Classification Model of Spikes Morphology Using Principal Components Analysis in Drug-Resistant Epilepsy

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Abstract. Epilepsy is one of the diseases that are more subject to consultation in neurological clinics. To help neurologists to accurately diagnose this disease, several technological tools have been developed. Electroencephalography (EEG) of scalp or deep is a signal acquisition tool from electrical discharges of the brain areas. These signals are often accompanied by transient events commonly called interictal paroxystic events (IPE) or spikes of short durations. Analysis of these IPE could help with the diagnosis of drug-resistant epilepsy. With this intention, we will first of all seek to detect IPE, by separating them from the basic activity of signal EEG. In this paper, we propose spike detection method based on Smoothed Nonlinear Energy Operator (SNEO) using adaptive threshold. Then we will implement a new approach using principal components analysis (PCA) before classification to separate the events detected according to their morphologies. The objective in the long term is to characterize their space-time distribution over all the duration of the EEG signal.

Keywords: Epilepsy · Spike detection · SNEO · PCA
Unsupervised classification

1 Introduction

Epilepsy is a neurologic affection which touches most of the world population. It is characterized by an abnormal and excessive discharge of a more or less important neuronal population. This disease poses, still today, of the problems of treatments (drugs) [1], and modern medicine does not encounter yet today difficulties of treating certain cases. Indeed, some forms of epilepsy called drug-resistant are resistant to all medication [2]. In these cases, a surgical treatment can be considered but its application requires a complex pre-surgical evaluation. In order to find new solutions therapeutic, the scientific communities and medical study, since years, the way in which the crises occur.

We distinguish two periods in the life cycle from an epileptic: critical periods characterized by the crises and the interictal periods characterized by interictal paroxystic

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events (IPE). IPE are observed at 1% of non-epileptic subjects and around 60 to 90% of epileptic subjects [3]. They are a complementary source of information in the diagnosis and localization of epilepsy. They are characterized by a brief initial phase, sharp and strong amplitude. The interictal spikes occurrence is higher than the seizures frequency. The clinical characterization of these events rests on their density, their topography or their morphology. The morphological definition of the IPE varies much from one patient to another. A simple spike (P: Positive or N: Negative) is characterized by a pointed peak or trough, according to their duration, between 20 and 70 ms.

For analyzing well, the spikes morphology, IPE must be detected. In literature, spikes detections methods were grouped according to their criterion of spike detection in nine (9) categories [4]: *Methods based on traditional recognition techniques, known as Mimetic Techniques*, *Methods based on morphological analysis, Methods based on parametric approaches, Methods based on independent component analysis, Methods based on artificial neural networks, Methods based on clustering techniques, Methods employed data Mining and other classification techniques and Methods utilizing knowledge-based rules*. Paper [5] gives some comparison methods that are more used in this research area. In this paper, we propose a new method of spike detection based on Smoothed Nonlinear Energy Operator (SNEO) using adaptive threshold. After the step of detection, we implement an algorithm of extraction of the all spikes detected by using a window. Spikes extracted will be assignment and clustering using principal components analysis (PCA) and k-means algorithm for unsupervised classification. This treatment would characterize the space-time distribution of the IPE in EEG signal. Brief replies on this distribution would enable us to characterize the bond still little known between the space-time distribution of IPE and the arrival of the crises, thus bringing a significant complement in the diagnosis of the epilepsies.

After the introduction, the Sect. 2 presents the adaptive spike detection. In the Sect. 3, we give of principal components analysis for the clustering. In the Sect. 4, we explain the proposed process of the spikes morphology classification. The Sect. 5 analyzes the results obtained starting from the real data recorded among patients suffering from drug-resistant epilepsy of the temporal lobe. An experimental validation of the results is made. The last section concludes the paper.

