Metastable brain waves

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Traveling patterns of neuronal activity – *brain waves* – have been observed across a breadth of neuronal recordings, states of awareness, and species, but their emergence in the human brain lacks a firm understanding. Here, we analyze the complex nonlinear dynamics that emerge from modeling large-scale spontaneous neural activity on a whole-brain network derived from human tractography. We find a rich array of three-dimensional wave patterns, including traveling waves, spiral waves, sources, and sinks. These patterns are metastable, such that system visits multiple spatiotemporal wave patterns in sequence. Transitions between metastable states correspond to reconfigurations of an underlying phase flow, characterized by complex nonlinear instabilities. These metastable dynamics accord with empirical data from multiple imaging modalities, including electrical waves in cortical tissue, the presence of sequential spatiotemporal patterns in resting state MEG data, and large-scale waves in human electrocorticography. By moving the study of functional networks from a static to an inherently dynamic frame, our work unifies apparently diverse phenomena across functional neuroimaging modalities and makes specific predictions for further experimentation.

Introduction

A central aim in neuroscience is to understand how complex brain dynamics emerge from brain structure. Thus far, attention has been largely directed toward understanding long-time averaged measures of brain activity such as correlations and power spectra – that is, static summaries of the underlying dynamics. While the importance of dynamics has long been known in electrophysiology experiments, human neuroimaging has been slow to embrace this additional information. But this is rapidly changing, due to advances in imaging technology, such as fast functional magnetic resonance imaging (fMRI), and accompanying analysis methods. Time-varying analyses have recently revealed richer dynamics than previously appreciated: brain activity exhibits switching between metastable states [1], stochastic jumps between multistable states [2], transiently-expressed functional networks [3], and large-scale waves [4]. Yet with the exception of the pathological strongly-nonlinear dynamics in epileptic seizures [5, 6], theory and modeling have fallen behind the body of empirical results. Various empirical debates have appeared in this vacuum, such as the existence and nature of non-stationary (dynamic) functional connectivity [3, 7, 8]. Models with physiologically-meaningful parameters have much to contribute here, through their ability to specify candidate causes of complex patterns in empirical data [9].

Waves are a canonical example of dynamical phenomena in biological systems [10]. A diversity of neuronal wave patterns have been observed on mesoscopic [11-15] and whole-brain scales [4, 16-18]. These waves are not merely epiphenomena: For example, they have been reproducibly observed in visual processing [19] – carrying the primary stimulus-evoked response in visual cortex [11, 20]; reflecting information flow in response to dynamic natural scenes [21]; encoding directions of moving stimuli [22]; encoding stimulus positions and orientations [23]; underlying bistable perceptual rivalry [24]; reinforcing recent visual experience [25]; and also occur pathologically during visual hallucinations [26]. Waves have been observed in primary motor cortex, where they mediate information transfer during movement preparation [12], can be induced by optogenetic stimulation [27], and reveal the nature of the excitability of neural tissue [28]. They have also been implicated in sensorimotor processing of saccades [29], and observed during sleep with a possible role in memory consolidation [4]. Waves have been reported in diverse neuroimaging modalities including voltage-sensitive dyes [11, 20, 25, 30], local field potentials [12, 15, 21, 22, 29], electrocortigraphy [4], electroencephalography (EEG) [16, 17], magnetoencephalography (MEG) [31], fMRI [24]; and inferred from close analysis of psychophysical phenomena [32].

The widespread occurrence of cortical waves opens many questions [18]: What is their basis? Is each instance a uniquely determined phenomenon or do there exist deeper unifying principles? How do particular waves appear and disperse, and how do they relate to stationary patterns of activity? Computational models are required to tackle these questions.

The linear treatment of cortical waves under idealized assumptions regarding cortico-cortical connectivity has been well-studied [33, 34], particularly for standing waves [35, 36], as has neuronal wave pattern formation in abstract mathematical settings [26, 37-41]. But large-scale waves and spontaneous transitions between different emergent patterns in models of brain dynamics constrained by empirical connectivity data have not been explored. Here, we show that large-scale metastable waves emerge and dynamically evolve on the human connectome, whereby the system visits multiple patterns in sequence, and no single wave pattern endures. We first construct a model of macroscopic brain dynamics composed of local brain regions interacting through diffusion-MRI derived connectivity data. We then simulate whole-brain dynamics, from which we characterize the emergent metastable wave dynamics and compare to resting-state data. Finally, we cast these metastable dynamics as reorganizations of the underlying wave flows, and relate the wave sources and sinks to the underlying brain anatomy. Importantly, we show that the presence of these waves does not depend upon the choice of neural model, and is replicated on two independent whole-brain connectomes.

Results

We modeled large-scale brain dynamics using a network of coupled neural masses [42-47]. This approach has two main components: a local mean-field model that describes neuronal dynamics in each region, and a structural connectome that introduces connectivity between regions [9]. We describe the local dynamics of each brain region with a conductance-based neural mass [48]. The model has three state variables per region: the mean membrane potential of excitatory pyramidal cells, the mean membrane potential of inhibitory interneurons, and the average proportion of open potassium ion channels. We concentrate on dynamics in the absence of noise.

Regions are coupled by connections between the excitatory populations. We use connectomic data derived from healthy subjects using probabilistic tractography [49]. This yields the connectivity matrix, which describes direct connections between regions and the strengths of these connections. Here, we define the connection weights as proportional to the numbers of

streamlines joining each pair of regions, averaged across subjects and divided by the streamline lengths between regions [49, 50]. A global coupling constant c scales all the connection weights, and operates as a tuning parameter that sets the overall excitability of the brain [51]. We also include delays between regions, which are important [42], particularly for inter-areal synchronization properties [44, 52]. As a first approximation, we use a constant delay τ for all connections.

The key novel model ingredients here are that we (i) explore a range of coupling strengths and delays beyond the narrow area of parameter space previously studied; (ii) use higher-quality and denser connectivity data than previous modeling studies [45, 46]; and (iii) focus on spatiotemporal dynamics unfolding on a wide range of time scales including the very short, not just long-time averages.

Emergent wave dynamics

We choose a coupling strength higher than has typically been explored previously [44-46, 52]. Along with short delays, this strong coupling means that each region exerts a strong influence on its neighbors, which tends to favor local synchronization [48]. Starting from a broad diversity of random initial conditions, we find that cortical activity reliably and rapidly self-organizes into spatiotemporal patterns (Fig. 1). There appears a diversity of patterns of wave dynamics: traveling waves (Fig. 1a, SI Movie 1), rotating (or *spiral*) waves (Fig. 1b, SI Movie 2), and sources and sinks (or *breathers*) in which activity either emanates from or converges toward a localized point (Fig. 1c, SI Movie 3). The wave patterns are highly coherent across the cortex, to the extent that most regions contribute to any given pattern. This large spatial scale is consistent with waves observed in human sleep spindles [4] and slow-wave sleep [53].

Propagation speeds represent a succinct and testable attribute of such predicted waves. Wave propagation speeds, estimated from the instantaneous phase velocities (see Methods), collated over all wave patterns and brain regions show an approximately lognormal distribution (Fig. 2a). Speeds across all regions and time points in our model have a median of 26 m s^{-1} although they vary widely with 10th percentile at 14 m s^{-1} and 90th percentile at 64 m s^{-1}. We next asked whether the speeds are homogenous across the brain. To test this, we calculated the mean speed in each brain region across all wave patterns. Nodal mean speeds range from 23-52 m s^{-1} (Fig. 2b), considerably narrower than the full set of instantaneous speeds. Spatially, the main trend is that nodal speeds are roughly bilaterally symmetric, and

increase with distance from midline (Fig. 2c). However, there is additional spatial structure (Fig. 2d). The regions supporting faster wave fronts form a roughly contiguous zone in each hemisphere, spanning from the frontal lobe to the occipital lobe, via the parietal lobe and posterior aspects of the temporal lobe. Slower regions primarily occur on the midline and toward the anterior pole of the temporal lobe. The bimodal nature of the speed distribution (Fig. 2b) suggests that slow and fast regions partition into two somewhat distinct clusters.

