Separation of Extracellular Spikes: When Wavelet Based Methods Outperform the Principle Component Analysis

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Abstract. Spike separation is a basic prerequisite for analyzing of the cooperative neural behavior and neural code when registering extracellularly. Final performance of any spike sorting method is basically defined by the quality of the discriminative features extracted from the spike waveforms. Here we discuss two features extraction approaches: the Principal Component Analysis (PCA), and methods based on the Wavelet Transform (WT). We show that the WT based methods outperform the PCA only when properly tuned to the data, otherwise their results may be comparable or even worse. Then we present a novel method of spike features extraction based on a combination of the PCA and continuous WT. Our approach allows automatic tuning of the wavelet part of the method by the use of knowledge obtained from the PCA. To illustrate the methods strength and weakness we provide comparative examples of their performances using simulated and experimental data.

1 Introduction

Current extracellular experiments provide recordings of multi-unitary activity, where several neurons nearby to the electrode tip produce short lasting electrical pulses, spikes, of different amplitudes and shapes (see for details e.g. [1]). Consequently, extracting useful information from these measurements relies on the ability of separating the recorded firing events into groups or clusters. Ideally each cluster should contain all spikes emitted by only one neuron. Errors occur when spikes belonging to different neurons are grouped together (false positive) or when some spikes emitted by a single neuron are not included into the group (false negative). The performance of this procedure defines the final quality and reliability of any bio-physical results obtained upon the analysis of spike timings. However, the quality of the spike separation by a human operator is significantly below the estimated optimum [2]. Besides, amount of the data generated by modern experimental setups is really huge, thus there is a big demand for automatic separation techniques.

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Nowadays there exist a number of numerical techniques targeting classification of the extracellular action potentials (see e.g. [1, 3] and references therein). Any method for sorting of spikes relays on two basic steps: i) Extracting the important (most discriminative) features of the spikes and thus lowering the dimension of the parametric set representing the spikes, and also reducing noise influence; and ii) Clustering of the parametric sets into groups, i.e. identifying the number of different spike types (neurons) and the membership of spikes in these groups. Also there are many clustering algorithms (see e.g. [4, 5]) showing different performances on different data sets, as a mater of fact, the final performance of the spike separation is mostly defined by the quality of the extracted spike features, i.e. the quality of the first step. Currently available features extraction methods may be divided into three groups: 1) "naive", threshold based; 2) based on the Principal Component Analysis (PCA); and 3) based on the Wavelet Transform (WT). First two methods are the most widely used now, while the third method becomes more popular and has been demonstrated to have advantages [6, 7, 8]. Although these methods show a good performance, the best representation of the spike feature is still a challenging problem. Here we analyze strength and weakness of the methods and present our novel approach that combines the PCA and Continous Wavelet Transform (CWT).

2 Spike Features Extraction Methods: General Possibilities and Limitations

The simplest approach to the problem of spike separation is high-pass filtering following by the amplitude thresholding. Obvious disadvantage of this approach is that the amplitude is not the only feature of a spike waveform, and separation of spikes close enough in amplitudes degenerates drastically the method performance.

Another simple but significantly more powerful tool for spike sorting is the PCA. Within this framework a set of orthogonal vectors is estimated being the eigenvectors of the covariance matrix constructed from the data. Each spike is completely represented by a sum of the principal component vectors with the corresponding weights or scale factors, so called scores. The latter ones are considered as spike features for sorting. In practice the use of first two or three components is optimal, since they account for the most important information about the shapes of action potentials, while higher components are usually very noisy and decreases the algorithm performance.

A problem occurs when among some number of different waveforms there are two types with similar shapes and clearly expressed distinctions appearing only on small time scales. Such distinctions are usually not reflected in the first principal components, and consequently the method fails to separate such spikes. To illustrate this we generated a test data set consisting of 500 spikes of five different waveforms (Fig. 1A) corrupted by a noise.