2 Adaptive Spike Detection Based on SNEO

In this part, we use the discrete operator of Teager - Kaiser [6] (Eq. 1) or Nonlinear Energy Operator (NEO) to measure the authorities of energy of the signal.

$$\psi_{\mathbb{R}}[x(n)] = x^2(n) - x(n-1)x(n+1) \tag{1}$$

Thus the operator can detect changes for instantaneous amplitudes (A) or instantaneous frequencies (Ω) of a signal (Eq. 2).

$$E_n = x_n^2 - x_{n+1}x_{n-1} \simeq A^2\Omega^2 \tag{2}$$

It is an analyzer time-frequency which can simultaneously consider the amplitude and the frequency of instantaneous information of the entry signal. By consequence NEO is used to amplify the activities in a signal. However, NEO is sensitive to the noises and has a problem of the growth of the terms of the operator [7]. To reduce this problem, Mukhopadhyay and Ray [8] suggested SNEO to detect the events of points in signals EEG by convoluting $\psi_{\mathbb{R}}[x(n)]$ with a smoothed window of time domain is expressed by:

$$\psi_S[\mathrm{x(n)}] = w(n) * \psi_{\mathbb{R}}[x(n)] \tag{3}$$

Where operator * represents the product of convolution and $w(n)$ the smoothed window. The choice of the type of window and its length is very important to carry out the sufficient reduction of interferences without losing much its temporal resolution which is very useful for the spike detection. In the order to achieve this goal, the window of Bartlett with the implementation of a numerical filter was selected to overcome the complexity of the algorithm as far as possible [8].

With a window of length L, Eq. 3 becomes then:

$$\psi_S[\mathrm{x(n)}] = \sum_{k=0}^{L-1} w(k).\psi_{\mathbb{R}}[x(n-k)] \tag{4}$$

The following figure gives the stages of the spikes detection with SNEO and an adaptive block for the threshold of detection.

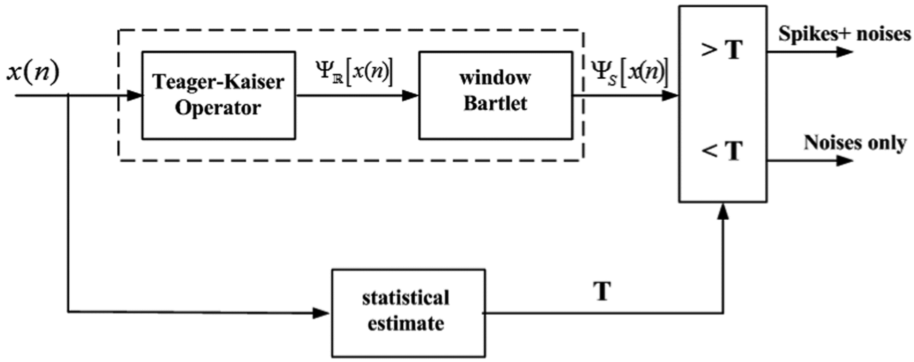

Fig. 1. Adaptive spike detection using SNEO

The main aim of the detector is to decide if there is presence of a spike in the noise of the bottom or if there is noise only. Values of ψ_S[x(n)] are continuously compared with a threshold T. Compared to the stage of the decision, a spike is present if ψ_S[x(n)] $> T$, if not the signal is considered to contain only noise. The threshold is the focal point with adaptive detection. Only the density of probability under the null assumption and the probability of false alarm (P_{fa}) are necessary. As the Teager-Kaiser operator is nonlinear, the density of probability cannot be evaluated in a firm way. In statistics, several approaches were proposed to circumvent this limitation. However, in accordance with the need for simplicity, a parametric approach is adopted. Thus, as the noise is a random process, the exit of the diagram (Fig. 1) is also a random process having like median value μ and standard deviation σ. The threshold can thus be estimated by the following equation:

$$T = \mu + p\sigma \tag{5}$$

Where T is the adaptive threshold of detection to determine the presence of a spike and the multiplier p depends P_{fa} [8].

