Abstract of Dissertation
論文の内容の要旨

Neurodynamics of Sequential Memory
(シーケンシャル記憶の神経動力学)

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Sequential memory has been the subject of intense research in recent years from the viewpoint of computational neuroscience. Experimental recordings of neural activity have been conducted at many different scales (EEG, local field potentials, multi-unit recordings etc.), notably with novel techniques that allow for the simultaneous analysis of large neuron populations. The identification of sequential patterns of activity remains however an intricate problem because it is difficult to distinguish between the random and deterministic contributions to neural fluctuations. Indeed, the code used by the brain to store, generate and manipulate sequential memories is not fully understood and, therefore, the means by which precise information could be extracted from neural signals are yet to be discovered.

In order to solve this problem, the most critical aspect to investigate is the origin and mechanisms of reliable generation, transmission and storage of temporal patterns of activity. The simulations and models of neural networks that we have developed have enabled us to identify some previously unknown conditions and dynamical regimes under which generation of temporal patterns can be achieved with robustness and flexibility as a result of well-known biological mechanisms operating in the brain. Our analysis shows that the difficulty in observing reproducible temporal patterns of activity may result from theoretical obstacles in addition to experimental ones. The models we have developed allow for the identification novel aspects of neural activity which are likely to encode sequential information, which may help improving the experimental protocols used for the analysis of neural activity in vivo, on which rely future discoveries.

Thesis

The fundamental hypothesis that motivated our research is that the encoding of sequential memory can be achieved by non linear dynamics of population averaged quantities. Previous studies have shown that low dimensional chaos has computational properties which are particularly adapted to the processing of spatio-temporal information in neural systems. However, it has been difficult to identify clearly chaotic patterns in vivo conditions, notably because neural networks are high-dimensional systems subject to fluctuations resulting from a large number of degrees of freedom. We demonstrate that at the level of neuron populations described by ensemble averaged quantities, for which the number of degrees of freedom is smaller, non linear dynamics can contribute to the encoding of temporal and sequential information.

Chaotic attractors and learning

First, we have studied how chaotic attractors encoding temporal information can be created by realistic learning mechanisms. We develop a mean field approximation of an analog neural network model to analyze the bifurcations, induced by the slow effect of learning on synaptic weights, which lead to the creation of novel chaotic attractors of activity. Attractors encoding persistent activity can notably appear via generalized period-doubling bifurcations, tangent bifurcations of the second iterates or boundary crises.

We consider the combined effects of LTP/LTD and synaptic scaling in the stabilization of these chaotic attractors. According to the rate of change of the external inputs, different types of attractors can be formed: line attractors for rapidly changing external inputs and discrete attractors for constant external inputs. Moreover, we found that fractal basin boundaries may form in neural systems when non-trivial attractors coexist.

Deterministic irregularity

We propose that the occurrence of these fractal basin boundaries have important consequences, notably concerning the change in irregularity and trial-to-trial variability of neural recordings. We evaluated the difference in complexity between coexisting attractors by calculating their Lyaponuv number and found that changes in deterministic dynamics may explain the change in irregularity observed in vivo during tasks involving the working memory.

When the encoding attractors are chaotic and basin boundaries are fractal, infinitesimal differences in the initial conditions induce sensitivity to initial conditions and final-state sensitivity, respectively, in response of the brain. We have shown that final state sensitivity can participate to the non-reproducibility characterizing physiological recordings.

We related this concept of non-reproducibility to the matching law and the hypothesis of Bayesien computation by considering the modulation of learning due to LTP and reward-dependent learning via dopamine. We show that, by modulating the area of fractal basin tongues, modulation by dopamine can favor or suppress final state sensitivity and thus the amount of trial-to-trial variability. We argue that final state sensitivity can be a candidate for the neural implementation of Bayesian computation.

Population spike coding

Furthermore, we developed a realistic model to demonstrate that population averaged activity can indeed exhibit chaotic dynamics and encode for temporal information in vivo. We developed a large scale simulation of a neural population and carefully implemented many realistic biological features and mechanisms which constrain the dynamics of biological networks, with a precise objective in mind: to not simplify artificially random fluctuations in our model as compared to in vivo conditions. Our purpose was indeed to show that, in spite of random fluctuations which are inherent to biological neural networks, some deterministic contribution can nonetheless encode temporal information.

The model is based on a network of leaky integrate and fire (LIF) neurons exposed to a noisy background, slow synaptic currents at different time scales (slow NMDA, and relatively fast AMPA and GABA currents), dynamic synapses with heterogeneous properties (depression and facilitation-dominant), delays in synaptic transmissions and slow oscillations from the cortical background modeling the modulating effect of sub threshold oscillations. All these phenomena were simulated with realistic parameters taken from the literature in neurophysiology.

We identified that the slow coordinated patterns of up and down states observed in the cortex can encode temporal information in their inter population spike intervals. We suggest that these patterns could result from the interactions between the synaptic dynamics of local neuron populations and slow modulating oscillations. We show that coupled excitatory and inhibitory networks can exhibit relaxation oscillations driven by slow oscillations, which can induce synchronization and chaotic dynamics of the population averaged activity. Implications of our model are consistent with the observation that slow oscillations are related to up and down state patterns recorded in vivo, correlated with the state of arousal during behavioral tasks and involved in memory replay.

The simulations were supported by a detailed theoretical analysis based on recent progress made in the theory of mean field approximations applied to leaky integrate and fire models. Due to our efforts in simulating a realistic network, its theoretical mean field approximation includes a large number of variables to be taken into account. We have proposed a method to simplify the analysis of the system by a fast-slow reduction. Our approach consists in aggregating the variables representing rapid membrane dynamics with the fastest components of dynamic synapses. Only the slowest contributions to short term plasticity are studied as a separate slow system.

The reduction of the fast-slow system relies on the computation of the critical manifold, i.e., steady state manifold of the fast system. We extended some results in the theory of mean field approximation applied to LIF neurons and achieved a bifurcation analysis to find conditions under which relaxation oscillations occur on the critical manifold. The analysis that we conducted is likely to be useful for the study of other systems and has a theoretical interest of its own.

Future directions

Our hypothesis that temporal information can be encoded in the imprecise timing of population spikes generated by the intrinsic properties of local neuron population contrasts with the idea of synchronous firing chains which existence is controversial.

This novel paradigm requires further theoretical investigation to test the temporal precision and limiting capacity of this code. Testing this hypothesis could suggest novel in vivo experiments.

The effect of noise on these relaxation oscillations is to haste or slow down the transition delay between up and down state, when the trajectory is at the proximity of a fold curve. It would be interesting to study in more details this phenomenon which is characteristic of noisy systems operating near a fold bifurcation. The change in spike synchrony at the transitions between up and down state observed in vivo recordings may be an important argument to support the hypothesis that these state transitions result from a deterministic contribution in addition to a stochastic one.