



Humanity's desire for self-understanding and curiosity about the brain has fueled research into its functions and connections for centuries. Early neuroscientists, such as Niels Stensen in the 1600s, recognized the brain's immense complexity and stressed the importance of studying its anatomy to draw connections between brain structure and cognitive function. However, it was only after the development of methods to stain and trace neural connections in the early 20th century that the groundwork was laid for more detailed anatomical descriptions of human brain connectivity.

When these techniques were coupled with noninvasive imaging technologies in the early 2000s the goal of gaining a comprehensive connectome map for the human brain began to take shape. This map is called the "connectome." It is used to decipher the electrical signals that generate thoughts and behaviors by identifying unique patterns in the circuitry of nerve fibers in the brain's cerebral cortex. This concept has become widely accepted within the field of neuroscience, bridging various attempts to map macroscopic neural connections to microscopic neural activity.^{1,3}

In the human brain, neural networks control cognitive functions including perception, learning, and decision making. These networks consist of neurons (specialized nerve cells) linked by synapses

to create complex webs that enable the brain to send signals and process information. Human neural networks are highly adaptable due to a property known as neuroplasticity, which allows the brain to restructure itself by forming new connections between neurons throughout an individual's life. Educational experiences and external environmental stimuli can either reinforce or diminish one's neural pathways, helping the brain adapt and optimize its performance according to how the individual engages with the environment. These networks generate coordinated patterns of electrical activity, known as brain waves, through the synchronized firing of neurons. Brain waves vary in frequency and types, such as delta (1.5 – 4 Hz), theta (4 – 8 Hz), alpha (8 – 12 Hz), beta (13 – 30 Hz), and gamma (30 – 80 Hz) waves.² Since the connectivity and organization of neural networks are directly responsible for the frequency at which brain waves are generated, it is possible to associate the cognitive states prevalent at these frequencies with certain neural structures. For example, when a person experiences calm and relaxed mental states, alpha waves are prevalent, but when the brain is engaged in higher levels of cognitive function focusing or remembering, gamma waves are observed.

Decoding the Connectome

The nervous system invents itself as it

grows, just as the rest of the body does, in predictable yet unexplainable ways. How this massive system of interconnected neurons produces a collection of given behaviors in a flexible and self-organized way remains a mystery. Neural networks show unexpected, collective wave patterns that change over space and time as a result of interactions between the networks' simpler components. Here, the term "unexpected" indicates the mathematical limitations in predicting these emergent patterns from the equations that govern the dynamics of the individual components within these systems. In an attempt to understand these patterns, researchers developed a mathematical framework based on the Fourier basis to study the human connectome. The Fourier basis can be thought of as a collection of simple, component patterns that can be blended to create more complex patterns. These fundamental patterns consist of sine and cosine waves at various frequencies, and they can be used to decode the complicated signals that they help form. The use of the Fourier basis to break down brain waves into their frequency specific constituents in order to reveal the organization of neural networks, has been termed "connectome harmonics."¹

When the Fourier transform is applied to a function, it allows that function to be expressed in terms of its frequency components. This transformation is followed

