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Sorting of neural spikes: When wavelet based methods outperform principal component analysis

ALEXEY PAVLOV[1], VALERI A. MAKAROV[2,*],
IOULIA MAKAROVA[2,3], and FIVOS PANETSOS[2]
[1]*Nonlinear Dynamics Laboratory, Department of Physics, Saratov State University, Astrakhanskaya St. 83, 410026, Saratov, Russia;* [2]*Neuroscience Lab, Department of Applied Mathematics, Escuela de Optica, Universidad Complutense de Madrid, Avda. Arcos de Jalon s/n, 28037, Madrid, Spain;* [3]*Departamento Investigacion, Hospital Ramon y Cajal, 28034, Madrid, Spain (*Author for correspondence, e-mail: vmakarov@opt.ucm.es)*

Abstract. Sorting of the extracellularly recorded spikes is a basic prerequisite for analysis of the cooperative neural behavior and neural code. Fundamentally the sorting performance is defined by the quality of discriminative features extracted from spike waveforms. Here we discuss two features extraction approaches: principal component analysis (PCA), and wavelet transform (WT). We show that only when properly tuned to the data, the WT technique may outperform PCA. We present a novel method for extraction of spike features based on a combination of PCA and continuous WT. The method automatically tunes its WT part to the data structure making use of knowledge obtained by PCA. We demonstrate the method on simulated and experimental data sets.

Key words: clustering, neural spikes, spike sorting, wavelet analysis

Abbreviations: PCA – principal component analysis; WF – wave form; WSAC – wavelet shape-accounting classifier; WSPC – wavelet-classifier with superparamagnetic clustering; WSC – wavelet-based spike classifier; WT – wavelet transform

1. Introduction

Current extracellular experiments provide recordings of multi-unitary activity, where several neurons nearby to an electrode tip produce short lasting electrical pulses or spikes different in amplitude and shape (Figure 1, for details see e.g., Lewicki, 1998). Consequently, the quality and reliability of an analysis of the cooperative neural behavior or single neuron spiking activity rely on the ability of separation (or sorting) of the recorded firing events into groups or clusters. Ideally each cluster should contain spikes emitted by only one neuron. Errors occur when spikes belonging to other neurons are

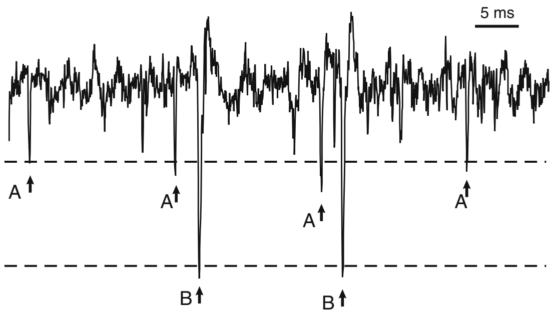

Figure 1. An example of extracellular potential recorded from the hippocampus of the rat. The simplest way to sort spikes (marked by arrows) is the amplitude thresholding. Two dashed lines delimit two groups of spikes, A and B, but a reliable sorting needs more careful investigation.

grouped together with the spikes of the target neuron (false positive) or when some spikes emitted by that neuron are not included into its group (false negative).

The quality of spike separation by a human operator is significantly below the estimated optimum (Harris et al., 2000). Besides, amount of the data generated by modern experimental setups is really huge (in a typical experiment one can easily have more than 10^4 spikes), hence there is a big demand for developing of automatic optimal separation techniques.

Currently there exist a number of numerical tools aiming at spike classification (see e.g., Lewicki, 1998; Wheeler, 1999; Shoham et al., 2003; Buzsaki, 2004 and references therein). Further on we shall consider empirical methods of spike sorting that rely on two basic steps: (i) Extraction of the most discriminative features from spike waveforms; and (ii) Clustering of the obtained parametric set into groups, i.e., identification of the number of different groups (neurons) and the membership of spikes in these groups.

Also there are many clustering algorithms (see e.g., Kaufman and Rousseeuw 1990; Downs and Barnard, 2002) showing different performances on different data sets, as a mater of fact, the final performance of the spike sorting is mostly defined by the quality of the extracted spike features. Currently available methods for feature extraction may be divided into three groups: (1) "naive", threshold based; (2) principal component analysis (PCA); and (3) wavelet transform (WT). The first two methods are the most widely used now, while the third technique has been shown to be superior and becomes more popular (Letelier and Weber, 2000; Hulata et al., 2002; Quian Quiroga et al., 2004).

