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# 1 Symmetry breaking organizes the brain's resting 2 state manifold

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## 8 **Abstract**

9 Spontaneously fluctuating brain activity patterns that emerge at rest  
10 have been linked to brain's health and cognition. Despite detailed descrip-  
11 tions of the spatio-temporal brain patterns, our understanding of their  
12 generative mechanism is still incomplete. Using a combination of compu-  
13 tational modeling and dynamical systems analysis we provide a mechanis-  
14 tic description of the formation of a resting state manifold via the network  
15 connectivity. We demonstrate that the symmetry breaking by the connec-  
16 tivity creates a characteristic flow on the manifold, which produces the  
17 major data features across scales and imaging modalities. These include  
18 spontaneous high amplitude co-activations, neuronal cascades, spectral  
19 cortical gradients, multistability and characteristic functional connectiv-  
20 ity dynamics. When aggregated across cortical hierarchies, these match  
21 the profiles from empirical data. The understanding of the brain's resting  
22 state manifold is fundamental for the construction of task-specific flows  
23 and manifolds used in theories of brain function such as predictive cod-  
24 ing. In addition, it shifts the focus from the single recordings towards  
25 brain's capacity to generate certain dynamics characteristic of health and  
26 pathology.

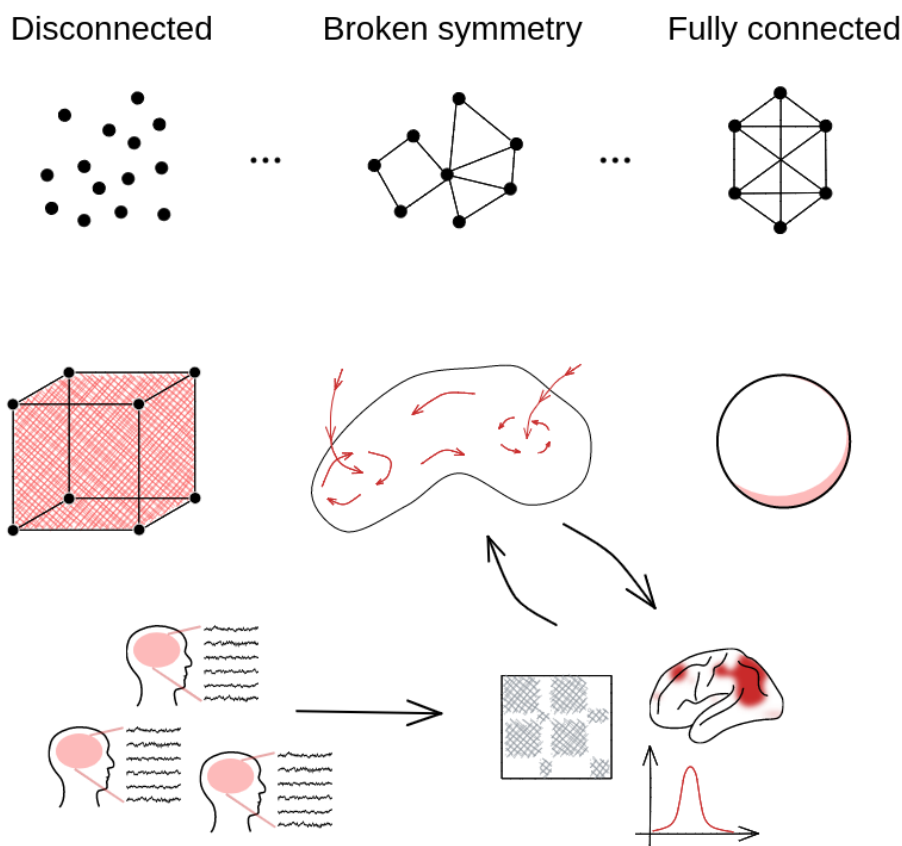
## 27 **1 Introduction**

28 The human brain at rest exhibits remarkable richness of neural activity struc-  
29 tured both in time and space. Early computational modeling studies explored  
30 how these spontaneous fluctuations are constrained and how their organisation  
31 is shaped by the anatomic connectivity [1–4] enabling to start disentangling  
32 the mechanisms of the resting state dynamics *in silico*. A substantial body of  
33 work has related the emergent activity patterns at rest to the brain functional  
34 networks involved in task conditions [5, 6], and shown that the spatio-temporal

35 variability of resting-state activity possesses functional significance [7–9], rel-  
36 evance to cognitive task performance [10], consciousness levels [11], changes  
37 during ageing [12, 13], mental disorders [14], and neurodegenerative diseases  
38 (e.g. Alzheimer’s dementia; [15]). The structure of the resting state dynam-  
39 ics changes over time [16] and is characterized by a range of properties such  
40 as metastability [17, 18], event-like coactivations [19–21] and traveling waves  
41 [22]. However, our understanding of the mechanisms underlying these spatio-  
42 temporal patterns of the brain activity at rest is still incomplete [23] and whole  
43 brain network models have a crucial role to play on that front [24].

44 There is general agreement that the resting brain operates near critical-  
45 ity [25]. This is supported by a large range of analyses performed on simu-  
46 lated and empirical data using network based measures (functional connectivity,  
47 functional connectivity dynamics), information theoretical measures (entropy,  
48 ignition) and descriptions of spatiotemporal dynamics (avalanches, cascades).  
49 Modeling efforts provide further evidence for the close relationship between the  
50 empirical data features and the properties of the structural network, local dy-  
51 namics, coupling strength, neural gain [4, 13, 26–31]. The resting state dynamics  
52 can then be understood as noise-driven fluctuations of brain activity, operat-  
53 ing near criticality and constrained by the brain connectivity [2, 32]. However,  
54 none of the above qualifies as a description of a mechanism. Descriptions of  
55 mechanisms require formulation in terms of causal activities of their constituent  
56 entities and render the end stage, in our context the resting state dynamics,  
57 intelligible by showing how it is produced [33]. To explain is thus not merely to  
58 redescribe one regularity (e.g. functional connectivity dynamics, or maximiza-  
59 tion of entropy) as a series of several (such as near-criticality, cascades, ignition).  
60 Rather, explanation involves revealing the productive relation between causal  
61 activities linked to their constituent entities.

62 In this paper we aim to remedy this situation and provide this explanation  
63 using Structured Flows on Manifolds (SFMs) [34–38]. SFMs is a mathematical  
64 framework explaining how low dimensional dynamics, reflecting generative sets  
65 of rules underlying behavior, emerges in high-dimensional nonlinear systems,  
66 specifically dynamical systems on networks modeling macroscale brain dynam-  
67 ics. When properly linked to the network’s constituent entities (functional nodes  
68 and connectivity), we will demonstrate how their causal activities lead to the  
69 formation of brain’s resting SFM, comprising all its dynamic signatures (see  
70 Figure 1). If we distill the previous reports of brain resting state data analysis  
71 from the dynamical systems point of view, we arrive at the following main em-  
72 pirical signatures that should be part of the end stage of a successful mechanistic  
73 description: bistability of single region activation [39–41], low-dimensionality of  
74 the global system dynamics in state space [7, 42, 43], cascade propagation [44],  
75 multistability of recurrent coactivation spatial patterns [18, 45] and their non-  
76 trivial temporal dynamics or intermittency [21, 32, 46]. These signatures will  
77 constitute the key features of what we will describe as structured flows on the  
78 low dimensional resting state manifold.



79

80 **Figure 1: Structured flows on manifolds as focus of resting state**  
 81 **characterization.** With respect to the structure of the connectivity of the  
 82 dynamical system, we consider spectrum defined by the two symmetrical limit  
 83 cases: fully connected and fully disconnected network. Driven by noise, the  
 84 disconnected system exhibits fully statistical, high-dimensional dynamics - it  
 85 explores the whole state space in an equidirectional manner. On the other hand,  
 86 the dynamics of the fully connected system is fully constrained corresponding to  
 87 a  $SO(n)$  hypersphere with zero flow. The dynamics on the sparsely connected  
 88 system leads to an object in between - a low-dimensional attractive manifold  
 89 with an associated flow (SFM). It is this object we wish to put in the center of  
 90 interest and characterize. While the SFM object remains the same, connections  
 91 are made to data of various modalities with the help of suitable data features.

