Spatiotemporal clustering of synchronized bursting events in neuronal networks

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Abstract

in vitro neuronal networks display Synchronized Bursting Events (SBEs), with characteristic temporal width of 100-500 ms and frequency of once every few seconds. We analyze such data using preprocessing by SVD for dimensional reduction, after which we apply quantum clustering to sort out the SBEs into different groups. Each SBE is described within a spatiotemporal template, allowing us to distinguish between neuronal activities (firing rates) and relative temporal variations of the spiking of each neuron within the SBE. Clustering assignments according to the two different kinds of information are very different from one another. SBEs may thus serve as carriers of different information in these two different implementations of the neuronal code.

Key words: Synchronized bursting events, clustering, spatiotemporal coding

1 Introduction

In vitro neuronal networks display Synchronized Bursting Events (SBEs), with characteristic temporal width of 100-500 ms and frequency of once every few seconds. These events can be registered over a period of many hours. Applying SVD (or PCA) to the PSTHs, i.e. vectors of neuronal activities per burst, (1) have demonstrated characteristic changes that take place over time scales of hours. This was done by simple clustering applied to the data in the reduced dimensions of the first few principal components. Here we extend this investigation in two directions. We distinguish between firing rate and temporal information and analyze these data separately, using the Quantum Clustering (QC) method (2) to reveal underlying structures [2].

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[2] Available software for SVD and QC can be found at `http://adios.tau.ac.il/compact`.

The data we analyze are from eight experiments carried out in the laboratory of E. Ben Jacob (3; 4). The experiments consist of registering the electrical activity of *in vitro* neuronal networks that are derived from cortical regions of rats, and are allowed to self-assemble into an active neuronal network for about a week, which is when the SBE activity is observed.

We first process the data to select the SBEs. We define an SBE by setting a threshold to the total activity within a given temporal bin of 10ms. Then, in order to define the SBE raster plot, we determine its beginning by the point where the total activity is 1/5 of the burst's peak. The end of the SBE is defined by the time when the activity decreases to the same threshold. On the average we find 2000 SBEs in each experiment. All SBEs were fit into a spatiotemporal template determined by the SBE with the longest time span, such that all peaks are set at the same time and zeros are added to the prefix and suffix of each temporal sequence defining an SBE.

Next we apply SVD processing to these data to achieve dimensional reduction. Let X denote an $m \times n$ matrix of real-valued data, e.g. firing rates of m neurons measured for n SBEs along the time-span of one experiment. The singular value decomposition of X is

$$X = USV^T \tag{1}$$

where S is diagonal, and U and V are orthonormal matrices. Consider a column vector in X. Clearly, it can be reconstructed from a linear combination of column vectors of U. Dimensional reduction means we limit ourselves to just a few of them, e.g. the first three columns of U. Afterward, we normalize the projections to the unit sphere, so that the squares of the three projections sum up to one.

Within this three-dimensional representation we perform clustering using the quantum clustering (QC) method (2). This method assigns a potential function to all data points. Data points that fall within different valleys of the potential are assigned to different clusters. To assure good separability of the different clusters we have selected points within the bottom half of each valley, regarding all others as outliers. An example of the potential for one of our experiments (231000) is shown in Fig. 1.

2 Clustering of firing rate data

Firing rate data are obtained from our SBE representation by summing over time within each SBE. Applying SVD to the resulting PSTHs, we reproduce the clusters of (1) in the three experiments analyzed there, and usually obtain three clusters in each of our eight experiments. However, whereas (1) have observed that different clusters occur at different times over the span of the experiment, we find that this is not a general characteristic. In four of the experiments that we have analyzed we observed a uniform temporal distribution, i.e. bursts belonging to a specific cluster may occur anytime within the many hours of the experiment.

3 Clustering of spatiotemporal data

Now we turn to spatiotemporal data, applying our SVD procedure and clustering to the spatiotemporal representation of the SBEs. The QC potential of one of the experiments is demonstrated in Fig. 1. The data in the three valleys of this potential are assigned to the three different clusters.