Although existing methods show a good performance on preselected data sets, the best procedure of the spike feature extraction is still a challenging issue. Here we analyze strengths and weaknesses of the methods and present our novel approach for spike feature extraction combining PCA and continous wavelet transform.

2. Potential and limitations of PCA and wavelet techniques

For illustration purpose we generated two testing data sets (Figure 2), both consisting of 500 spikes of five different waveforms. The original spike waveforms where selected from electrophysiological recordings. The two sets have three clearly different waveforms (WFs 1–3) and two similar ones (WFs 4, 5). Similar waveforms in Set #1 exhibit differences in small time scale only, while WFs 4 and 5 in Set #2 have more pronounced difference on larger scales. To simulate the noisy background we mixed a colored noise, band-pass (300 Hz–3 kHz) filtered Poisson process, with the noise-free spike waveforms.

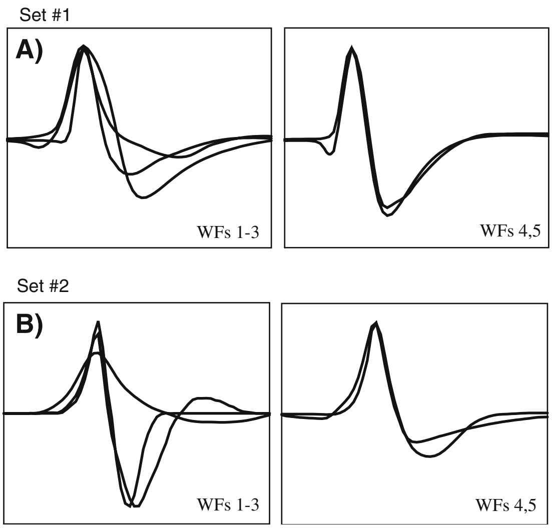

Figure 2. Original spike waveforms used for generation of two data sets (Sets #1 and #2). We use three clearly different waveforms (WFs 1–3) and two similar waveforms (WFs 4 and 5). Difference between the similar WFs appears on small time scales for Set #1 and on larger scales for Set #2.

Within the PCA framework a set of orthogonal eigenvectors of the covariance matrix of the spike waveforms is estimated. Then each spike is completely represented by a sum of the principal component vectors with the corresponding scale factors, so called scores. The scores are considered as spike features for sorting. In practice the use of the first two or three scores is the optimal, since they account for the largest variance in the spike waveforms.

A problem with the PCA method occurs when among different waveforms there are two types with similar shapes and clearly expressed distinctions appearing only on small time scales (Set #1 in Figure 2). Such distinctions are usually not reflected in the first principal components, and consequently the method may fail to separate such spikes. Indeed, sorting of Set #1 by PCA reveals four different clusters (Figure 3A). The first three clusters correspond to spikes of WFs 1–3, so confirming potential of the PCA approach. However, the fourth cluster contains a mixture of spikes of the two similar waveforms: WFs 4 and 5. Analysis of the first principal components proves that the difference between WFs 4 and 5 is not reflected by them.

The wavelet approach (Letelier and Weber, 2000; Hulata et al., 2002; Quian Quiroga et al., 2004) represents spikes by coefficients of the WT (somehow similar to the Fourier transform):

$$C(a,b) = \frac{1}{\sqrt{a}} \int_{-\infty}^{+\infty} s(t)\psi_{a,b}(t)\,\mathrm{d}t,\ \ \psi_{a,b}(t) = \psi\left(\frac{t-b}{a}\right), \tag{1}$$

where $s(t)$ is the spike waveform, and $\psi\ (t)$ is the translated and scaled mother wavelet with b and a defining the time localization and scale, respectively. The WT (1) of a spike can be considered as a set of filters with different bandwidth controlled by the scale parameter a. Then the value of the energy found in a specific frequency band for each spike is considered as its feature. For the first time this idea has been adopted within the framework of the wavelet-based spike classifier (WSC) (Letelier and Weber, 2000). Tuning parameter a, one can successfully resolve the multi-scale structure of the data Set #1 (Figure 2). Indeed, the WSC technique finds all five clusters including those corresponding to WFs 4 and 5 (Figure 3B).