## 92 2 Results

93 In what follows we employ whole-brain modeling to study the low dimensional  
 94 manifold and the associated structured flows of the spontaneous resting state

95 dynamics, and how these relate to the structural connectome. We constructed a  
96 brain network model (BNM) in the Virtual Brain [47] using the two-dimensional  
97 mean-field model of an ensemble of quadratic integrate-and-fire neurons ([48];  
98 MPR) to govern the regional dynamics coupled with a connectome derived from  
99 a subject from the Human Connectome Project [49]. We applied Balloon-  
100 Windkessel model [50] to the simulated neuronal mass activity to generate  
101 realistic BOLD signals. From these, we computed the Dynamical Functional  
102 Connectivity (dFC) that captures the changes in the system’s dynamics on the  
103 slow time scale, which we compared with empirical recordings. The fast neu-  
104 ronal activity is decomposed in a  $2N$ -dimensional state space using Principal  
105 Component Analysis (PCA) to unveil the low-dimensional manifold on which  
106 the system evolves (see Materials and Methods for more details).

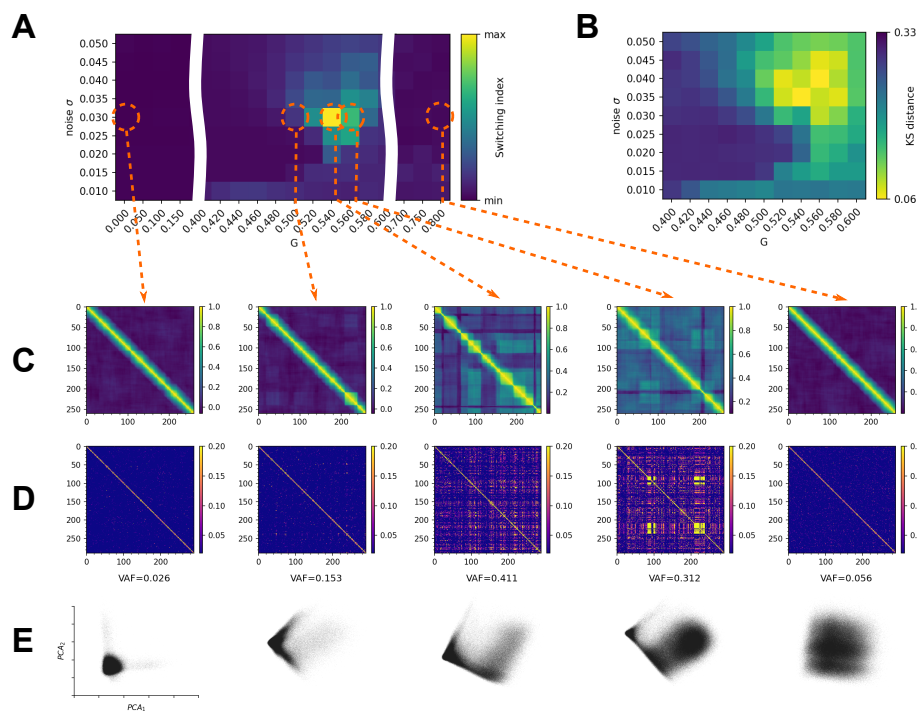
107 When driven by noise, the network of the bistable MPR nodes has the ca-  
108 pacity to exhibit realistic dFC when the network input is scaled appropriately  
109 [44]. The noise together with the network input drives the switching between  
110 up- and down-state of the individual nodes, while the network mediates the co-  
111 ordination reflected in the functional connectivity. In the following sections, we  
112 explore how the manifold of the resting state activity arises from the networked  
113 interactions, how it shapes the multistability of the functional connectivity in  
114 the simulated BOLD, and how it relates to empirical observations.

## 115 2.1 Symmetry breaking: working point for dFC

116 To assess the impact of the symmetry breaking by the connectome, we simu-  
117 lated 10 minutes of spontaneous activity for a range of values of the coupling  
118 scaling parameter  $G$  and noise variance  $\sigma$ , and applied PCA to the source signal  
119  $\Psi(t)$  and dFC to the BOLD (Figure 2). We used the variance accounted for  
120 (VAF) of the first two PCA components as an estimate for the dimensionality  
121 of the system’s dynamics in the state-space (Figure 2D), and the variance of the  
122 upper triangle of the dFC matrix as a measure of the *fluidity* of the system’s  
123 dynamics—that is the propensity to dwell in specific brain states (defined by the  
124 functional connectivity) and shift and return between several such states (Fig-  
125 ure 2A). In addition, using Kolmogorov-Smirnov distance between the centered  
126 distributions of the values of the upper triangle of the  $dFC_w$  in the empirical  
127 and simulated data, we have verified that the region of the parameter space  
128 where dFC is most similar to the one derived from empirical data overlaps with  
129 the region with the highest fluidity, Figure 2A.

130 For low values of  $G$ , the system exhibits high-dimensional dynamics as re-  
131 flected in the low variance explained by the first PCA components and low  
132 values of the variance of the off-diagonal values of dFC with the mean around  
133 0—reflecting the absence of recurrence in the system dynamics (Figure 2B,C).  
134 Note, that the explained variance for each PCA component is equal to  $1/N$   
135 (in this case  $N = 84$  nodes of the network), and the projection in panel D  
136 reflects the independent infrequent switching of two nodes, each captured by  
137 one PCA component. Around the value of  $G = G_w = 0.525$  and  $\sigma_w = 0.030$   
138 (working point) the variance explained by the first two components of the PCA

139 increases substantially, and so does the fluidity of the dFC as the characteristic  
140 intervals of FC invariance (on-diagonal nonzero blocks) appear together with  
141 similarity across time (high off-diagonal correlations). Past the working point  
142 ( $G > 0.6$ ) the explained variance in PCA drops as well as the off-diagonal dFC  
143 correlations, signifying increase in dimensionality of the spontaneous dynamics.



144

145 **Figure 2: Brain network model and symmetry breaking.** The brain  
 146 network model is simulated for varying levels of global coupling parameter  $G$   
 147 and noise variance  $\sigma$  to produce both time-series of the state space variables  
 148  $\mathbf{r}(t)$ ,  $\mathbf{V}(t)$ , and the BOLD signal. For each combination of  $G$  and  $\sigma$  we compute  
 149 the sliding window  $dFC_w$  matrix from the simulated BOLD signal, and quantify  
 150 the "switching index" of the dFC as the variance of the upper triangle (A).  
 151 Kolmogorov-Smirnov distance of the centered (mean-subtracted) distributions  
 152 of the values of the upper triangle of the dFC computed from empirical and  
 153 simulated resting state BOLD time series. The region of parameter space where  
 154 the distributions are closest overlaps with the region with high fluidity of dFC  
 155 (B). For selected values of  $(G, \sigma)$  we show the sliding window  $dFC_w$  (C), edge  
 156 based  $dFC_e$  (D) and the projection of  $\mathbf{r}(t)$  time series in the first two PCA  
 157 components (E) annotated with corresponding fractional variance accounted  
 158 for (VAF). In the working point around  $G = 0.54$  and intermediate values of  $\sigma$   
 159 the system exhibits recurrence in the large-scale dynamics as captured by non-  
 160 zero switching index, and reduction of dimensionality as captured in the increase  
 161 in explained variance by the first PCA components and the asymmetry in the  
 162 respective projection. For values of  $G$  below or above the working point, the  
 163 systems loses the fluidity property as reflected in the absence of the off-diagonal  
 164 blocks on the dFC, and exhibits high-dimensional dynamics.

