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Wave-like properties of functional dynamics across the cortical sheet

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The human cortex is organized in a hierarchical manner. Pines et al.[1] show that wave-like hemodynamic activity flows along this architecture, from unimodal through association cortices, providing fertile ground for researchers seeking to map links across behavioral and cognitive states.

The cerebral cortex is composed of a dense tapestry of areal parcels that are woven into large-scale function networks and corresponding information-processing hierarchies. Over the past century, we have made great strides in our understanding of how this complex neurobiological architecture underlies aspects of the human experience, ranging from discrete facets of cognition and behavior to health and disease. Initially, work in this area was restricted to invasive techniques including histology, anatomical tract tracing, electrophysiology, and lesion methods that largely treat the brain as a set of independent and functionally specialized regions or circuits. At the turn of the century, the development of new imaging technologies enabled the *in vivo* localization of behavior-related regions and the observation of coactivation patterns that link functionally coupled yet spatially distributed processes. However, despite a recent shift from the study of the segregation of brain functions within isolated regions toward analytic frameworks that target functional integration, research in this domain often relies on static analytic approaches that assume stable patterns of connectivity across time (Figure 1). Human cognition is a time-varying process, and there is growing evidence that brain functions exhibit complex dynamic properties across multiple timescales. In a report in this issue of *Neuron*, Pines et al.[1] directly consider this fundamental aspect of brain organization, characterizing the spatiotemporal propagation of hemodynamic activity across the cortical sheet.

Patterns of wave-like activity have been a focused topic of study in non-human animal models, where neural and vascular events have been observed locally[2] and been shown to spread across cortex, tracking both physiological changes and expressed behavior.[3] Similar time-varying profiles have been reported in humans, for instance, intracranial electroencephalography recordings of traveling brain rhythms or "spectral fingerprints" that correlate with memory task performance.[4] However, outside select examples within visual cortices,[5] the robust characterization of widespread wave-like propagations using functional MRI (fMRI) has proven difficult. While classic systems neuroscience approaches have sought to parcel the cerebral cortex into "discrete" functional units and network communities, there is clear evidence for continuous gradients of brain function, gene expression, receptor densities, and cellular distributions across cortex. This organization is theorized to support the flow of information from unimodal cortices, including somato/sensory, motor, and visual regions, through the transmodal association territories that support parallel cognitive processing and complex cognitive functions.[6] In this regard, a major technical bottleneck has been the lack of accessible and data-driven methods to measure the direction, magnitude, and source of cortical signals, impeding our ability to map and model the order of functional events across the cortical sheet.

Theories regarding a hierarchy of information processing within the cortex are well supported by anatomical and physiological data, but direct *in vivo* evidence in humans has been limited. As reported in this issue of *Neuron*, Pines et al.[1] take an important step in this direction, creatively borrowing methodology from computer vision research, optical flow, to capture the direction of propagation of hemodynamic activity. Optical flow has been used for decades in artificial intelligence research to track the motion of objects in a sequence of images, based on apparent motion of pixels between two consecutive frames. Adapting this method to human cortical fMRI data, the authors demonstrate that hemodynamic activity preferentially moves in a wave-like manner along a hierarchy from unimodal regions through association cortices.

As is often the case, while Pines et al.[1] demonstrate the presence of functional propagations that systematically ascend and descend a cortical hierarchy, revealing the influence of task demands and development across select points in the lifespan, this work raises intriguing questions that warrant future study. The macro-scale correlation structure of fMRI changes markedly from childhood through adolescence and into adulthood.[7] The analyses reported in Pines et al.[1] suggest that "top down," descending hierarchical propagations become more prevalent with greater demands for cognitive control as well as with development in youth. However, the physiological, cellular, and molecular mechanisms providing for the emergence of these properties and the nature of their refinement across the lifespan remain to be established. Moreover, open questions remain regarding the associated relationships that may