Although Figure 3A, in accordance with earlier studies (Letelier and Weber, 2000; Hulata et al., 2002; Quian Quiroga et al., 2004),

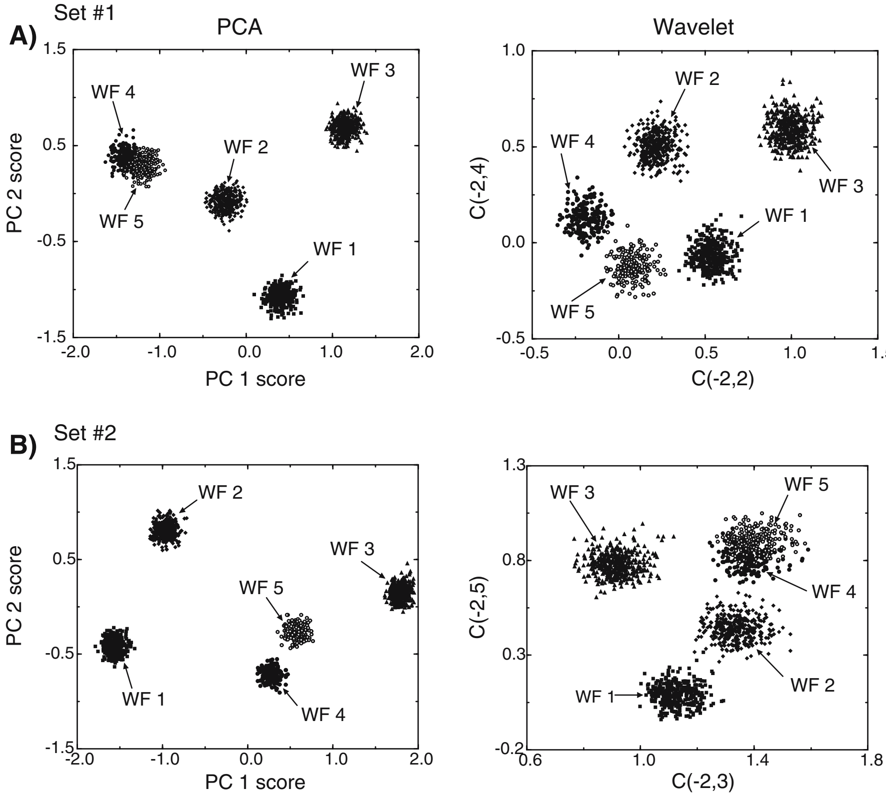

Figure 3. Sorting of the data sets shown in Figure 2 by PCA and wavelet techniques. (A) The wavelet-based approach outperforms the spike separation by PCA for Set #1. In the PCA feature space spikes of WFs 1–3 are clearly clustered, but WFs 4 and 5 (open and solid circles, respectively) are mixed together. The wavelet space provides five well separated clusters for all spikes (WFs 1–5). B) The PCA method provides better separation of Set #2, than the WSC method. The chosen suboptimal wavelet coefficients exhibit multi-modal distributions allowing separation of clearly different spikes (WFs 1–3), but not similar WFs 4 and 5.

shows that the WT approach is potentially more powerful, there are a number of issues restricting its considerable application for spike separation. Here we discuss main of them:

(i) An arbitrary choice of the mother wavelet. Apparently the wavelet coefficients, $C(a,b)$, depend on the mother wavelet ψ. Generally, no standard answer providing an optimal choice exists. A number of different wavelets have been advocated for spike separation: Daubechies (Letelier and Weber, 2000), Coiflet (Hulata et al., 2002), Haar (Quian

Quiroga et al., 2004). Possible advantage or pitfall of one or another depend on the particular experimental data set. In our experience, a success of the classification is often achieved with a mother wavelet similar to the shape of spikes. For instance, in the above discussed example (Figures 2A and 3A) we employed so-called "Wave" – wavelet:

$$\psi_{\text{wave}} = te^{-t^2/2}, \tag{2}$$

that is similar to the complicated WFs 4 and 5.

