A MIXTURE MODEL FOR SPIKE TRAIN ENSEMBLE ANALYSIS USING SPECTRAL CLUSTERING

Rong Jin[*], *Yasir Suhail*[†], *Karim Oweiss*[‡]

[*] Computer Science and Engineering Dept., Michigan State University, East Lansing MI, USA
[‡] Electrical and Computer Engineering Dept., Michigan State University, East Lansing MI, USA
[†] Biomedical Engineering Dept., The Johns Hopkins University, MD, Baltimore, USA

ABSTRACT

Identifying clusters of neurons with correlated spiking activity in large-size neuronal ensembles recorded with high-density multielectrode array is an emerging problem in computational neuroscience. We propose a nonparametric approach that represents multiple neural spike trains by a mixed point process model. A spectral clustering algorithm is applied to identify the clusters of neurons through their correlated firing activities. The advantage of the proposed technique is its ability to efficiently identify large populations of neurons with correlated spiking activity independent of the temporal scale. We report the clustering performance of the algorithm applied to a complex synthesized data set and compare it to multiple clustering techniques.

1. INTRODUCTION

One of the key issues to understand the general computational principles underlying the dynamic interactions between populations of neurons in systems neuroscience is to identify the topology of the neuronal circuits that is transiently configured to process and store information. This may be feasible by identifying the subsets of neurons within a recorded ensemble that collectively and cooperatively respond to external stimuli with possibly non-random temporal relationships among their spiking activity patterns. This identification problem has received attention for several decades since single electrode recordings were performed to isolate pairs or triplets of single units. Large scale ensembles of neurons became more feasible to record with the advent of high-density microelectrode arrays (e.g. [1]) that enabled high resolution mapping of neuronal activity to be obtained in a network context [2]. As a result, large volumes of physiological and behavioral data became available in the past few years that triggered numerous neurobiological discoveries.

Traditionally, spike trains have been considered multi-dimensional point processes due to their stochastic and dynamic nature [3, 4]. Although a handful of probabilistic models have been largely used to describe the likelihood of a neuron firing at any given time , techniques for identifying functional interdependencies in these large data sets remain relatively limited to resolving correlations of a few neurons [5, 6]. These are either time domain, frequency domain, pattern classification or likelihood based approaches.

Generally speaking, two important aspects mitigate the performance of these approaches in clustering spike train data. First, nonstationarity in neuronal firing, and second, the uncertainty in existing spike sorting techniques. The former is problematic for many existing approaches because of the underlying stationarity assumption within the analysis interval. The later, on the other hand, generally leads to a large number of unresolved neurons that contaminate the accuracy of clustering. Traditionally, averaging is performed across trials to reduce the variability in the analysis, which unfortunately makes the identification of the rapid dynamic changes in neural representation of sensory inputs a formidable task.

The objective of this paper is to propose an unsupervised, nonparametric clustering approach for identifying clusters of functionally interdependent neurons from multiple single unit activity, independent of the time scale at which they are dependent. There are two main advantages of the proposed approach: First, the ability to map to a single cluster units in local neuronal circuits that receive common inputs and respond with relatively fast temporal synchrony, as well as units in global circuits with extended synaptic activation that exhibit slower temporal dependency that arise later in the response. Second, the approach relies on the wavelet transform as a preprocessing tool before actual clustering is performed. Besides the superior capability of wavelets in modeling nonstationary signals [7], it is considered a natural extension to the wavelet-based spike sorting algorithm developed recently by the third author [8] in which large margins of spike sorting errors from previous techniques were efficiently remedied.

2. THEORY

Suppose we have array of M electrodes that records P spike trains within the discrete interval $T = [t_1, \ldots, t_N]$. The observed raw data is an $M \times N$ matrix that can be modeled as

$$\mathbf{Y} = \mathbf{AS} + \mathbf{Z} \tag{1}$$

where $\mathbf{A} \in \mathbf{R}^{M \times P}$ denotes the mixing matrix that expresses the array response to P single units, $\mathbf{S} \in \mathbf{R}^{P \times N}$ denotes the P spike trains, and $\mathbf{Z} \in \mathbf{R}^{M \times N}$ denotes a zero-mean additive noise component. A scale space array model can be obtained from (1) by expressing the data matrix across multiple time scales by means of the discrete wavelet transform (DWT) [7] up to J scale levels, i.e.,

$$\mathbf{Y}_j = \mathbf{A}\mathbf{S}_j + \mathbf{Z}_j,\ j = 0, 1, \ldots, J \tag{2}$$

where spike trains in each scale level are represented by the matrix $\mathbf{S}_j$. Our objective is to identify groups of functionally interdependent neurons given the scale representation of the sorted neuronal spike trains $\{\mathbf{S}_j, j = 1, \ldots, J\}$.