## 165 2.2 Network dynamics

166 Before we delve into the characterization of the low-dimensional manifold, let  
167 us first describe the network dynamics in detail. For the MPR model, the dy-  
168 namical profile of an isolated node in the bistable parametrization consists of  
169 an unstable fixed point (saddle node) and two stable fixed points: down-state  
170 stable node and up-state focus (Figure 3A). Considering the uncoupled system,  
171 that is, the joint dynamics of the  $N$  populations (nodes) in the absence of any  
172 inter-population synaptic coupling, the phase flow is represented by  $2^N$  stable  
173 fixed points that contain all possible combinations of the populations firing at  
174 either their low or high mean firing rates (down or up state, respectively). Start-  
175 ing from an initial condition, the system will settle into the nearest accessible  
176 such fixed point, a stable network state composed of a corresponding combina-  
177 tion of regions in their up or down state. Thus, the dynamics of the uncoupled  
178 system in phase space can be thought of as being driven by a potential energy  
179 landscape with multiple stable local minima representing the stable attractor  
180 states of the network. In fact, the uncoupled system, as such, is invariant under  
181 permutation of the indexes of the populations, such that these latter attractor  
182 network states are distinguished only in terms of the respective number of nodes  
183 in up and down states. The global dynamics of the system, thus, collapses in  
184 finite time onto this stable attractor state composed of a finite set of stable  
185 equilibrium points that is invariant under shuffling of indexes of the nodes.  
186 The associated global phase flow can be decomposed into  $N$  projections onto  
187 the identical 2D phase planes of individual populations, depicted in Figure 3A.  
188 Viewed from this perspective, the structure of the basins of attraction of the  
189  $2^N$  stable system equilibrium points redundantly inherits, in higher dimensions,  
190 the relative structure of the basins of attraction of the two stable fixed points  
191 of an individual population. For an isolated node, varying the external input  
192  $I_i$  changes the size of the basins of attraction of the stable fixed points. This  
193 modulates the probability of switching between the two states when driven by  
194 noise as captured by the mean escape times (Figure 3A, see Methods for more  
195 detail). For a connected node, the external input  $I_e$  depends on the state of the  
196 neighboring nodes (see Equation 4), fluctuating as they transition between the  
197 up- and down-state. On the network level, given right scaling of the network  
198 connections, this enables the cascades of up- and down-state switching at the  
199 fast time-scale, and the co-fluctuation of the BOLD signal (Figure 3B).

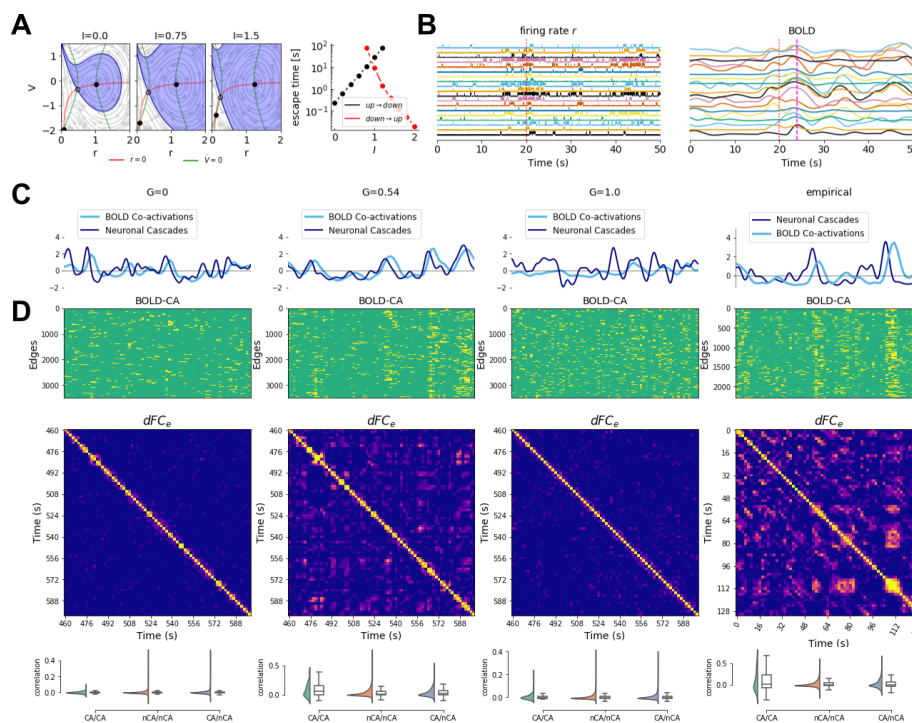
200 To understand better the dynamical underpinning of the increase of fluidity  
201 of the dFC we assess the characteristics of the co-fluctuations of the BOLD  
202 signal and the cascades in the source signal. For the co-activations, we start  
203 from the edge time series which is defined as pairwise dot product of z-scored  
204 BOLD signal (an average over the edge time series would correspond to the  
205 pearson correlation). The correlation across time-points yield the  $dFC_e$  matrix  
206 capturing the recurrence of the edge configurations, and the root sum squared  
207 (RSS) over the edges at each time point captures the contribution of that par-  
208 ticular time point to the overall functional connectivity (see Methods for more  
209 details). The time-points crossing the 95-th percentile threshold of the RSS are



210 considered as strong co-activation events. The neuronal cascades [44] are long  
211 lasting perturbations of the neuroelectric activity and are measured on a global  
212 level as a sum over regions of the binarized firing rate activity (at the threshold  
213 of 3 standard deviations). We compared these measures between the working  
214 point  $G_w$ , the disconnected system  $G = 0$ , the strong network coupling regime  
215  $G \gg G_w$ , and the empirical data (Figure 3C,D).

216 In the working point  $G_w$  the co-activations include large number of edges  
217 (Figure 3D) and the RSS follows the number of cascades up to a short delay  
218 corresponding to the delay of the BOLD signal. Moreover, some of the strong  
219 co-activations re-occur partially in time as reflected in the non-zero elements  
220 of the  $dFC_e$  matrix. The same profiles can be observed in the empirical data,  
221 namely in the simultaneous EEG and fMRI recordings. On the other hand,  
222 the characteristic spatial and temporal structure is lost outside of the working  
223 point, that is either for the weakly coupled system ( $G \ll G_w$ ), or for too strong  
224 coupling ( $G \gg G_w$ ).

225 To quantify how the co-activation events contribute to the characteristic  
226 similarity across time, we compare the correlation of the edge vectors during the  
227 events, during the non-events, and between events and non-events. As a result  
228 we observe an increased similarity of the edge vectors during the events both in  
229 the empirical data and in the simulations in the working point  $G_w$ . Again, this  
230 property is lost for too weak ( $G \ll G_w$ ) or for too strong coupling ( $G \gg G_w$ ).  
231 Together, these results show, that the system has a similar dynamical profile  
232 in the working point  $G_w$  as observed in the empirical data with respect to the  
233 network-carried fluctuations on both the fast and slow timescales (as captured  
234 by  $dFC$  and cascades respectively).



235

236 **Figure 3: Network dynamics.** (A) The network input  $I$  modulates the  
 237 probability of a noise-driven transition between the down- and up-state. (B)  
 238 Example of a cascade—coordinated increase in activity translating to a delayed  
 239 correlated peak in the BOLD signal. Below we compare the network dynamics  
 240 in and outside the working point, and the empirical data. In both empirical  
 241 data and the working point ( $G = 0.54$ ), the BOLD co-activations follow the  
 242 neuronal cascades with a latency (C), and show distinct spatial profiles which  
 243 are recurrent in time (D): edge time series on the (top panel) captures the  
 244 spatial profiles of the co-activations, the similarity across time is captured by  
 245 the  $dFC_e$  matrix (middle panel), and the distributions of correlation between  
 246 co-activation events (CA) and non-events (nCA) is compared (bottom panel).

