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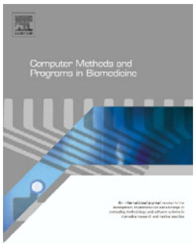

In quest of the missing neuron: Spike sorting based on dominant-sets clustering

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ABSTRACT

Spike sorting algorithms aim at decomposing complex extracellular signals to independent events from single neurons in the electrode's vicinity. The decision about the actual number of active neurons is still an open issue, with sparsely firing neurons and background activity the most influencing factors. We introduce a graph-theoretical algorithmic procedure that successfully resolves this issue. Dimensionality reduction coupled with a modern, efficient and progressively executable clustering routine proved to achieve higher performance standards than popular spike sorting methods. Our method is validated extensively using simulated data for different levels of SNR.

1. Introduction

The basis of every spike sorting algorithm is the assumption that all the action potential traces of a particular neuron have nearly the same amplitude and shape. In extracellular recordings, the shapes of neural waveforms reflect the neuron's geometry and its distance to the recording electrode [1,2]. The goal of a spike sorting process is to identify the number of active neurons and extract detailed time courses of their spiking activity from extracellular neural recordings. The related algorithms display a variety of applications ranging from clinical neurophysiology to cortex–machine interfaces.

The battery of available spike sorting routines includes mainly automated techniques that analyze the recorded signals by means of their waveforms. In a first step, linear techniques like principal component analysis (PCA) [3,4] and wavelets [5–7] are often employed to reduce the dimensionality of the input data and enhance the signal dynamics. PCA representation is most often restrained within the subspace spanned by the first two or three principal components, although the incorporation of additional components is often advantageous [8]. Alternatively, the wavelet transform can be employed in the representation step so as to enhance the subsequent spike discrimination by emphasizing particular morphological characteristics. In both cases, the representation step serves as a preprocessing stage for a clustering framework that would take over the detection of distinct signal sources (i.e. active neurons) and the classification of the corresponding spiking contributions.

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Regarding clustering, Bayesian [9] and expectation maximization [10] methods have been proposed for spike sorting. A stationary Gaussian profile for the background noise is a popular assumption in the related methodologies [11]. Both the above methods consider Gaussian characteristics for the potential clusters residing in the PCA representation subspace. However, background noise in realistic neural recordings may only be approximately modeled as stationary Gaussian process [12]. Actually, deviations from stationarity and normality are the usual case. Synaptic coupling among neurons, superimposed field potentials, electrode drifts and bursting neurons are all factors that constitute a non-stationary non-Gaussian cluster profile more plausible [7,9,13–15]. To avoid Gaussian considerations, clustering approaches featuring hierarchical algorithms have appeared [7,16]. In particular, the work described in [7], namely *Waveclus*, is currently considered as a state-of-the-art technique in the spike sorting domain [17]. It employs a stochastic algorithm, known as super-paramagnetic clustering (SPC), which makes no prior assumptions about the statistical properties of the data. Furthermore, online spike sorting techniques have appeared incorporating data-dependent feedback so as to directly adapt to the non-stationarities of the recording [18].

There are two important parameters when one evaluates a spike sorting classification process: the number of clusters (i.e. the number of active neurons) being decided by the process and the number of spikes assigned to each cluster. Both are well incorporated by Type I/II errors [10] in the spike sorting domain. Type I (false positive (FP))/II (false negative (FN)) errors derive from the traditional classification schemes and conceptualize misclassification. A false-positive corresponds to a misplaced spike (most often represented by an ambiguous waveform), wrongly assigned to the cluster of waveforms for a particular neuron. Likewise, a false-negative corresponds to a spike missing from the cluster of a neuron's waveforms. Thus, the identification of fewer neurons than expected (under-clustering) leads to high false positive errors, while the opposite case (over-clustering) results in a large amount of false negatives. Although a correct estimation of the number of clusters would limit both errors in cluster-delineation, the identification of the actual number of active neurons is still an open issue. Even popular methods (like SPC) do not often incorporate a satisfactory treatment of this issue, leading to erroneous results [17]. It is worth noting that, in laboratory practice, over-clustering is most often addressed in a less time-consuming way than under-clustering. In a recently published work [8], we have stressed the importance of the previous fact and defined a new clustering-error measure that penalizes under-clustering more than over-clustering.

There are two main reasons that obstruct the estimation of the 'true' number of active neurons. The first relates to the low SNR of the signals and the subsequent poor representation (in the original or reduced space) of the waveforms. The second relates to the existence of sparsely firing neurons among those contributing to the recorded signal. The identification of the relatively rare events corresponding to their activations is an issue left untreated by the vast majority of contemporary algorithms targeting the activity of dominating 'hyperactive' neurons. However, the involvement of this type of neurons in the formation of neural code has been recently emphasized [19–23] and the development of a spike sorting algorithm capable of recognizing sparsely-firing neurons is necessary. Currently, only Waveclus has been considered as 'an optimal spike sorting algorithm that is particularly suited to detect sparsely firing neurons, which typically have very low baseline firing rates' [21].

Here we propose a sequential, subtractive algorithmic procedure which, apart from the reliable classification of activations from 'conventional' neurons, can treat equally well activations from 'occasional' or 'sporadic' neurons. The principal algorithm stems from graph theoretic ideas and in particular the notion of dominant sets [24]. It works in an iterative fashion by operating on a neighborhood graph. It identifies the core of the graph, using replicator dynamics formulation, and then removes it from the graph and feeds back the remaining graph. The procedure terminates when all the data have been assigned to distinct groups or no more compact groups can be formed. The incorporated algorithm is engaged to work within a representation space which is derived via a fully compatible dimensionality reduction technique, namely the isometric feature mapping (ISOMAP) [25]. ISOMAP is known to reveal the intrinsic data variation and is therefore expected to be insensitive to random variations due to background noise. Hence, the resulting low-dimensional parameterization of the waveform variation is expected to enhance the clustering performance.

A preliminary version of this work has appeared in the Proceedings of the 12th Mediterranean Conference on Medical and Biological Engineering and Computing (MEDICON2010) [26]. The use of iterative dominant-sets algorithm for spike sorting was originally introduced therein. Here the algorithm is incorporated in a noise-assisted, pattern-analytic framework and extensively evaluated (A Matlab implementation of the algorithm is available online at http://neurobot.bio.auth.gr/spike-sorting).

The remainder of this article is organized as follows. Section 2 describes the proposed methodology. Section 3 presents the comparative evaluation of our spike sorting technique in relation with a state-of-the-art alternative [7], using simulated data. Section 4 concludes the paper.

2. Method

2.1. Low-dimensional representation

The neural waveform segments, extracted from the time-series of extracellular recordings, are considered as the initial raw representation of spiking activity. The ensemble of these loosely aligned spike-waveforms can be thought as a point-swarm residing in a multidimensional feature space with axes corresponding to signal amplitudes at particular latencies. Following the standard convention, the ith spike waveform is depicted as $x_i(t)$, $t = 1, 2, \ldots, T$, $i = 1, 2, \ldots, N$ (with t denoting discrete time or latency) and represented via the row-vector $\mathbf{x_i} = [x_i(1), x_i(2), \ldots, x_i(t), \ldots, x_i(T)] \in R^T$. Similarly the whole ensemble is represented in a data-matrix format as $\mathbf{X}_{[N \times T]} = [\mathbf{x_1} | \mathbf{x_2} | \ldots \mathbf{x_i} | \ldots \mathbf{x_N}]$, where '|' denotes a line separator.

Here, we employ ISOMAP embedding as a dimensionality reduction (denoising) step. The goal is to achieve a