.H., de Montjoye, Y.-A., Clauset, A., Apr. 2010. Performance of modularity maximization in practical contexts. Phys. Rev. E 81 (4), 046106. https://doi.org/10.1103/PhysRevE.81.046106.

Hagmann, P., et al., Jul. 2008. Mapping the structural core of human cerebral cortex. PLoS Biol. 6 (7), e159. https://doi.org/10.1371/journal.pbio.0060159.

Hilgetag, C.C., Kötter, R., Stephan, K.E., Sporns, O., 2002. Computational methods for the analysis of brain connectivity. In: Ascoli, G.A. (Ed.), Computational Neuroanatomy: Principles and Methods. Humana Press, Totowa, NJ, pp. 295—335. https://doi.org/10.1007/978-1-59259-275-3_14.

Imms, P., et al., May 2021. Navigating the link between processing speed and network communication in the human brain. Brain Struct. Funct. 226 (4), 1281—1302. https://doi.org/10.1007/s00429-021-02241-8.

Jeub, L.G.S., Sporns, O., Fortunato, S., Feb. 2018. Multiresolution consensus clustering in networks. Sci. Rep. 8 (1). https://doi.org/10.1038/s41598-018-21352-7.

Lancichinetti, A., Fortunato, S., Mar. 2012. Consensus clustering in complex networks. Sci. Rep. 2 (1). https://doi.org/10.1038/srep00336.

Liu, Z.-Q., Vázquez-Rodríguez, B., Spreng, R.N., Bernhardt, B.C., Betzel, R.F., Misic, B., Jun. 2022. Time-resolved structure-function coupling in brain networks. Commun. Biol. 5 (1). https://doi.org/10.1038/s42003-022-03466-x.

Meunier, D., Lambiotte, R., Fornito, A., Ersche, K., Bullmore, E., 2009. Hierarchical modularity in human brain functional networks. Front. Neuroinf. 3. https://www.frontiersin.org/articles/10.3389/neuro.11.037.2009. (Accessed 6 July 2022).

Mišić, B., et al., Jun. 2015. Cooperative and competitive spreading dynamics on the human connectome. Neuron 86 (6), 1518—1529. https://doi.org/10.1016/j.neuron.2015.05.035.