The first important observation is that the assignment of SBEs to clusters according to the spatiotemporal structure, is different, almost orthogonal, to the assignments derived from the firing-rate analysis. Hence the two different representations seems to carry different information. Next we wish to point out that all spatiotemporal clusters seem to have uniform distribution along the time scale of the experiment.

Since the clusters were derived from the SVD reduced representation, we return now to the original data and ask whether the spatiotemporal clustering can be observed directly in it. We randomly select 100 SBEs from each one of the three clusters, and measure the Pearson correlations between their original raster plots. The results, shown in Fig. 2, demonstrate that correlations within the clusters are significantly higher than correlations between SBEs that belong to different clusters, i.e. the clustering selection is indeed meaningful. The dimensional reduction, while very helpful in the clustering analysis, did not distort the important features in the data.

To exemplify the differences between the spatiotemporal clusters we display in Fig. 3a the average activity of a specific neuron within the SBEs of three different clusters in one of the experiments. Clearly this profile is strongly cluster dependent. Moreover we observe different inter-neuron relations in different clusters. As an example we display in Fig. 3b the profiles of two neurons in two different clusters, taken from another experiment, showing synchrony in one cluster and out-of-phase behavior in the other.

4 Discussion

The question may arise whether our results can contribute to the old question regarding the nature of the neural code, i.e. is information carried only by neuronal firing rate or also by the timing of its spikes. A well-known debate on this issue took place in 1995 between Softky (5), who claimed that temporal coding is much more efficient than rate coding, hence evolution was supposed to prefer it, and Shadlen and Newsome (6) who pointed out that there was no clear biological evidence found for the more complex temporal coding.

In our case, we analyze experiments in which neurons self-assemble and act without any obvious external stimuli. Hence the information carried by their firing patterns cannot be specified because it is not clear what it should be associated with. We may regard the different clusters as representing candidates for neuronal cell assemblies that may be used as such if and when the neuronal system becomes part of a general information-carrying organism. Our contribution to the important neuronal code problem is that we observe independent clusters in the two different modes of firing rate and temporal variation within SBEs. In other words, information may be simultaneously and independently carried by these two different modes. Thus the two different codes may coexist within the same system.

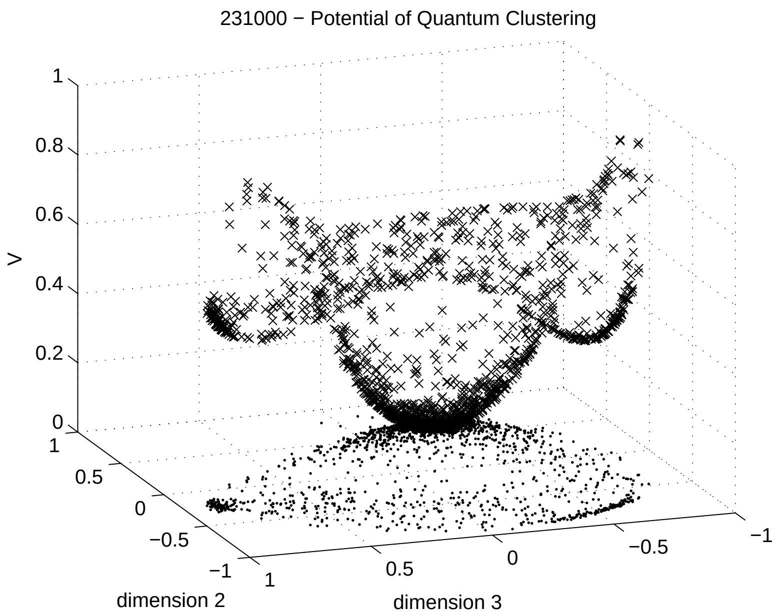

Fig. 1: The values (x) of the QC potential function for data points (dots) displayed in a plane spanned by the second and the third principal components of SVD.

