Experiments on Clustered Neuronal Networks

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Neuronal cultures are excellent systems to study the interplay between dynamics and connectivity in neuronal networks. Cultures not only bring a wealth of knowledge on the dynamics in living neuronal networks, but also provide fruitful insight on general principles governing brain processes. Neuronal cultures are highly versatile and can be prepared to fit diverse experimental requirements[1]. Cultures show a rich repertoire of spontaneous activity already few days after preparation, and although this activity is ultimately dictated by the underlying connectivity, the mechanisms that relate a particular network architecture with a specific dynamic behavior are still not well understood[2].

In order to investigate the dependence of neuronal network dynamics on architecture, we study spontaneous activity in a particular configuration of neuronal cultures known as clustered neuronal networks[3]. As shown in Fig. 1, these networks are formed by interconnected islands of highly packed neurons (clusters). By using different patterning techniques we can control the size and location of the clusters, therefore tailoring different network architectures.

In the experiments we monitor the spontaneous activity of the clustered network using high-speed calcium fluorescence imaging. Network's firing is characterized by bursts of activity, in which the clusters fire sequentially in a short time window, remaining silent until the next bursting episode (Fig.2a). With sufficient spatial and temporal resolution we are able to resolve, for a given burst, the activation sequence of the clusters (Fig.2b). The extension of this analysis for all the bursts of the recording finally provides the family of activation sequences.

The analysis of the experiments revealed interesting features. For instance, we observed that some activation sequences appeared more frequently than others, suggesting that a particular network architecture favors a specific dynamic motif. We also observed that the disruption of connectivity in the network by chemical or physical means preserved some dynamic motifs, hinting at the existence of dynamic robustness, even under strong perturbation of the nodes or links of the network.

Our experiments provide an interesting approach to study self-organization mechanisms in living neuronal networks and their interplay with neuronal architecture and dynamics. The analysis of the experiments in the context of network theory is providing new insights on the repertoire of activity in networks, as well as its origin, robustness and adaptability.

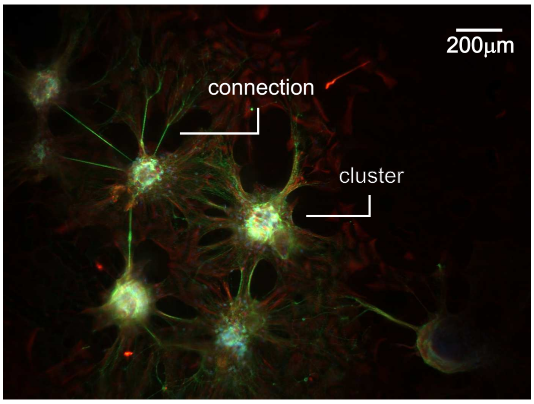

FIG. 1. Example of a clustered network. Colors corresponds to the fluorescence immunostaining of the different cell types: neurons and connections in green, glia in red and cells' soma in blue.

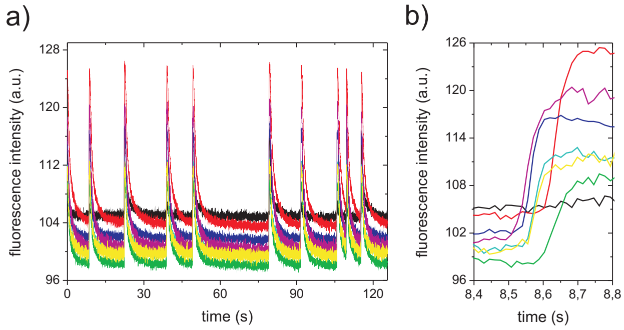

FIG. 2. **(a)** Temporal evolution of clusters bursting activity through fluorescence calcium imaging (fluorescence intensity in arbitrary units). Each color corresponds to a different cluster of the network. **(b)** Detail of a bursting episode showing that clusters fire at different times. The order of firing provides the clusters' activation sequence within the burst.

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