Small worlds inside big brains

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Neuroscientists face the challenge of explaining how functional brain states emerge from the interactions of dozens, perhaps hundreds, of brain regions, each containing millions of neurons. Much evidence supports the view that highly evolved nervous systems are capable of rapid, real-time integration of information across segregated sensory channels and brain regions. This integration happens without the need for a central controller or executive: It is the functional outcome of dynamic interactions within and between the complex structural networks of the brain. In this issue of PNAS, the study by Bassett *et al.* (1) reveals the existence of large-scale functional networks in magnetoencephalographic (MEG) recordings with attributes that are preserved across multiple frequency bands and that flexibly adapt to task demands. These networks exhibit "small-world" structure, i.e., high levels of clustering and short path lengths. The authors' analysis reveals that the small-world topology of brain functional networks is largely preserved across multiple frequency bands and behavioral tasks.

The structure of networks has been analyzed extensively in the social sciences (2) and in physics and information technology (3). In the life sciences, network approaches already have provided quantitative insights into cellular metabolism and transcriptional regulation (4). In neuroscience, researchers have examined the structure of axonal networks connecting individual neurons (5, 6) and whole-brain networks of interregional pathways (7–9). Across these systems and disciplines, network analysis is founded on the graph-theoretic characterization of a network in terms of nodes and connections (vertices and edges). A landmark study by Watts and Strogatz (10) revealed that a disparate set of natural and artificial networks shared small-world attributes. The canonical small-world network is one in which the majority of edges are recruited to form small, densely connected clusters, whereas the remainder are involved in maintaining connections between these clusters. The conjunction of local clustering and global interaction provides a structural substrate for the coexistence of functional segregation and integration in the brain (11), a hallmark of brain network complexity (12).

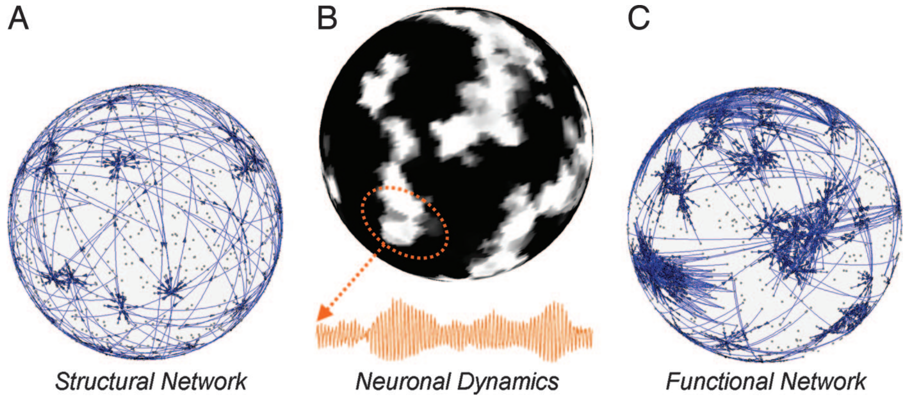

Fig. 1. Relationship of structural to functional connectivity networks. We built a demonstration model consisting of a set of 1,600 modeled neural mean field units arranged on a sphere and engaging in noise-driven spontaneous activity. (*A*) The anatomical connection pattern, shown only for a few randomly selected neural units, consists of a mix of mostly local (clustered) connections and a few connections made over longer distances. (*B*) A snapshot and an EEG-like recording trace of the dynamical neuronal activity pattern. Neuronal dynamics is characterized by complex spatial and temporal structure across multiple scales [supporting information (SI) Movie 1]. (*C*) A functional connectivity network obtained from a thresholded correlation matrix calculated from the dynamics shown in *B*. In this example, both structural and functional connectivity patterns exhibit small-world attributes.