(ii) Complicated selection of the best wavelet-parameters. Once the mother wavelet has been somehow selected, the WT of spike waveforms can be performed for a set of parameters (a,b). The right choice of only few sets is also crucial for an optimal sorting. Different authors suggested different empirical procedures, e.g., maximize standard deviation of the wavelet coefficients $C(a,b)$, big average, multi-modal distribution (Letelier and Weber, 2000). There is a more complicated but at the same time mathematically better justified method based on the information theory (Hulata et al., 2002). However, there is no one universal approach for the choice of the WT-features capable to provide all the time the best classification and a counterexample can be always found.

The difficulties with the WT technique particularly occur when dealing with data containing spikes of many neurons among which there are both clearly different and rather similar spike waveforms. A general procedure (Letelier and Weber, 2000; Quian Quiroga et al., 2004) relies on a search of parameters (a,b) that provide multi-modal distribution of the wavelet coefficient $C(a,b)$. However, in a case of many clearly different and similar waveforms, the former will produce multi-modal distributions for many if not for all wavelet parameters and will mask the differences between similar waveforms. There is no clue on how to perform an automatic comparison in order to unmask similar waveforms. For example a pronounced difference between spikes at relatively large scales for Set #2 (Figure 2B) favors the PCA separation (Figure 3B). The wavelet technique gets in a pitfall of numerous multi-modal distributions and selects for sorting suboptimal parameter sets. Accordingly in the wavelet space we have only four clusters for five neurons (Figure 3B). Thus a multi-modal distribution of wavelet coefficients not always provides the best spike sorting.

3. Novel approach for extraction of discriminative spike features

Let us now sketch our three-steps approach for extraction of spike features based on a combination of PCA and wavelet technique. The algorithm which we shall refer to as wavelet shape-accounting classifier (WSAC) is the following:

1. Find representative waveforms (rWFs).
2. Search for wavelet parameters (a,b) maximizing distance between the rWFs in the wavelet space.
3. Evaluate wavelet coefficients for the found parameter sets for all spikes, $C_i(a^*, b^*)$.

To demonstrate the method we start with a typical situation frequently found when processing real electrophysiological recordings. A conventional method of spike features extraction e.g., PCA gives two badly separated overlapping clouds (Figure 4A). For the sake of simplicity we suppose that these clouds consist of spikes of two neurons (or spikes of one neuron and other possibly noisy spike-like pulses).

First (step 1) we localize the cloud centers, i.e., positions of the spike density maxima in the PCA space. Then we average spike waveforms over spikes falling in a small neighborhood of each cloud center (insets in Figure 4A). The mean or representative waveforms (rWFs) thus obtained approximate noise free spike waveforms of the two neurons. Here we assume that each neuron emits spikes of the same shape that are linearly mixed with noise at the electrode, so the noise impact near the cloud centers is minimal and is canceled by averaging.

Second (step 2) we apply the WT, Eq. 1, to rWFs and search such a set of parameters, (a^*,b^*), that maximizes the distance $|C_{\mathrm{rWF1}}(a^*,b^*) - C_{\mathrm{rWF2}}(a^*,b^*)|$. Figure 4B shows the distance between rWFs as a function of scale a for different values of b. Frequently the crucial differences between spike waveforms occur in the beginning and the end of firing. To better account for the spike morphology we search separately the maximal distance in the first and second halfes of the spike time window. Circles mark two points (one per a half window) where the distance between the representative waveforms is maximal.

Third (step 3) we apply the WT for all spikes using the above found parameter sets (a^*,b^*). Obtained coefficients are new spike features (Figure 4C). Visually the clouds corresponding to two