2.1. The Mixture Point Process Model

Inferring correlation between any given pair of neurons in existing methods usually assumes that the interval over which correlation is assessed remains fixed for both neurons. Such assumption does not take into account the fact that rapid modulation of a neuron's firing rate may trigger slow modulation of rate function of another neuron. The converse is also true when neuronal local synchrony is inhibited by slow wave local field potentials or global unit firing activity over relatively longer periods of time. In order to capture both the short term and the long term correlation, we propose a non-parametric mixture point process model. We assume each of the P neurons may belong to any of K clusters. Each cluster represents neuronal elements that exhibit all types of short and long range temporal interdependency. We also assume that each neuron can belong to more than one cluster. This implies that a neuron can belong to a short rapid synchronized population as well as a slow asynchronous population in response to both *local* and *global* inhibition/excitation from other populations.

Let the function $f_p(t)$ denote the firing rate of a neuron spike train p, and $\mathbf{f}_p = [f_p(1), \ldots, f_p(N)]$ denote the sampled version of $f_p(t)$ within the discrete interval $T = [t_1, \ldots, t_N]$. Let $\{\mathbf{F}_k, k = 1, \ldots, K\}$ denote an underlying unknown "base" rate function of each cluster. Then, for neuron p, its firing rate function can be expressed as

$$\mathbf{f}_p = \sum_{k=1}^{K} a_{pk}\mathbf{F}_k \tag{3}$$

where a_{pk} describes the degree of membership of neuron p to cluster k. The spike train $\mathbf{s}_p$ can be modeled as the sum of the sampled firing rate $\mathbf{f}_p$ plus an independent error term i.e.,

$$\mathbf{s}_p = \mathbf{f}_p\delta T + \mathbf{z}_p \tag{4}$$

where δT represents the bin width of the spike train, and $\mathbf{z}_p$ represents the estimation error incurred in the approximation of the true rate function $f_p(t)$ in a minimum mean square error sense.

2.2. Scale-Space Representation

Let $W^{(j)}$ denote the lumped matrix operator of a discrete wavelet transform at time scale j, then the spike train at level j, denoted $\mathbf{s}_p^j$, can be expressed as

$$\mathbf{s}_p^j = \mathbf{W}^{(j)}\mathbf{s}_p$$

By substituting from (3) and (4), we have

$$\mathbf{s}_p^j = \sum_{k=1}^{K} a_{pk}\mathbf{F}_k^j\delta T + \mathbf{W}^{(j)}\mathbf{z}_p \tag{5}$$

where $\mathbf{F}_k^j$ represents the k-th cluster base rate function estimated at time scale j. The sampled cross correlation between neurons p_1 and p_2 at time scale j is determined as

$$c_{p_1p_2}^j = \frac{1}{N}\sum_{n=1}^{N} s_{p_1}^j(n)s_{p_2}^j(n)$$

Using (5), we have

$$\begin{aligned} E[c_{p_1p_2}^j] &= \frac{(\delta T)^2}{N}\sum_{k=1}^{K} a_{p_1k}a_{p_2k}(\mathbf{F}_k^j)^T\mathbf{F}_k^j + E[(\mathbf{z}_{p_1}^j)^T\mathbf{z}_{p_2}^j] \\ &= \frac{1}{N}\sum_{k=1}^{K} a_{p_1k}a_{p_2k}e_k^j + \epsilon_{p_1p_2}^j \end{aligned} \tag{6}$$

where $e_k^j = (\mathbf{F}_k^j)^T\mathbf{F}_k^j(\delta T)^2$ and $\epsilon_{p_1p_2}^j = E[(\mathbf{z}_{p_1}^j)^T\mathbf{z}_{p_2}^j]$. When noise terms of two neurons p_1 and p_2 are loosely correlated, $\epsilon_{p_1p_2}^j$ will be small, and therefore the pairwise correlation between p_1 and p_2 is mainly determined by a_{p_1k}'s and a_{p_2k}'s, the degree of membership of the neurons in each cluster. Moreover, the dependence of the sample correlation on e_j^k, the energy of each cluster at different time scales, plays an essential role in identifying the appropriate time scale at which any two neurons are correlated.