Bassett *et al.* (1) provide strong new evidence for the existence in the human brain of functional networks exhibiting small-world attributes. Their approach is based on a novel application of wavelet analysis to MEG recordings obtained from human subjects who were either at rest or engaged in a finger-tapping task. Patterns of functional connectivity across a large number of recording sites were obtained for each of six distinct temporal scales ranging over all classical EEG frequency bands, from low δ (1.1–2.2 Hz) to γ (37.5–75 Hz). These correlations between signals in wavelet space express a statistical association between recording sites, a signature of dynamical interactions between brain regions. The authors then transform the continuous symmetric matrix of wavelet correlations obtained for each frequency band to a binary symmetric matrix by applying a threshold. The symmetric binary matrix is interpreted as an undirected graph and is analyzed by using network-analytic tools that measure clustering, path length, centrality, and synchronizability. Bassett *et al.* (1) find that the global topology of the functional networks at different frequency bands is both highly clustered and highly integrated, forming a small world, in accordance with several earlier reports of small-world brain functional networks obtained from neurophysiological and neuroimaging data sets (13–15).

Previous work on the large-scale structure of brain networks in several mammalian species has demonstrated the existence of small-world attributes within the anatomical substrate (11, 16, 17). Patterns of interregional connections were shown to partition the brain into distinct clusters that resembled known or postulated functional subdivisions (16). The work by Bassett *et al.* (1) now raises the question of how functional networks as revealed by MEG wavelet analysis relate to the underlying structural networks of the human brain (Fig. 1). Addressing this central structure–function question will require a comprehensive structural description of the human brain, the human connectome (18).

Perhaps the most remarkable finding of the study by Bassett *et al.* (1) is the relative invariance of the network topology across all physiologically relevant frequency bands, forming a self-similar or fractal architecture. What might explain this experimental result? It has

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been argued (9, 11) that small-world attributes reflect the need of the network to satisfy simultaneously the opposing demands of local and global processing and that they may reflect an organization that tends to minimize the number of processing steps (19). Because of significant variations in axonal conduction delays across brain regions and cell types, the spatial separation of network nodes induces temporal constraints on information transmission. Given the spatial complexity of neural dynamics, it seems likely that functionally relevant communication would have to occur across multiple frequency bands. If the small-world functional architecture revealed by Bassett *et al.* (1) indeed promotes efficient interregional communication, then it should be found across multiple temporal scales.

A second major finding of Bassett *et al.* (1) concerns the task dependence of the functional networks they observe. Comparing MEG data from subjects at rest against data from subjects engaged in a simple motor task, they find that, although some individual interactions do exhibit significant changes, the global topological properties are once again largely invariant. Thus, it appears that brain networks preserve global topological characteristics (continually maintaining the balance of efficient local and global processing) while flexibly adapting the specifics of the topology to satisfy changing task demands. Changes in functional connectivity patterns across tasks have been widely documented (e.g., ref. 20), but the degree to which these networks combine topological stability with adaptive reconfiguration had not been investigated. Interestingly, it appears that higher-frequency bands (β and γ) exhibit more extensive changes in connection patterns across tasks, specifically in the form of new long-range functional relationships between sensory and motor regions during the execution of a motor task.

The idea that perception and cognition depend critically on patterns of synchronization and desynchronization, e.g., the dynamic binding of neural assemblies (21) or neuronal groups (22), has received support from a range of electrophysiological studies (e.g., ref. 23). The work by Bassett *et al.* (1) is consistent with the observations of numerous other authors in claiming that that the dynamic coupling and uncoupling of distant neural sites reflect changes in sensory inputs, task demands, or attention. The fact that these synchronization patterns occur at multiple frequencies might mean that brain functional networks contain multiple "frequency channels" along which information is transmitted. The utility of this interpretation depends crucially on whether these channels are truly separable entities, and this question remains open. One way of beginning to answer it is to investigate what happens when the global topology of human brain functional networks changes across all frequency bands or within a specific range of frequencies. Empirical evidence suggests that such changes in global network topology occur between sleep and waking (24), and at least some forms of mental disease are associated with disruptions in integrative neural communication (25).

Human cognition is the result of dynamical processes unfolding within the networks of the human brain. Network dynamics offers a fresh perspective on brain function by emphasizing the role of network topology (1) on systemwide coordination (26) and the dependence of local function on neural context (27) and degeneracy (28). The study by Bassett *et al.* (1) brings us an important step closer to understanding how cognitive function depends on the structure of the human brain as an integrated network.

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