3 Principal Components Analysis

Principal components analysis (PCA) is a fundamental method in multidimensional descriptive statistics [9]. It is used for visualization of complex data. This technique is based on the reduction of the attributes. It calculates initially the matrix of correlation R of N_a attributes (number of elements in complex data). In the second time, it seeks the eigenvalues λ_i and the eigenvectors v_i of R. To finish, it selects among the N attributes, N_{PCA} which have the greatest eigenvalues [10]. It is thus a question of obtaining the most relevant summary of the initial data.

2D representation is made through the first two eigenvalues. These determine the factors (principal components) that return alone almost all of the dispersion of the point cloud. In addition, the axes passing through the origin 0 are generated by the eigenvectors associated with the selected values. These axes must pass the best in the middle clouds. And they are not correlated. Each component is a linear combination of the two eigenvectors. Therefore, we use PCA for mixtures data before applying the clustering.

4 Classification of Spikes Morphology

In this paper, cityblock distance [11] is used because it is very simple for their implementation. Cityblock distance or Manhattan is determinate by the following expression.

$$d_{CB}\left(x_1(k), x_2(k)\right) = \sum_{k=1}^{N} \left|x_1(k) - x_2(k)\right| \tag{6}$$

4.1 Extraction of Detected Spikes

We use the wavelets [12] transform after the phase of detection to be able well to extract IPE. So a window of extraction is open around the moment of occurrence of each IPE: by using information a priori over the intermediate duration of IPE. We chose a window of length L = 128 samples, that is to say 0.5 s (256 is the sample frequency for our data). A matrix $\underset{pre-ext}{E}(t)$ then is obtained. The matrix contains events pre-extracts defined by: $\underset{pre-ext}{e}{}_i(t)$ with $i \in \left\{0, 1, \ldots, N^{IPE} - 1\right\}$ ($t \in \{0, 1, \ldots, L\}$ and N^{IPE} or N_{spike} is the number of detected spikes). The event is to represent by:

$$\underset{pre-ext}{e}{}_{i}(t) = v(t)\ \mathrm{x} \prod_{[\hat{\tau}_i - a, \hat{\tau}_i + b]} (t) \tag{7}$$

Where $v(t)$ is an EEG signal and $\prod_{[\hat{\tau}_i - a, \hat{\tau}_i + b]} (t)$ is rectangular function ($\hat{\tau}_i$ is the moment of occurrence or the instant detection of the IPE extracted, a = 32 and b = 95). We will apply the wavelet Daubechies 6 to the matrix obtained after extraction.

4.2 Application of K-Means Algorithm

There are several approaches of clustering, the unsupervised is selected. The algorithm must be executed several times $N_{execution}$ before choosing the best execution. The operation of K-means could be described step by step:

- **Stage 1**: *choice* N_C *randomness elements* $x_i(k)$ *among* N_{spike}. *They represent the centroids at the first execution.*
- **Stage 2**: *calculation distance elements-centroids by using cityblock.*
- **Stage 3**: *attribution each element* $x_i(k)$ *nearest cluster* C_j *of the centroid among* N_{spike}.
- **Stage 4**: *calculation the centroid of each cluster* $Cent_j(k)$*: mean of the elements* $x_i(k)$ *belonging to a cluster* C_j. *And we replace the old centroids by these new centroids. If there is no movement compared to the preceding iteration, the execution is stopped.*
- **Stage 5**: *return at stage 2.*

The following figure gives us the various phases and loops of K-means (Fig. 2).

