Inference of Global States Stability in Cortical Networks

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The Default Global State of the Cerebral Cortex [1]

Phenomenology

- Slow Oscillations ($\leq$1Hz)
  - at the neuron level (membrane potential and firing rate)
  - at the network level (extracellular electrical activity: LFP and MUA)
- Observed in:
  - slow wave sleep
  - deep anaesthesia
  - deafferentation
  - cortical slices

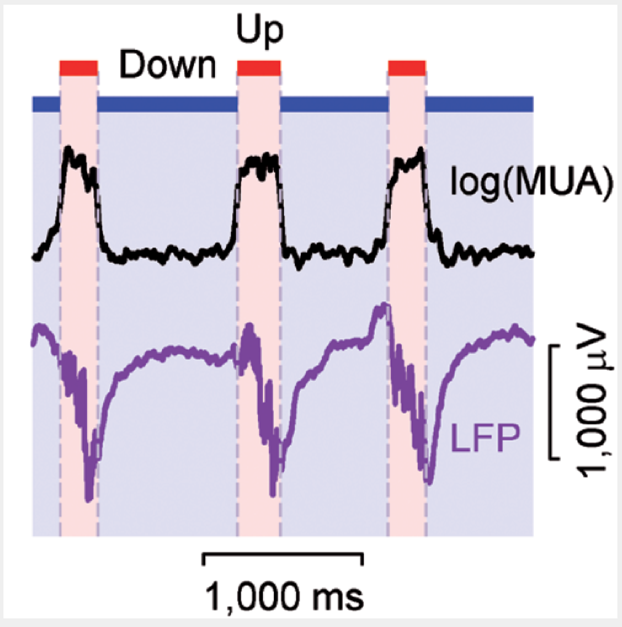

Figure 1: Slow oscillations recorded from the frontal cortex of an anaesthetized mouse [1]

Key Features

- Bistability
  - existence of two attractors: UP state and DOWN state
- Intrinsic fluctuations between these attractors
- Regularity of the UP/DOWN states alternance

$\rightarrow$ behaves as a relaxation oscillator

Advantages

- Resilience to perturbances:
  - the relaxation-oscillator regime acts as an equilibrium of the network.
- Facilitation of the transition towards more connected, awake-like states.

Motivation

- Can we detect and characterize other global network states apart from the SO regime?

Cortical Networks Parameters: Literature Review

In fact, the dynamics of the network states are not fully understood [3]. The stability of such states seems to be strongly influenced by:

- the input stimulus [4]
- the connectivity properties of the network
  - either unshaped or structured in clusters [5]
- the excitatory-inhibitory balance [6]
- the network architecture
  - either predominantly feedforward or recurrent [7]
- the kind of noise
  - intrinsic or extrinsic [8]

Problem: Although multiple mechanistic hypotheses have been proposed in models, the current analysis tools do not enable us to discern empirically the dynamics of the network states.

References

[1] Sanchez-Vives MV, Mattia M. (2014) *Slow wave activity as the default mode of the cerebral cortex.* Arch Ital Biol. 152(2-3):147-55.

[2] D'Andola M, Rebollo B, Casali AG, Weinert JF, Pigorini A, Villa R, Massimini M, Sanchez-Vives MV. (2017) *Bistability, Causality, and Complexity in Cortical Networks: An in Vitro Perturbational Study.* Cereb Cortex, 112:105-113

[3] Balaguer-Ballester E. (2017) *Cortical Variability and Challenges for Modeling Approaches.* Front. Syst. Neurosci. 11:15.

[4] Bujan AF, Aertsen A, Kumar A. (2015) *Role of input correlations in shaping the variability and noise correlations of evoked activity in the neocortex.* J Neurosci. 35(22):8611-25.

[5] Rosenbaum R, Smith MA, Kohn A, Rubin JE, Doiron B. (2017) *The spatial structure of correlated neuronal variability.* Nat Neurosci. 20(1):107-114.

[6] Denève S, Machens CK. (2016) *Efficient codes and balanced networks.* Nat Neurosci. 19(3):375-82.