### 247 2.3 Manifold of the resting state and characteristic sub- 248 spaces

249 Having characterized the dynamics of the system in the working point with an  
 250 appropriate measure, we proceed with the description of the manifold on which  
 251 it evolves—that is to show that this behavior is low-dimensional and constrained  
 252 to a specific subspace. To relate cascades and co-activations to the trajectories  
 253 of the system in the  $2N$ -dimensional state space, we first select time intervals  
 254 with similar functional connectivity. Starting from the edge time series for  
 255 the magnitude of co-fluctuations, we clustered the time points using k-means

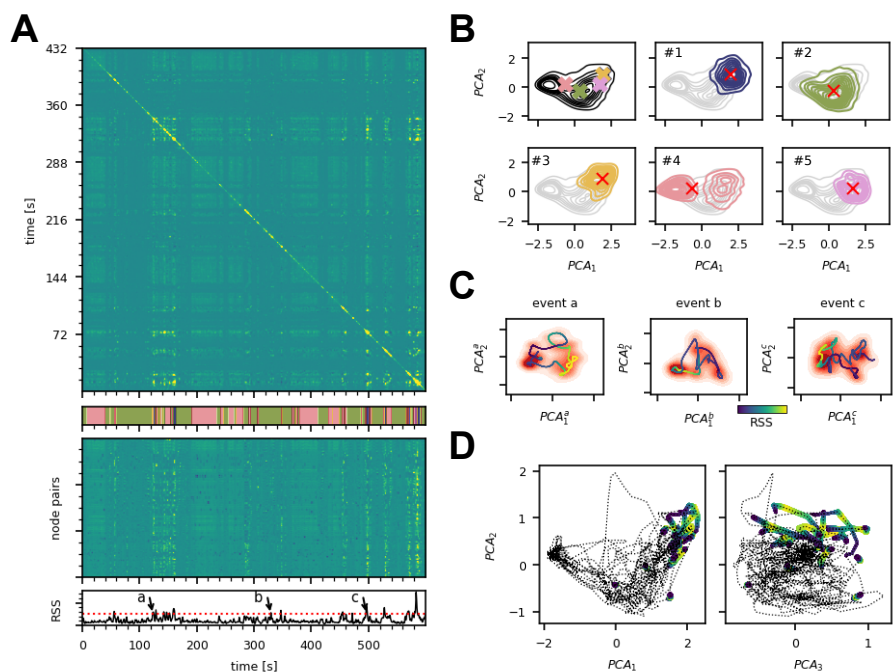
256 ( $k=5$ ). This separated the high-activity intervals (majority of the nodes in the  
257 up-state), low-activity intervals (majority of the nodes in the down-state), and  
258 the co-fluctuation events (Figure 4A).

259 Next, we identified the trajectories of the system underlying each cluster  
260 in the low dimensional projection of state space. For each cluster, we have  
261 selected the corresponding time points in the state space of the system, and  
262 projected them into the first two principal components of the PCA computed  
263 on the complete time series. We have observed that while the corresponding  
264 subspaces overlap partially in the projection (Figure 4B, colors correspond to  
265 the clusters), the activity within the clusters concentrates to different subspaces.  
266 This concentration in different subspaces is reflected in the distance between the  
267 centroids of the cluster time points in the PCA projection.

268 While the cluster activity overlaps in the projection in the components of  
269 the PCA computed from the whole time series, the co-activation trajectories be-  
270 come clearer by choosing different basis to span the low-dimensional space, that  
271 is, to compute the PCA from the time points corresponding to the individual  
272 co-activation events. To project the trajectories of the events observed at the  
273 slow time scale of the BOLD on the manifold, we have shifted the BOLD signal  
274 by the characteristic lag, and for each BOLD time point belonging to the cluster  
275 we selected the corresponding time points in  $\mathbf{r}(t)$ , and convolved the resulting  
276 data with a Gaussian kernel to smoothen out the noisy fluctuations (see Meth-  
277 ods for details). We then spanned the subspace corresponding to the first two  
278 PCA components of the co-fluctuation trajectory and overlaid the smoothened  
279 trajectory over the density plot of the full  $\mathbf{r}(t)$  time series. The density plots  
280 (shades of red, Figure 4C) of the example events show a separation of the event  
281 subspace marked by the peak in the RSS (shown in yellow in Figure 4C) on  
282 the smoothened trajectory from the rest of the manifold. This suggests that  
283 the event subspace is relatively stable, allowing the system to dwell in it long  
284 enough to cause the significant peaks in the slow BOLD signal, and that the  
285 intermediate states are less stable than the event subspace or the rest of the  
286 manifold and visited only transiently.

287 Although the linear embedding of the whole time-series does not separate  
288 the event trajectories well when applied to the  $\mathbf{r}(t)$  time series, the event trajec-  
289 tories concentrate in the high-activity subspace spanned by the first two PCA  
290 components of the BOLD signal (Figure 4D).

291 Together, these results chart the low-dimensional manifold of the system in  
292 the working point regime, associating the subspaces with specific flows. The  
293 fluid dynamics as characterized in the previous section then arise from the slow  
294 transitions between the low- and high-activity subspaces, where the latter sup-  
295 ports the strong co-activation events which are reflected in the  $dFC$ .



296

297 **Figure 4: Manifold subspaces and characteristic dynamics.** (A) The  
 298 edge-based dynamic functional connectivity  $dFC_e$  of a simulation of the model  
 299 in the working point (top) shows the off-diagonal structure of similarity of the  
 300 system's activity across time. The edge time series (middle) shows the time evolu-  
 301 tion of the functional connectivity of the simulated BOLD signal between each  
 302 of the node pairs, and exhibits the characteristic co-activation events defined as  
 303 time points with the root sum squared (RSS, bottom) crossing the threshold of  
 304 95th percentile. Dividing the edge-time series into 5 clusters (k-means, shown  
 305 in the colorbar under the dFC) has separated the event and non-event time  
 306 points, and also differentiated the events based on their respective similarity.  
 307 (B) The time intervals in  $\mathbf{r}(t)$  corresponding to the 5 clusters were selected; in  
 308 the first panel the centroids of the time points of the individual clusters are  
 309 marked with a cross in the projection to the first two principal components of  
 310 the whole time series, following panels show the projection of the  $\mathbf{r}(t)$  intervals  
 311 of particular clusters. Cluster #2 captures the high-activity subspace, cluster #4  
 312 corresponds to the low-activity state, and the clusters #1, #3, and #5 capture  
 313 the co-activation events. (C) Local trajectories in the manifold subspaces: the  
 314 time series of the three example events (a,b,c, marked in the panel A bottom)  
 315 was projected to the first two components of PCA applied to each time seg-  
 316 ment individually. The smoothened trajectory marks the advance of the system  
 317 through the event and out of it, and is colored by the value of RSS (yellow at the  
 318 peak of the event blue at the beginning and the end). (D) The event trajectories  
 319 on the manifold. The trajectory of the simulated BOLD signal is projected in  
 320 the space defined by the first three PCA components with the events colored  
 321 by the RSS value (yellow at the peak of the event).

## 322 2.4 Fixed point skeleton and structured flow

323 To understand how the resting state manifold arises, we start by considering the  
324 uncoupled system, that is, the joint dynamics of the  $N$  populations (nodes) in  
325 the absence of any inter-population synaptic coupling. This uncoupled system's  
326 phase flow is dominated by  $2^N$  stable fixed points that represent all possible  
327 combinations of the populations firing at either their low or high mean firing  
328 rates (down or up state, respectively). Starting from an initial condition and  
329 in the absence of noise, the BNM will settle into the nearest accessible such  
330 fixed point, a stable network state composed of a corresponding combination of  
331 regions in their up or down state.

332 The dynamical effects of the symmetry breaking in the BNM are delineated  
333 by the topology of the connectome. The heterogeneity of the in-degree (to-  
334 tal connectivity) of individual nodes of the network drives a variation in the  
335 relative positioning of the separatrices between the basins of attraction of the  
336 equilibrium points, mirrored in the variation of the corresponding projections  
337 onto the 2D phase planes of corresponding nodes (see Figure 3A). In conjunc-  
338 tion, connectivity strength and topology give rise to gradients in the relative  
339 attractiveness of the system's equilibrium states. This attractiveness (or sta-  
340 bility) can be quantified by the largest negative real eigenvalues obtained from  
341 the linearization of the system about the respective equilibrium state (linear  
342 stability analysis).