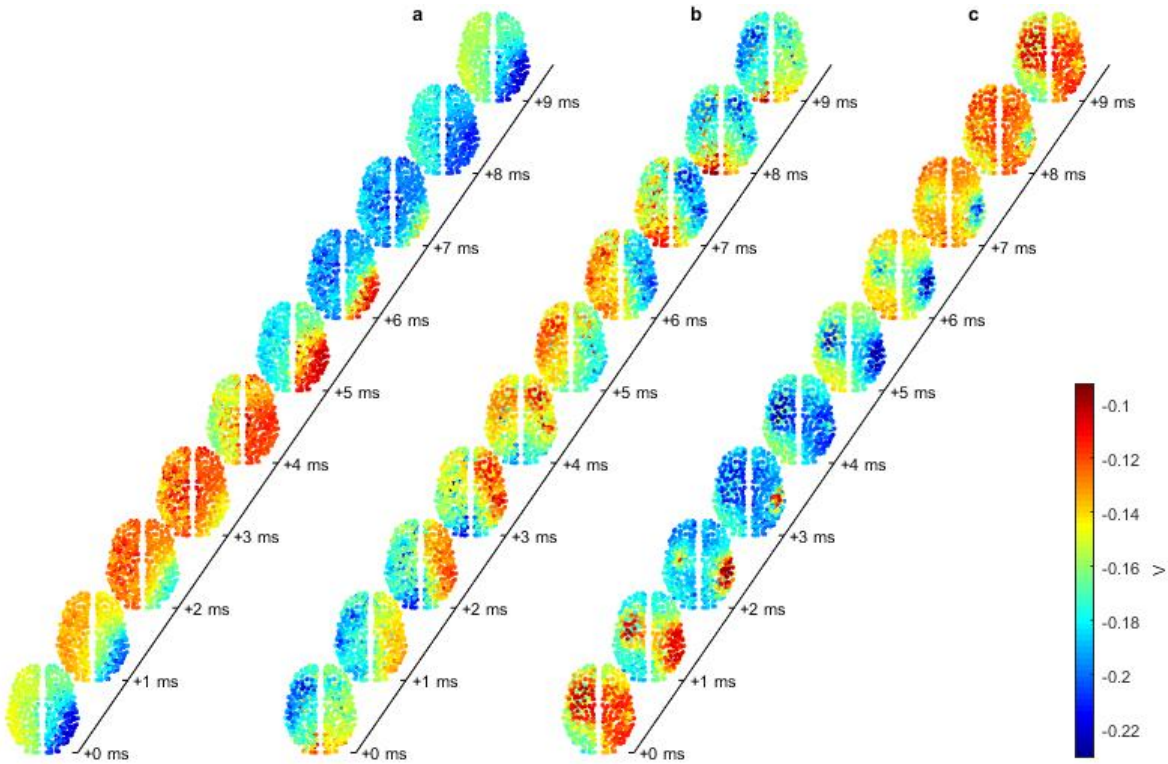

Figure 1: Large-scale wave patterns in the model. Ten snapshots of the dynamics of the pyramidal mean membrane potential V at latencies indicated on the time axes, for (**a**) a traveling wave; (**b**) a rotating wave; and (**c**) a pattern with sinks (red areas shrinking for latencies 0-3 ms) and diffuse sources (broad red areas emerging for latencies 6-9 ms). These results are for strong coupling $c = 0.6$ and short delay $\tau = 1$ ms.

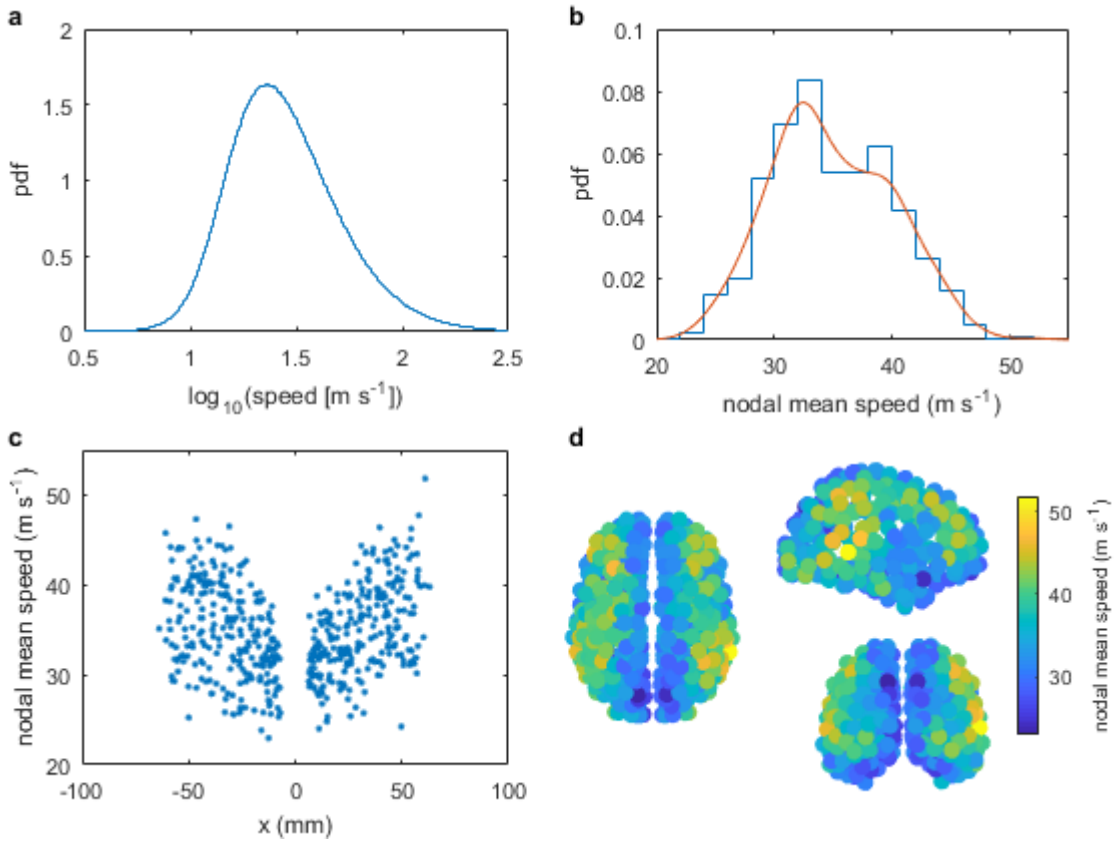

Figure 2: Wave propagation speeds. (**a**) Histogram of $\log_{10}$(speed) across all nodes and times. (**b**) Histogram of average speed (in m/s) at each node. Red line shows a kernel density estimate. (**c**) Mean speed in each region as a function of lateral position. (**d**) Spatial distribution of nodal mean speeds as viewed (clockwise from left) from the top, right, and back. These results are for strong coupling $c = 0.6$ and short delay $\tau = 1$ ms, as in Fig. 1.

Metastable transitions

The observed diversity of types of wave patterns (i.e., traveling waves, rotating waves, and sources and inks) occurs for a fixed set of parameters – the dynamics shown in Fig. 1 transition spontaneously between different patterns (SI Movie 4). The system dwells in a single wave pattern for many repeats of a particular wave oscillation, then exhibits a relatively rapid reconfiguration into the next pattern. These are spontaneous transitions that occur in the absence of noise or other external inputs. This rules out *multistability* as a mechanism for the transitions, which requires the application of a perturbation to kick the system between attractors [2, 54]. Instead, what we observe is *metastability*, a form of "winnerless competition" whereby the system's orbits visit multiple patterns in sequence, and no single pattern endures [54].

To quantify these metastable transitions, we use the fact that any particular wave pattern is composed of specific phase relationships that vary relatively smoothly across space and time. The waves we observe have long wavelengths on the whole-brain scale, so signals averaged over a large area of cortex typically do not cancel out, as would be expected if short incoherent wavelengths dominated. To capture a metric of these patterns, we hence partition the brain into the two hemispheres and calculate the instantaneous coherence within each hemisphere. We then calculate the sliding-window, time-lagged cross-correlation between these two intrahemispheric coherences. We term this the *interhemispheric cross-correlation function* (see Methods).

As a particular wave pattern propagates across the brain, this pattern of correlated phase lags between the hemispheres is relatively constant. To see this, notice that during a metastable pattern (Fig. 3a), the same "signature" (alternating blue and red as a function of lag) persists on the time scale of hundreds of milliseconds, varying relatively slowly in time within any individual pattern (as shown by the way the blue and red stripes evolve slowly). At the time of a metastable transition, the large-scale wave pattern breaks up and disorganized short wavelengths dominate. Thus, the metastable wave signatures are separated by narrow periods of time with relatively low correlation between the hemispheres. That is, metastable transitions exhibit a brief desynchronization during which wave patterns reconfigure.

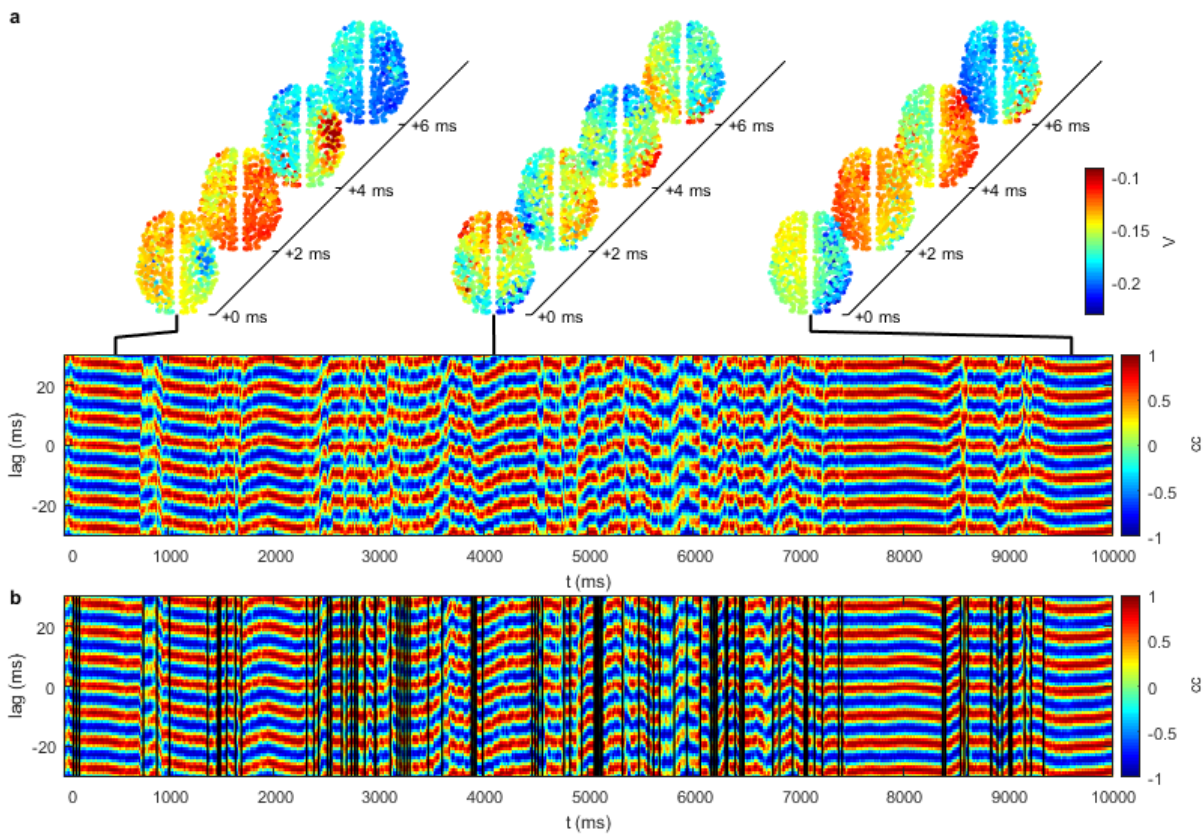

Figure 3: Metastable transitions. (**a**) Each pattern has a "signature" in the interhemispheric cross-correlation, with transitions between different patterns revealing a brief period of desynchronization. (**b**) Vertical lines depict instances of low values of the interhemispheric cross-correlation function, corresponding to wave transitions. These results are for strong coupling $c = 0.6$ and short delay $\tau = 1$ ms, as in Fig. 1.