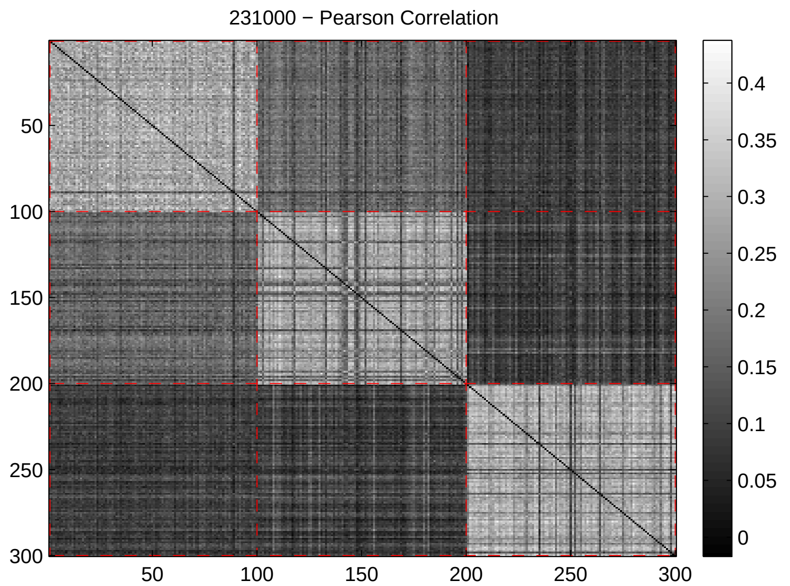

Fig. 2: Pearson correlations between the raster plots of SBEs assigned to the three clusters corresponding to the bottom halves of the three valleys in Fig. 1.

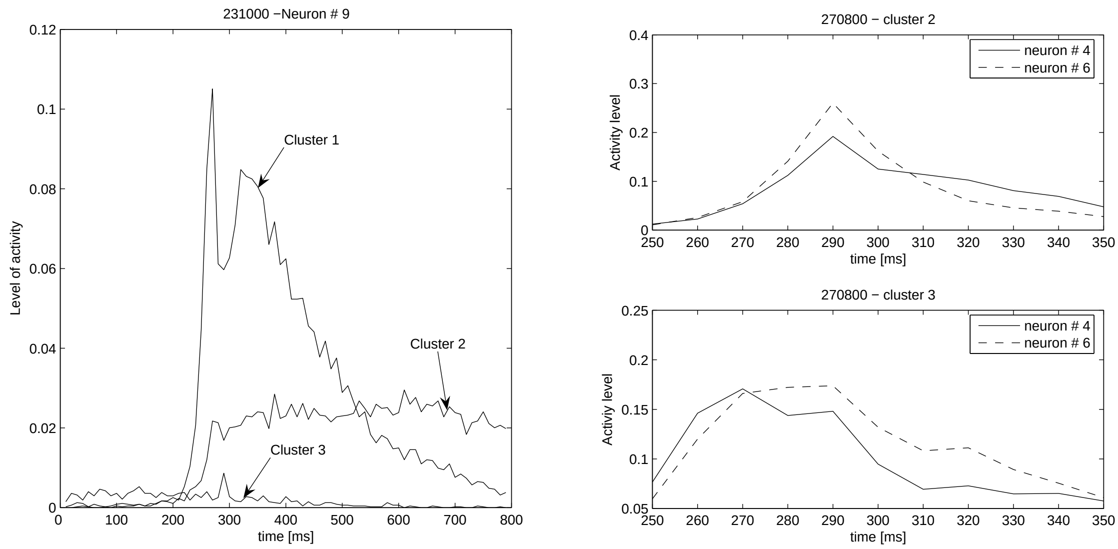

Fig. 3: (a) Activity characteristics of a particular neuron in the SBEs belonging to the three different clusters display clearly different profiles. (b) Profiles of two neurons in another experiment show different relative phases depending on the clusters.

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