343 To map the complete manifold outside the simulated trajectories we sampled  
344 the stable fixed points for varying coupling scaling parameter  $G$  from the  $2^N$   
345 combinations of up- and down-states, and evaluated their stability (see Methods  
346 for more details). We found that the number of stable fixed points in the sample  
347 decreases with increasing  $G$ . This decrease is due to the loss of states with mixed  
348 composition of up- and down-state due to the bifurcation of the down state in  
349 nodes with high input (Figure 5A). Projecting the  $\mathbf{r}$  component of the fixed-  
350 points in the first two eigenvectors of the Laplacian confirms this thinning of the  
351 intermediate compositions biased towards those with higher number of nodes in  
352 the up-state (corresponds to the first Laplacian eigenvector  $\lambda_1$ ). Additionally,  
353 the stability of the fixed points was inversely proportional to the number of  
354 nodes in the up-state, that is in the direction of  $E_1$  the first eigenvector of the  
355 Laplacian (Figure 5B).

356 To put this into the context of the simulated trajectories, we have next iden-  
357 tified the fixed points around which the simulated trajectory evolved by taking  
358 initial conditions from the simulated trajectory, and integrating the system with-  
359 out noise to the equilibrium. We have confirmed that in all instances the system  
360 reached a stable fixed point composed of combination of up- and down-states,  
361 and that the stability of these fixed points follows the same gradient in terms  
362 of the composition (Figure 5C).

363 Furthermore, the nodes of the network exhibit a frequency gradient of the  
364 oscillations in the up-state (Figure 5D). This gradient reflects variability of the  
365 characteristic frequency in the up-state across nodes in the network. In the  
366 fixed-point state, if the nodes are treated as isolated systems with an input

367 current term based on the existing network state, then

$$\begin{aligned} r_i^* &= r^* + \delta_i^r \\ v_i^* &= v^* + \delta_i^v \end{aligned} \quad (1)$$

368 where  $(r^*, v^*)$  are the symmetric fixed-points of the network and  $(\delta_i^r, \delta_i^v)$  are the  
369 excursions from the symmetric fixed-point and change according to the existing  
370 network state. These excursions depend directly on the in-strength of the  $i$ th  
371 node and the local states of its first neighbours.

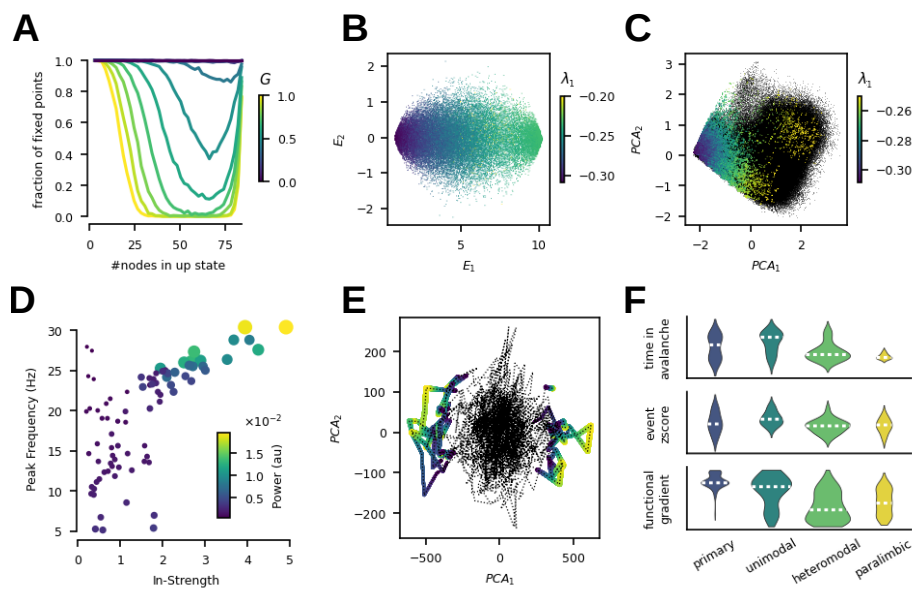
372 Following linear stability analysis of the  $i$ th system around the fixed-point  
373 (see Methods), the eigenvalues of the Jacobian matrix are given by

$$\begin{aligned} \lambda_{1,2} &= 2v_i^* \pm \sqrt{Jr_i^* - 4\pi^2 r_i^{*2}} \\ &= 2v_i^* \pm \sqrt{2Jr_i^* - 4\pi^2 r_i^{*2} + 2J\delta_i^r - 4\pi^2 \delta_i^{r2} - 8\pi^2 r^* \delta_i^r} \end{aligned} \quad (2)$$

374 From the above equation, we see that the frequency of oscillations in the up-  
375 state of the  $i$ th node increases proportional to  $\delta_i^r$  and therefore proportional to  
376 the in-strength of the node, which we also observe in the simulation (Figure 5D).

377 Furthermore, applying the PCA projection on the empirical BOLD time-  
378 series, we have identified a similar separation of the event trajectories in the  
379 global embedding as observed in the simulations (Figure 5E). However in the  
380 case of the empirical data the system exhibits both the co-activations and co-  
381 deactivations as seen on the separation through the first PCA component.

382 Lastly, symmetry breaking by the connectivity alone results in a spatial  
383 organization of the above described flow which is aligned with empirically ob-  
384 served trends (Figure 5F). In particular, per region the time spent in avalanches  
385 and the cumulative z-scored BOLD signal within events both decrease across  
386 the cortical hierarchy from the primary to paralimbic regions. The established  
387 principal functional gradient extracted from the empirical fMRI data is also  
388 aligned along this axis .



389

390 **Figure 5: Mechanistic structure of the manifold.** (A) Composition of  
 391 the sampled stable fixed points in terms of number of nodes in the up-state as  
 392 a function of  $G$ , normalized to  $G = 0$ . (B) Projection of the stable fixed points  
 393 into the first two leading eigenmodes of the network Laplacian  $E_1, E_2$ , color  
 394 coded with the value of the largest eigenvalue in the linear stability analysis.  
 395 (C) Fixed points (colored) derived by noise-free integration to equilibrium from  
 396 the trace of a simulation (black) in the working point  $G_w$ , color coded by the  
 397 value of the largest eigenvalue  $\lambda_1$ . (D) Frequency peak in the simulated source  
 398 activity of each of the regions plotted against the node structural connectivity  
 399 in-strength. (E) Empirical BOLD time series projected into the first two PCA  
 400 components with the events colored by the RSS value (yellow in the peak). (F)  
 401 Across the cortical hierarchy, the time spent in avalanches of the  $\mathbf{r}(t)$  time-  
 402 series (top) decreases, as does the cumulative z-scored simulated BOLD from  
 403 the event time-segments (middle). The spatial distribution of the principal  
 404 functional gradient extracted from empirical fMRI is also aligned along the  
 405 cortical hierarchy (bottom).

### 406 3 Discussion

407 Using a combination of computational modeling and dynamical systems analy-  
 408 sis we have provided a complete mechanistic description in terms of constituent  
 409 entities and their causal activities leading to spontaneous co-activations and  
 410 neuronal cascades in the brain's resting state [44]. We showed how the breaking  
 411 of the symmetry of the BNM's connectivity gives rise to the structured low-  
 412 dimensional dynamics in the phase space and recurrent fluctuations of the func-



413 tional connectivity (Figure 2). These fluctuations arise from network-mediated  
414 cascades of up- and down-state switching and capture well the empirically found  
415 relationship between the strong co-activation events and the recurrence struc-  
416 ture reflected by the functional connectivity dynamics (Figure 3). The subspace  
417 accessible to the brain in this regime was charted and partitioned according to  
418 the characteristic flow associated with each of the partition (Figure 4). Finally,  
419 this subspace and its associated flows arise from the rich fixed point structure  
420 of the system and the differential stability of the nodes in these fixed points is  
421 not only reflected in the propensity to state switching that reflects the corti-  
422 cal hierarchy, but also influences the dominant oscillation frequency (Figure 5).  
423 In summary, these results support our hypothesis that the recurrent functional  
424 connectivity states of the resting state correspond to distinct subspaces on a  
425 low-dimensional manifold associated with distinct structured flows.