We use these brief periods of phase desynchronization, yielding low values of the interhemispheric cross-correlation function, to identify transitions (vertical black lines in Fig. 3b). Extracting all times corresponding to low synchronization thus yields an automatically-computed set of transition times, from which we can calculate the distribution of dwell-times (Fig. 4a). We find that dwell times follow a skewed unimodal distribution.

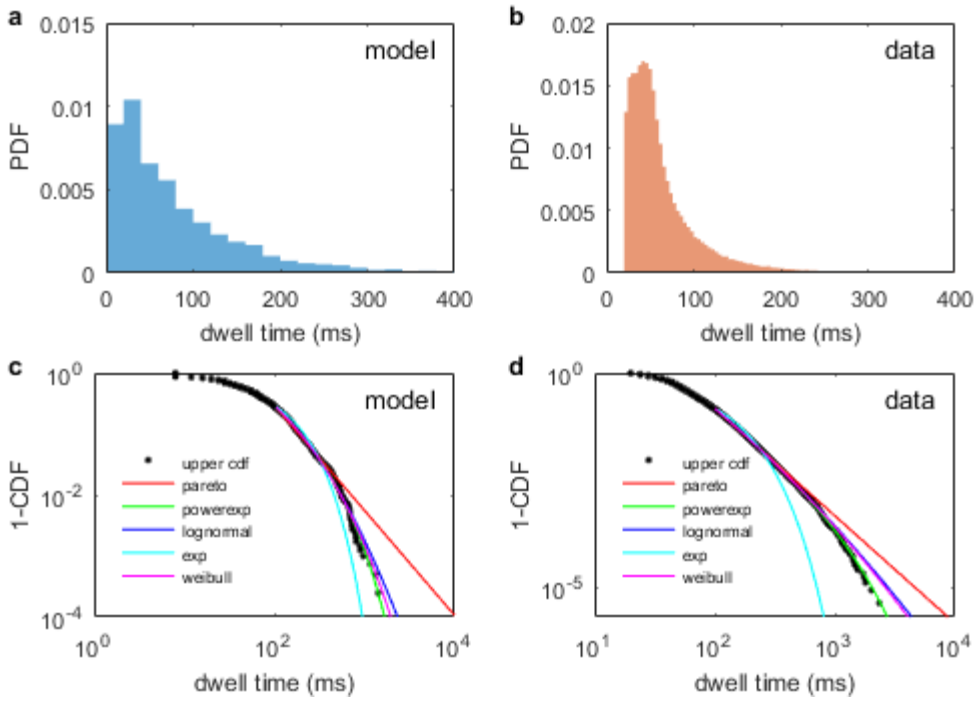

Figure 4: Dwell time distributions. (**a**) Model for c=0.6, d=1 ms. (**b**) Resting-state MEG data from [55]. (**c,d**) Upper cumulative distributions (black circles) on double logarithmic axes for dwell times in (**c**) the model, and (**d**) MEG data. Lines are maximum likelihood fits to upper tails for the power law (Pareto, red), exponentially-truncated power law (green), lognormal (blue), exponential (cyan), and stretched exponential (Weibull, magenta) distributions. Tail cutoffs at dwell times of 100 ms.

Comparison to resting-state data

Transitions between dynamic spatial patterns have been recently reported in empirical resting state MEG data [1, 55]. Dwell-time distributions in these data were calculated as the times between transitions from consecutive spatial patterns using in a hidden Markov model with 12 states [55]. As in our model, these dwell time distributions exhibit skewed unimodal distributions (Fig. 4b). The individual states have median dwell time 48 ms, similar to the 56 ms median dwell time found in the model (p=0.064, Wilcoxon rank-sum test). More importantly, the distributions are of a very similar shape in their upper tails. To show this more clearly, we plot the upper cumulative distributions (Fig. 4c-d). Both distributions exhibit heavier tails than a simple Gaussian or exponential distribution (cyan lines), but have a thinner tail than a power law. Both exhibit good agreement with an exponentially-truncated power law (green), particularly in the data where the truncated power law outperforms the

alternative candidate fits (two-sided p=1×10^{-5} and p=4×10^{-6} for truncated power law versus lognormal and stretched exponential, respectively, using Vuong's test). In the model, while the exponentially-truncated power law again yielded the best fit, similar quality fits were found for lognormal and stretched exponential distributions (two-sided p=0.067 and p=0.14 for truncated power law versus lognormal and stretched exponential, respectively, using Vuong's test). Our model thus provides a plausible mechanism for these metastable transitions.

Although the waves observed in our model are highly dynamic, they nonetheless bear a time-averaged signature. We thus asked what our metastable waves would look like through the standard lens of resting-state functional connectivity (FC) as studied in fMRI. The metastable states here are relatively long-lived (mean lifetime 89 ms) but still much shorter than the typical temporal resolution of fMRI. Despite this temporal mismatch, there is empirical evidence that short-lived states visible in electrophysiology do leave an imprint on the correlations between regions at time scales visible to fMRI [1]. Calculating FC in this way on our modeled time series, after convolution with a hemodynamic response function, reveals that edgewise FC values in the model correlate with those in resting-state fMRI from the same group of subjects both without (r=0.30, 95% CI [0.293, 0.303], two-sided $p<10^{-15}$) and with (r=0.41, 95% CI [0.409, 0.418], two-sided $p<10^{-15}$) global signal regression. This agreement compares favorably with that established in other biophysical models (~r=0.1–0.5) [45, 56, 57], which is particularly notable given that our finely-parcellated network has an order of magnitude more regions and two orders of magnitude more connections than those typically used to study whole-brain dynamics. Note that here we have not tuned parameters to optimize this relationship. Instead, this shows that when viewed on the long time-scale of average FC, complex wave dynamics have similar explanatory power to other model mechanisms that have been used to link brain network structure to FC.

Spatiotemporal scaffold

We next sought to quantify the wave dynamics in a manner that would allow a better understanding of the dynamic processes underlying the wave transitions. To achieve this, we exploited the fact that the phase velocities form a time-varying vector field (Fig. 5a, Supplementary Movie 5), which evolves more slowly than the waves themselves (compare Fig. 5a middle to Fig. 5a left). That is, for any specific wave pattern, the vector field is almost invariant while the waves themselves evolve. Transitions between distinct wave patterns

coincide with reconfigurations of this vector field. We hence treated the phase-velocity vector field at each time as a snapshot of the flow of activity implied by the waves. To infer the instantaneous flow, we employed a streamline algorithm to trace the paths along the flow vectors, similar to the methods underpinning tractography using tensor-based diffusion imaging data. We calculated the streamlines starting at the 513 nodes in both the forward and backward directions (by inverting the flow vectors). This reveals *sinks* where the flow congregates and *sources* where the flow emerges.

