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► **To cite this version:**

Jennifer S Goldman, Núria Tort-Colet, Matteo Di Volo, Eduarda Susin, Jules Bouté, et al.. Bridging single neuron dynamics to global brain states. *Frontiers in Systems Neuroscience*, 2019, 13, pp.75. 10.3389/fnsys.2019.00075 . hal-02506324

**HAL Id: hal-02506324**

**<https://hal.science/hal-02506324v1>**

Submitted on 12 Mar 2020

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# Bridging single neuron dynamics to global brain states

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Published in: *Frontiers in Systems Neuroscience*, 13, Dec 2019,

doi:10.3389/fnsys.2019.00075

<https://www.frontiersin.org/article/10.3389/fnsys.2019.00075>

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## 2 ABSTRACT

3 Biological neural networks produce information on backgrounds of multi-scale spontaneous  
4 activity that become more complex in brain states displaying higher capacities for cognition, for  
5 instance, attentive waking versus anesthetized states. Here, we review brain state-dependent  
6 mechanisms spanning ionic currents (microscale) to the dynamics of brain-wide, distributed,  
7 transient functional assemblies (macroscale). Not unlike how microscopic interactions between  
8 molecules underlie structures formed in macroscopic states of matter, using statistical physics,  
9 the dynamics of microscopic neural phenomena can be linked to macroscopic brain dynamics.  
10 Beyond spontaneous dynamics, it is observed that stimuli produce collapses of complexity, more  
11 remarkable over highly complex background dynamics present in conscious than unconscious  
12 brain states. In contrast, complexity may not be further collapsed in already low-dimensional  
13 unconscious spontaneous activity. We propose that increased complexity of spontaneous  
14 dynamics during conscious states supports responsiveness, enhancing neural networks'  
15 emergent capacity to robustly encode information over multiple scales.

16 **Keywords:** cerebral cortex, consciousness, computation, empirical, theoretical, statistical physics, mean-field model, manifold,  
17 coupling, synchrony, regularity, complexity, dimensionality, entropy

## INTRODUCTION

18 Brain activity transitions between healthy states, including stages of sleep, restful and aroused waking, as  
19 well as pathological states such as epilepsy, coma, and unresponsive wakefulness syndrome. From such  
20 a diversity of brain states, phenomenological categories encompassing similar spatio-temporal activity  
21 patterns can roughly, but usefully, be defined: unconscious (e.g., sleep and anesthesia) and conscious  
22 (e.g., waking and dreaming) brain states. At the macroscopic, global scale, unconscious brain states are  
23 dominated by high voltage, low frequency oscillatory brain activity related to the microscopic alternation

24 of synchronous neuronal spiking and near silence (Steriade et al., 1993; Brown et al., 2010). Conversely,  
25 conscious states are macroscopically characterized by low voltage, high frequency, complex "disorganized"  
26 dynamics resulting from more asynchronous irregular (AI) microscopic network activity (Brunel, 2000;  
27 Tsodyks and Sejnowski, 1995; Van Vreeswijk and Sompolinsky, 1996), thought to be important for neural  
28 coding (Van Vreeswijk and Sompolinsky, 1996; Zerlaut and Destexhe, 2017; Skarda and Freeman, 1987;  
29 Tononi and Edelman, 1998).

30 Much as different states of matter like solids, liquids, and gases emerge from interactions between  
31 populations of molecules, different brain states may emerge from the interactions between populations  
32 of neurons. Statistical physics provides a mathematical framework to uncover structures of microscopic  
33 interactions underlying macroscopic properties. In this sense, macroscopically observed high synchrony,  
34 low complexity brain signals recorded from unconscious states may be accounted for by an increased  
35 coupling in the system's components, behaving more like a solid (Peyrache et al., 2012; Le Van Quyen  
36 et al., 2016; Olcese et al., 2016; Nghiem et al., 2018a). In contrast, conscious brain states may be described  
37 as higher complexity (Sitt et al., 2014; Engemann et al., 2018; Nghiem et al., 2018a), perhaps liquid-like.

38 Though quantitative expressions directly linking order and complexity are not straightforward, various  
39 definitions and metrics of complexity have been described to vary between brain states. Reports of enhanced  
40 complexity in conscious compared to unconscious states may be understood as increased dimensionality  
41 (El Boustani and Destexhe, 2010), namely the number of degrees of freedom needed to capture a system's  
42 dynamics. Intuitively, dimensionality relates, though is not reducible to, algorithmic complexity which  
43 quantifies the length of a deterministic algorithm required to reproduce an exact signal. For a random signal  
44 resulting from purely stochastic dynamics (similar to neural activity observed during conscious states),  
45 the length of the algorithm would be as long as the signal itself. In contrast, a purely oscillatory signal  
46 (reminiscent of unconscious brain dynamics) can be recapitulated by a shorter algorithm, easily described  
47 by a periodic trajectory in few dimensions.

48 Here, we aim to connect spatial scales from microscopic (nanometers to micrometers - molecules to whole  
49 neurons) to macroscopic brain activity (centimeters to meters - brain areas to individual subjects' brains),  
50 describing both spontaneous and evoked dynamics. Toward linking interpretations of studies between  
51 scales, mesoscopic data (micrometers to millimeters - populations of thousands to tens of thousands  
52 of neurons) have been useful to inform models of neuronal assemblies. The perspective concludes by  
53 discussing a hypothesis best tested with a multi-scale understanding of brain function: the global complexity  
54 of neural activity increases in conscious brain states so as to enhance responsiveness to stimuli. We suggest  
55 responsiveness may depend on the capacity of neural networks to transiently collapse the dimensionality  
56 of collective dynamics - in particular neural assemblies sensitive to stimulus features - into evoked  
57 low-dimensional trajectories supporting neural codes (Fig. 1A).

## MACROSCOPIC SIGNALS VARY ROBUSTLY BETWEEN BRAIN STATES

58 Both spontaneous and evoked (Fig. 1A-B) neural signals vary macroscopically across brain states, as  
59 demonstrated in electroencephalography (EEG), magnetoencephalography (MEG), and functional magnetic  
60 resonance imaging (fMRI). In unconscious states, neural activity is dominated by low-frequency, high-  
61 amplitude signals (Niedermeyer and da Silva, 2005). Accordingly, analyses of entropy (Sitt et al., 2014;  
62 Engemann et al., 2018), complexity (Tononi and Edelman, 1998), and dimensionality (El Boustani and  
63 Destexhe, 2010) during unconscious states indicate a relative simplicity of signals compared to conscious  
64 states. In unconscious states, synchronous activity slowly sweeps across the cortex (Massimini et al., 2004)  
65 along paths formed by cortical tracts (Capone et al., 2017). In both conscious resting and unconscious states,

66 the default mode network (Raichle et al., 2001; Boly et al., 2008) establishes a pattern of synchronization  
67 between brain areas, producing correlations in ultra-slow ( $< 1$  Hz) dynamics (Brookes et al., 2011).  
68 Sustained, slow oscillations were initially reported in the thalamocortical system (Steriade, 2003), but are  
69 also observed experimentally in isolated cortex, without thalamus (Timofeev et al., 2000; Sanchez-Vives  
70 and McCormick, 2000). Thalamocortical connections shape slow wave dynamics (David et al., 2013;  
71 Crunelli et al., 2015; Destexhe et al., 2007; Zucca et al., 2019; Poulet et al., 2012) although slow oscillations  
72 appear to be the default state of cortical networks (Sanchez-Vives and McCormick, 2000; Sanchez-Vives  
73 et al., 2017).