Application of the PCA to the data set reveals four different clusters. First three clusters correspond to spikes of the WFs 1–3, so demonstrating the poten-

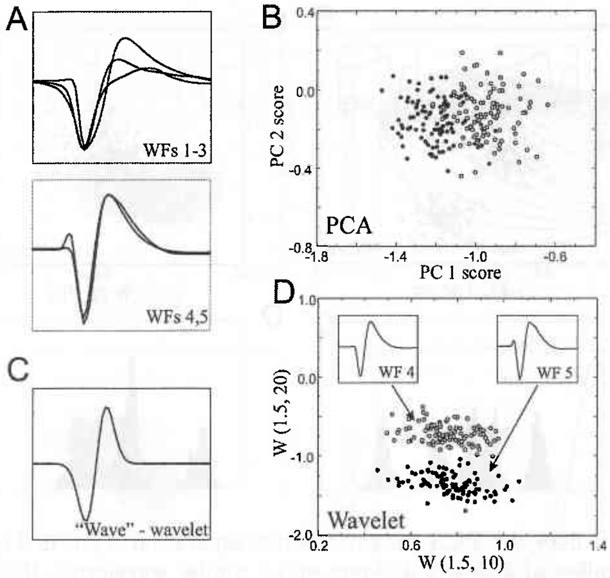


Fig. 1. An example where the wavelet-based approach outperforms the spike separation by the PCA. A) Original spike waveforms used for generation of the data set. We use 3 clearly different waveforms (WF 1-3) and 2 similar waveforms (WF 4 and 5). The difference between two similar WFs appears on small time scales. B) Feature space of the first two principal components. A zoomed region corresponding to the fourth cluster is shown. Spikes of two waveforms (open and solid circles for WFs 4 and 5, respectively) are mixed, and their acceptable separation is impossible. C) The Wave - function chosen for the wavelet-analysis. D) Zoomed region corresponding to fourth and fifth clusters (WF4 and 5) in the wavelet space. Two clearly distinct clouds are formed, and separation with high fidelity is possible

... of the PCA approach. However, fourth cluster contains a mixture of spikes of two similar waveforms: WFs 4 and 5 (Fig. 1B). Analysis of the Principle Components confirms that the difference between WFs 4 and 5 is not reflected in the first of them. Thus PCA based methods fail to separate spikes with differences appearing on small scales.

Recently a new approach for spike sorting based on the WT has been developed [6, 7, 8]. This approach is claimed to have advantages in comparison with the techniques traditionally used for classification of action potentials. The Continuous Wavelet Transform (CWT) of a one-dimensional signal $f(t)$ involves its decomposition (somehow similar to the Fourier transform):

$$W(a,b) = \frac{1}{\sqrt{a}} \int_{-\infty}^{+\infty} f(t)\psi_{a,b}(t)\, dt, \quad \psi_{a,b}(t) = \psi\left(\frac{t-b}{a}\right), \tag{1}$$

where $\psi_{a,b}(t)$ is a translated and scaled mother wavelet, $\psi(t)$, with b and a defining the time location and scale. Instead of the continuous transform (1), its