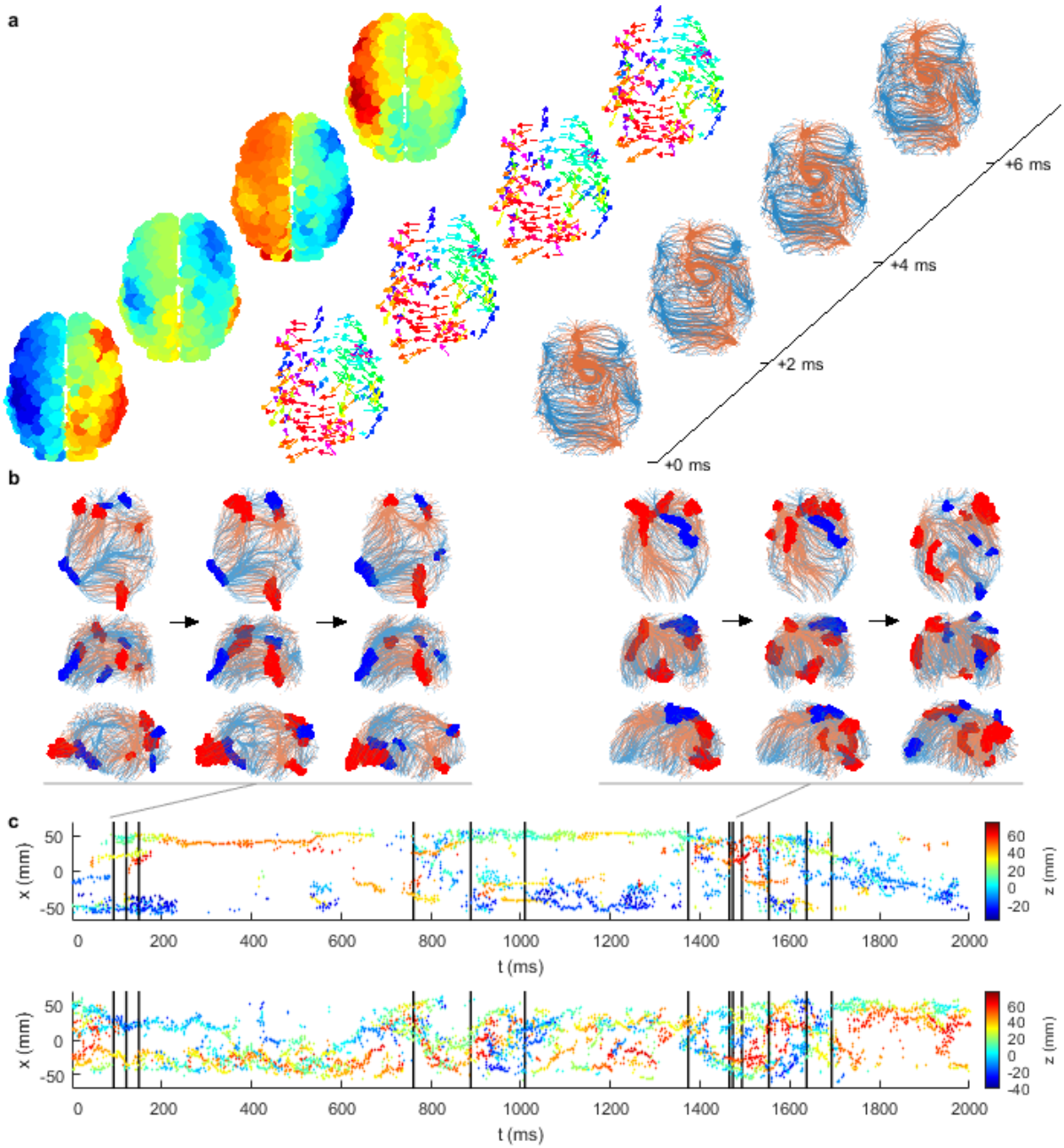

Figure 5: Phase flow tracked across space and time. (**a**) Snapshots of waves (left, colored by voltage as in Fig. 1), the corresponding phase flow vectors (middle, colored by orientation in the plane), and phase flow streamlines (right, blue and red denote forward and backward

streamlines, respectively). (**b**) Exemplar streamlines near metastable transitions, colored as in panel (a), viewed from the top, back, and right (rows 1-3, respectively). Shown are two sets of three snapshots, each surrounding a transition as indicated (gray) in the panel below. Highlighted points (filled circles) denote clusters that form sources (red) and sinks (blue). (**c**) Sinks (top) and sources (bottom) plotted across time, colored by vertical (dorsoventral) position *z*. Vertical black lines denote transition times calculated using interhemispheric cross-correlation.

Doing this reveals that streamlines typically exhibit a complex spatial arrangement, with multiple dense areas – these are the sources and sinks (Fig. 5a, right). When patterns exhibit stable travelling wave or breather solutions, the sinks and sources are typically isolated single points reflecting the dominant flow of the waves. Even though we have not imposed any temporal smoothness (e.g. as done in optical flow methods [15]), the streamlines are well-behaved across time, reflecting the stability and order of the underlying activity patterns. In the example shown here, there are sources along the midline and sinks positioned laterally in both hemispheres. Occasionally the flow converges onto or diverges from a closed loop (e.g. the source loop on the midline), corresponding to rotating wave patterns. The streamlines also form 'bundles', where nearby trajectories bunch together on approach to a sink (or from a source), revealing major pathways of activity flow.

Similar to the stable and unstable fixed points in a dynamical system, the sinks and sources allow us to summarize the dynamics of a given wave pattern more succinctly. They essentially form a scaffold around which the dynamics are organized. We identify these points by finding where streamline points form dense clusters, after transients (see Methods). The sources and sinks are relatively stable on time scales of ~100 ms, with these stable periods punctuated by relatively rapid reconfigurations in space (Supplementary Movie 6). We find that metastable transitions typically coincide with the abrupt dissolution or collision of one or more sources and/or sinks. Two exemplar metastable transitions are shown here. The first (Fig. 5b, left) shows two frontal left-hemisphere sources and a sink that merge and reconfigure to yield one left frontal source, while in the right hemisphere one frontal source and one frontal sink move closer together and a temporal sink emerges. The second example (Fig. 5b, right) exhibits complex frontal clusters of sources and sinks that split and move posteriorly, plus the emergence of an occipital sink. Tracking all sources and sinks over time suggests that these reconfigurations typically coincide with desynchronizations in the interhemispheric cross-correlation function (black lines in Fig. 5c denote the same times as in

Fig. 3b). To quantify this, we estimated the temporal variability of sources (and sinks) by calculating the standard deviation of visits to each node within sliding windows (non-overlapping of length 20 ms), and averaged this across nodes. Windows containing a cross-correlation-derived transition exhibit 14-20% higher temporal variability than those without a transition (medians for sources: 0.018 vs 0.015, $p<10^{-15}$; medians for sinks: 0.024 vs 0.021, $p<10^{-15}$; two-sided Wilcoxon rank-sum tests). We also observe that sinks tend to be more localized and less variable in time than the sources, which are often diffuse. The differences in temporal variability are highly significant (medians for sources vs sinks, 0.022 vs 0.016, $p<10^{-15}$, two-sided Wilcoxon rank-sum test). The more erratic nature of the source locations is evident when comparing the upper (sinks) and lower (sources) panels of Fig. 5c. Moreover, there is a tendency for sources and sinks to remain within a single hemisphere (i.e., the trajectories traced by colored dots in Fig. 5c tend not to cross x=0). In sum, the positions of sources and sinks reflect the nature of the wave pattern at that instant in time. Metastable transitions between wave patterns correspond to their dissolution, emergence, or collisions, analogous to bifurcations in low-dimensional dynamic systems.

Wave sources and sinks are distributed heterogeneously across the network

We next determined how the organizing centers of the waves are spatially distributed across the cortex. Similar to the mean speeds in Fig. 2d, the sources and sinks are heterogeneously distributed (Fig. 6a, b). While this is to be expected to an extent because singularities of the flow tend to occur where flow is zero (cf. the center of a spiral wave in 2-D), we also find regions that are highly-visited sinks but have relatively fast average flow. Sinks primarily cluster in frontal and lateral parietal areas (Fig. 6a), while sources are more diffuse, occurring more frequently in midline and temporal areas (Fig. 6b).

Do these preferential sites of sources and sinks overlap with classic functional networks? To study this, we assigned brain regions to twelve subnetworks (somatomotor hand, somatomotor mouth, cingulo-opercular, auditory, default mode, memory, visual, fronto-parietal, salience, subcortical, ventral attention, and dorsal attention) according to a broadly-used functional subdivision of the brain [58] (Supplementary Fig. S1). Both sinks (Fig. 6c) and sources (Fig. 6d) overlap non-uniformly with these functional networks (sinks: $F(12,500)=3.5$, $p=5.7\times10^{-5}$; sources: $F(12,500)=3.7$, $p=1.9\times10^{-5}$; ANOVA). For example, the ventral attention subnetwork is visited by sinks more often than each of cingulo-operculum

and subcortical, while sources visit the somatomotor hand network more often than others including the default mode.

We also studied how these waves were shaped by the network properties of the structural connectome, finding a positive but relatively weak correlation between node strength and visits to sources (r=0.098, 95% CI [0.012, 0.18], p=0.026) but not sinks (r=-0.025, 95% CI [-0.11, 0.061], p=0.57). That is, stronger hubs are more likely to be sources than nodes that are more topologically peripheral. To further elucidate the role of hubs we compared the top 75 nodes by strength (the strongest hubs) with the bottom 75 nodes by strength (the non-hubs) and the middle "feeder" 363 nodes. This analysis confirmed that the feeder nodes act as sinks significantly more often than hubs and non-hubs (Fig. 6e), while the hubs act as sources significantly more often than the non-hubs (Fig. 6f).