74 Patterns of neocortical regions activated in resting state networks have been successfully retrieved using  
75 eigenmodes of the structural connectivity matrix, i.e. the possible oscillatory patterns at frequencies allowed  
76 by white matter tract lengths (Atasoy et al., 2016). In active states, the executive control network replaces  
77 the default mode (Fox et al., 2005), and the co-activation of different cortical regions is more strongly  
78 controlled by correlations in external stimuli than by white matter structural connectivity (Gilson et al.,  
79 2018), with patterns of activity propagating recurrently between low-level, sensory areas and high-level,  
80 associative areas.

81 During conscious states, on the background of globally disorganized neural activity, transient patterns  
82 emerge (Singer, 2013; Uhlhaas et al., 2009; Duncan-Johnson and Donchin, 1982; Goodin and Aminoff,  
83 1984; Sur and Sinha, 2009; Luck and Kappenman, 2011; Sato et al., 2012; Chemla et al., 2019; Churchland  
84 et al., 2012). Under an interpretation of brain states in analogy to states of matter, microscopic changes in  
85 the interactions between neurons could permit the emergence of larger-scale structures in brain activity.

## MICROSCOPIC MECHANISMS; BIOPHYSICS OF BRAIN STATES

86 Experiments have demonstrated that during unconscious brain states, the membrane potential ( $V_m$ ) of  
87 single cells slowly oscillates between hyperpolarized and depolarized potentials associated with alternating  
88 periods of silence (Down states, also termed “OFF periods”) and AI-like firing (Up states, also termed  
89 “ON periods”)(Steriade et al., 1993) (Fig. 2A). During conscious brain states, neurons show sustained but  
90 sparse and irregular AI firing patterns (Vreeswijk and Sompolinsky, 1998; Destexhe et al., 1999; Steriade,  
91 2000; Brunel, 2000; Renart et al., 2010; Dehghani et al., 2016; di Volo and Torcini, 2018). It was found  
92 that, during AI states, excitatory (E) and inhibitory (I) synaptic inputs are near-balanced (Dehghani et al.,  
93 2016), as predicted theoretically (Van Vreeswijk and Sompolinsky, 1996). In AI states, voltage fluctuations  
94 drive neurons over the threshold for firing action potentials, resulting in irregular spiking dynamics, also  
95 known as fluctuation-driven regimes (Destexhe, 2007; Destexhe and Rudolph-Lilith, 2012; Kuhn et al.,  
96 2004). To understand mechanisms at work during fluctuation-driven dynamics, computational models have  
97 further shown that three parameters are important to capture neuronal responses in this regime, the average  
98 membrane voltage  $V_m$ , the amplitude of  $V_m$  fluctuations, and the conductance state of the membrane (Reig  
99 et al., 2015; Zerlaut et al., 2016).

100 Neuromodulators, including acetylcholine, play important biological roles in modulating the membrane  
101 properties of neurons (McCormick, 1992) and thus transitions between AI and slow oscillatory dynamics  
102 through the regulation of membrane currents (Hill and Tononi, 2005). Neuromodulators are present  
103 at higher concentrations during conscious states (McCormick, 1992; Jones, 2003) and, most generally,  
104 inhibit potassium (activity-dependent and leak  $K^+$ ) channels, which leads to depolarization of cells and  
105 suppression of *spike-frequency adaptation*. At low neuromodulatory concentrations, during unconscious  
106 states,  $K^+$  leak channels are constitutively open and activity-dependent  $K^+$  open when neurons spike,  
107 allowing  $K^+$  ions to exit the cells thus hyperpolarizing cells. Accumulating self-inhibition in the form

108 of spike-frequency adaptation during Up periods results in the transition to Down states. Conversely,  
109 spike-frequency adaptation wears off during Down states, allowing noise fluctuations (present ubiquitously  
110 (Destexhe and Rudolph-Lilith, 2012)) to trigger transitions to Up states (Destexhe, 2009; Jercog et al.,  
111 2017; di Volo et al., 2019; Nghiem et al., 2018c) (Fig.2B). Computationally speaking, for high values of  
112 spike-frequency adaptation, bistability can be observed, with solutions at firing rate zero (Down state)  
113 and non-zero (Up state) values (di Volo et al., 2019; Holcman and Tsodyks, 2006). The more chaotic  
114 dynamics of AI states associated with states of consciousness allows for more reliable stimulus encoding  
115 (D'Andola et al., 2017), more reliable propagation (Zerlaut and Destexhe, 2017), and more sustained  
116 responses (Nghiem et al., 2018c) to stimuli over time. In contrast, during unconscious states, neuronal  
117 responses are more unreliable and vary greatly depending on the stimulus amplitude and whether cells  
118 receive inputs in Up or Down periods (Rosanova and Timofeev, 2005; Reig et al., 2015).

119 The Ising model for spin glasses (Jaynes, 1982) fitted to neural data (Schneidman et al., 2006) has  
120 revealed divergent types of emergent neuronal dynamics in conscious and unconscious states. While  
121 neuronal interactions are pairwise in wakefulness (Nghiem et al., 2017), coupling becomes population-wide  
122 in deep sleep compared to wakefulness (Nghiem et al., 2018b; Tavoni et al., 2017). In particular, inhibitory  
123 neurons organize synchronous activity across populations (Nghiem et al., 2018b; Zanoci et al., 2019),  
124 especially during deep sleep (Peyrache et al., 2012; Le Van Quyen et al., 2016; Olcese et al., 2016) where  
125 inhibitory neurons regulate rhythms of slow wave dynamics (Compte et al., 2008; Zucca et al., 2017; Funk  
126 et al., 2017; Zucca et al., 2019).

127 To summarize, between unconscious and conscious brain states, microscopic data appear intuitively  
128 related to macroscopic data: synchronous microscopic Up and Down states resulting from constitutive  
129 and activity-dependent, hyperpolarizing currents due to reduced neuromodulation correspond to relatively  
130 simple, high-amplitude macroscopic dynamics observed in unconscious states. Active, disorganized,  
131 desynchronized, AI, low adaptation, high neuromodulation conditions correspond to low amplitude,  
132 complex, conscious brain signals. On backgrounds of differing spontaneous dynamics, generalizable  
133 patterns of activity (a.k.a. neural graphoelements) are observed. Cash et al. have shown that K-complexes  
134 (graphoelements characteristic of sleep stage 2) are complementarily observed both at microscopic and  
135 macroscopic scales (Cash et al., 2009). Other identifiable patterns also begin to emerge in empirical and  
136 theoretical data, including phase cones (Freeman and Barrie, 2000) and interacting traveling waves (Sato  
137 et al., 2012; Chemla et al., 2019). Since statistical physics has successfully described neuronal interactions  
138 for different brain states, we ask next whether mesoscale methods from statistical physics can help represent  
139 spontaneous and evoked dynamics of neuronal populations, thus formally linking knowledge between  
140 micro- and macroscopic scales.

## MESOSCALE BRIDGES; POPULATIONS OF NEURONS

141 Brain dynamics at mesoscopic scales, describing thousands of neurons, are investigated empirically by  
142 electrophysiology and more recently, voltage-sensitive dyes (Arieli et al., 1996; Chemla and Chavane,  
143 2010). At mesoscales, brain activity follows the trend of increasing complexity of spontaneous activity  
144 with consciousness (Fig.2A). Studying the effects of inputs at the mesoscale, studies have shown that  
145 perturbations during deep sleep states induce slow waves, but, during waking states, perturbations can result  
146 in chains of phase-locked activity (Pigorini et al., 2015) leading to causal global interactions (Rosanova  
147 et al., 2018).