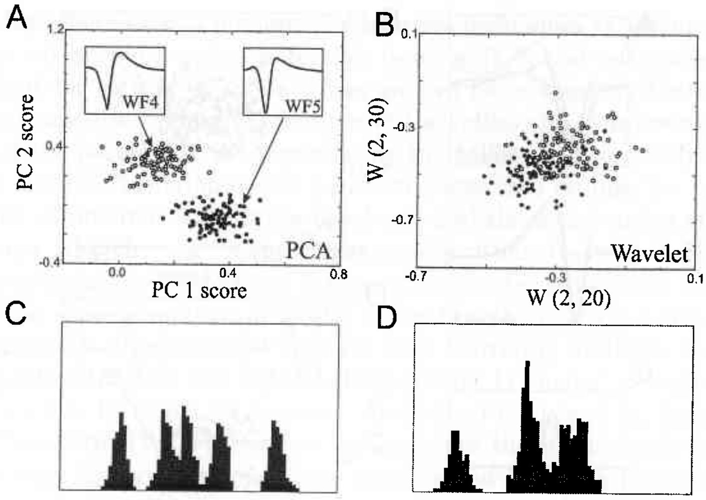


Fig. 2. A case where the PCA provides better separation. Like in Fig. 1, we use a data set with spikes of 3 clearly different and 2 similar waveforms. However, now the difference between similar spikes is not so pronounced and is not in small scales. A) Principle components show a good separation of spikes of WF4 and WF5 (open and solid circles, respectively). B) Wavelet classification. The chosen wavelets-coefficients demonstrate multi-modal distributions allowing separation of clearly different spikes. However, separation of WF4 and 5 is not achieved. C,D) Histogram of spike density along the first component score (C) and one of the wavelet-coefficients (D). The wavelet-coefficient demonstrates a multi-modal distribution however the number of peaks (four in (D)) corresponding to clusters is less than in the PCA case (five in (C))

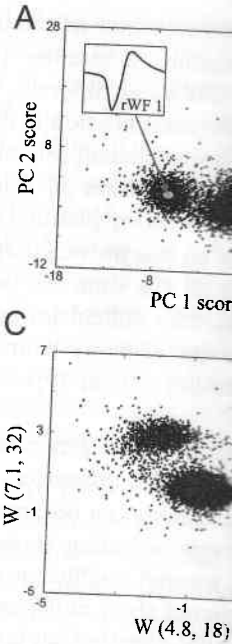
discrete counterpart (DWT) is usually used. In the DWT the scale takes only some fixed values (usually $a = 2^i$).

Several methods for spike separation based on the DWT have been proposed [6, 7, 8]. They use the fact that the WT of a signal (spike) can be considered as a set of filters with different bandwidth controlled by the scale parameter a. Then the values of the energy found in specific frequency bands during each spike profile are considered as quantities for spike classification within the framework of the Wavelet-based Spike Classifier (WSC) [6].

In the case where spike waveforms have a multi-scale structure with any significant characteristics appearing on small scales, like in the data set used in Fig. 1, the wavelets are able to resolve these features. Indeed, application of the wavelet technique to the data set of Fig. 1 shows that this approach finds all five clusters. Figure 1D illustrates a good separation of WF 4 and 5 into two clusters, where the PCA had difficulties (Fig. 1B).

Although the WT is potentially more powerful there are a number of problems restricting its considerable application for spike separation. Here we discuss main of them:

i) An arbitrary choice of the mother wavelet
ii) Complicated selection of the best wavelet-coefficients



