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Bridging single neuron dynamics to global brain states

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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

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

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

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

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

MACROSCOPIC SIGNALS VARY ROBUSTLY BETWEEN BRAIN STATES

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

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

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

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

MICROSCOPIC MECHANISMS; BIOPHYSICS OF BRAIN STATES

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

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

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

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

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

MESOSCALE BRIDGES; POPULATIONS OF NEURONS

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

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

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

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

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

DISCUSSION

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

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

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

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

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

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

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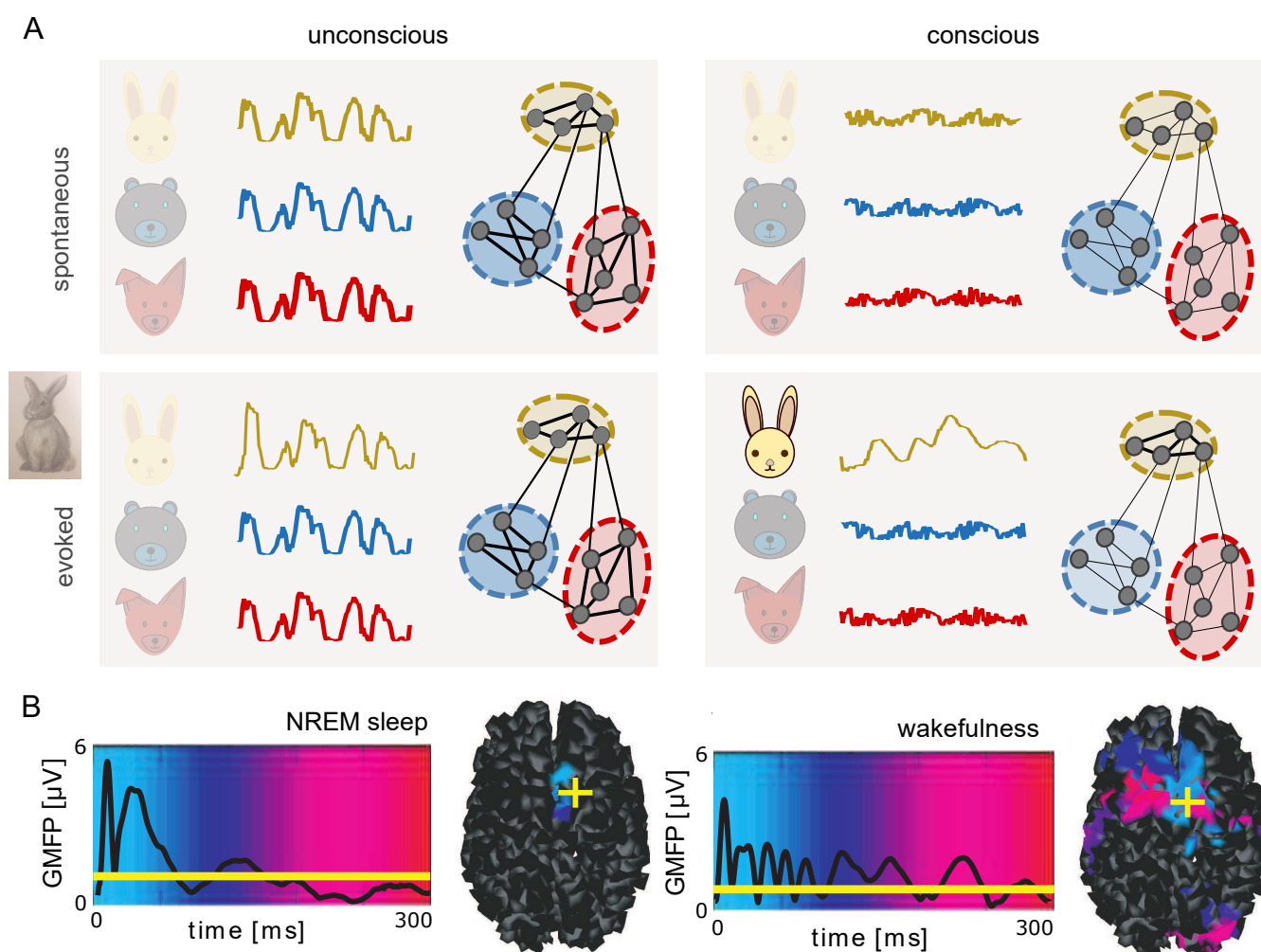


Figure 1. Complex dynamics associated with conscious brain states provide a potential substrate for neural coding. **A** Schematics of spontaneous (top) and evoked (bottom) dynamics in connected neuronal assemblies encoding different related concepts (different colors) in unconscious (left) and conscious (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.