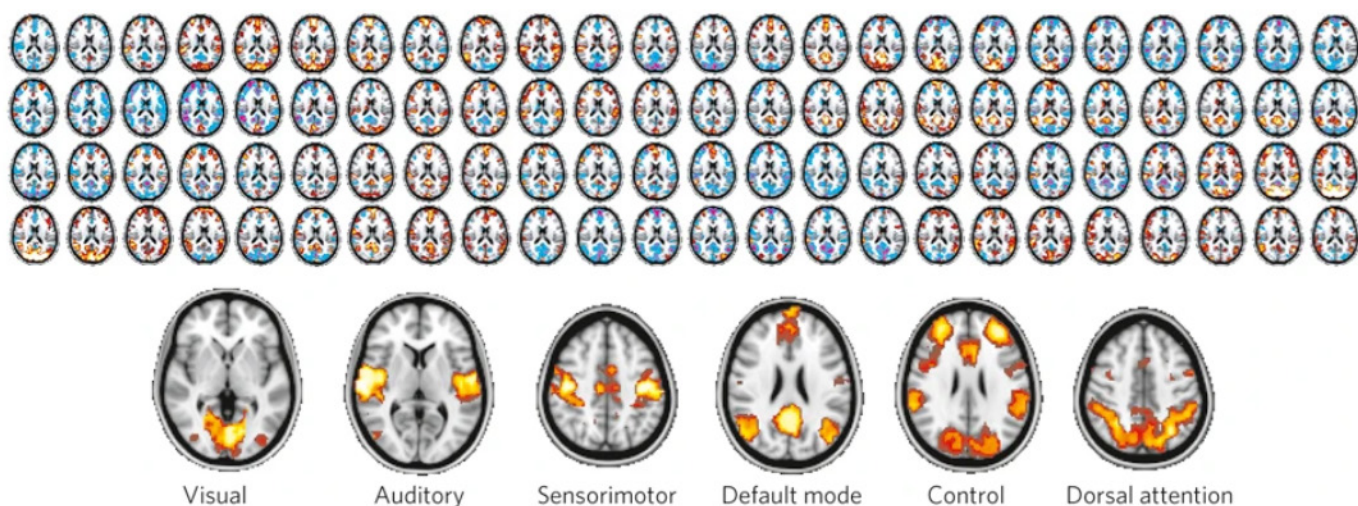


Figure 1: Spontaneous human-brain spatiotemporal patterns identified from neural networks.

by the Laplace operator, which connects the behavior of the original function to its frequency components, measuring how the function's output values shift over space. In the context of the human brain, the Fourier transform and Laplace operator work to break down the complex patterns of brain waves into simpler elements, a process similar to breaking down a piece of music into its individual notes. A more deconstructed view of the connectome harmonics at play helps model how neural activity is organized and distributed across different spatial regions of the brain.

Neural Field Modeling

In their exploration, scientists found that connectome harmonics could accurately predict the brain's resting state networks (RSNs). RSNs reflect how the brain operates when it is not actively focused on a task. These networks are important for self-related thoughts, daydreaming, and remembering personal experiences. By mapping the brain's resting-state waves to the neural connections that create them, researchers found that

these connections match the spatial layout of resting state networks.¹ This suggests that the brain's anatomical structure influences the formation of behavior dependent neural networks.

Recent studies have also investigated the biological mechanisms behind connectome harmonics. Using a neural field model based on the Wilson-Cowan equations, researchers were able to determine how the balance between excitatory neuron activity (neurons that activate other neurons) and inhibitory neuron activity (neurons that suppress the actions of other neurons) can predict the frequency of resulting brain waves.¹ These equations outline the dynamic behavior of excitatory and inhibitory neurons over time, taking into account variables affecting the strength of interactions and activation barriers. Interestingly, the model mirrored the neurophysiological changes observed when consciousness is lost and regained, indicating a potential link between connectome harmonics and awareness.

While there is still a lot to uncover about the connectome, advances in computational

models are expediting the process. This research carries implications for better medical care, tailored treatment, neurological research, and technology. A key application involves the improved identification of biomarkers related to certain neurological and psychiatric conditions by examining abnormal connectivity patterns associated with disorders such as Alzheimer's disease, schizophrenia, and autism. This personalized approach could lead to earlier diagnosis and targeted treatment plans depending on each person's distinct connectome. Additionally, mapping the connectome enhances neuroscience research by providing an explanation for the neural mechanisms underlying more complicated cognitive functions. By integrating connectome data with computational simulations, researchers can model brain activity across a massive range of scenarios, demonstrating how differences in connectivity impact cognitive function.⁴ The connectome harmonics approach has deepened our theoretical understanding of the brain and offers exciting possibilities for new neurotechnology and therapeutics.