426 The central result of our work is that the symmetry breaking via the struc-  
427 tural connectivity carves out an attractive subspace of all the possible states  
428 of the brain, and that the flow on this manifold governs the characteristic dy-  
429 namics of the brain (that is discarding the transient towards the manifold from  
430 arbitrary initial conditions). In this regime, the model captures the multistabil-  
431 ity and noise-driven exploration of the dynamic repertoire explored previously  
432 in computational studies [2, 31, 32, 51, 52]. The data features extracted from  
433 the time series provides a link between the empirical data and the model. Here,  
434 the functional structure in the brain is carried by the rare high amplitude co-  
435 fluctuation events as it was previously demonstrated in empirical fMRI data [19,  
436 21, 53], and in simultaneous EEG and fMRI measurements [44]. Similarly, re-  
437 cent modeling study has shown the role of structural modules of the network in  
438 shaping the co-fluctuation events [54], which is aligned with the brain network  
439 as the symmetry breaking gives rise to the low-dimensional dynamics.

440 The slow time scale fluctuations of the dynamical functional connectivity  
441 reflect the movement of the brain activity between the low- and high-activity  
442 subspaces of the manifold. The flow in the high-activity subspace supports  
443 the cascades, which in turn are reflected in the high activity coactivations. This  
444 movement points to the multistable rather than metastable interpretation of the  
445 resting state dynamics [55], and reflects the observation of switching between a  
446 low-amplitude incoherent and high-amplitude coherent states in empirical data  
447 [56]. Furthermore, the slow transitions between the high- and low-activity sub-  
448 spaces is compatible with the reports on the spontaneous infra-slow brain ac-  
449 tivity [57, 58] and the detailed reports on its spatio-temporal structure. For  
450 example, the slow traveling waves [22] propagating along the principal gradi-  
451 ent of cortical organization [59, 60] would provide a refined description of the  
452 trajectory through the manifold subspaces.

453 The attractive subspace of the low-dimensional manifold and the associated  
454 structured flow arise in the presented system from the changes in the fixed-  
455 point structure due to the irregular connectivity. In particular, the network  
456 input mediates the modulation of the escape times of the noise-induced transi-  
457 tions. These chain into domino-like sequences [61, 62], which in turn constitute  
458 the neuronal cascades. On a network level, our results elaborate the previous



459 analytical results of increased entropy of the attractors in an Ising-spin network  
460 model for intermediate values of coupling strength [63]. The relationship to  
461 the dimensionality of the exhibited dynamics is such that for the low values of  
462 coupling strength  $G$ , where the Ising model is in the trivial state with all spins  
463 equal to 0, the model presented here is also driven by noise to the all-down  
464 state due to the significantly larger basin of attraction of the down-state, and  
465 the nodes make uncoordinated noise-driven excursions to the up-state reflected  
466 in the high-dimensionality of the dynamics. For high values of  $G$  the situation is  
467 opposite, and for intermediate values of  $G$  the Ising model exhibits high entropy  
468 of attractors, which is in our case reflected in the available states organized in  
469 the low-dimensional manifold with the structured flow governed by the stability  
470 of these states.

471 Overall, the movement of the system through the subspaces of a low-dimensional  
472 manifold is in accordance with empirical and modeling results on recurrence and  
473 state clustering of resting state fMRI BOLD recordings. Using clustering algo-  
474 rithms to partition the BOLD time series yields statistically similar and tempo-  
475 rally recurrent whole brain spatial coactivation patterns [18, 45] associated  
476 with specific dwell times and transition probabilities. However, compared to the  
477 clustering approaches applied to the BOLD time-series, the SFMs allows us to  
478 refine the partitioning of the state-space in two aspects: we unfold the subspaces  
479 based on the similarity of the coactivations on the level of the BOLD signal, and  
480 we provide a detailed description of the flow of the system in these subspaces  
481 e.g. in terms of the cascades. The former is in line with the recent advances  
482 regarding the low-dimensional representation of meso- [64, 65] and macroscopic  
483 [66, 67] brain dynamics, but the latter describes the origin of those subspaces  
484 as constrained by the connectome. Interestingly, the clustering of phase-locking  
485 BOLD states [43] leads to very similar low-dimensional representation of the  
486 resting state dynamics to our approach, with a single dominant global phase  
487 locked state and a number of transient partially phase-locked states related to  
488 functional networks. Similarly, by embedding the resting state data onto the  
489 task manifold extracted with the help of diffusion maps, [68] found that rest-  
490 ing state time-points concentrate in the task-fixation and transition subspaces,  
491 and only a minority of time-points reach to the cognitive subspaces of the task  
492 manifold.

493 The description of the structured flow addresses also the fast time-scale by in-  
494 cluding the cascades, which we previously showed to relate to the co-activations  
495 observed in the BOLD signal [44]. In EEG literature, the spatio-temporal struc-  
496 ture of the resting state dynamics is characterized with the help of microstates—  
497 sensor-level transient patterns lasting on average for 60-150 ms [69]. Attempts  
498 have been made to relate the microstates to BOLD activation clusters [70, 71],  
499 but identifying the sources generating the microstates with clustering or regres-  
500 sion analysis has been challenging so far due to unclear relationship between the  
501 broadband EEG activity and the BOLD signal fluctuations [72]. To advance  
502 we propose to reframe the question as a search for a shared manifold of the  
503 neuronal activity with specific slow and fast time-scale characteristics which in  
504 turn are reflected in the EEG and the BOLD observables.

505 The manifold we describe is conceptually reminiscent of energy landscapes  
506 described in previous works [40, 41]. However, previous energy landscape mod-  
507 els, such as in [41], implicitly assume energy minimization and thus, by con-  
508 struction, encode the hypothesis that the activation of two brain regions that  
509 are connected via a direct structural connection is more energetically favorable  
510 than that of two regions that are not directly connected. We make no such  
511 assumption here and, instead, the effective energy landscape emerges, in the  
512 form of a low dimensional manifold, out of the interplay of the non-linearity in  
513 the local neural mass model and the connectome, thus fully embracing the the  
514 network impact, beyond the pair-wise interactions. In addition, previous en-  
515 ergy landscape analysis [40] assumed that the network changes only gradually  
516 by flipping one region at a time, and did not account for transitions in which  
517 several regions flip simultaneously. Treating the brain as a whole, the BNM  
518 that we presented here instead allows for such latter transitions of the system  
519 in state space, which may very well be due to strongly connected regions that  
520 are able to simultaneously influence their nearest neighbors during coactivation  
521 events.

522 It is worth pointing that our framework covers only one part of the mecha-  
523 nisms that shape the brain’s manifold and the flow on it, that is the connectome.  
524 We have assumed identical parameters for each region, ignoring the known struc-  
525 tural hierarchies [73], which have been shown to improve the predictive value of  
526 the BNMs [56, 74, 75]. While we observed differential functional properties of  
527 the nodes across the cortical hierarchy [76], we didn’t recover the exact spatial  
528 correspondence to the established functional gradients [59]. Neuromodulation  
529 and the subcortical drives [77] are another missing aspect that similarly improve  
530 the performance of BNMs [78]. However, both of these elements are not yet es-  
531 tablished in the framework of BNMs, as is the impact of the connectome [24].  
532 Thus our goal here is not to generate *in silico* observables that are as close as  
533 possible to the empirical one, which nevertheless differ a lot depending on the  
534 preprocessing, e.g. see [79], but to focus on the generative mechanisms for the  
535 key data features across time-scales and neuroimaging modalities that render  
536 functional activity identifiable across subjects [12, 13, 80].

537 A natural next step will be to extend the analysis to include the impact  
538 of the data-informed regional variance [81] which is now reachable by TVB  
539 through Ebrains [82]. Similarly intriguing direction for the extension of the  
540 framework presented here is in more refined inclusion of the subcortical struc-  
541 tures, especially their impact through the neuromodulation. Notably, recent  
542 works [77, 83, 84] exploring the role of thalamus, locus coeruleus, and basal nu-  
543 cleus of Meynert in shaping of the dynamical landscape of the cortical activity  
544 are already formulated in the dynamical systems language while incorporating  
545 carefully the detailed anatomical and cytoarchitectural knowledge. Integrating  
546 these advances in the SFM framework is a natural next step towards the origi-  
547 nal motivation of SFM, that is to link the mesoscopic neuronal activity to the  
548 behaviour, as the intricate interactions between cortex and the subcortical areas  
549 are one of the organizing principles of the underlying the biological mechanisms  
550 supporting behaviour [85].