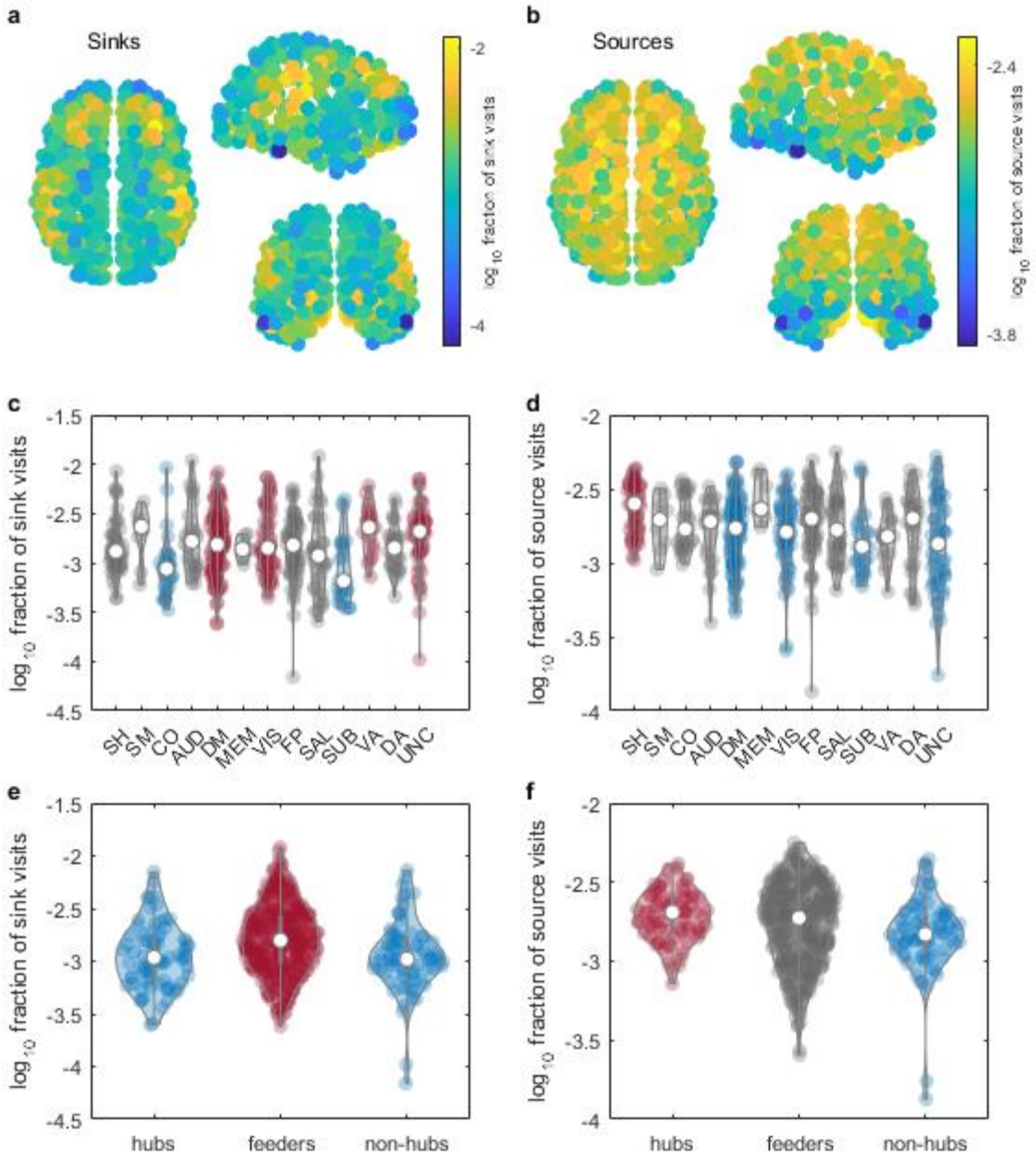

Figure 6: Source and sink properties. (**a**) Spatial distribution of sinks. (**b**) Spatial distribution of sources. (**c**) Overlap of sinks with functional networks. Blue denotes networks with fewer visits than red, and gray denotes no significant difference from any other group. Networks are labeled as: SH=Somatomotor Hand, SM=Somatomotor Mouth, CO=Cingulo-Opercular, AUD=Auditory, DM=Default Mode, MEM=Memory, VIS=Visual, FP=Fronto-Parietal, SAL=Salience, SUB=Subcortical, VA=Ventral Attention, DA=Dorsal Attention, UNC=Unclassified. (**d**) Overlap of sources with functional networks. Colors as per panel (c). (**e**) Overlap of sinks with hubs (top 75 nodes by strength), feeders, and non-hubs (bottom 75 nodes by strength). Colors as per panel (c). (**f**) Overlap of sources with hubs, feeders, and non-hubs. Colors as per panel (c). White circles in violin plots denote group medians, violins are kernel density estimates. Statistics for panels (**c**)-(**d**) are given in Supplementary Table S1 and for panels (**e**)-(**f**) in Supplementary Table S2.

Robustness to changes in parameters, connectivity, and models

We explored the robustness of the wave patterns to changes in the model and network details. First, we explored how the model dynamics vary over a range of coupling strengths and delays. Our aim here was to ensure that waves are not rare (confined to a unique combination of parameters), and to link the present findings to previously-studied dynamical regimes. The diversity of patterns across parameter space is complex (Supplementary Movie 7). The broad differences are captured by functional connectivity matrices (Fig. 7a). We find four main classes of dynamics: waves, discrete clusters, near fully-synchronized states, near fully-desynchronized states, as well as hybrids of these. Broadly speaking, waves exhibit much stronger intrahemispheric FC than interhemispheric FC – or equivalently, stronger short-range than long-range correlations – yielding a clear block diagonal structure (e.g. the c = 0.6, τ = 1 ms case studied in detail above). Wave patterns (Supplementary Movie 8) can be relatively smooth (as above), or less coherent (e.g. for c = 0.5, τ = 1 ms) such that the longest spatial scales exhibit wave patterns but within these waves, the phases are only partially synchronized between spatial neighbors. Waves are also primarily observed for stronger coupling combined with longer delays, occurring across relatively large regions of parameter space (e.g. for c = 0.4-0.6, τ = 6-10 ms). In contrast, discrete (non-propagating) clusters are observed for weaker coupling (e.g. for c = 0.1, τ = 0, 3, 5 ms). These discrete clusters exhibit a marked bimodal distribution of FC values, where nodes within a cluster exhibit FC $\approx$ 1 (dark red) while between clusters FC $\approx$ 0 (green). In the discrete cluster regime, nodes split into phase-locked clusters, with each cluster being activated sequentially (Supplementary Movie 8), as explored in more detail previously [44-46, 52]. A hybrid of waves and clusters, which we term *lurching* waves, exists for strong coupling and delays of 6-9 ms (Supplementary Movie 8). Within this regime, travelling waves occur within clusters but do not propagate continuously between clusters.

Our interhemispheric cross-correlation measure captures many of these dynamics (Fig. 7b). For example, it is sensitive to metastable transitions in partially-synchronized waves, as evidenced by periods of strong interhemispheric cross-correlation punctuated by brief desynchronizations (Fig. 7c). This measure is also sensitive to metastable dynamics even in cases where the functional connectivity is globally weak (Fig. 7d). Conversely, there exist desynchronized states with strong FC but no temporal dynamics in the interhemispheric

cross-correlation (e.g. c = 0.6, τ = 2 ms). Lurching waves exhibit two timescales, with relatively-slowly evolving correlation structure interleaved with a faster cluster-switching time (Fig. 7e).

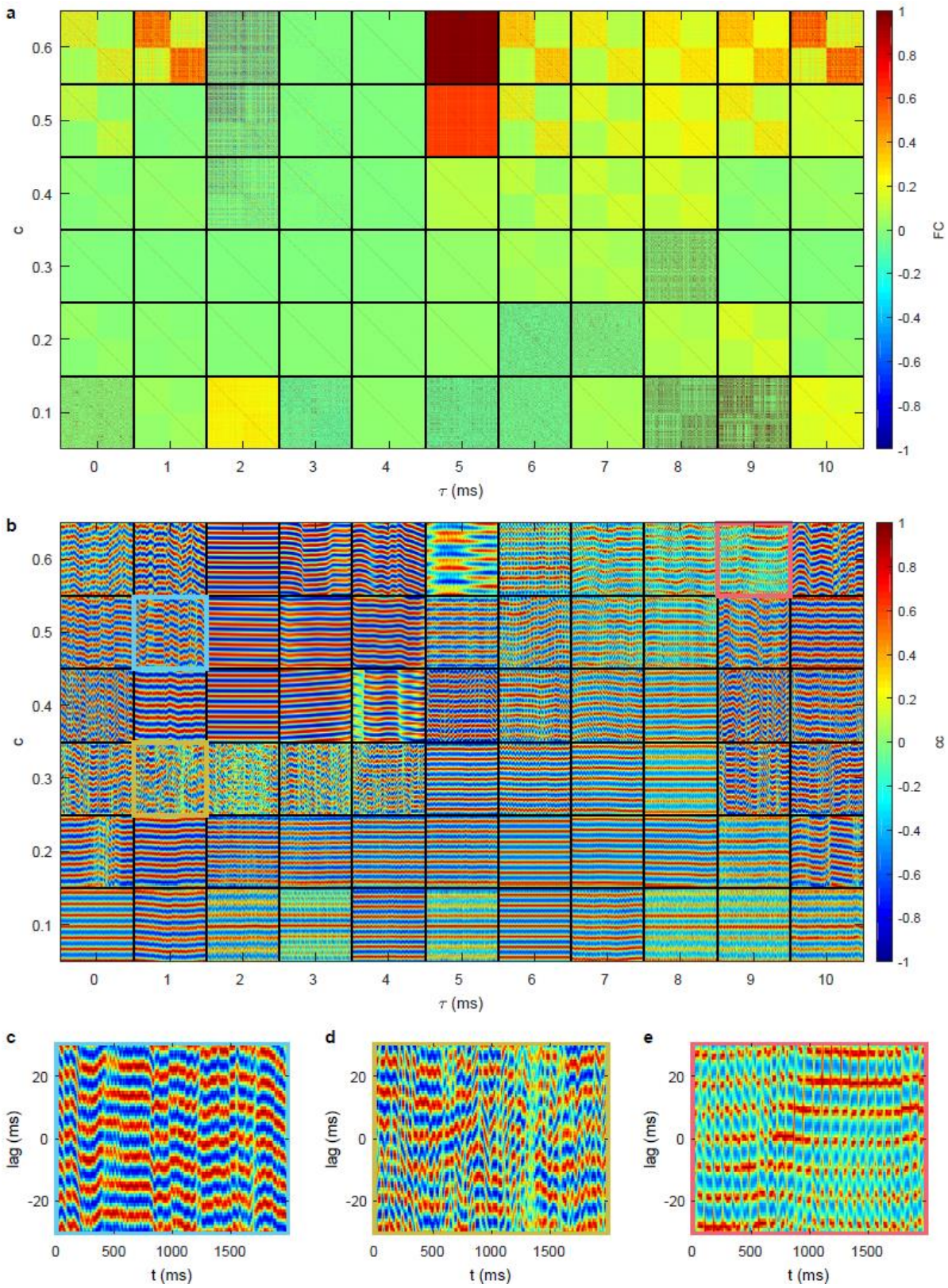

Figure 7: Dynamics as a function of coupling strength c and delay τ. (**a**) Functional connectivity matrices calculated after convolution of the neuronal time series with a hemodynamic response function. Each tile shows one FC matrix with axes indexing the nodes 1-513. (**b**) Interhemispheric cross-correlation functions, showing a 1 s segment (time is on the horizontal axis in each tile) for lags between -30 ms and 30 ms (lag is on the vertical axis in each tile). Exemplars in the text are highlighted here with colored outlines and shown in corresponding panels: (**c**) weakly-coherent waves; (**d**) interhemispheric cross-correlation dynamics despite negligible average FC; and (**e**) lurching waves.