Mišić, B., et al., Jul. 2018. Network-based asymmetry of the human auditory system. Cerebr. Cortex 28 (7), 2655–2664. https://doi.org/10.1093/cercor/bhy101.
Newman, M.E.J., Jan. 2003. The structure and function of complex networks. SIAM Rev. 45 (2), 167–256. https://doi.org/10.1137/S003614450342480.
Newman, M.E.J., Girvan, M., Feb. 2004. Finding and evaluating community structure in networks. Phys. Rev. E 69 (2), 026113. https://doi.org/10.1103/PhysRevE.69.026113.
Oldham, S., et al., Jun. 2022. Modeling spatial, developmental, physiological, and topological constraints on human brain connectivity. Sci. Adv. 8 (22), eabm6127. https://doi.org/10.1126/sciadv.abm6127.
O'Reilly, J.X., et al., Aug. 2013. Causal effect of disconnection lesions on interhemispheric functional connectivity in rhesus monkeys. Proc. Natl. Acad. Sci. U. S. A. 110 (34), 13982–13987. https://doi.org/10.1073/pnas.1305062110.
Park, H.-J., Friston, K., Nov. 2013. Structural and functional brain networks: from connections to cognition. Science 342 (6158), 1238411. https://doi.org/10.1126/science.1238411.
Passingham, R.E., Stephan, K.E., Kötter, R., Aug. 2002. The anatomical basis of functional localization in the cortex. Nat. Rev. Neurosci. 3 (8). https://doi.org/10.1038/nrn893.
Peixoto, T.P., Mar. 2014. Hierarchical block structures and high-resolution model selection in large networks. Phys. Rev. X 4 (1), 011047. https://doi.org/10.1103/PhysRevX.4.011047.
Puxeddu, M.G., Faskowitz, J., Betzel, R.F., Petti, M., Astolfi, L., Sporns, O., Sep. 2020. The modular organization of brain cortical connectivity across the human lifespan. Neuroimage 218, 116974. https://doi.org/10.1016/j.neuroimage.2020.116974.
Puxeddu, M.G., Petti, M., Astolfi, L., 2021a. Multi-layer analysis of multi-frequency brain networks as a new tool to study EEG topological organization. In: 2021 43rd Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC), pp. 924–927. https://doi.org/10.1109/EMBC46164.2021.9630173.
Puxeddu, M.G., Petti, M., Astolfi, L., 2021b. A comprehensive analysis of multilayer community detection algorithms for application to EEG-based brain networks. Front. Syst. Neurosci. 15. https://www.frontiersin.org/articles/10.3389/fnsys.2021.624183. (Accessed 1 March 2023).
Puxeddu, M.G., Faskowitz, J., Sporns, O., Astolfi, L., Betzel, R.F., Dec. 2022. Multi-modal and multi-subject modular organization of human brain networks. Neuroimage 264, 119673. https://doi.org/10.1016/j.neuroimage.2022.119673.
Puxeddu, M.G., et al., Feb. 2024. Relation of connectome topology to brain volume across 103 mammalian species. PLoS Biol. 22 (2), e3002489. https://doi.org/10.1371/journal.pbio.3002489.
Roberts, J.A., et al., Jan. 2016. The contribution of geometry to the human connectome. Neuroimage 124, 379–393. https://doi.org/10.1016/j.neuroimage.2015.09.009.
Rosenthal, G., et al., Jun. 2018. Mapping higher-order relations between brain structure and function with embedded vector representations of connectomes. Nat. Commun. 9 (1). https://doi.org/10.1038/s41467-018-04614-w.
Rosvall, M., Bergstrom, C.T., Jan. 2008. Maps of random walks on complex networks reveal community structure. Proc. Natl. Acad. Sci. U. S. A. 105 (4), 1118–1123. https://doi.org/10.1073/pnas.0706851105.
Rosvall, M., Grönlund, A., Minnhagen, P., Sneppen, K., Oct. 2005. Searchability of networks. Phys. Rev. E 72 (4), 046117. https://doi.org/10.1103/PhysRevE.72.046117.
Rubinov, M., Sporns, O., Sep. 2010. Complex network measures of brain connectivity: uses and interpretations. Neuroimage 52 (3), 1059–1069. https://doi.org/10.1016/j.neuroimage.2009.10.003.
Schröter, M., Paulsen, O., Bullmore, E.T., Mar. 2017. Micro-connectomics: probing the organization of neuronal networks at the cellular scale. Nat. Rev. Neurosci. 18 (3). https://doi.org/10.1038/nrn.2016.182.
Seguin, C., van den Heuvel, M.P., Zalesky, A., Jun. 2018. Navigation of brain networks. Proc. Natl. Acad. Sci. U. S. A. 115 (24), 6297–6302. https://doi.org/10.1073/pnas.1801351115.