148 *Mean-field* models offer a formalism for scaling up microscopic detail to collective macroscopic dynamics  
149 using few equations, offering a computational advantage for simulations. In describing states of matter,



150 mean-field models simplify the probabilistic behavior of molecules to the relatively more predictable  
151 behavior of macroscopic states (Kadanoff, 2009). A rich literature has begun to develop mean-field models  
152 of neuronal populations, showing that global variables describing population activity can be usefully  
153 derived from the biophysics of neurons and their interactions (Ohira and Cowan, 1993; Ginzburg and  
154 Sompolinsky, 1994; El Boustani and Destexhe, 2009; Buice et al., 2010; Dahmen et al., 2016). Mean-field  
155 models have qualitatively reproduced temporal features of spontaneous dynamics including AI (El Boustani  
156 and Destexhe, 2009), Up and Down dynamics (Compte et al., 2003; Jercog et al., 2017; Tartaglia and Brunel,  
157 2017; di Volo et al., 2019), and transitions between these states (Tort-Colet et al., 2019; di Volo et al., 2019).  
158 In addition, connecting mean-fields provides a tool for simulating the propagation of patterns through time  
159 and space, across mesoscale structures. For example, recent work deriving mean-field models of networks  
160 with conductance-based synapses has reproduced the suppressive interaction between travelling waves  
161 observed in visual cortex during conscious states, a biological phenomenon that could not be captured by  
162 current-based networks (Chemla et al., 2019).

163 Mean-field models have highlighted that, while complicated to apply mathematically in the framework of  
164 conductance-based models (di Volo et al., 2019), voltage-dependent interactions constitute a significant  
165 non-linearity in the membrane evolution equations. Voltage-dependent interactions appear to be important  
166 for explaining non-trivial responses of biological neurons, through the mean and fluctuations of the cells'  
167 membrane voltage (Reig et al., 2015). In fact, while these results do not imply that this effect is due only  
168 to conductances, they show that voltage dependent synapses play a role in the nonlinear state-dependent  
169 response of a neural network. As shown in Fig.2C, various levels of membrane conductance, regulated by  
170 voltage-dependent synapses, are shown to differently shape population responses.

171 Finally, renormalization group theory, a method of coarse-graining microscopic detail to obtain  
172 macroscopic laws helping to understand how order can emerge from apparent disorder (Cardy, 1996;  
173 Goldenfeld, 2018; Wilson, 1979) has recently begun to be applied to neural assemblies (Meshulam et al.,  
174 2019), laying further foundation for the formal connection of our understanding of brain function across  
175 scales.

## DISCUSSION

176 In this paper, we briefly reviewed work on the measurement and modeling of brain states at different  
177 scales, from single neurons to cell assemblies and global brain activity, considering both spontaneous and  
178 evoked dynamics. In particular we highlighted that increased complexity in the dynamics of conscious  
179 brain states relates to changes in single-neuron biophysics, tuned by neuromodulation. In unconscious  
180 states, reduced neuromodulation promotes activity-dependent self-inhibition of excitatory neurons as they  
181 spike, leading to alternating, synchronous transients of silence and firing, that produce high-amplitude, low-  
182 complexity, synchronous signals, on resonant frequencies of the structural connectome. During conscious  
183 states, neuronal discharges are asynchronous, irregular and fluctuation-driven, resulting from sustained  
184 membrane depolarization in cortical neurons, promoting effective neural communication.

185 Beyond conscious and unconscious categories proposed here for the sake of brevity, important differences  
186 exist within categories of unconscious and conscious states (Brown et al., 2010; El Boustani and Destexhe,  
187 2010; Nghiem et al., 2018a). Unlike healthy wakefulness and sleep, epileptic networks display both  
188 excessively high conductance and strongly synchronized, regular dynamics (El Boustani and Destexhe,  
189 2010). Further, brain signals in coma are both low-amplitude and low-complexity, in contrast to high-  
190 amplitude signals observed in other unconscious states, but also to complex signals observed in conscious  
191 states (El Boustani and Destexhe, 2010). Such anomalous deviations from the overall trend of coordinated

192 changes in complexity and amplitude may illuminate mechanisms underlying disease-causing deviations  
193 from healthy brain states (Mackey and Glass, 1977).

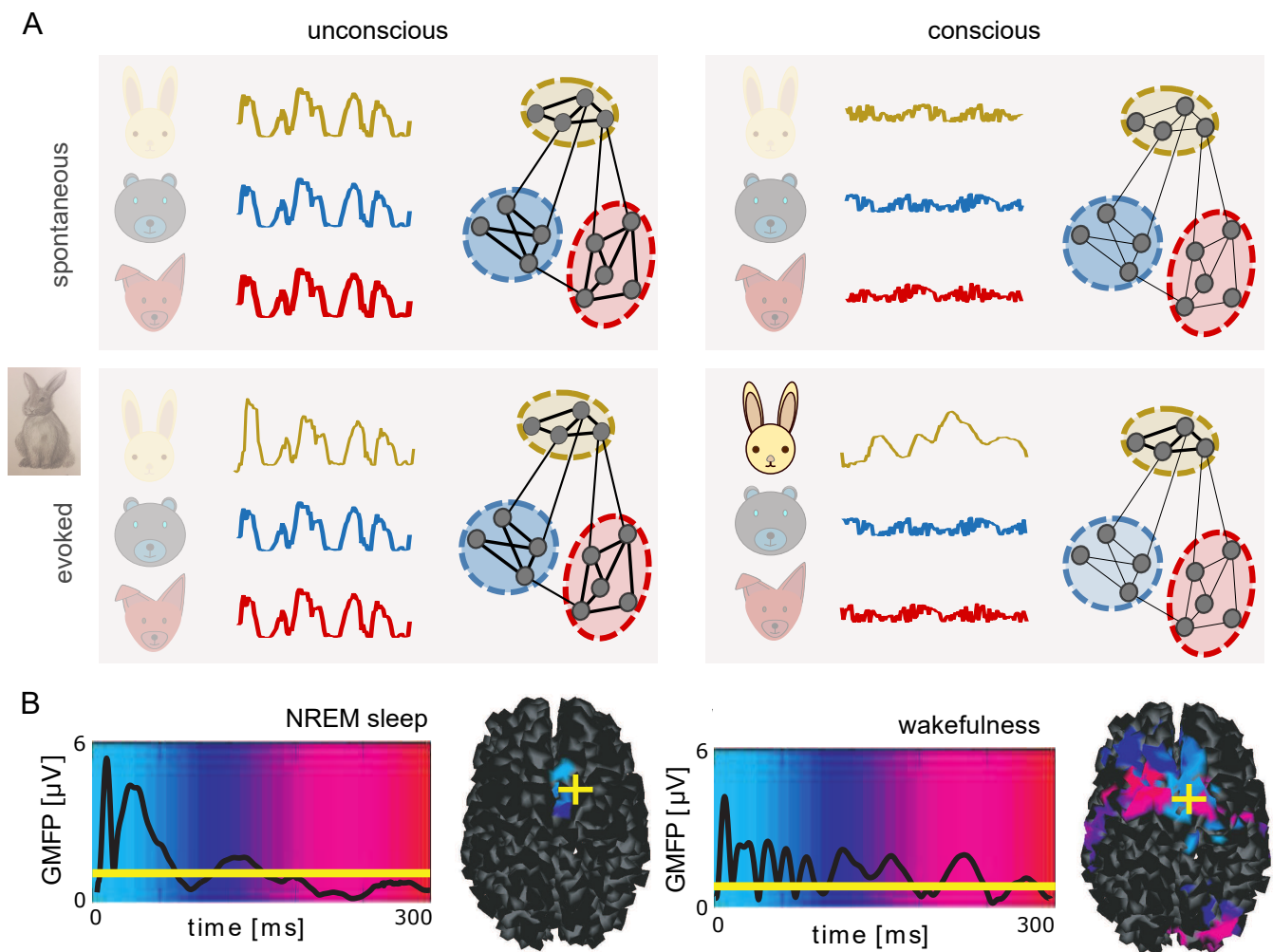
194 To characterize brain states, it has been useful to consider not only spontaneous dynamics but also patterns  
195 evoked by perturbations. It was found that macroscopic responsiveness highly depends on brain state and  
196 different patterns of responses are evoked in conscious versus unconscious states (Massimini et al., 2005).  
197 Such state-dependent responsiveness can also be seen at the level of local networks *in vivo* and *in silico*,  
198 for example in the different reliability of responses to perturbations given during Up and Down periods of  
199 slow waves (Reig et al., 2015; Zerlaut and Destexhe, 2017). In simulations, different responsiveness could  
200 be accounted for by three parameters: membrane voltage, voltage fluctuation amplitude, and membrane  
201 conductance (Reig et al., 2015). These parameters could be well described by mean-field models (di Volo  
202 et al., 2019), able to capture fundamental properties of spontaneous dynamics and also state-dependent  
203 responses at mesoscales. As such, the data-driven connection of such mean field models may serve as  
204 natural candidates for modeling the emergence of mesoscopic and macroscopic-scale patterns.