2.3. Assessing Pairwise Correlation in Scale Space

Let the pairwise correlation matrix of the neurons in the k-th cluster be denoted by $\mathbf{C}_k \in \mathbf{R}^{P \times P}$. Then, the correlation of neurons at the j-the time scale, denoted by $\mathbf{C}^j$, can be expressed as:

$$\mathbf{C}^j = \sum_{k=1}^{K} \mathbf{C}_k e_k^j + \Delta^j \tag{7}$$

where $\Delta_{p_1p_2}^j = \epsilon_{p_1p_2}^j$. To reduce the uncertainty in estimating time scale correlation using cluster correlation, we use principal components to suppress the error term Δ^j. In particular, we construct a block diagonal matrix $\mathbf{T} \in \mathbf{R}^{(P \times J) \times (P \times J)}$ that has the j-th $P \times P$ block as $\mathbf{C}^j$, i.e.,

$$\mathbf{T} = \begin{bmatrix} \mathbf{C}^0 & & & \\ & \mathbf{C}^1 & & \\ & & \ddots & \\ & & & C^J \end{bmatrix} \tag{8}$$

With $\{(\lambda_i, \mathbf{u}_i), i = 1, \ldots, P \times J\}$ as the eigenvectors and eigenvalues of matrix $\mathbf{T}$, we then reconstruct matrix $\mathbf{T}$ by only using its dominant eigenvectors using the low rank approximation

$$\mathbf{T}_{p_1 p_2} = \sum_{q=1}^{Q} \lambda_q |c^q_{p_1 p_2}| \tag{9}$$

where $c^q_{p_1 p_2}$ denotes the correlation between neurons p_1 and p_2 in the direction of the eigenvector $\mathbf{u}_q$. Each entry $\mathbf{T}_{p_1 p_2}$ provides a *similarity measurement* between neuron p_1 and p_2, which will be used to form the graph representation for spectral clustering.

2.4. Spectral Clustering in Scale-Space

The above steps outline the basic preprocessing needed to map the neuronal spike trains to a scale-space graph representation using adequately defined similarity measures. This representation allows using a powerful unsupervised clustering approach drawn from Machine Learning [9]. Briefly, a spectral clustering algorithm views the problem of identifying clusters of strongly correlated objects as a graph partition problem. In particular, each object, in our case a neuronal spike train, is represented as a vertex in a graph. Any two objects are connected by an undirected edge whose weight is the similarity between the two objects. With the graph representation, a minimum cut algorithm is applied to identify clusters of strongly related objected and only edges of small weights are removed. In order to allow each neuron to belong to multiple clusters, we use "soft" memberships. In particular, we use a_{pk} to represent the probability for the p-th object to be in the k-th cluster. Then, the minimum cut problem is to find the set of probabilities $\{a_{pk}\}$ that maximizes the following objective function:

$$\mathcal{L} = \sum_{k=1}^{K} \frac{\sum_{p_1=1}^{P} \sum_{p_2=1}^{P} a_{p_1 k} a_{p_2 k} w_{p_1 p_2}}{\sum_{p_1=1}^{P} \sum_{p_2=1}^{P} a_{p_1 k} w_{p_1 p_2}} \tag{10}$$

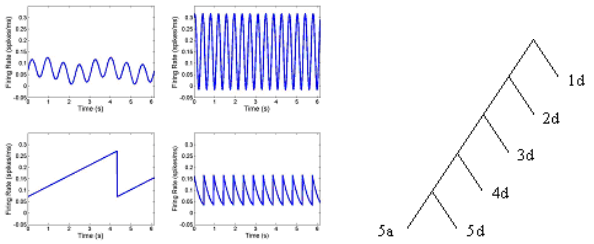
An efficient bound algorithm [10] can be used to optimize the objective function in equation (10). The final cluster memberships are derived from $\{a_{pk}\}$ by assigning each object to the cluster with the largest probability, i.e.,

$$k^*_p = \text{argmax}_{k \in \{1,\ldots,K\}} a_{pk} \tag{11}$$

Finally, to apply the probabilistic spectral clustering in scale space, we set $w_{p_1 p_2} = \mathbf{T}_{p_1 p_2}$ as determined from (9).