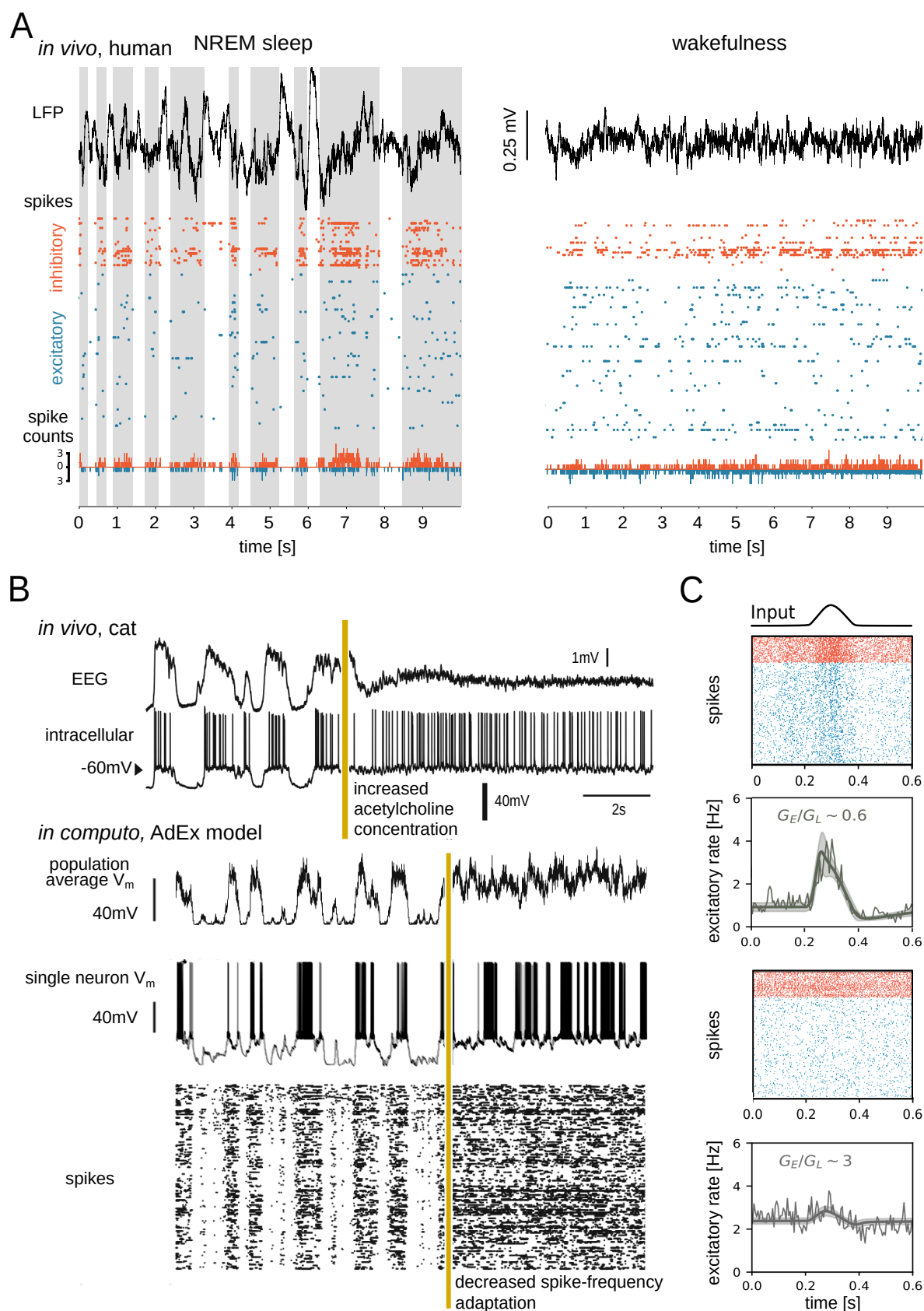


Figure 2. Simple, high-amplitude signals in unconscious brain states are associated with synchronous regular neuronal firing, whereas complex, low-amplitude signals in conscious brain states emerge from asynchronous irregular firing. **A** Data sample from (Peyrache et al., 2012; Le Van Quyen et al., 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

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

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

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