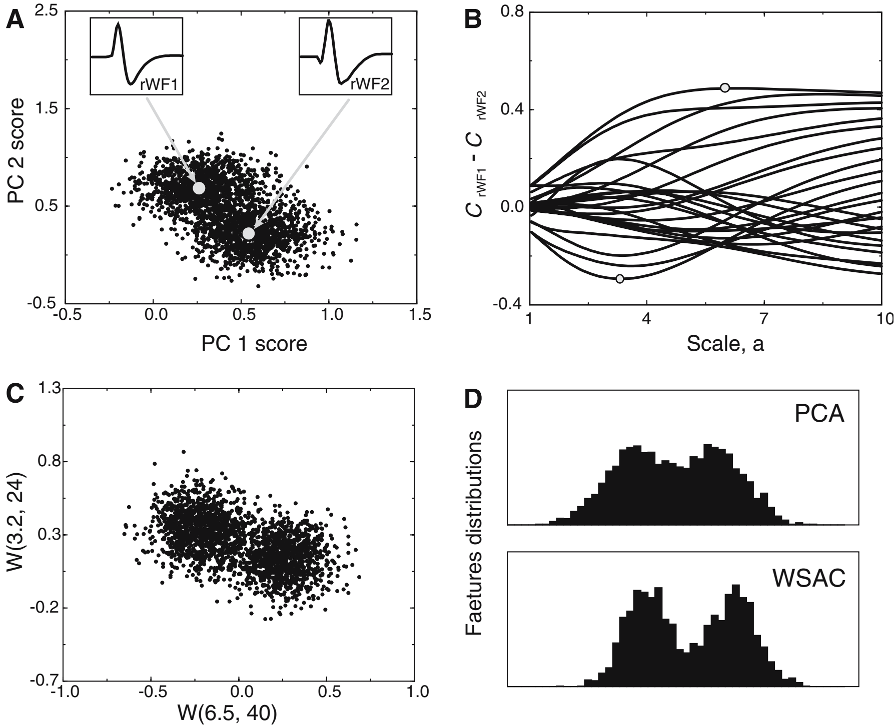

Figure 4. Working principle of the WSAC method demonstrated on a real electrophysiological recording. (A) Conventional PCA provides two strongly overlapping clouds corresponding to spikes of different neurons. Insets show representative spike waveforms (rWFs) obtained by averaging over neighborhoods of the cloud centers. (B) Distance between the rWFs in the wavelet space as a function of scale *a* for different localization parameters *b*. Circles mark the parameters sets (*a*,*b*) maximizing the distance between rWFs: (6.5, 40) and (3.2, 24). (C) New wavelet feature space better resolving spikes. (D) Histograms of spike distribution along the clouds for the PCA space (A) and wavelet space (C). The WSAC distribution shows more prominent peaks providing better localization of spike clouds in the wavelet feature space.

neurons are better delimited in the wavelet plane than in the PCA space (compare Figure 4A and C). Indeed, the histogram of distribution of spike features in the wavelet spaces (WSAC method) exhibits significantly more pronounced peaks in comparison with the PCA method (Figure 4D). This means that one can now better delimit clouds reducing considerably classification errors originated from a misclassification of spikes in the overlapping part of the clouds.

4. Performance test

We assess the method performance on three different data sets (S1, S2, and S3). Each data set has been obtained in the following way. We select an electrophysiological recording such that spikes of one type can be easily separated from the rest by a conventional sorting method. Then these spikes are mixed with another experimental recording demonstrating complex spiking activity. Thus obtained data set, from one side, conserves all characteristics (level and type of noise, spike waveform variation etc.) typical for a real electrophysiological recording, and from the other we have a priori information about the membership of spikes from the first recording.

The generated data sets are supplied to feature extraction algorithms above discussed. Then clustering by the superparamagnetic method (Blatt et al., 1996) is performed and we calculate the number of misclassified spikes in the target cluster (spikes whose membership we know a priory).

Figure 5 illustrates results obtained for the data set S1 consisting of 16568 spikes including 3069 "targeting" spikes. PCA gives two clusters (Figure 5A) shown in black and gray. Squares mark unclassified spikes not related to either of the clusters. Classification of spikes by using of the first three principal components (PCs) gives 290 misclassified spikes: 24 false negative and 266 false positive, i.e., 0.8% and 8.6% from the total number of spikes in the target cluster. Histograms of spike densities in the features space show a bi-modal distribution for PC1, and uni-modal distribution for PC2. Thus PC1 does provide a separation of the spikes into two clusters, while PC2 gives no additional information.