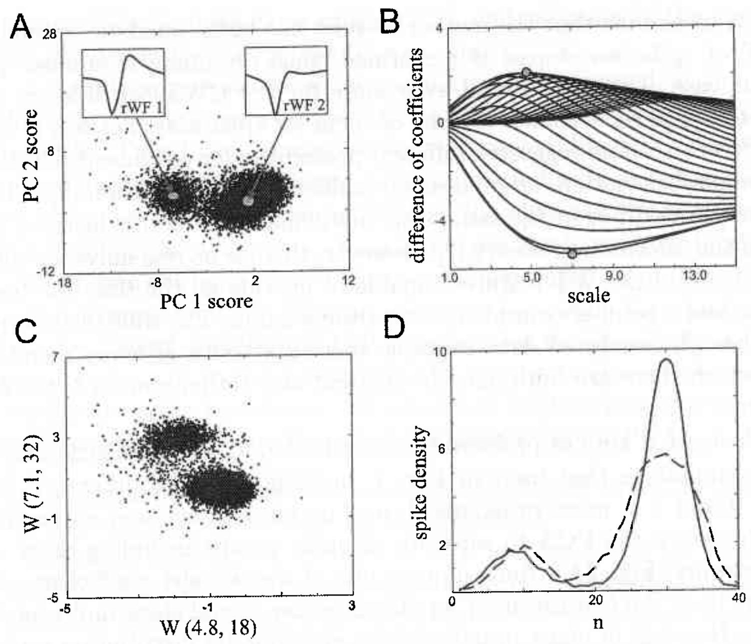


Fig. 3. Working principle of the WSAC method. A) Two overlapping clouds correspond to spikes of different types on the PCA plane. Insets show representative spike waveforms obtained by averaging over neighborhoods of the cloud centers. B) The difference between the wavelet-coefficients for the representative spikes as a function of scale. Circles mark the coefficient pairs ($a = 4.8$, $b = 18$ and $a = 7.1$, $b = 32$) that correspond to the most prominent distinctions between rWF1 and rWF2. C) New spike features space. The found coefficients are used. D) Spike density along the clouds. Peaks correspond to the centers of the clouds. Dashed line corresponds to the PCA space, and solid line shows the results obtained in the wavelet space. The later distribution shows better separated and prominent peaks resulting in a better localization in feature space of spike of different waveforms (compare clouds in (A) and (C))

i) Apparently, the results of the analysis, e.g. the wavelet-coefficients, depend on the mother wavelet ψ. Generally, there is no standard answer on how to choose the mother wavelet in a particular case. Thus the performance of the method may strongly vary from one case to another. For spike separation different mother wavelets have been advocated: Daubechies [6], Coiflet [7], Haar [8]. Possible advantages of one or another depend on the particular spike waveforms of the analyzed data set, and no a-priori assumption which mother wavelet will perform better can be given. In our experience, success of the classification can be often achieved by selection of the mother wavelet similar to the shape of spike waveforms. For instance, in the example shown in Fig. 1, to obtain a good separation we used the so-called "Wave" – wavelet (Fig. 1C). Visually, this wavelet is very similar to the WFs 4 and 5 (Fig. 1A), and a good separation of all waveforms, including WF4 and WF5, has been obtained.

ii) Let us assume that the mother wavelet has been somehow selected. Then the WT of spike waveforms is performed, thus obtaining a number (usually 64 in the case of the DWT and even more for the CWT) of different wavelet coefficients. The right choice of some of them for spike classification is also crucial. Different authors suggested different procedures for coefficient selection, e.g. large standard deviation, large average, multi-modal distribution [6]. There is a more complicated but at the same time mathematically better justified method based on the information theory [7]. 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 especially occur when the analyzed data contains spiking activity of many neurons, and among which there are both, clearly different and rather similar types of spike waveforms.

To illustrate a kind of problem that can be found we again generated a test data set similar to that used in Fig. 1, however now the difference between the WF 4 and 5 is more pronounced, and no clear differences on small scales exist. This helps the PCA to separate all spike groups including those of similar waveforms (Fig. 2A). According to one of the wavelet coefficient selection procedure [6, 8] the features used for classification should show multi-modal distribution. However in many practical cases multi-modal distribution is obtained for many wavelet-coefficients and there is no clue on how to perform their automatic comparison in order to select the most informative ones. An example of such quasi arbitrary (unsuccessful) choice of the coefficients is illustrated in Fig. 2B. Although the chosen wavelets coefficients have multi-modal distributions (Fig. 2D) allowing separation of the first three clearly different spike waveforms, the wavelet approach gives worse classification of two similar waveforms than that provided by the PCA (Fig. 2AC).

3 Our Novel Approach for Spike Features Extraction

Let us start with a typical situation frequently appearing when processing real electrophysiological data. We assume that a conventional method of spike features extraction (e.g. the PCA) gives two overlapping clouds. For the sake of simplicity we suppose that these clouds consist of spikes of two types (or we may aim at separation of spikes of a given type, say WF1, from the rest, possibly noisy spike-like pulses). Figure 3A shows such an example with the PCA of spikes from a real electrophysiological recording. Let us now sketch our three-steps approach based on a combination of the PCA-method and the CWT method that we shall refer to as Wavelet Shape-Accounting Classifier (WSAC).

First step: Calculation of the representative WaveForms (rWFs).

The usual PCA is performed on the all available waveforms. Then we average spike waveforms in a small neighborhood of each cloud center. As a result two representative (mean) spike waveforms are obtained (insets in Fig. 3A). Since these waveforms are related to the centers of the corresponding clouds we can suppose that they represent "real" spike waveforms with lowest noise impact.

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4 Results

We test the proposed approa
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Figure 4 illustrates results
spike waveforms including 3069
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Second step: Wavelet transform of the rWFs and selection of the coefficients that optimally depict the differences between them.