205 Transient collapses of dimensionality found in encoding networks were also discussed as substrates  
206 potentially supporting neural codes. Such collapses in complexity have been observed in active ensembles  
207 at scales spanning microscopic (Churchland et al., 2010; Fairhall, 2019) to macroscopic (Quiroga et al.,  
208 2001; Zang et al., 2004) activity. This echoes recent work studying recordings of neural populations which  
209 highlighted that neural representations of stimuli may lie on low-dimensional manifolds (Gallego et al.,  
210 2017; Stringer et al., 2019; Chaudhuri et al., 2019; Sadtler et al., 2014; Golub et al., 2018; Chaudhuri  
211 et al., 2019; Churchland et al., 2012; Zhao and Park, 2017; Recanatesi et al., 2019). Indeed neurons do  
212 not fire independently, which would yield dynamics of dimensionality as high as the number of neurons,  
213 but instead follow constrained trajectories of activity that can be captured by descriptions of much lower  
214 dimensionality that depend on spontaneous and evoked dynamics. For example, a neural population firing  
215 in synchrony could be fully described by a periodic orbit trajectory constrained to a low-dimensional space  
216 (Churchland et al., 2012). Since spontaneous global network activity increases in dimensionality during  
217 conscious states, we ask whether the transient collapse of complexity in specific networks, translating the  
218 emergence of simpler dynamical structures from disorder, may be associated to neural codes.

219 As an analogy, windmills facing all in one direction display low complexity, but can only be synchronously  
220 active or inactive. Windmills facing in random directions, in contrast, are a higher complexity configuration  
221 able to represent wind from any direction through the activity of a subset. The activity of an ensemble  
222 of windmills tuned to a particular direction of wind could represent a collapse of complexity and the  
223 generation of information by that subset (in this case, about the direction of wind). Similarly, enhanced  
224 dimensionality associated with conscious states could subserve neural information through the collapse of  
225 complexity in neural assemblies tuned to encode particular representations.

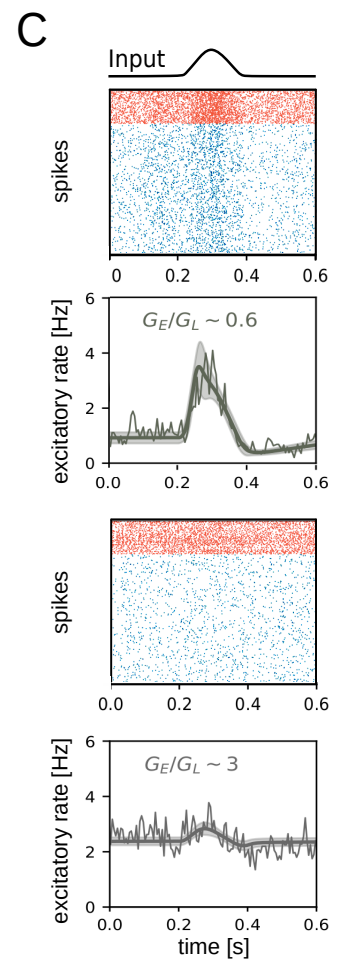
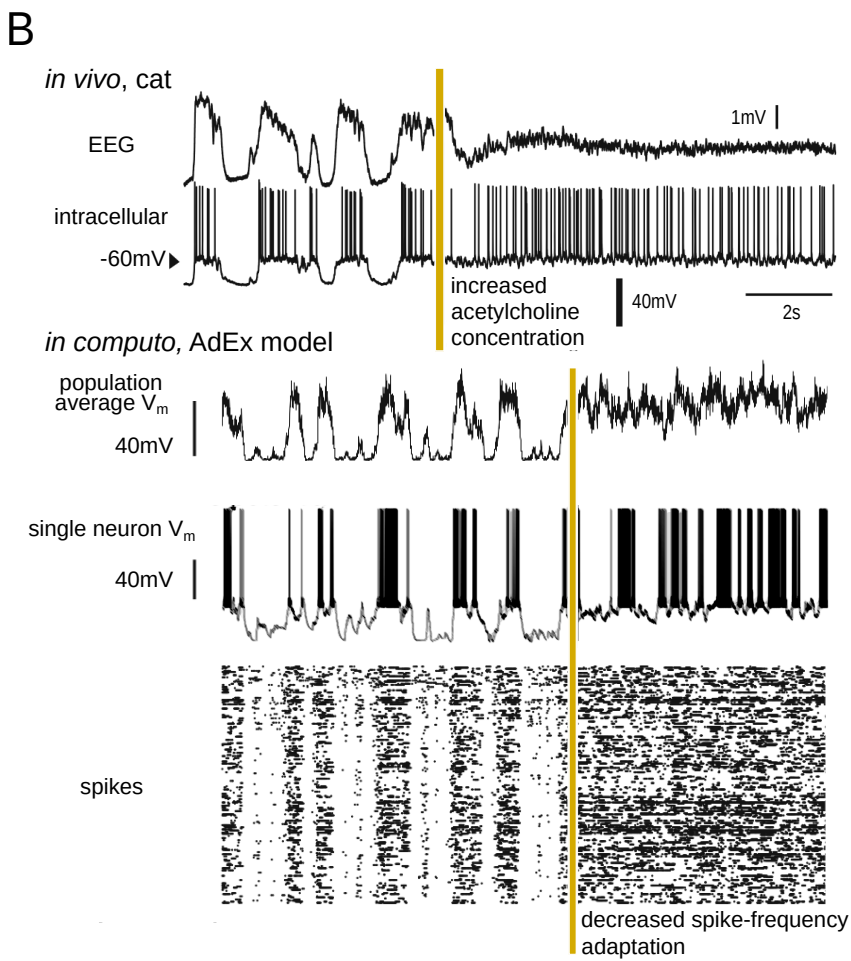
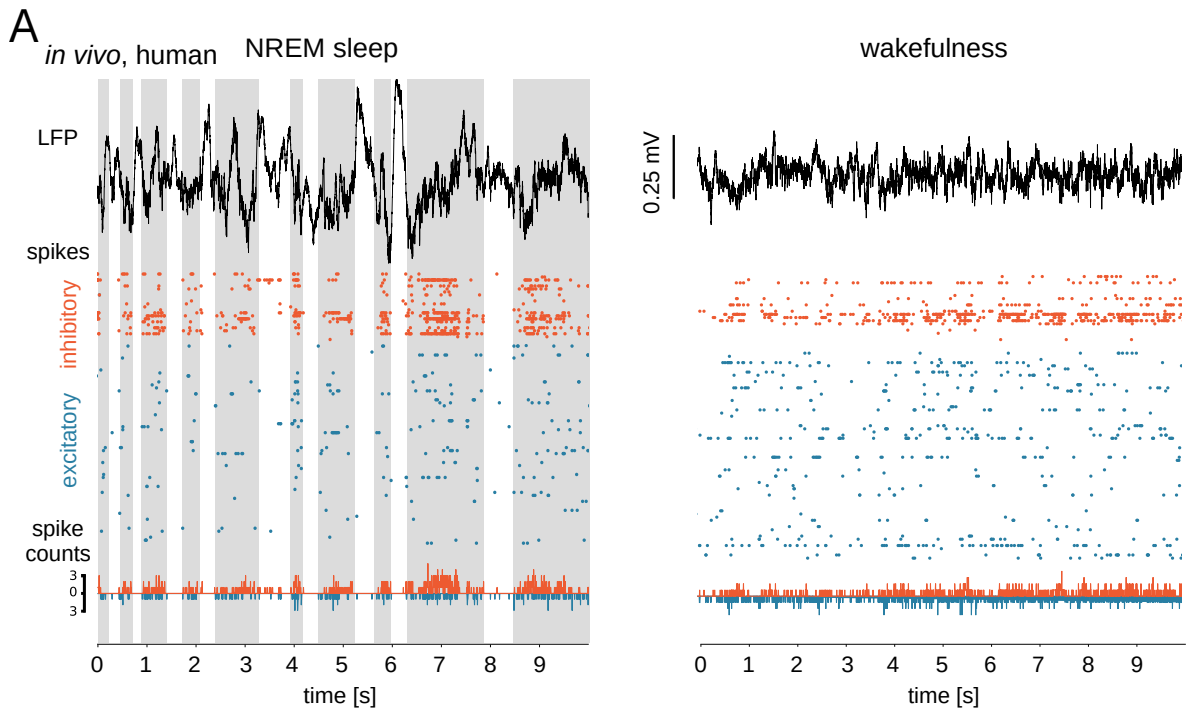
## 226 Acknowledgments