[7] Doiron B, Litwin-Kumar A, Rosenbaum R, Ocker GK, Josić K. (2016) *The mechanics of state-dependent neural correlations.* Nat Neurosci. 19(3):383-93.

[8] Sancristóbal B, Rebollo B, Boada P, Sanchez-Vives MV, Garcia-Ojalvo J. (2016) *Collective stochastic coherence in recurrent neuronal networks.* Nat Phys. 12, 881887.

[9] Muandet K, Fukumizu K, Sriperumbudur B, Schölkopf B. (2017) Kernel Mean Embedding of Distributions: A Review and Beyond. arXiv:1605.09522 [stat.ML].

Cortical Slices Recordings

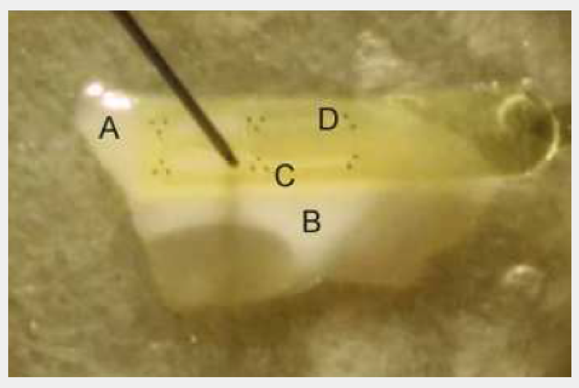

Figure 2: Cortical slice recording setup: (A) cortex, (B) white matter, (C) infragranular layers' electrodes and (D) supragranular layers' electrodes

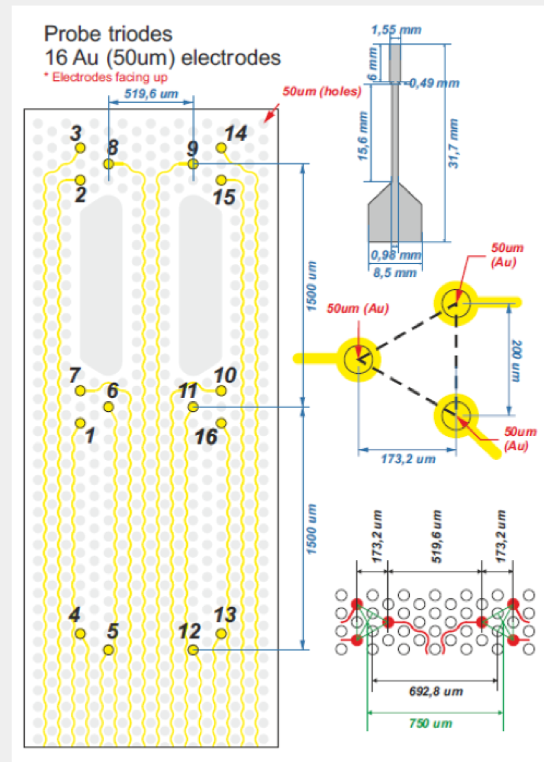

Figure 3: Schematic of the 16-channel SU-8-based flexible microprobe used for the recordings

Experimental Conditions [2]

- Pharmacological Modulations
  - adding Carbachol (0.5 μM) + Norepinephrine (50 μM)
  - reducing extracellular Calcium (to 0.8-0.9 mM)
  - Reducing temperature (to 31-32 °C)
- Electrical Stimuli
  - 150 μA pulses every 10 s at layer 5.

$\rightarrow$ Experimental model to explore the transitions from a state of slow oscillations towards a higher complexity state (awake-like asynchronous state).