551 Parcellation-induced variation of empirical and simulated brain connectomes  
552 at group and subject levels is another issue that needs to be considered [86].  
553 Nevertheless, we focus on general mechanisms without going on regional level  
554 specificities, so the choice of parcellation should not play such a role.

555 In conclusion, our results show how the low-dimensional dynamics arises  
556 from breaking the symmetry in the brain on the level of the connectome. De-  
557 scribing these dynamics as structured flows on manifolds allows us to bridge the  
558 gap between the observational measures and the state-space trajectories of the  
559 system. As such, this object is well suited for comparison across different mod-  
560 els, scales, and neuroimaging modalities, and provides means for integration of  
561 the diverse descriptions of the resting state dynamics.

## 562 4 Materials and methods

### 563 4.1 Brain network model

564 Computational brain network model [87] is used to simulate resting state activity  
565 under varying values of network coupling scaling parameter  $G$ . The dynamics  
566 of each of the network nodes were governed by the neural mass model (NMM)  
567 derived analytically as the limit of infinitely all-to-all coupled  $\theta$ -neurons [48],  
568 namely for  $i$ -th node for the firing rate  $r_i$  and membrane potential  $v_i$  as:

$$\begin{aligned}\tau_c \dot{r}_i &= \frac{\Delta}{\pi \tau_c} + 2r_i v_i, \\ \tau_c \dot{v}_i &= v_i^2 + \eta - (\tau_c \pi r_i)^2 + J \tau_c r_i + I_i,\end{aligned}\tag{3}$$

569 where  $I_i$  is the input current,  $\eta$  is the average neuronal excitability,  $J$  is the  
570 synaptic weight,  $\Delta$  is the spread of heterogeneous noise distribution, and  $\tau_c$   
571 is the characteristic time.

572 The  $N$  nodes are then coupled with a connectome derived from empirical  
573 data as

$$I_i(t) = G \sum_j W_{ij} r_j(t - D_{ij}),\tag{4}$$

574 where  $G$  is the network scaling parameter,  $W_{ij}$  is the connection weight,  $D_{ij} =$   
575  $L_{ij}/S$  is the delay caused by propagation of the signal on a tract of length  
576  $L_{ij}$  with finite speed  $S$ . We picked the speed  $S = 2m/s$  from the biologically  
577 plausible range [88], and a connectivity matrix of a subject from the Human  
578 Connectome Project [49] in the Desikan-Killiany parcellation [89] with 84 regions  
579 including subcortical structures.

580 The equations 3 and 4 comprise the drift  $a(\Psi, t)$  in the stochastic delay  
581 differential equation formulation with linear additive noise reading:

$$d\Psi(t) = a(\Psi(t))dt + b(\Psi(t))dW(t),\tag{5}$$

582 where  $\Psi$  is the state vector  $[\psi_1, \dots, \psi_n]$  with  $\psi_n = [r_n, V_n]$ ,  $dW(t)$  is a differential  
583 of a Wiener process with Gaussian increment with variance  $\sigma^2$ , and  $b(\Psi, t) = 1$   
584 is the diffusion coefficient—here constant yielding the noise term additive.

585 The model was implemented in The Virtual Brain [47] and equipped with  
 586 BOLD forward solution comprising the Balloon-Windkessel model applied to  
 587 the firing rate  $\mathbf{r}(t)$  [50].

588 The model parameters  $\eta = -5.0$ ,  $J = 15.0$ ,  $\tau_c = 1.0$ , and  $\Delta = 1.0$  were  
 589 selected to set the nodes in the bi-stable regime in the absence of coupling [48].  
 590 We then varied the global coupling parameter  $G$  and the noise variance  $\sigma$ , and  
 591 simulated 10 minutes of resting state BOLD activity with  $TR = 720ms$  after  
 592 discarding 10 seconds of the initial transient from random initial conditions.

## 593 4.2 Functional connectivity dynamics

594 In order to track the time-dependent changes in the functional connectivity, we  
 595 compute the windowed dynamical functional connectivity  $dFC_w$  [32, 90] and  
 596 edge dynamical functional connectivity  $dFC_e$  [44]. Starting from the regional  
 597 BOLD time-series  $B_n(t)$  for each node  $n$ , we compute functional connectivity  
 598 matrices  $FC(w)$  for each time window  $w = 1 \dots W$  defined as  $B_n(t)|_{t_w}^{t_w + \tau}$  with  
 599 window length  $\tau = 60s$  and window step size  $t_{(w+1)} - t_w = 2s$ . Next we compute  
 600 the  $dFC_w$  matrix of order  $W$  as

$$dFC_w(i, j) = \text{corr}(FC(w_i)^\Delta, FC(w_j)^\Delta), \quad (6)$$

601 where  $FC(w)^\Delta$  is the vectorized upper part of the  $FC$  matrix.

602 For the window-less  $dFC_e$  [44] we start from the edge time-series [21] defined  
 603 as  $E_{nm}(t) = z_n(t)z_m(t)$  for  $n, m = 1 \dots N$  where  $z_n(t) = \frac{B_n - \mu_n}{\sigma_n}$  is the z-scored  
 604 BOLD time-series of a node  $n$ . The edge dynamical functional connectivity  
 605 is then computed as correlation between the edge vectors at each pair of time  
 606 points  $t_1, t_2$ :

$$dFC_e(t_1, t_2) = \text{corr}(E_{nm}(t_1), E_{nm}(t_2)). \quad (7)$$

607 The co-fluctuation events (CF) are defined as time points in the edge time-  
 608 series  $E_{nm}(t)$  during which the root sum squared  $RSS = \sqrt{\sum_{nm} E_{nm}^2(t)}$  crosses  
 609 a given threshold, here chosen as 95th percentile. Time points where  $RSS$  is  
 610 below the threshold are then labeled as non-events (nCF).

611 The avalanches were computed on the binary mask  $\mathbf{a}(t)$  on the  $\mathbf{r}(t)$  such  
 612 that  $a_i(t) = 1 \iff z(r_i(t)) > 3$  where  $z(r_i(t))$  is the z-score of firing rate  $r$  of a  
 613 node  $i$ .

## 614 4.3 Manifold subspaces

615 As a first step in the analysis of the local dynamics specific to a particular  
 616 attractive subspace, we have extracted the time-points belonging to these sub-  
 617 spaces with k-means clustering applied to the edge time series  $E_{nm}(t)$ . We  
 618 varied the number of clusters  $k$  and selected  $k = 5$  at which the co-fluctuation  
 619 events separated to distinct cluster.

620 To extract the segments of  $\mathbf{r}(t)$  corresponding to the  $E_{nm}(t)$  time points  
 621 we first estimated the BOLD signal lag  $l = 2500ms$  as optimal peak-to-peak

622 alignment with  $\mathbf{r}(t)$  smoothed by a Gaussian filter with same effective width  
 623 ( $\sigma = 700$ ). Then for all BOLD time points in a given cluster  $c$  we selected the  
 624 2000 corresponding time points in  $\mathbf{r}(t)$  and concatenate these to get the fast  
 625 time-scale activity  $\mathbf{r}_c(t)$  in the subspace corresponding to cluster  $c$ . Each of the  
 626  $\mathbf{r}_c(t)$  was then projected to space spanned by the first two PCA components  
 627 of the whole  $\mathbf{r}(t)$  time-series to evaluate how much of the overall state-space is  
 628 covered by individual clusters.

629 The local trajectory for a given event  $e$  was computed by selecting interval  
 630  $\mathbf{r}_e(t)$  corresponding to BOLD timepoints above the RSS threshold and three  
 631 timepoints before and after the event. Local  $PCA^e$  of was then computed from  
 632  $\mathbf{r}_e(t)$ , and the smoothed trajectory was computed by convolving  $\mathbf{r}_e(t)$  with a  
 633 Gaussian filter ( $\sigma = 100$ ).