227 Research supported by the Centre National de la Recherche Scientifique (CNRS), the European  
228 Community (Human Brain Project, H2020-785907), and by École des Neurosciences de Paris (ENP).  
229 The authors would like to thank Simone Blanco Malerba, Cristiano Capone, Stephen E. Clarke, Damien  
230 Depannemaecker, Anton Filipchuk, Enrique Hansen, J.N.K. Jaynes, Vicente Medel, Archibald Parsons,  
231 Mattias Peuvrier, Wolf Singer, Kat Uesat, Bahar Hazal Yalçınkaya, and Yann Zerlaut for useful discussion  
232 of the manuscript.



**Figure 1. Complex dynamics associated with conscious brain states provide a potential substrate for neural coding.** **A** Schematics of spontaneous (top) and evoked (bottom) dynamics in connected neuronal assemblies encoding different related concepts (different colors) in unconscious (left) and conscious (right) brain states. In unconscious brain states, slow, synchronous, large amplitude oscillations are observed. Stimuli delivered during unconscious states evoke large amplitude, transient responses similar to spontaneous activity. In contrast, during conscious states, asynchronous, irregular firing of neurons results in macroscopically desynchronized, low amplitude signals. Only networks recruited by the perturbation (here, a rabbit) produce lower-dimensional patterns that propagate relatively further in time and space. **B** Global mean field power (GMFP) recorded with EEG in response to transcranial magnetic stimulation, during deep, non-rapid eye movement (NREM) sleep versus wakefulness. Mean EEG signal is represented by black traces. Background colors represent temporal latency (light blue, 0 ms; red, 300ms) of maximum current sources, also shown in cortical space on the right, where yellow crosses represent the location of stimulation (right dorsolateral premotor cortex). Reprinted with permission from AAAS (Massimini et al., 2005). If brain dynamics between states may be described in analogy to states of matter, perturbing unconscious brains results in large, brief signals perhaps akin to a small perturbation of a solid, which can displace the solid briefly, but will not modify its internal structure. In contrast, the same perturbation delivered during conscious, liquid-like brain states results in smaller but more complex patterns that propagate further in time and space. Under this interpretation, in coding networks, responses evoked during conscious states could represent a form of transient 'crystallization', consistent with neural trajectories lying on low-dimensional manifolds.





**Figure 2. Simple, high-amplitude signals in unconscious brain states are associated with synchronous regular neuronal firing, whereas complex, low-amplitude signals in conscious brain states emerge from asynchronous irregular firing.** **A** Data sample from (Peyrache et al., 2012; Le Van Quyen et al., 2016; Teleńczuk et al., 2017; Dehghani et al., 2016; Nghiem et al., 2018b), containing local field potential (LFP; top), spike times (action potentials; middle), and spike counts (bottom) recorded from a human subject during NREM sleep (left) and wakefulness (right). Spikes from inhibitory (orange) and excitatory (blue) neurons were separated and spike counts were calculated in bins of 5ms. Up states shaded in the left panel. **B** Transition between slow-wave (unconscious) and activated (conscious) state dynamics *in vivo* (top) and *in silico* (bottom). Experimentally the transition is generated by electrical stimulation of acetylcholine neurons in the pedunculopontine tegmentum (PPT) in anesthetized cat (Volgushev et al., 2011), triggering awake-like, desynchronized dynamics in cortex (Rudolph et al., 2005). A prominent consequence of enhancing cholinergic signaling in cortex is a reduction of spike-frequency adaptation (McCormick, 1992). *In silico*, a similarly desynchronizing effect can be generated by reducing the parameter responsible for spike-frequency adaptation. Simulated traces shown in the bottom were modified from (Destexhe, 2009), which used a network of adaptive exponential integrate-and-fire neurons. The average  $V_m$  of the network, the  $V_m$  of a randomly chosen neuron, and the raster plot of the network are shown. Reproduced with permission from (Destexhe, 2009). **C** State dependence of network responsiveness. The responsiveness of two spiking networks to a sinusoidal pulse is shown. Raster plots display spike times of excitatory (blue) and inhibitory (orange) neurons connected by voltage-dependent synapses. Population activity (spike counts, thin line), as well as mean (thick line), and standard deviation (shaded area) of population firing rate generated by a mean field model developed in (di Volo et al., 2019). Responsiveness is found to vary between levels of conductance, obtained by changing the ratio of the time-averaged global excitatory conductance ( $G_E$ ) (Destexhe et al., 2003) to membrane leakage conductance ( $G_L$ ) from low (top) to high values (bottom).