Two obtained representative spike waveforms are analyzed in the wavelet space. We seek for those wavelet coefficients that maximize the difference between the rWFs. Thus the differences between corresponding wavelet coefficients are estimated and coefficients showing maximal dissimilarity are selected. Figure 3B shows examples of the differences between the obtained wavelet coefficients (for rWFs 1 and 2) as a function of scale. Circles mark two points where the differences between the wavelet-coefficients are maximized. Note that there may be more than two extrema for different scales, so increasing the number of features (i.e., the wavelet-coefficients) that may be used for classification. Because the given procedure performs a search of the most prominent distinctions for the representative spike waveforms, the estimated features can provide a better resolution between the clusters than that obtained with the PCA.

Third step: Estimation of the selected coefficients for all available spike waveforms and their use as new features for classification.

The coefficients selected at the second step are estimated for all available spike waveforms and then considered as spike features for classification (Fig. 3C). Figure 3D shows densities of spikes in the PCA and Wavelet feature spaces. Main peak in the wavelet space becomes narrower and more pronounced in comparison with the distribution obtained for the PCA method. This means that we can now better separate clouds into clusters and reduce classification errors that mostly originate from a misclassification of spikes in the intermediate (common) part of the clouds.

4 Results

We test the proposed approach on three different data sets (S1, S2, and S3). Each data set has been obtained in the following way. We take two experimental electrophysiological recordings. One of the recordings is selected in the way that spikes of one type can be easily separated from the rest by the conventional thresholding method. Then these spikes are mixed with another experimental recording demonstrating complex spiking activity. This procedure, from one side, allows keeping all characteristics (level and type of noise, spike waveform variation etc.) essential to a real electrophysiological experiment, and from the other hand we possess the a-priori information about the membership of spikes for one target cluster formed by the "additional" spikes. Hence we can estimate the classification error for the given cluster.

The generated data sets have been used as an input to four feature extraction algorithms above discussed. Then clustering by the superparamagnetic method [9] has been performed and the number of misclassified spikes has been estimated.

Figure 4 illustrates results obtained for the data set S1 consisting of 16568 spike waveforms including 3069 "additional" spikes. The PCA gives 2 clusters (Fig. 4A) shown in black and gray corresponding to the additional (targeting) and the original action potentials, respectively. Squares mark unclassified spikes

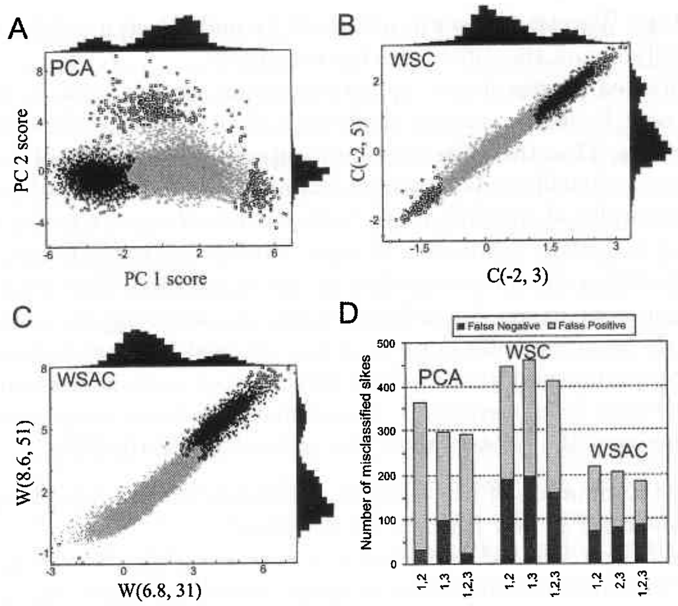

Fig. 4. Results of spike separation by different methods for the data set S1. A) Projection of the feature space for the PCA into first two components, and corresponding histograms of spike densities. Black points correspond to spikes classified to be belonging to the targeting cluster. B) The same as 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 methods and for different spike features subsets used for classification

being not related to either of the clusters. Classification of spikes by three first 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 this cluster. The histograms of spike densities for each coordinate in the features space show a bimodal distribution for the PC1, and uni-modal distribution for the PC2. The former allows separation of different waveforms into two clusters, while the later does not actually provide additional information for spike classification.