Figure 5B shows spike sorting by the WSC method (Letelier and Weber, 2000). We note, that unlike to PCA, the both histograms in Figure 5B are bi-modal, and therefore the two spike features provide useful information for the sorting. However, we obtain higher classification error: 410 misclassified spikes (5.2% of false negative and 8.1% of false positive). This confirms our conclusion that a suboptimal choice of the wavelet-parameters may provide a worse classification than the PCA method (see Figure 3B).

Figure 5C shows results of spike classification obtained by our WSAC method. We found that three pairs of parameters: (6.8, 31), (8.6, 51), and (6.2, 20) maximize distance between the representative

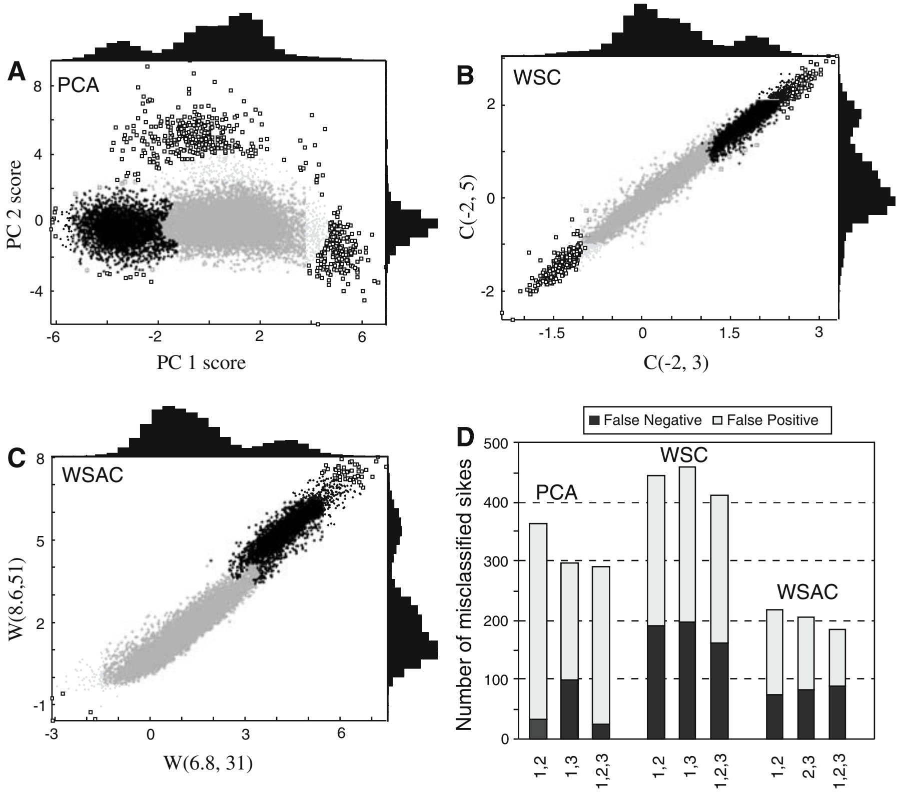

Figure 5. Results of spike separation by different methods for the data set S1. (A) PCA feature space and corresponding histograms of spike densities. Black points correspond to spikes classified to be in the targeting cluster. (B) The same as in (A) but for the WSC method. (C) The same as in (A) but for the WSAC method. (D) Number of misclassified spikes for different subsets of spike features used for classification.

waveforms. Using them we obtain the best sorting results: 185 errors or 2.8% of false negative and 3.1% of false positive.

Figure 5D summarizes results of spike classification done by these three methods for different combinations of feature sets used by each particular technique. For instance, classification performed by the use of first two principal components gives 364 errors (first bar in Figure 5D), while the same done with PC1 and PC3 results in 296 errors. Hence for this data set PC3 captures better the variation in the spike waveforms than PC2. The use of all three components improves a bit the sorting reducing the error to 290. Considering the WSC we note

Table 1. Classification error rates for three data sets and different methods (percentage of the misclassified spikes to the total number of spikes in the cluster)

	S1		S2		S3	
	FN/FP	Sum	FN/FP	Sum	FN/FP	Sum
PCA	0.8/8.6	9.5	41.6/11.8	53.4	0.1/2.6	2.7
WSC	5.2/8.1	13.3	34.2/13.8	48.0	6.7/2.9	9.6
WSPC	7.5/8.9	16.4	28.7/0.8	29.5	9.5/4.4	13.9
WSAC	2.8/3.1	5.9	26.4/8.2	34.6	1.8/0.3	2.1

FN and FP denote False Negative and False Positive errors.

that each coefficient improves results of classifications, but the overall performance is the worst over all methods. The WSAC approach is the winner giving in average the minimal classification error for any combination of the spike features.