Seguin, C., Razi, A., Zalesky, A., Sep. 2019. Inferring neural signalling directionality from undirected structural connectomes. Nat. Commun. 10 (1). https://doi.org/10.1038/s41467-019-12201-w.
Seguin, C., Tian, Y., Zalesky, A., Nov. 2020. Network communication models improve the behavioral and functional predictive utility of the human structural connectome. Netw. Neurosci. 4 (4), 980–1006. https://doi.org/10.1162/netn_a_00161.
Seguin, C., Mansour L, S., Sporns, O., Zalesky, A., Calamante, F., May 2022. Network communication models narrow the gap between the modular organization of structural and functional brain networks. Neuroimage 119323. https://doi.org/10.1016/j.neuroimage.2022.119323.
Seguin, C., Sporns, O., Zalesky, A., 2023a. Brain network communication: concepts, models and applications. Nat. Rev. Neurosci. 24 (9). https://doi.org/10.1038/s41583-023-00718-5.
Seguin, C., Jedynak, M., David, O., Mansour, S., Sporns, O., Zalesky, A., 2023b. Communication dynamics in the human connectome shape the cortex-wide propagation of direct electrical stimulation. Neuron. https://doi.org/10.1016/j.neuron.2023.01.027.
Sejnowski, T.J., Churchland, P.S., Movshon, J.A., Nov. 2014. Putting big data to good use in neuroscience. Nat. Neurosci. 17 (11). https://doi.org/10.1038/nn.3839.
Simon, H.A., 1962. The architecture of complexity. Proc. Am. Philos. Soc. 106 (6), 467–482.
Sporns, O., Apr. 2013. Network attributes for segregation and integration in the human brain. Curr. Opin. Neurobiol. 23 (2), 162–171. https://doi.org/10.1016/j.conb.2012.11.015.
Sporns, O., Betzel, R.F., 2016. Modular brain networks. Annu. Rev. Psychol. 67 (1), 613–640. https://doi.org/10.1146/annurev-psych-122414-033634.
Sporns, O., Tononi, G., Kötter, R., Sep. 2005. The human connectome: a structural description of the human brain. PLoS Comput. Biol. 1 (4), e42. https://doi.org/10.1371/journal.pcbi.0010042.
Suárez, L.E., Markello, R.D., Betzel, R.F., Misic, B., Apr. 2020. Linking structure and function in macroscale brain networks. Trends Cognit. Sci. 24 (4), 302–315. https://doi.org/10.1016/j.tics.2020.01.008.
Towlson, E.K., Vértes, P.E., Ahnert, S.E., Schafer, W.R., Bullmore, E.T., Apr. 2013. The rich club of the *C. elegans* neuronal connectome. J. Neurosci. 33 (15), 6380–6387. https://doi.org/10.1523/JNEUROSCI.3784-12.2013.
Vaiana, M., Muldoon, S.F., Oct. 2020. Multilayer brain networks. J. Nonlinear Sci. 30 (5), 2147–2169. https://doi.org/10.1007/s00332-017-9436-8.
van den Heuvel, M.P., Mandl, R.C.W., Kahn, R.S., Hulshoff Pol, H.E., 2009. Functionally linked resting-state networks reflect the underlying structural connectivity architecture of the human brain. Hum. Brain Mapp. 30 (10), 3127–3141. https://doi.org/10.1002/hbm.20737.
Van Essen, D.C., Smith, S.M., Barch, D.M., Behrens, T.E.J., Yacoub, E., Ugurbil, K., Oct. 2013. The Wu-Minn human connectome Project: an overview. Neuroimage 80, 62–79. https://doi.org/10.1016/j.neuroimage.2013.05.041.
Vázquez-Rodríguez, B., et al., Oct. 2019. Gradients of structure–function tethering across neocortex. Proc. Natl. Acad. Sci. U. S. A. 116 (42), 21219–21227. https://doi.org/10.1073/pnas.1903403116.
Winding, M., et al., Mar. 2023. The connectome of an insect brain. Science 379 (6636), eadd9330. https://doi.org/10.1126/science.add9330.
Zamani Esfahlani, F., et al., Dec. 2021. Modularity maximization as a flexible and generic framework for brain network exploratory analysis. Neuroimage 244, 118607. https://doi.org/10.1016/j.neuroimage.2021.118607.
Zamani Esfahlani, F., Faskowitz, J., Slack, J., Mišić, B., Betzel, R.F., Apr. 2022. Local structure-function relationships in human brain networks across the lifespan. Nat. Commun. 13 (1). https://doi.org/10.1038/s41467-022-29770-y.
Zhang, F., et al., Apr. 2022. Quantitative mapping of the brain's structural connectivity using diffusion MRI tractography: a review. Neuroimage 249, 118870. https://doi.org/10.1016/j.neuroimage.2021.118870.