Figure 4B illustrates the results of spike sorting performed by the WSC method [6]. Following the author recommendations, we have chosen for classification the wavelet-coefficients showing the largest standard deviations, the largest values and the bimodal distributions. Note, that unlike to the PCA, the histograms in Fig. 4B are both bi-modal, and therefore they actually provide useful information for spike sorting. However, for the considered example we obtain higher classification error: 410 misclassified spikes (5.2% of false negative and 8.1% of false positive). Thus a quasi arbitrary choice of the wavelet-coefficients satisfying the mentioned recommendations did not allowed improving classification in comparison to the PCA method.

Figure 4C shows results of spike classification obtained by our WSAC method. We found that three pairs of coefficients: (6.8, 31), (8.6, 51), and (6.2, 20) max-

Table 1. Classification error rate
of the misclassified spikes to the
denote False Negative and False

	S1
	FN/FP
PCA	0.8/8.6
WSC	5.2/8.1
WMMC	7.5/8.9
WSAC	2.8/3.1

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5 Conclusions

Addressing the question: when th
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Table 1. Classification error rates for all data sets and different methods (percentage of the misclassified spikes to the total number of spikes in the cluster). FN and FP denote False Negative and False Positive errors

	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
WMMC	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

imize the difference between the characteristic spike shapes, and used them for classification. This method provides the best results: 185 errors or 2.8% of false negative and 3.1% of false positive.

Figure 4D shows results of spike classification done by these three methods for different combinations of features used in each particular technique. For instance, classification performed by the use of first two principle components gives 364 errors (first bar in Fig. 4D), while the same done with PC1 and PC3 results in 296 errors. This means that in this case PC3 describes better the variation in the data set than PC2. The use of all three components improves a bit the classification resulting in 290 errors. Considering WSC we note that each coefficient improves the results of classifications, but the overall performance is the worst. 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. We also included in the table classification errors obtained by the WMMC method based on the approach proposed in [8]. This approach performs considerably better for the set S2, while showing poor performance in S1 and S3.

5 Conclusions

Addressing the question: when the wavelet-based methods outperform the PCA, we have shown that the main advantage of the WT techniques reveals when dealing with the detailed structure of experimental signals in a wide range of scales. Considering the WT-approach as a "mathematical microscope", the following interpretation can be given: the wavelets can resolve fine details of a signal structure, but we need to choose appropriately the focusing point and the resolution of this "microscope". From the mathematical viewpoint the latter means that the selection of the parameters a and b in (1) responsible for the resolution and focusing is of a crucial importance. In the case of successful selection, the "microscope" elucidates the differences in spike waveforms. That is why the problem of selection of the optimal wavelet-coefficients is an important trend in the problem of spike separation. Unlike the PCA-based methods where the first principal component scores are used as spike features due to their natural order, optimal selection of features within the framework of the WT techniques is significantly more complicated procedure.

In order to eliminate arbitrariness in the selection of the spike features here we have proposed a novel technique, the WSAC method. It is based on the choice of the wavelet-coefficients tuned to the spikes shapes. The main idea of the method is to find such features of the WT that maximize the differences between two or more kinds of representative waveforms selected from the experimental recordings, and then to use them for classification of all spikes. Using different data set we have shown that the proposed method of features selection outperforms the PCA and the other wavelet-based techniques.

Summarizing, we emphasize that there are at least two cases when the wavelet-based techniques potentially are preferable than the Principal Component Analysis: (i) the presence of small-scale structure in waveforms that is not reflected in the first principal components, and (ii) the presence of strong enough low-frequency noise that strongly reduces the PCA-method performance whereas this noise statistics is less essential for the wavelets. In other situations the WT-based approaches show results comparable with the classical technique.

Acknowledgments

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Structural St
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Abstract. We show expe
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1 Introduction

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