## REFERENCES

- 233 Arieli, A., Sterkin, A., Grinvald, A., and Aertsen, A. (1996). Dynamics of ongoing activity: explanation of  
 234 the large variability in evoked cortical responses. *Science* 273, 1868–1871
- 235 Atasoy, S., Donnelly, I., and Pearson, J. (2016). Human brain networks function in connectome-specific  
 236 harmonic waves. *Nature communications* 7, 10340
- 237 Boly, M., Phillips, C., Tshibanda, L., Vanhaudenhuyse, A., Schabus, M., Dang-Vu, T. T., et al. (2008).  
 238 Intrinsic brain activity in altered states of consciousness: how conscious is the default mode of brain  
 239 function? *Annals of the New York Academy of Sciences* 1129, 119
- 240 Brookes, M. J., Woolrich, M., Luckhoo, H., Price, D., Hale, J. R., Stephenson, M. C., et al. (2011).  
 241 Investigating the electrophysiological basis of resting state networks using magnetoencephalography.  
 242 *Proceedings of the National Academy of Sciences* 108, 16783–16788
- 243 Brown, E. N., Lydic, R., and Schiff, N. D. (2010). General anesthesia, sleep, and coma. *New England*  
 244 *Journal of Medicine* 363, 2638–2650
- 245 Brunel, N. (2000). Dynamics of sparsely connected networks of excitatory and inhibitory spiking neurons.  
 246 *Journal of computational neuroscience* 8, 183–208
- 247 Buice, M. A., Cowan, J. D., and Chow, C. C. (2010). Systematic fluctuation expansion for neural network  
 248 activity equations. *Neural computation* 22, 377–426
- 249 Capone, C., Rebollo, B., Muñoz, A., Illa, X., Del Giudice, P., Sanchez-Vives, M. V., et al. (2017). Slow  
 250 waves in cortical slices: how spontaneous activity is shaped by laminar structure. *Cerebral Cortex* ,  
 251 1–17
- 252 Cardy, J. (1996). *Scaling and renormalization in statistical physics*, vol. 5 (Cambridge university press)
- 253 Cash, S. S., Halgren, E., Dehghani, N., Rossetti, A. O., Thesen, T., Wang, C., et al. (2009). The human  
 254 k-complex represents an isolated cortical down-state. *Science* 324, 1084–1087
- 255 Chaudhuri, R., Gerçek, B., Pandey, B., Peyrache, A., and Fiete, I. (2019). The intrinsic attractor manifold  
 256 and population dynamics of a canonical cognitive circuit across waking and sleep. *Nature neuroscience* ,  
 257 1–9
- 258 Chemla, S. and Chavane, F. (2010). Voltage-sensitive dye imaging: technique review and models. *Journal*  
 259 *of Physiology-Paris* 104, 40–50
- 260 Chemla, S., Reynaud, A., di Volo, M., Zerlaut, Y., Perrinet, L., Destexhe, A., et al. (2019). Suppressive  
 261 traveling waves shape representations of illusory motion in primary visual cortex of awake primate.  
 262 *Journal of Neuroscience* , 2792–18
- 263 Churchland, M. M., Byron, M. Y., Cunningham, J. P., Sugrue, L. P., Cohen, M. R., Corrado, G. S.,  
 264 et al. (2010). Stimulus onset quenches neural variability: a widespread cortical phenomenon. *Nature*  
 265 *neuroscience* 13, 369
- 266 Churchland, M. M., Cunningham, J. P., Kaufman, M. T., Foster, J. D., Nuyujukian, P., Ryu, S. I., et al.  
 267 (2012). Neural population dynamics during reaching. *Nature* 487, 51
- 268 Compte, A., Reig, R., Descalzo, V. F., Harvey, M. A., Puccini, G. D., and Sanchez-Vives, M. V. (2008).  
 269 Spontaneous high-frequency (10–80 hz) oscillations during up states in the cerebral cortex in vitro.  
 270 *Journal of Neuroscience* 28, 13828–13844
- 271 Compte, A., Sanchez-Vives, M. V., McCormick, D. A., and Wang, X.-J. (2003). Cellular and network  
 272 mechanisms of slow oscillatory activity ( $\approx 1$  hz) and wave propagations in a cortical network model.  
 273 *Journal of neurophysiology* 89, 2707–2725
- 274 Crunelli, V., David, F., Lőrincz, M. L., and Hughes, S. W. (2015). The thalamocortical network as a single  
 275 slow wave-generating unit. *Current opinion in neurobiology* 31, 72–80

- 276 Dahmen, D., Bos, H., and Helias, M. (2016). Correlated fluctuations in strongly coupled binary networks  
277 beyond equilibrium. *Physical Review X* 6, 031024
- 278 D'Andola, M., Rebollo, B., Casali, A. G., Weinert, J. F., Pigorini, A., Villa, R., et al. (2017). Bistability,  
279 causality, and complexity in cortical networks: an in vitro perturbational study. *Cerebral cortex* 28,  
280 2233–2242
- 281 David, F., Schmiedt, J. T., Taylor, H. L., Orban, G., Di Giovanni, G., Uebele, V. N., et al. (2013). Essential  
282 thalamic contribution to slow waves of natural sleep. *Journal of Neuroscience* 33, 19599–19610
- 283 Dehghani, N., Peyrache, A., Telenczuk, B., Le Van Quyen, M., Halgren, E., Cash, S. S., et al. (2016).  
284 Dynamic balance of excitation and inhibition in human and monkey neocortex. *Scientific reports* 6,  
285 23176
- 286 Destexhe, A. (2007). High-conductance state. *Scholarpedia* 2, 1341
- 287 Destexhe, A. (2009). Self-sustained asynchronous irregular states and up–down states in thalamic,  
288 cortical and thalamocortical networks of nonlinear integrate-and-fire neurons. *Journal of computational*  
289 *neuroscience* 27, 493
- 290 Destexhe, A., Contreras, D., and Steriade, M. (1999). Spatiotemporal analysis of local field potentials and  
291 unit discharges in cat cerebral cortex during natural wake and sleep states. *Journal of Neuroscience* 19,  
292 4595–4608
- 293 Destexhe, A., Hughes, S. W., Rudolph, M., and Crunelli, V. (2007). Are corticothalamic ‘up’states  
294 fragments of wakefulness? *Trends in neurosciences* 30, 334–342
- 295 Destexhe, A., Rudolph, M., and Paré, D. (2003). The high-conductance state of neocortical neurons in  
296 vivo. *Nature reviews neuroscience* 4, 739
- 297 Destexhe, A. and Rudolph-Lilith, M. (2012). *Neuronal Noise* (Springer Series in Computational  
298 Neuroscience)
- 299 di Volo, M., Romagnoni, A., Capone, C., and Destexhe, A. (2019). Biologically realistic mean-field models  
300 of conductance-based networks of spiking neurons with adaptation. *Neural computation* 31, 653–680
- 301 di Volo, M. and Torcini, A. (2018). Transition from asynchronous to oscillatory dynamics in balanced  
302 spiking networks with instantaneous synapses. *Physical review letters* 121, 128301
- 303 Duncan-Johnson, C. C. and Donchin, E. (1982). The p300 component of the event-related brain potential  
304 as an index of information processing. *Biological psychology* 14, 1–52
- 305 El Boustani, S. and Destexhe, A. (2009). A master equation formalism for macroscopic modeling of  
306 asynchronous irregular activity states. *Neural computation* 21, 46–100
- 307 El Boustani, S. and Destexhe, A. (2010). Brain dynamics at multiple scales: can one reconcile the  
308 apparent low-dimensional chaos of macroscopic variables with the seemingly stochastic behavior of  
309 single neurons? *International Journal of Bifurcation and Chaos* 20, 1687–1702
- 310 Engemann, D. A., Raimondo, F., King, J.-R., Rohaut, B., Louppe, G., Faugeras, F., et al. (2018). Robust  
311 eeg-based cross-site and cross-protocol classification of states of consciousness. *Brain* 141, 3179–3192
- 312 Fairhall, A. L. (2019). Whither variability? *Nature neuroscience* 22, 329
- 313 Fox, M. D., Snyder, A. Z., Vincent, J. L., Corbetta, M., Van Essen, D. C., and Raichle, M. E. (2005). The  
314 human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proceedings of*  
315 *the National Academy of Sciences* 102, 9673–9678
- 316 Freeman, W. J. and Barrie, J. M. (2000). Analysis of spatial patterns of phase in neocortical gamma eegs in  
317 rabbit. *Journal of neurophysiology* 84, 1266–1278
- 318 Funk, C. M., Peelman, K., Bellesi, M., Marshall, W., Cirelli, C., and Tononi, G. (2017). Role of  
319 somatostatin-positive cortical interneurons in the generation of sleep slow waves. *Journal of Neuroscience*  
320 37, 9132–9148