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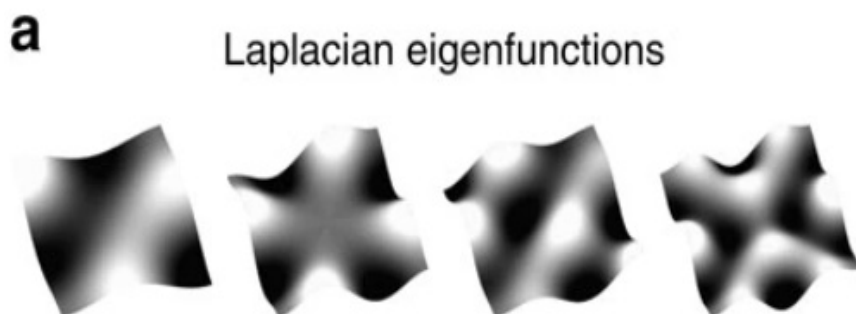
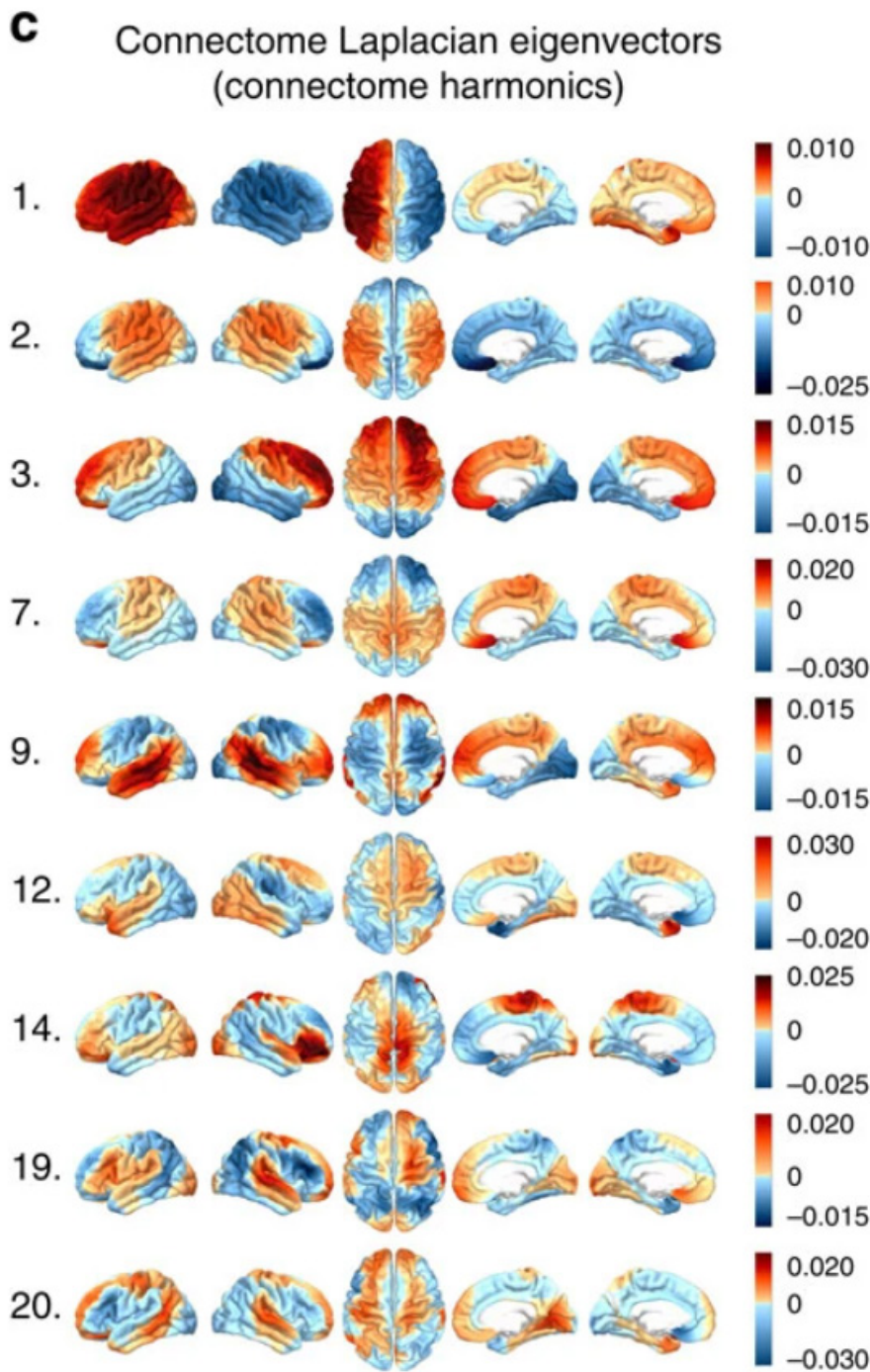


Figure 2: Patterns in Laplace eigenfunctions.



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Figure 3: Examples of the 20 lowest frequency connectome harmonics. Left: wave number. Right: spatial patterns of synchronous oscillations estimated by the eigenvectors of the connectome Laplacian.

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