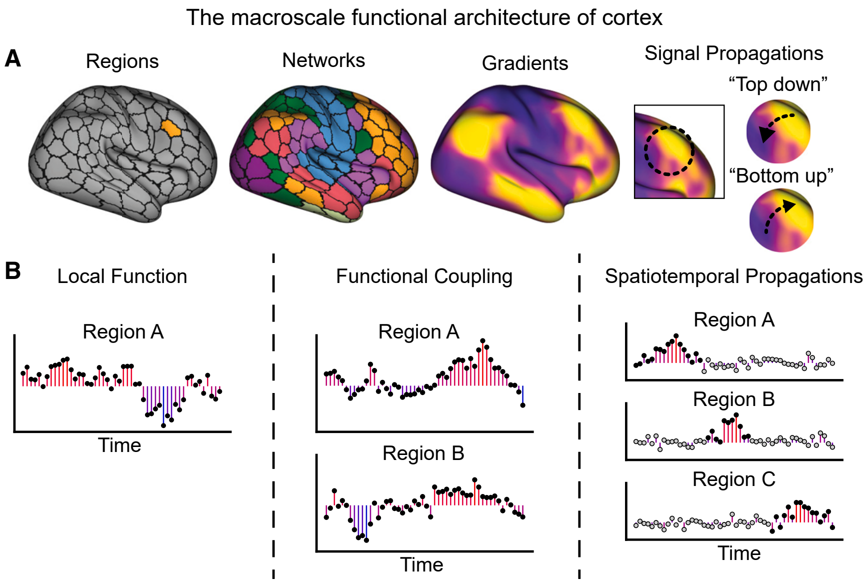

Figure 1. Alternate approaches for the analysis of *in vivo* imaging data reveal complementary aspects of cortical organization

(A) Surface maps display analytic approaches that range from modular to mobile views of information processing in the human cerebral cortex, reflecting a selection of common analysis methods. Regional, or local, methods treat adjacent vertices/voxels sharing similar temporal activation patterns as the unit of interest. Network-based approaches consider "functionally connected" brain regions, for instance, through the examination of correlated fluctuations in the fMRI blood oxygenation level dependent (BOLD) signal. Gradient techniques capture spatial variation across the cortex continuously along overlapping organizing axes, offering a complementary approach to standard network parcellations. Dynamic approaches, such as those used by Pines et al.,[1] consider spatial and temporal patterns of signal propagations across the cortical sheet. Here, "top down" and "bottom up" refer to the sequencing of time-varying signal fluctuations across the association and unimodal territories theorized to anchor discrete ends of the cortical information-processing hierarchy.

(B) Stick and ball plots display simulated signal fluctuations within a given region, between functionally coupled or correlated network parcels, and as signals propagate across both regions and time. Here, region refers to the selected spatial unit of measurement (e.g., voxels, vertices, parcels, etc.).

influence the wave-like propagation of signals across cortex and population-level behavioral variability through health and disease.

The discoveries reported by Pines et al.[1] are inherently influenced by a host of theoretical assumptions. The geometric properties of the cortical surface, from folding patterns through laminar properties and white matter topology, reflect a powerful physical constraint on brain functions and associated network dynamics.[8] By restricting analyses to an inflated spherical abstraction of the cortical surface, Pines and colleagues may have obscured biologically relevant information crucial for characterizing the spatiotemporal patterns that best capture activity propagations across functional systems. Perhaps most critically, the roles of non-cortical structures are almost entirely neglected in human brain imaging.[9] Although prior models of large-scale neuronal dynamics posit a role for the thalamus in driving waves of propagating activity across cortex,[10] many investigations examining functional dynamics continue to restrict their analyses to the cortical sheet. As such, the potential influence of subcortical and cerebellar connections on the initiation, development, and maintenance of the observed functional propagations remain to be determined. Moreover, the existence of a strict and universal flow-chart-like hierarchy of cortical functions across diverse aspects of cognition and behavior should not be assumed. The organization of information propagation within the brain, especially when integrating the contribution of non-cortical regions, likely involves a combination of hierarchical and heterarchical principles, with the latter potentially providing additional nuance on the complex, flexible, and distributed properties of brain organization.

Across the brain sciences, there is perhaps no fundamentally more important topic of study than the characterization of the spatiotemporal properties of information processing. Making use of advances in functional neuroimaging and computer vision, Pines et al.[1] establish the presence of cortical propagations that systematically ascend and descend along the cortical hierarchy. While open questions remain, these data provide a framework for the study of hierarchical cortical organization with clear relevance for models of neurodevelopment and human behavior.

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DECLARATION OF INTERESTS

The authors declare no competing interests.

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