We also verified that the existence of wave patterns reproduces across connectomic data (Supplementary Movie 9). Waves similar to those in our fully-connected weighted connectome exist also in sparser networks (thresholded down to 10% density), and occur whether using traditional weight-based thresholding [59] or consistency-based thresholding [60]. Waves exist also on a 10%-density binary network thresholded by weight (with all weights set to 1). This is consistent with the lattice-like formation of binary networks, such that shorter connections are much more probable than longer connections. This is a natural substrate to support the increased local synchrony required for wave patterns. We also observed waves arising on two entirely independent connectomes: an elderly connectome derived using probabilistic tractography [61], and the 998-node Hagmann et al. connectome derived using deterministic tractography from diffusion spectrum imaging [50].

Finally, we verified that emergent waves are not restricted to our particular choice of neural mass model. We tested two additional models: a network extension of the Wilson-Cowan model [47, 62, 63] and the Kuramoto model [64, 65]; see Methods for details. In both models we found large-scale waves (Supplementary Movie 10). In the Wilson-Cowan case, we observed complex dynamics with smooth waves in competition with partially-coherent activity that slowly intrudes onto the waves, leaving wave-like but less-coherent dynamics in its wake. This coexistence of coherent and incoherent states is an example of a chimera state [39]. In the Kuramoto case we observed waves when the model is in a regime of partial synchronization. Both of these models have complex dependencies on parameter values, similar to the neural mass model studied here.

Discussion

In this computational study, we have shown that the human connectome supports large-scale wave dynamics in the resting state. Moreover, these waves exhibit metastability, with

spontaneous transitions from one pattern to the next. While metastability and waves in neural systems have been studied in isolation, here we show for the first time that these dynamical regimes are compatible, can arise from the human connectome, and can be explained with a unified mechanism. We have developed analysis tools to quantify these dynamics, one sensitive to coarse-grained phase dynamics and one sensitive to the spatiotemporal details of the underlying dynamical flows. These new methods (available in the public domain) enable tests of our model predictions, and open new avenues in the analysis of large-scale brain activity.

The existence and distribution of sources and sinks in the wave flows organize the spatiotemporal structure of the dynamics. This suggests a different conceptualization of how information can flow around the connectome. In network studies, the prevailing paradigm is that brain regions communicate via the structural connectivity, through a composite of the direct and indirect pathways between the two regions of interest. The net effect of the many paths remains inadequately described in this picture. Our results provide an interpretation in terms of spatial pathways along which activity preferentially flows – and hence potentially also pathways of information flow, e.g. via communication through coherence [66]. This is a higher-level description than simply following the fiber pathways, instead describing the net effect of the communication between brain regions as mediated through the organization of the large-scale wave patterns.

The decomposition of waves into their sources and sinks naturally yields directionality in the dynamics, providing information inaccessible to standard functional connectivity. For example, sources can be thought of as "controlling" the resulting wave pattern, and intriguingly we find that these tend to associate with hub regions more so than non-hubs. This may also speak to the purported role of costly rich-club connections between hubs in coordinating dynamics [67]. Wave sources and sinks also overlapped heterogeneously with functional network properties. This suggests that waves have functional specificity. For instance, one subnetwork in which sinks tend to congregate is the default mode, consistent with its purported unique role in task-free/resting state acquisitions. Note also that waves contain information in their wavelength and carrier frequency that can be “read out” by dendritic trees with the matching orientation and spatial wavelength [68] – the dynamic and metastable patterns could hence yield distinct cognitive and behavioral consequences. Moreover, the spontaneous transitions in metastability are similar to the itinerancy that emerges in coupled oscillator systems [69], and to the heteroclinic cycles that have been

proposed as a mechanism for sequential cognitive processes and decision making [70]. Such theories of functional switching could be tested by moving beyond dwell times to study transition probabilities between specific patterns, as has been done for two-dimensional waves [15] and transient MEG patterns [1]. Future application of our modelling and analysis methods to task-related data will enable elucidation of these potential functional roles.

In the past decade, much of our understanding of large-scale resting-state brain dynamics has been obtained through the lens of fMRI. With the exception of slow hemodynamic waves in visual cortex [71, 72], it is not expected that fast neuronal wave dynamics can be easily resolved through the low temporal resolution of fMRI. This speaks to a need for imaging technologies that are sensitive to fast neuronal activity to observe such dynamics, such as MEG and ECoG. Indeed, excellent spatiotemporal resolution is the norm in the animal preparations where waves have been studied in the most detail. For human neuroimaging, progress will require source reconstruction techniques that can appropriately accommodate the complex amplitude-phase relationships that reflect metastable waves.

The present analysis was performed in the absence of added system noise. Intrinsic sustained fluctuations in this system emerge from the chaotic dynamics of each coupled node. Future work could add noise, and thereby enable assessment of the relative contributions of noise-driven fluctuations versus endogenous metastable dynamics. Incorporating noise and other input stimuli also opens the possibility of exploring multistability – that is extrinsically perturbed jumps between states. The present model is capable of exhibiting multistability: e.g. for $c = 0.5$ and $\tau = 15$ ms, wave or discrete cluster dynamics may emerge, depending on the choice of initial condition. Analysis of transitions between multistable states would require incorporation of stimuli or stochastic influences [2, 54, 73], which will be the subject of future work.

A key parameter in our model is the coupling strength, which scales the overall influence of activity from connected regions. There are several important points here. First, the connectome exhibits a rapid, roughly exponential drop-off in connection weight with distance [49]. In fact, this exponential drop-off is similar to the connectivity kernels used in neural field models, where pattern formation is well-known [41]. Although there has been some debate in the field as to the relative merits of continuum neural field models versus networks of discrete coupled neural masses, we contend that these two approaches are more complementary than has previously been appreciated, beyond the trivial point that continuum

models are routinely discretized for numerical simulations. Second, modeling studies typically use coarse parcellations with 50-100 nodes. Given the exponential spatial kernel, this means that most of the coupling influence is relatively local ($\lesssim$ 50 mm). Local patches of this scale are often lumped together in typical coarse parcellations. This simplification reduces the spatial resolution and may hinder wave formation, which is a spatiotemporal collective phenomenon of many regions. Third, the most strongly-coherent waves were observed for strong coupling (in comparison to the coupling used in earlier studies). It is possible that highly coherent waves observed here for strong coupling are more common in states such as seizures, anesthesia, and sleep [4] than in healthy awake adults. The locally less coherent and lurching waves we observed may be a more likely candidate for the higher-complexity associated with conscious states. The lurching waves encompass both the functional segregation offered by sequentially-activated discrete clusters and the transient localized (e.g. to within V1) wave patterns observed empirically [11].

Another important component of the coupling between regions is the propagation delay. We made the simple approximation of uniform delays between all regions, where the delay is to be interpreted as a mean effective delay. This is a common approach, and while there is some evidence for regional variation in myelination supporting near-uniform delays between thalamus and cortex [74], it remains an approximation. The next simplest approximation would be to assume a fixed conduction velocity instead, implying a distribution of delays that increase with distance, as has been used in some studies [42, 47]. The reality is that both delays and velocities vary between regions [75]. Future work could address the roles of distributed delays on wave dynamics and metastable switching times. Since distributed delays have been linked to increased stability of dynamics [76, 77], we conjecture that wave dynamics may be more stable to perturbation with broader delay distributions.

We observe that the nature (probability distribution) of the metastable transitions of our model bear close resemblance to those derived from the analysis of metastable switching in resting state MEG data [1, 55], although there is a modest quantitative mismatch in the precise form. Reducing this mismatch could act as a cost function if fitting the wave dynamics more formally to empirical data. Both sets of dwell times are broadly similar to a lognormal distribution, although formal testing shows other long-tailed distributions (e.g. exponentially-truncated power law) can provide a similar quality fit to the upper tails. Alternatively, the hidden Markov model method employed in the MEG study could be

applied to our model simulations, after application of an appropriate forward model. There is also scope to improve our phase-flow streamline methods.

In sum, waves of cortical activity appear in empirical recordings, across broad recording modalities, species, and behavioral states. Here, we show that the human connectome supports the spontaneous emergence of complex metastable brain waves. These are robust to changes in model parameters, the choice of model, and the thresholding of the underlying connectome. They reproduce across connectome data sets and yield qualitative matches with empirical resting state data. The widespread empirical observation of travelling wave phenomena reproduced suggests a range of functional and potentially pathological roles in cognition and states of awareness [18]. The present modeling study makes specific predictions that can be further tested in these data and, moreover, yields novel quantitative analysis techniques that allow for a fundamental shift from static to nonstationary analytic frames.