3. EXPERIMENTAL RESULTS

We evaluate the proposed algorithm on a simulated data set with pre-defined relationships among neuronal elements. This simulation consisted of 120 neurons divided into 4 clusters of



(a) (b)

Fig. 1. (a) Basis firing functions, and (b) the number scheme for Wavelet transform tree

30 neurons each. Neurons within a cluster were functionally interdependent but were independent of neurons outside the cluster. Every cluster was assigned a base rate function $\mathbf{F}_k$ that was distinct for each of the four clusters. These function are illustrated in Figure 1(a). Within each cluster, firing rate functions $\mathbf{f}_p$ were generated for all neurons belonging to that cluster according to the following relationship

$$f_p(n) = \alpha_p \mathbf{F}_k \left(\frac{n - \tau_p}{\sigma_p} \right) + \gamma_p \tag{12}$$

where α_p, τ_p, δ_p, and γ_p were randomly generated parameters for each neuron. In this simulation, it was assumed that for $a_{pk} = 1$ when neuron p belongs to the k-th cluster and 0 otherwise (i.e., no overlap between clusters). A spike train $\mathbf{s}_p$ was obtained as a realization of a Non Homogenous Poisson Process with rate $\mathbf{f}_p$.

A discrete wavelet transform representation of the spike trains was obtained up to eight decomposition levels. We used the Haar wavelet basis in our experiment. The correlation of neurons on different time scales is illustrated in Figure 2, following the numbering scheme of Figure 1(b). For visual clarity, spike trains belonging to one cluster were numbered consecutively. Hence, a cluster appears as a continuous band of 30 rows or columns. It is clearly observed that the clusters have distinct timescale correlation structures as evident from the representations across multiple levels. For example, cluster 2 is strongly represented at time scales corresponding to levels "4d" and "5d", while cluster 3 is best represented at time scales corresponding to levels "7d", "8d", and "8a", respectively. Furthermore, the projection of correlation matrix on different principle eigenvectors, i.e., $c^q_{p_1 p_2}$ in (9), is illustrated in Figure 3. It is clear that PCs beyond the sixth component do not possess any significant energy.

The clustering error of the proposed algorithm for this simulation is only 2.5%, or only 3 neurons out of 120 were incorrectly clustered. To put these results into perspective, they were compared to those of the k-means and Bayesian clustering and listed in Table 4. Given that each neuron spike train is represented by a large number of data points, a principle component analysis is applied to reduce the dimensional-

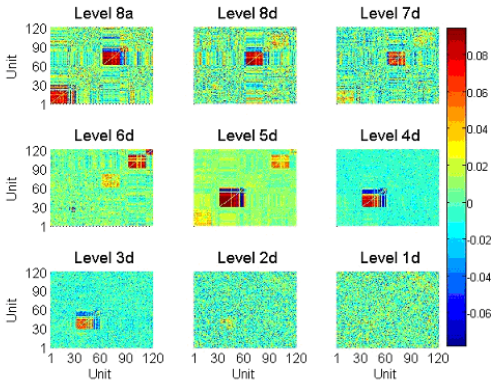


Fig. 2. Correlation matrix across multiple time scales for 8-Haar wavelet transform. The number scheme of Wavelet transform is illustrated in Figure 1(b).

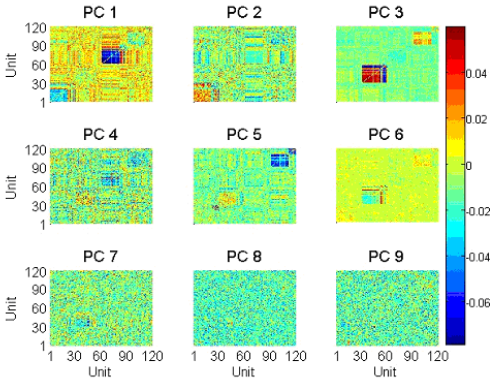


Fig. 3. Dominant 9 principal components of the augmented matrix $\mathbf{T}$.

ity before the k-means and the Bayesian clustering algorithms are applied.

4. CONCLUSION

We presented a novel approach for analyzing multiple spike trains in large-size neuronal ensembles. The technique relies on scale-space spectral clustering, in which neurons exhibiting functional interdependency across a multitude of time scales will be clustered together. This intrinsic feature is of crucial importance to short-term and long-term dependency typically encountered in ensemble neural recordings in multiple brain structures that inherently characterizes the distributed processing mechanism of the nervous system. Furthermore, unlike pairwise, fixed bin-width correlation techniques, the spectral clustering works with the distance/similarity information independent of the temporal scale at which neurons might be correlated, which allow for sophisticated distance/similarity measures (e.g., kernel function), especially

Number Of Features	K-Means	Bayesian
5	25.8%	43.0%
10	25.8%	48.3%
20	46.6%	60.0%
40	65.8%	60.0%

Table 1. Clustering errors for K-Means and Bayesian Algorithm

when the firing rate functions are nonlinearly related.

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