Table 1 summarizes results obtain for all data sets where for comparison we also included results of wavelet-classifier with superparamagnetic clustering (WSPC) proposed in (Quian Quiroga et al., 2004). This wavelet approach performs considerably better for set S2, while shows quite poor performance for S1 and S3.

5. Conclusions

Investigation of algorithms of automatic spike features extraction is an important trend in development of mathematical tools for analysis of biophysical data. Addressing question: when wavelet-based methods outperform PCA, we have shown that the main advantage of the WT technique reveals when dealing with the detailed structure of experimental signals in a wide range of scales. Particularly, the presence of an essential small-scale structure in spike waveforms may be missed by PCA, but perfectly captured by the wavelet approach.

We have shown that unlike to PCA, where principal components are naturally ordered, an optimal selection of spike features within the WT framework is significantly more complicated procedure. Considering the WT-approach as a ‘‘mathematical microscope’’, we offer the following interpretation of an optimal spike feature extraction. To resolve fine details of the data set structure we need appropriately select resolution and focusing point of the microscope, i.e., parameters of scale a and localization b in Eq. 1. Correctly tuned microscope elucidates the differences in spike waveforms and provides the best possible spike sorting. Accordingly an optimal method should account for the data set under question, and not rely just on general empirical assumptions.

Here we have proposed a novel technique, WSAC, based on a choice of the wavelet-parameters tuned to spike shapes of a particular experimental data set. The main idea is to find parameter values maximizing the distance between two (or more) representative waveforms estimated from the experimental recordings. Then such parameters are used for wavelet extraction of spike features.

Using different data sets we have shown that the proposed method outperforms PCA and other empirically "fixed" wavelet-based techniques.

In conclusion we note that the proposed approach can also be useful in a number of other applications, e.g., in radiolocation for identification and separation of spike-like signals received from different objects, in image processing (Acharya and Ray, 2005) one may use a combination of PCA and WT techniques to improve the performance of denoising or edge identification. Our research is also in line with the problem of speaker identification from sound signals based on a similar to the wavelet classifier method.

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References

Acharya T and Ray AK (2005) Image Processing: Principles and Applications. Wiley

Blatt M, Wiseman S and Domany E (1996) Superparamagnetic clustering of data. Physical Review Letters 76: 3251–3254

Buzsaki G (2004) Large-scale recording of neuronal ensembles Nature Neuroscience 7(5): 446–451

Downs GM and Barnard JM (2002) Clustering methods and their uses in computational chemistry. Reviews in Computational Chemistry 18: 1–40

Harris KD, Henze DA, Csicsvari J, Hirase H and Buzsaki G (2000) Accuracy of tetrode spike separation as determined by simultaneous intracellular and extracellular measurements. Journal of Neurophysiology 84: 401–414

Hulata E, Segev R and Ben-Jacob E (2002) A method for spike sorting and detection based on wavelet packets and Shannon's mutual information. Journal of Neuroscience Methods 117: 1–12

Kaufman L and Rousseeuw PJ (1990) Finding Groups in Data: An Introduction to Cluster Analysis. Wiley-Interscience

Letelier J and Weber P (2000) Spike sorting based on discrete wavelet transform coefficients. Journal of Neuroscience Methods 101: 93–106

Lewicki M (1998) A review of methods for spike sorting: the detection and classification of neural action potentials. Network: Computational Neural Systems 9: R53–78

Quian Quiroga R, Nadasdy Z and Ben-Shaul Y (2004) Unsupervised spike detection and sorting with wavelets and superparamagnetic clustering. Neural Computation 16: 1661–1687

Shoham S, Fellows MR and Normann RA (2003) Robust, automatic spike sorting using mixtures of multivariate *t*-distributions. Journal of Neuroscience Methods 127: 111–122

Wheeler B (1999) Automatic Discrimination of Single Units. CRC Press, Boca Raton, FL