Methods

Connectomic data

We derived estimates of whole brain structural connectivity from diffusion images of 75 healthy subjects (aged 17-30 years, 47 females). Diffusion MRI data were acquired on a Philips 3T Achieva Quasar Dual MRI scanner (Philips Medical Systems, Best, Netherlands). We estimated the fiber orientation distribution (FOD) within each voxel constrained spherical deconvolution [78], implemented in MRtrix [79]. Tractograms were generated using a probabilistic streamline algorithm [79], which produces a set of connection trajectories by randomly sampling from the orientation uncertainty inherent in each FOD along the streamline paths. Our connectivity matrices were reconstructed from densely seeded tractography (10^8 seeds) and parcellated into a relatively fine representation of 513 uniformly sized cortical and sub-cortical regions [80]. The resulting weighted, undirected matrices were nearly fully connected in each subject. The weights are the number of streamlines linking each pair of regions, divided by the streamline lengths (see Ref. [49] for full details).

Resting-state fMRI was recorded from the same subject cohort; 69 subjects had a full set of both diffusion and resting-state images. Functional images were collected using a T2* weighted echo-planar imaging sequence (TE = 30 ms, TR = 2000 ms, flip angle = 90º, FOV

250 mm, 136 x 136 mm matrix size in Fourier space) and consisted of twenty-nine contiguous 4.5 mm axial slices (no gap) covering the entire brain. Participants were requested to clear their mind without falling asleep. Preprocessing of data used included realignment, unwarping, anatomical co-registration, and spatial normalization. The functional data were corrected for white matter and cerebrospinal fluid signal. Further details of image acquisition and preprocessing are provided in Ref. [81]).

Neural mass model

The neural mass model we used has been presented in detail elsewhere [48, 73]; here we give a brief overview. This simple conductance-based neural mass model has three state variables at each node j: mean membrane potential of local pyramidal cells V_j, mean membrane potential of inhibitory interneurons Z_j, and the average number of open potassium ion channels W_j. Its dynamics are governed by:

$$\begin{aligned}\frac{dV_j}{dt} = &-\{g_{Ca} + r_{NMDA}a_{ee}[(1-c)Q_V(V_j) + cQ_j^{\text{network}}]\}m_{Ca}(V_j)(V_j - V_{Ca}) \\ &- [g_{Na}m_{Na}(V_j) + a_{ee}Q_V(V_j)](V_j - V_{Na}) \\ &- g_K W(V_j - V_K) - g_L(V_j - V_L) \\ &+a_{ie}Z_jQ_Z(Z_j)+a_{ne}I_0,\end{aligned} \tag{1}$$

$$\frac{dZ_j}{dt} = b[a_{ni}I_0 + a_{ei}V_jQ_V(V_j)], \tag{2}$$

$$\frac{dW_j}{dt} = \phi[m_K(V_j) - W_j]. \tag{3}$$

Here, delayed inputs from other regions in the network enter through the term $Q_j^{\text{network}} = \sum_k C_{jk}Q_V(V_k(t-\tau)) / \sum_k C_{jk}$, where τ is the delay time and c is the global coupling strength. Equations (1)-(3) are nondimensionalized to have unit capacitance such that nondimensional time is numerically equivalent to milliseconds [48]. Here I_0 is nonspecific input to excitatory and inhibitory populations. The model distinguishes between AMPA and NMDA channels, where r_{NMDA} denotes the ratio of NMDA receptors to AMPA receptors, and a_{xy} terms parameterize the strength synaptic coupling from population x ($= e, i, n$, where n is a non-specific input) to population y ($= e, i$). Parameters b and ϕ are rate parameters (inverse time constants) that determine the time scales of Z and W, respectively. The g_{ion} terms in Eq. (1) are conductances of the corresponding ion channels, and the $m_{ion}(V)$ functions describe the voltage-dependent fractions of open channels. They take the sigmoidal form

$$m_{ion}(V) = 0.5\left[1 + \tanh\left(\frac{V - T_{ion}}{\delta_{ion}}\right)\right], \tag{4}$$

where T_{ion} and δ_{ion} are the mean and standard deviation, respectively, of the threshold membrane potential for a given ion channel. The self-feedback of the pyramidal cells is split into a conventional voltage-dependent term for sodium channels $a_{ee}Q_V(V)(V - V_{Na})$, and a state-dependent term for NMDA-gated calcium channels, $r_{NMDA}a_{ee}Q_V(V)m_{Ca}(V)(V - V_{Ca})$.

The voltage-dependent functions Q_V and Q_Z are the mean firing rates of the excitatory and inhibitory populations, respectively, also given by sigmoidal forms

$$Q_V(V) = 0.5Q_{V_{\max}}\left[1 + \tanh\left(\frac{V - V_T}{\delta_V}\right)\right], \tag{5}$$

$$Q_Z(Z) = 0.5Q_{Z_{\max}}\left[1 + \tanh\left(\frac{Z - Z_T}{\delta_Z}\right)\right], \tag{6}$$

where $Q_{V_{\max}}$ and $Q_{Z_{\max}}$ are the maximum firing rates of the excitatory and inhibitory populations, respectively, and V_T and Z_T are the corresponding thresholds for axon potential generation, and δ_V and δ_Z are the standard deviations in these thresholds.

The inhibitory population Z is passively slaved to the pyramidal population: its membrane potential (and resulting firing rate) is driven by the firing rate of the output of the pyramidal cells, responding on a slow time scale parameterized by the factor b. The inhibitory population thus acts as a passive low-pass filter of the pyramidal cells.

Parameter values are given in Table 1.

Table 1: Parameters for the neural mass model (in nondimensional units)

Parameter	Description	Value
g_{Ca}	Maximal conductance of calcium ion channel	1
g_{Na}	Maximal conductance of sodium ion channel	6.7
g_K	Maximal conductance of potassium ion channel	2
g_L	Conductance of passive leaky membrane	0.5
V_{Ca}	Equilibrium potential of calcium ion channel	1

V_{Na}	Equilibrium potential of sodium ion channel	0.53
V_K	Equilibrium potential of potassium ion channel	-0.7
V_L	Equilibrium potential of passive leaky membrane	-0.5
T_{Ca}	Threshold for calcium ion channels	-0.01
T_{Na}	Threshold for sodium ion channels	0.3
T_K	Threshold for potassium ion channels	0
δ_{Ca}	Threshold standard deviation for calcium ion channels	0.15
δ_{Na}	Threshold standard deviation for sodium ion channels	0.15
δ_K	Threshold standard deviation for potassium ion channels	0.3
V_T	Firing threshold potential for excitatory population	0
Z_T	Firing threshold potential for inhibitory population	0
δ_V	Firing threshold standard deviation for excitatory population	0.65
δ_Z	Firing threshold standard deviation for inhibitory population	0.65
$Q_{V_{\max}}$	Maximum firing rate for excitatory population	1
$Q_{Z_{\max}}$	Maximum firing rate for inhibitory population	1
b	Rate constant for inhibitory dynamics	0.1
ϕ	Rate constant for potassium dynamics	0.7
r_{NMDA}	Ratio of NMDA to AMPA receptors	0.25
a_{ee}	Synaptic strength from excitatory to excitatory	0.36
a_{ie}	Synaptic strength from inhibitory to excitatory	2
a_{ne}	Synaptic strength from nonspecific to excitatory	1
a_{ei}	Synaptic strength from excitatory to inhibitory	2
a_{ni}	Synaptic strength from nonspecific to inhibitory	0.4
I_0	Mean nonspecific input strength	0.3

Functional connectivity

To estimate functional connectivity from the model simulations we calculated the pairwise linear Pearson correlation coefficient between each pair of time series. We calculated functional connectivity both on the mean pyramidal cell body potential, and after estimating the BOLD signal. We approximated the BOLD signal for each region using linear convolution with a hemodynamic response function (as implemented in SPM12's `spm_hrf`). This entailed downsampling to a 0.1 s time step using an antialiasing Chebyshev Type I IIR filter of order 8 (as implemented in MATLAB's `decimate` function). We compared this convolution method to full solution of the nonlinear Balloon-Windkessel model [82] and found the results similar, so employed the faster convolution method.

Interhemispheric synchrony

We use a measure of interhemispheric synchrony derived as follows. Using the Hilbert phase $\phi_j(t)$ at each node j we calculate the coherence for a set of nodes S in terms of an order parameter $R_S(t)$, given by

$$R_S(t) = \left| \sum_{j \in S} e^{i\phi_j(t)} \right|. \tag{7}$$

We can then calculate the two intrahemispheric coherences $R_L(t)$ for nodes L in the left hemisphere and $R_R(t)$ for nodes R in the right hemisphere. We define the interhemispheric synchrony as the sliding-window time-lagged cross-correlation $C(t, l)$ between $R_L(t)$ and $R_R(t)$. This quantity depends on time (via the windowing) and the cross-correlation lag l. We use windows of length 100 ms and 90% overlap; like all sliding-window methods there is a tradeoff between resolution and uncertainty in the estimates within each window. Here we opt for increased smoothing at the expense of temporal resolution.

Phase velocities

We calculated the velocity vector field at each time point using a method similar to that of Rubino et al. [12]. First we extracted the instantaneous phase at each node using the Hilbert transform. The phase velocity $\mathbf{v}$ can be calculated from the spatial and temporal derivatives of the phase $\phi(x, y, z, t)$, as $\mathbf{v} = -\left(\left|\frac{\partial \phi}{\partial t}\right| / \|\nabla \phi\|^2\right) \nabla \phi$. To calculate the spatial derivatives, we used the constrained natural element method [83], a meshless method for solving calculus problems on non-convex domains. This allowed us to calculate nodal quantities (specifically

the components of the gradient vector) without needing to interpolate to and from a 3-D grid, which can introduce edge effects for nodes on the brain's convex hull. To handle phase unwrapping, we calculated the gradient of $e^{i\phi(x,y,z,t)}$ and used the identity $\frac{\partial\phi}{\partial x} = -ie^{-i\phi}\frac{\partial}{\partial x}e^{i\phi}$.