- 321 Gallego, J. A., Perich, M. G., Miller, L. E., and Solla, S. A. (2017). Neural manifolds for the control of  
322 movement. *Neuron* 94, 978–984
- 323 Gilson, M., Deco, G., Friston, K. J., Hagmann, P., Mantini, D., Betti, V., et al. (2018). Effective connectivity  
324 inferred from fmri transition dynamics during movie viewing points to a balanced reconfiguration of  
325 cortical interactions. *Neuroimage* 180, 534–546
- 326 Ginzburg, I. and Sompolinsky, H. (1994). Theory of correlations in stochastic neural networks. *Physical*  
327 *review E* 50, 3171
- 328 Goldenfeld, N. (2018). *Lectures on phase transitions and the renormalization group* (CRC Press)
- 329 Golub, M. D., Sadtler, P. T., Oby, E. R., Quick, K. M., Ryu, S. I., Tyler-Kabara, E. C., et al. (2018).  
330 Learning by neural reassociation. *Nature neuroscience* 21, 607
- 331 Goodin, D. S. and Aminoff, M. J. (1984). The relationship between the evoked potential and brain events  
332 in sensory discrimination and motor response. *Brain* 107, 241–251
- 333 Hill, S. and Tononi, G. (2005). Modeling sleep and wakefulness in the thalamocortical system. *Journal of*  
334 *neurophysiology* 93, 1671–1698
- 335 Holcman, D. and Tsodyks, M. (2006). The emergence of up and down states in cortical networks. *PLoS*  
336 *computational biology* 2, e23
- 337 Jaynes, E. T. (1982). On the rationale of maximum-entropy methods. *Proceedings of the IEEE* 70, 939–952
- 338 Jercog, D., Roxin, A., Bartho, P., Luczak, A., Compte, A., and de la Rocha, J. (2017). Up-down cortical  
339 dynamics reflect state transitions in a bistable network. *Elife* 6, e22425
- 340 Jones, B. E. (2003). Arousal systems. *Front Biosci* 8, 438–51
- 341 Kadanoff, L. P. (2009). More is the same; phase transitions and mean field theories. *Journal of Statistical*  
342 *Physics* 137, 777
- 343 Kuhn, A., Aertsen, A., and Rotter, S. (2004). Neuronal integration of synaptic input in the fluctuation-driven  
344 regime. *Journal of Neuroscience* 24, 2345–2356
- 345 Le Van Quyen, M., Muller, L. E., Telenczuk, B., Halgren, E., Cash, S., Hatsopoulos, N. G., et al. (2016).  
346 High-frequency oscillations in human and monkey neocortex during the wake–sleep cycle. *Proceedings*  
347 *of the National Academy of Sciences* 113, 9363–9368
- 348 Luck, S. J. and Kappenman, E. S. (2011). *The Oxford handbook of event-related potential components*  
349 (Oxford university press)
- 350 Mackey, M. C. and Glass, L. (1977). Oscillation and chaos in physiological control systems. *Science* 197,  
351 287–289
- 352 Massimini, M., Ferrarelli, F., Huber, R., Esser, S. K., Singh, H., and Tononi, G. (2005). Breakdown of  
353 cortical effective connectivity during sleep. *Science* 309, 2228–2232
- 354 Massimini, M., Huber, R., Ferrarelli, F., Hill, S., and Tononi, G. (2004). The sleep slow oscillation as a  
355 traveling wave. *Journal of Neuroscience* 24, 6862–6870
- 356 McCormick, D. A. (1992). Neurotransmitter actions in the thalamus and cerebral cortex and their role in  
357 neuromodulation of thalamocortical activity. *Progress in neurobiology* 39, 337–388
- 358 Meshulam, L., Gauthier, J. L., Brody, C. D., Tank, D. W., and Bialek, W. (2019). Coarse graining, fixed  
359 points, and scaling in a large population of neurons. *Physical Review Letters* 123, 178103
- 360 Nghiem, T.-A., Lina, J.-M., di Volo, M., Capone, C., Evans, A. C., Destexhe, A., et al. (2018a). State  
361 equation from the spectral structure of human brain activity. *arXiv preprint arXiv:1806.07365*
- 362 Nghiem, T.-A., Marre, O., Destexhe, A., and Ferrari, U. (2017). Pairwise ising model analysis of human  
363 cortical neuron recordings. In *International Conference on Geometric Science of Information* (Springer),  
364 257–264



- 365 Nghiem, T.-A., Telenczuk, B., Marre, O., Destexhe, A., and Ferrari, U. (2018b). Maximum-entropy models  
366 reveal the excitatory and inhibitory correlation structures in cortical neuronal activity. *Physical Review E*  
367 98, 012402
- 368 Nghiem, T.-A. E., Tort-Colet, N., Gorski, T., Ferrari, U., Moghimi-firoozabad, S., Goldman, J. S., et al.  
369 (2018c). Cholinergic switch between two different types of slow waves in cerebral cortex. *bioRxiv*,  
370 430405
- 371 Niedermeyer, E. and da Silva, F. L. (2005). *Electroencephalography: basic principles, clinical applications,*  
372 *and related fields* (Lippincott Williams & Wilkins)
- 373 Ohira, T. and Cowan, J. D. (1993). Master-equation approach to stochastic neurodynamics. *Physical*  
374 *Review E* 48, 2259
- 375 Olcese, U., Bos, J. J., Vinck, M., Lankelma, J. V., van Mourik-Donga, L. B., Schlumm, F., et al. (2016).  
376 Spike-based functional connectivity in cerebral cortex and hippocampus: loss of global connectivity  
377 is coupled to preservation of local connectivity during non-rem sleep. *Journal of Neuroscience* 36,  
378 7676–7692
- 379 Peyrache, A., Dehghani, N., Eskandar, E. N., Madsen, J. R., Anderson, W. S., Donoghue, J. A., et al. (2012).  
380 Spatiotemporal dynamics of neocortical excitation and inhibition during human sleep. *Proceedings of*  
381 *the National Academy of Sciences* 109, 1731–1736
- 382 Pigorini, A., Sarasso, S., Proserpio, P., Szymanski, C., Arnulfo, G., Casarotto, S., et al. (2015). Bistability  
383 breaks-off deterministic responses to intracortical stimulation during non-rem sleep. *Neuroimage* 112,  
384 105–113
- 385 Poulet, J. F., Fernandez, L. M., Crochet, S., and Petersen, C. C. (2012). Thalamic control of cortical states.  
386 *Nature neuroscience* 15, 370
- 387 Quiroga, R. Q., Rosso, O. A., Başar, E., and Schürmann, M. (2001). Wavelet entropy in event-related  
388 potentials: a new method shows ordering of eeg oscillations. *Biological cybernetics* 84, 291–299
- 389 Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., and Shulman, G. L. (2001).  
390 A default mode of brain function. *Proceedings of the National Academy of Sciences* 98, 676–682
- 391 Recanatesi, S., Ocker, G. K., Buice, M. A., and Shea-Brown, E. (2019). Dimensionality in recurrent  
392 spiking networks: global trends in activity and local origins in connectivity. *PLoS computational biology*  
393 15, e1006446
- 394 Reig, R., Zerlaut, Y., Vergara, R., Destexhe, A., and Sanchez-Vives, M. V. (2015). Gain modulation of  
395 synaptic inputs by network state in auditory cortex in vivo. *Journal of Neuroscience* 35, 2689–2702
- 396 Renart, A., De La Rocha, J., Bartho, P., Hollender, L., Parga, N., Reyes, A., et al. (2010). The asynchronous  
397 state in cortical circuits. *science* 327, 587–590
- 398 Rosanova, M., Fecchio, M., Casarotto, S., Sarasso, S., Casali, A., Pigorini, A., et al. (2018). Sleep-like  
399 cortical off-periods disrupt causality and complexity in the brain of unresponsive wakefulness syndrome  
400 patients. *Nature communications* 9, 4427
- 401 Rosanova, M. and Timofeev, I. (2005). Neuronal mechanisms mediating the variability of somatosensory  
402 evoked potentials during sleep oscillations in cats. *The Journal of physiology* 562, 569–582
- 403 Rudolph, M., Pelletier, J.-G., Paré, D., and Destexhe, A. (2005). Characterization of synaptic conductances  
404 and integrative properties during electrically-induced eeg-activated states in neocortical neurons in vivo.  
405 *Journal of neurophysiology*
- 406 Sadtler, P. T., Quick, K. M., Golub, M. D., Chase, S. M., Ryu, S. I., Tyler-Kabara, E. C., et al. (2014).  
407 Neural constraints on learning. *Nature* 512, 423
- 408 Sanchez-Vives, M. V., Massimini, M., and Mattia, M. (2017). Shaping the default activity pattern of the  
409 cortical network. *Neuron* 94, 993–1001