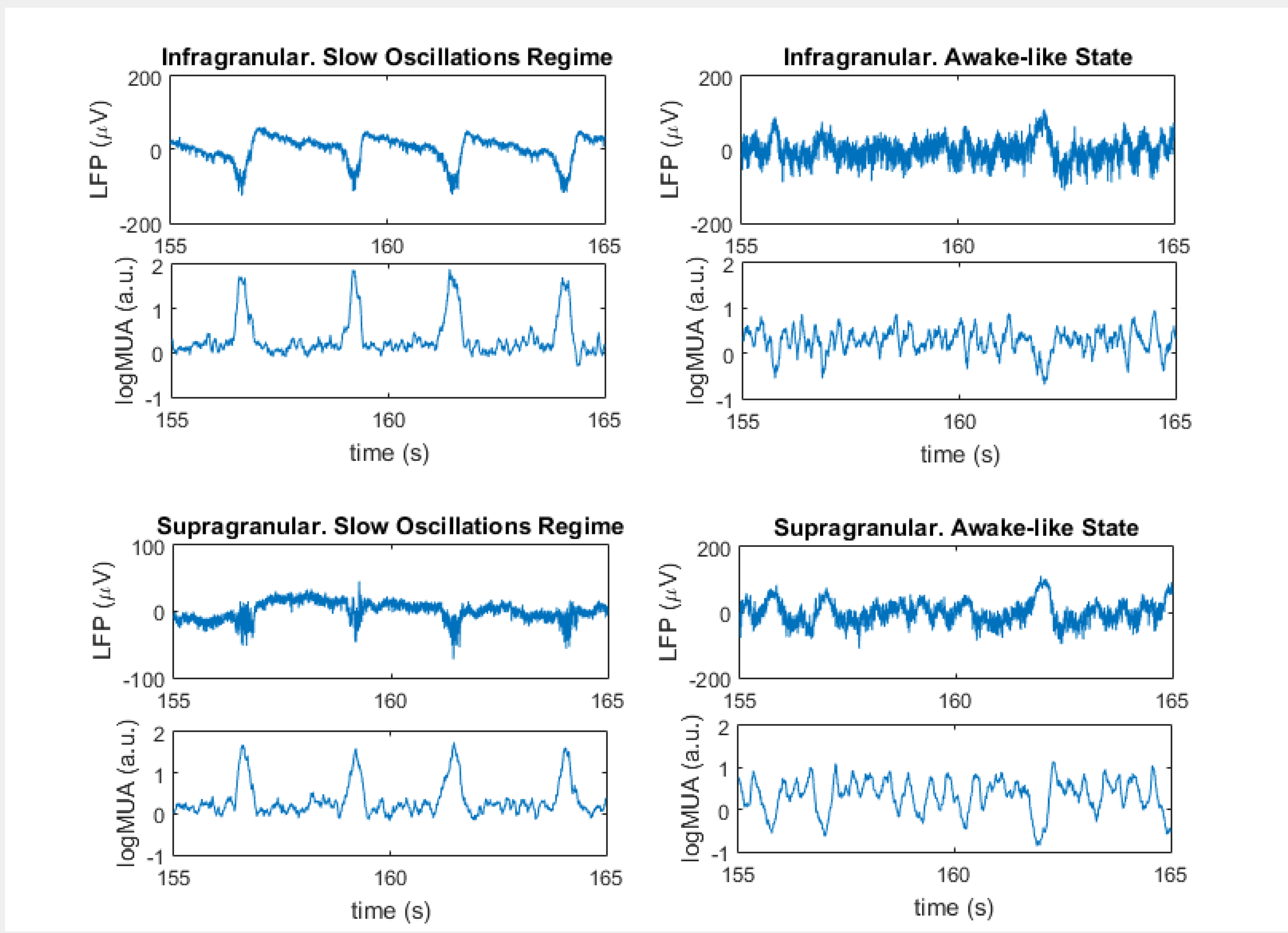

Figure 4: Example of extracellular activity (LFP and logMUA) issued from recordings at two different layers under two different experimental conditions

Our Approach

Aims

- To identify the stability of the global network states in isolated cortical networks under experimental manipulations that alter key network parameters (excitability, input, connectivity, etc.).
- To develop a novel theoretical tool which empirically captures the metastable regions of the network, i.e. transient states that temporarily behave as attractors.

Methodology

- With the aid of kernel mean embedding techniques for clustering [9], we will detect the convergence regions of the system.
- By studying how the phase portrait of the system evolves when the slow-oscillation regime is perturbed, we will map the bifurcations or transient states with the network parameters.