Flow streamlines

To calculate streamlines following the velocity vector field, we used a simple Euler stepping routine starting from the individual nodes. Flow at each point was estimated using constrained natural neighbor interpolation [83]. We used a maximum step length of 8 mm, and stopping criteria of the streamline leaving the brain or reaching a maximum of 200 steps. Dense clusters of streamline points were identified by first discarding streamlines shorter than 20 steps (these tended to exit the brain rather than converge onto a source/sink), then discarding transients by restricting attention to the last 5 points of each streamline, and passing these to a density-based clustering algorithm DBSCAN [84]. Parameters of the clustering algorithm were a cluster radius of 6 mm and a minimum cluster size of 10 points.

Replication datasets and models

We verified our results using independently-acquired connectomic data from both the elderly connectome [61], and the higher spatial resolution 998-node Hagmann et al. dataset [50]. We also exhibited waves in two different models, the Wilson-Cowan model extended in network form [62] and the Kuramoto model [64, 65].

In the Wilson-Cowan network model, each region j is described by two state variables u_j and v_j, representing firing rates for excitatory and inhibitory populations, respectively. Their dynamics are governed by

$$\frac{du_j}{dt} = -u_j + f\left(a_{ee}u_j - a_{ie}v_j - z_e + cu_j^{\text{network}}\right), \tag{8}$$

$$\tau_0\frac{dv_j}{dt} = -v_j + f\left(a_{ei}u_j - a_{ii}v_j - z_i\right), \tag{9}$$

where $f(x) = 1/[1 + \exp(-x)]$ is a sigmoidal firing rate function, and delayed inputs from other nodes in the network enter via $u_j^{\text{network}} = \sum_k C_{jk}u_k(t-\tau) \,/\, \sum_k C_{jk}$. The simulations here used $a_{ee} = a_{ie} = a_{ei} = 10$, $a_{ii} = -2$, $z_e = 1.5$, z_i=6, and $\tau_0 = 1$ [62].

In the Kuramoto model, each region is described by a single state variable θ_j describing a local oscillatory phase, and a natural frequency ω_j. Their dynamics are governed by

$$\frac{d\theta_j}{dt} = \omega_j + c\sum_k C_{jk}\sin(\theta_k - \theta_j), \tag{10}$$

where $c = 0.0028$ is a constant set in previous work to match empirical functional connectivity results [64]. In this example there are no delays between regions. Natural frequencies ω_j were determined as a function of the anatomical node strength $s_j = \sum_{k=1}^{513} C_{jk}$ to incorporate a hierarchy of timescales across the cortex. As in previous work [64], each region's intrinsic frequency is given by

$$\omega_j = a - (a - b)\left(\frac{s_j - s_a}{s_b - s_a}\right)^2, \tag{11}$$

where a = 0.1 Hz and b = 0.01 Hz are the maximum and minimum oscillatory frequencies, and $s_a = \min(s)$ and $s_b = \max(s)$ are the corresponding maximum and minimum strengths.

Data availability

All data are available from the corresponding authors upon request.

Code availability

MATLAB code is available at www.sng.org.au/Downloads.

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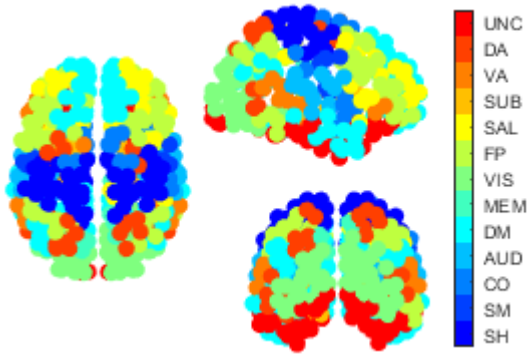
Author Contributions

J.A.R., L.L.G., and M.B. designed the study, J.A.R. and L.L.G. performed the simulations, J.A.R., L.L.G., and M.B. performed the analyses, R.A. and M.W.W. provided the MEG

resting-state dwell times. P. B. M. and G. R. provided the structural and functional MRI data. All authors discussed the results and contributed to writing the paper.

SUPPLEMENTARY INFORMATION

Supplementary Figure



Supplementary Figure S1: Spatial map of functional networks. Nodes are labeled by color according to their functional network membership: SH=Somatomotor Hand, SM=Somatomotor Mouth, CO=Cingulo-Opercular, AUD=Auditory, DM=Default Mode, MEM=Memory, VIS=Visual, FP=Fronto-Parietal, SAL=Salience, SUB=Subcortical, VA=Ventral Attention, DA=Dorsal Attention, UNC=Unclassified.

Videos

Supplementary Movie 1

Traveling wave. An example of a traveling wave pattern, for coupling $c = 0.6$ and delay $\tau = 1$ ms, as in Figure 1a.

Supplementary Movie 2

Rotating wave. An example of a rotating wave pattern, for coupling $c = 0.6$ and delay $\tau = 1$ ms, as in Figure 1b.

Supplementary Movie 3

Sources and sinks. An example of a wave pattern with sources and sinks, for coupling $c = 0.6$ and delay $\tau = 1$ ms, as in Figure 1c.

Supplementary Movie 4

Example of spontaneous metastable transitions. Top row shows three views of the brain (l-r: top, right, back). Bottom row shows the interhemispheric cross-correlation (see Fig. 3), with the time of the frame frames above annotated by the sliding vertical line.

Supplementary Movie 5

Waves, flow vectors, and streamlines. Left: Pyramidal membrane potential, same dynamics as in Supplementary Movie 4. Middle: Unit vectors for the direction of instantaneous flow. Color denotes angle in the plane. Right: Streamlines propagated forward (blue) and backward (red) from the seed positions. Highlighted clusters of points are sinks (asterisks) and sources (circles), colored by position along the dorsoventral axis (red=high, blue=low).

Supplementary Movie 6

Streamlines and reconfigurations of sources and sinks. Streamlines propagated forward (blue) and backward (red) from the seed positions. Highlighted clusters of points are sinks (asterisks) and sources (circles), colored by position along the dorsoventral axis (red=high, blue=low). Three views: top (left), right side (middle), and back (right).

Supplementary Movie 7

Mosaic of brain dynamics across (c, τ)-space. Rows from bottom to top denote c=0.1,…,0.6 , columns from left to right denote τ=0, …, 10 ms. Each panel has color scale spanning the individual top and bottom percentile of pyramidal membrane potential.

Supplementary Movie 8

Examples of different dynamical regimes. Left to right: partially-coherent waves; weakly-coherent waves; lurching waves; periodic clusters; and aperiodic clusters.

Supplementary Movie 9

Examples of waves on different connectomes. Left to right: same connectome as main paper but at 10% density after thresholding by consistency; same connectome as main paper but at 10% density after thresholding by weight; same connectome as main paper but binarized at 10% density after thresholding by weight; a connectome from a healthy elderly population; the 998-node Hagmann et al. connectome.

Supplementary Movie 10

Examples of waves in different models. In all cases the connectivity is the same as in the main paper. Left to right: the Kuramoto model; the Wilson-Cowan model, showing a chimera state from early in the simulation run; the Wilson-Cowan model, from later in the same simulation run as the preceding frames, showing partially-coherent waves.

Supplementary Tables

Supplementary Table S1

Statistics for comparisons in Fig. 6c,d, bolded entries correspond to the colored comparisons in the figure. Numbers are two-tailed *p*-values for t-tests, corrected for multiple comparisons (Bonferroni). Upper triangle is for comparisons between sink visits and functional networks, lower triangle (shaded) is for comparisons between source visits and functional networks.

	SH	SM	CO	AUD	DM	MEM	VIS	FP	SAL	SUB	VA	DA	UNC
SH		1	0.46	1	1	1	1	1	1	0.43	1	1	1
SM	1		0.97	1	1	1	1	1	1	0.81	1	1	1
CO	1	1		0.053	**0.039**	1	**0.033**	0.57	1	1	**0.0048**	1	**0.0033**
AUD	0.25	1	1		1	1	1	1	1	0.051	1	1	1
DM	**0.0053**	1	1	1		1	1	1	1	**0.048**	1	1	1
MEM	1	1	1	1	1		1	1	1	1	1	1	1
VIS	**0.0034**	1	1	1	1	0.8		1	1	**0.038**	1	1	1
FP	1	1	1	1	1	1	1		1	0.54	1	1	1
SAL	0.81	1	1	1	1	1	1	1		1	0.47	1	1
SUB	**0.0068**	1	1	1	1	0.39	1	1	1		**0.0049**	1	**0.0045**
VA	0.11	1	1	1	1	1	1	1	1	1		1	1
DA	0.82	1	1	1	1	1	1	1	1	1	1		1
UNC	**7.8×10^{-6}**	1	0.36	1	1	0.1	1	0.088	1	1	1	1	

Supplementary Table S2

Statistics for comparisons in Fig. 6e,f, bolded entries correspond to the colored comparisons in the figure. Numbers are two-tailed *p*-values for t-tests, corrected for multiple comparisons (Bonferroni). Upper triangle is for comparisons between sink visits and hub status, lower triangle (shaded) is for comparisons between source visits and hub status.

	Hubs	Feeders	Non-hubs
Hubs		**0.00016**	1
Feeders	0.25		**0.00024**
Non-hubs	**0.0093**	0.11	

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