- 410 Sanchez-Vives, M. V. and McCormick, D. A. (2000). Cellular and network mechanisms of rhythmic  
411 recurrent activity in neocortex. *Nature neuroscience* 3, 1027
- 412 Sato, T. K., Nauhaus, I., and Carandini, M. (2012). Traveling waves in visual cortex. *Neuron* 75, 218–229
- 413 Schneidman, E., Berry II, M. J., Segev, R., and Bialek, W. (2006). Weak pairwise correlations imply  
414 strongly correlated network states in a neural population. *Nature* 440, 1007
- 415 Singer, W. (2013). Cortical dynamics revisited. *Trends in cognitive sciences* 17, 616–626
- 416 Sitt, J. D., King, J.-R., El Karoui, I., Rohaut, B., Faugeras, F., Gramfort, A., et al. (2014). Large scale  
417 screening of neural signatures of consciousness in patients in a vegetative or minimally conscious state.  
418 *Brain* 137, 2258–2270
- 419 Skarda, C. A. and Freeman, W. J. (1987). How brains make chaos in order to make sense of the world.  
420 *Behavioral and brain sciences* 10, 161–173
- 421 Steriade, M. (2000). Corticothalamic resonance, states of vigilance and mentation. *Neuroscience* 101,  
422 243–276
- 423 Steriade, M. (2003). *Neuronal substrates of sleep and epilepsy* (Cambridge University Press)
- 424 Steriade, M., Nunez, A., and Amzica, F. (1993). A novel slow (< 1 Hz) oscillation of neocortical neurons  
425 in vivo: depolarizing and hyperpolarizing components. *Journal of neuroscience* 13, 3252–3265
- 426 Stringer, C., Pachitariu, M., Steinmetz, N., Carandini, M., and Harris, K. D. (2019). High-dimensional  
427 geometry of population responses in visual cortex. *Nature* , 1
- 428 Sur, S. and Sinha, V. (2009). Event-related potential: An overview. *Industrial psychiatry journal* 18, 70
- 429 Tartaglia, E. M. and Brunel, N. (2017). Bistability and up/down state alternations in inhibition-dominated  
430 randomly connected networks of lif neurons. *Scientific reports* 7, 11916
- 431 Tavoni, G., Ferrari, U., Battaglia, F. P., Cocco, S., and Monasson, R. (2017). Functional coupling  
432 networks inferred from prefrontal cortex activity show experience-related effective plasticity. *Network*  
433 *Neuroscience* 1, 275–301
- 434 Teleńczuk, B., Dehghani, N., Le Van Quyen, M., Cash, S. S., Halgren, E., Hatsopoulos, N. G., et al. (2017).  
435 Local field potentials primarily reflect inhibitory neuron activity in human and monkey cortex. *Scientific*  
436 *reports* 7, 40211
- 437 Timofeev, I., Grenier, F., Bazhenov, M., Sejnowski, T., and Steriade, M. (2000). Origin of slow cortical  
438 oscillations in deafferented cortical slabs. *Cerebral cortex* 10, 1185–1199
- 439 Tononi, G. and Edelman, G. M. (1998). Consciousness and complexity. *science* 282, 1846–1851
- 440 Tort-Colet, N., Capone, C., Sanchez-Vives, M. V., and Mattia, M. (2019). Attractor competition enriches  
441 cortical dynamics during awakening from anesthesia. *bioRxiv* , 517102
- 442 Tsodyks, M. V. and Sejnowski, T. (1995). Rapid state switching in balanced cortical network models.  
443 *Network: Computation in Neural Systems* 6, 111–124
- 444 Uhlhaas, P., Pipa, G., Lima, B., Melloni, L., Neuenschwander, S., Nikolić, D., et al. (2009). Neural  
445 synchrony in cortical networks: history, concept and current status. *Frontiers in Integrative Neuroscience*  
446 3, 17. doi:10.3389/neuro.07.017.2009
- 447 Van Vreeswijk, C. and Sompolinsky, H. (1996). Chaos in neuronal networks with balanced excitatory and  
448 inhibitory activity. *Science* 274, 1724–1726
- 449 Volgushev, M., Chauvette, S., and Timofeev, I. (2011). Long-range correlation of the membrane potential in  
450 neocortical neurons during slow oscillation. In *Progress in brain research* (Elsevier), vol. 193. 181–199
- 451 Vreeswijk, C. v. and Sompolinsky, H. (1998). Chaotic balanced state in a model of cortical circuits. *Neural*  
452 *computation* 10, 1321–1371
- 453 Wilson, K. G. (1979). Problems in physics with many scales of length. *Scientific American* 241, 158–179

- 454 Zang, Y., Jiang, T., Lu, Y., He, Y., and Tian, L. (2004). Regional homogeneity approach to fmri data  
455 analysis. *Neuroimage* 22, 394–400
- 456 Zanoci, C., Dehghani, N., and Tegmark, M. (2019). Ensemble inhibition and excitation in the human  
457 cortex: An ising-model analysis with uncertainties. *Physical Review E* 99, 032408
- 458 Zerlaut, Y. and Destexhe, A. (2017). Enhanced responsiveness and low-level awareness in stochastic  
459 network states. *Neuron* 94, 1002–1009
- 460 Zerlaut, Y., Teleńczuk, B., Deleuze, C., Bal, T., Ouanounou, G., and Destexhe, A. (2016). Heterogeneous  
461 firing rate response of mouse layer v pyramidal neurons in the fluctuation-driven regime. *The Journal of*  
462 *physiology* 594, 3791–3808
- 463 Zhao, Y. and Park, I. M. (2017). Variational latent gaussian process for recovering single-trial dynamics  
464 from population spike trains. *Neural computation* 29, 1293–1316
- 465 Zucca, S., D’Urso, G., Pasquale, V., Vecchia, D., Pica, G., Bovetti, S., et al. (2017). An inhibitory gate for  
466 state transition in cortex. *Elife* 6, e26177
- 467 Zucca, S., Pasquale, V., de Leon Roig, P. L., Panzeri, S., and Fellin, T. (2019). Thalamic drive of  
468 cortical parvalbumin-positive interneurons during down states in anesthetized mice. *Current Biology* 29,  
469 1481–1490