#### 634 4.4 Manifold sampling

635 To identify the fixed point scaffold of the manifold as traced by the trajectory  
 636 resulting from integrating the Equation 5, we sample the segments from the  
 637 simulated trajectory  $(r_i(t), v_i(t))|_{t_s}^{t_s + \tau_{max}}$ , and use them as initial conditions  
 638 for integration of the deterministic interpretation of Equation 5, i.e.  $d\Psi(t) =$   
 639  $a(\Psi(t))dt$ . From each such an initial condition, we integrated the system to  
 640 steady state equilibrium corresponding to a fixed point  $(\mathbf{r}^*, \mathbf{v}^*)$ .

641 The number of stable fixed points  $(\mathbf{r}^*, \mathbf{v}^*)$  of system with  $G = 0$  is  $2^N$   
 642 reflecting all the combinations of up- and down-states of the  $N$  nodes. To  
 643 sample the stable fixed points of the system with  $G > 0$  we solve repeatedly the  
 644 system of equations:

$$\begin{aligned} 0 &= \frac{\Delta}{\pi\tau_c} + 2r_i^*v_i^*, \\ 0 &= v_i^{*2} + \eta - (\tau_c\pi r_i^*)^2 + J\tau_c r_i^* + I_i \end{aligned} \quad (8)$$

645 using Newton-Raphson method with the initial conditions chosen randomly as a  
 646 vector of up- and down-state fixed points of the isolated nodes, i.e.  $(r_i^{*0}, v_i^{*0}) \in$   
 647  $\{(r_\uparrow^*, v_\uparrow^*), (r_\downarrow^*, v_\downarrow^*)\}$ ,  $\forall i$  where  $(r_\uparrow^*, v_\uparrow^*)$  and  $(r_\downarrow^*, v_\downarrow^*)$  are the up- and down-state fixed  
 648 points for the isolated node. For each initial condition  $(\mathbf{r}^{*0}, \mathbf{v}^{*0})$  we then check  
 649 if the corresponding solution of Equation 8 is equivalent up to the composition  
 650 in terms of up- and down-states. If not, it is discarded, otherwise we evaluate  
 651 the stability of the found fixed point using linear stability analysis.

652 As a low-dimensional projection of the sampled manifold we have used the  
 653 two slowest eigenmodes of the structural connectivity. These are computed as  
 654 eigendecomposition of the graph Laplacian  $\mathbf{L} = \mathbf{W} - \mathbf{I}$ , that is  $\mathbf{L}\mathbf{U} = \mathbf{U}\mathbf{\Lambda}$ , where  
 655 eigenvalues  $\lambda_k$  can be interpreted as structural frequencies and the eigenmodes  
 656  $\mathbf{u}_k$  as structural connectome harmonics [91].

#### 657 4.5 Linear stability analysis

658 We perform a linear stability analysis to identify the fixed-points obtained from  
 659 the NR method. If each fixed-point  $(\mathbf{r}^*, \mathbf{v}^*)$  is perturbed by  $(\epsilon^r, \epsilon^v)$ , then the

660 evolution of the perturbations depend on the Jacobian matrix ( $J$ ) and are given  
 661 by:

$$\begin{bmatrix} \dot{\epsilon}_1^r \\ \dot{\epsilon}_2^r \\ \vdots \\ \dot{\epsilon}_N^r \\ \dot{\epsilon}_1^v \\ \dot{\epsilon}_2^v \\ \vdots \\ \dot{\epsilon}_N^v \end{bmatrix} = \begin{bmatrix} 2v_1^* & 0 & \dots & 0 & 2r_1^* & 0 & \dots & 0 \\ 0 & 2v_2^* & \dots & 0 & 0 & 2r_2^* & \dots & 0 \\ \vdots & \vdots & \ddots & \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \dots & 2v_N^* & 0 & 0 & \dots & 2v_N^* \\ J - 2\pi^2 r_1^* & w_{12} & \dots & w_{1N} & 2v_1^* & 0 & \dots & 0 \\ w_{21} & J - 2\pi^2 r_2^* & \dots & w_{2N} & 0 & 2v_2^* & \dots & 0 \\ \vdots & \vdots & \ddots & \vdots & \vdots & \vdots & \ddots & \vdots \\ w_{N1} & w_{N2} & \dots & J - 2\pi^2 r_N^* & 0 & 0 & \dots & 2v_N^* \end{bmatrix} \cdot \begin{bmatrix} \epsilon_1^r \\ \epsilon_2^r \\ \vdots \\ \epsilon_N^r \\ \epsilon_1^v \\ \epsilon_2^v \\ \vdots \\ \epsilon_N^v \end{bmatrix} \quad (9)$$

662 The stability of a fixed-point depends on the eigenvalues of the Jacobian evalu-  
 663 ated at the fixed-point. The fixed-point is stable iff all the eigen-values of  $J$  are  
 664 negative. Therefore, we numerically evaluate the largest eigenvalue of Jacobian  
 665 for each fixed-point and label the point as stable if its real-part is negative.

#### 666 4.6 Fixed point sampling from simulated trajectory

667 From a given trajectory of the system given as 10 minutes of  $\psi(t)$  we have  
 668 selected a restart point  $t'$  each 50 ms (12000 starting points altogether). For  
 669 each of the restart point  $t'$  we extracted the segment  $\Psi(t)|_{t'}^{t'-\tau_{max}}$  where  $\tau_{max}$   
 670 is the length of the longest delay, and used as initial condition to a equivalent  
 671 system to Equation 5 with  $b = 0$ :

$$d\Psi(t) = a(\Psi(t))dt. \quad (10)$$

672 Integrating this system to equilibrium yielded then for each restart point  $t_r$  a  
 673 fixed point  $\Psi^* = (\mathbf{r}^*, \mathbf{v}^*)$ . The stability of each of the fixed points  $\Psi^*$  was  
 674 then evaluated using the linear stability analysis as the largest eigenvalue of the  
 675 respective Jacobian matrix.

#### 676 4.7 Escape time analysis

677 The switching behaviour of a single node is driven by the stability of the up-  
 678 and down-state fixed points in the presence of noise. We employed escape time  
 679 analysis [92] to measure the stability of these fixed points for range of values of  
 680 external input  $I$ . In detail, for a single node of the system given by Equation 3  
 681 we found the up- and down-state stable fixed points  $(r^*, v^*)^\uparrow$  and  $(r^*, v^*)^\downarrow$ , and  
 682 the unstable saddle node  $(r^*, v^*)^\times$ . Next we computed the separatrix between  
 683 the two basins of attraction by integration of the model backwards in time  
 684 resulting in an closed curve  $\omega$ . To find the characteristic escape time for a  
 685 fixed point  $(r^*, v^*)$  we have integrated the system from the initial condition  
 686  $(r_0, v_0) = (r^*, v^*)$  for a given value of  $I$  100 times, measuring the time  $t_E$  at  
 687 which the trajectory crosses  $\omega$  for the first time. The values of  $I$  were drawn

688 from the range given by  $[0, I_{\max}]$  where  $I_{\max} = \max\{I_i(t), \forall i\}$  is the largest value  
689 of  $I_i$  encountered in the integration of the full system in the working point.

## 690 4.8 Empirical data and spatial analysis

691 The functional gradient on empirical data was computed from the group connectiv-  
692 ity matrix of the Human Connectome Project dataset using the brainspace  
693 toolbox [93]. For a simulated resting state session with  $G_w$ , the time in avalanche  
694 was computed for each node as total time for which the  $\mathbf{r}_i(t)$  was above the  
695 threshold of 3 standard deviations, and the event z-score as a sum of z-scored  
696 BOLD signal in time-points marked as events. The nodes were then grouped  
697 according to the cortical hierarchy [76] projected to the Desikan-Killiany par-  
698 cellation.

699 A parcellation-based BOLD signals of a resting-state session from a subject  
700 from the Human Connectome Project [94] were used to validate the separation  
701 of the events in the low-dimensional embedding. The data consisted of 1200  
702 time points sampled at 720 ms in the Desikan-Killiany parcellation [89] with 70  
703 cortical regions.

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