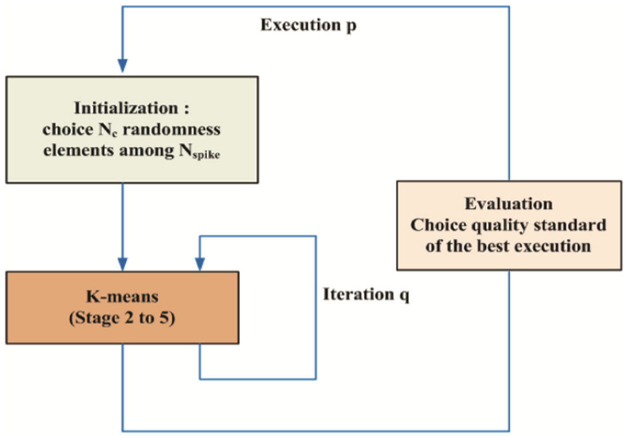

Fig. 2. Functioning of our k-means algorithm

4.3 Criterion of Stop an Execution of the K-means

The Eq. (8) calculate the mean error; after each iteration of index q of an execution p of K-means.

$$E_q^p = \sum_{j=0}^{N_c-1} \sum_{x(n)\in C_i} d\left(x(n), Cent_j^p(n)\right), q \in \{0, \ldots, N_{execution} - 1\} \tag{8}$$

The criterion of stop an execution of the K-means is given by the following expression:

$$\left| \frac{E_q^p - E_{q-1}^p}{E_{q-1}^p} \right| < \varepsilon \tag{9}$$

This criterion is attained with the iteration $q = N_{iterations}^p$, $p \in \{0, \ldots, N_{execution} - 1\}$. We choose $\varepsilon = 10^{-5}$.

4.4 Quality Standard of an Execution of K-means

The results of clustering vary according to the bad or good initialization of the centroids. After $N_{execution}$ executions, the best in the N_C clouds can be chosen. Then, the execution which minimizes the following equation must be selected:

$$p_{chosen} = \arg \min_{p\in\{0,\ldots,N_{execution}-1\}} \left\{ E_{N_{iteration}^p}^p \right\} \tag{10}$$

5 Analysis and Validation Results

In this part, real neuronal data are used for different patients. These data were extracted in the database of the Signal and Image Processing Laboratory of Renne1 University, France [13]. We will indicate the two databases by “Base BIG” and “Base GONT”. They contain hundreds of IPE of the type P, PP, N, NN, NP, PN, PW, PPW, NW, NNW, NPW and PNW. In more these data were labeled by an expert of the laboratory.

The simulations were made using a DELL-PC INSPIRON 1440 Pentium (R) dual-core CPU T4400 @ 2.20 GHz and 3 GB RAM. And all the solutions proposed were implemented under the environment of Matlab.

5.1 Evaluation of Adaptive Spike Detection Using SNEO

In this section, we present the results of proposed spike detection. To evaluate this method, we use several indices. By definition, false alarms (FA) give us the detected parts while they are not spikes. As for true positive (TP), they inform us that the spikes were well detected. Finally, non-detections (false negative: FN) represent spikes not found by the detector.

- The rate of false alarms is calculated as follow: $R_{FA} = \dfrac{FA}{TP + FA}$
- The sensitivity (rate of true positive) is a measure of the detector's ability to detect the spikes: $sensitivity = R_{TP} = \dfrac{TP}{TP + TN}$
- The selectivity is a measure of the ability of the detector to reject false alarms $selectivity = \dfrac{TP}{TP + FA} = 1 - R_{FA}$

The detection methods are often based on the principle of thresholding deciding event detection if any measurement exceeds a predetermined threshold. The higher this threshold is, the lower the algorithm is permissive and if false alarms decrease of sensitivity for its fall.

Similarly, a detection algorithm requires a third measure, it is the detection time (DT), that is to say, the time difference between the actual beginning of the spike to the electrical point of view (with the EEG, not so clinically) and the time when it is detected.

$$DT = \left| t_{spike} - t_{algo} \right| \tag{11}$$

Where t_{spike} is the actual start time of the spike and t_{algo} given by the detection algorithm. This performance indicator is calculated for each spike and evaluates the ability of the algorithm to detect an IPE more or less early.

Finally, taking into account these performance indicators, we trace the ROC curves for the detector.

Unlike many detection methods, with SNEO we don't use a lot of parameters to entry. Just give the length of the smoothing window and the estimation parameter of the adaptive threshold.

In the Fig. 3, we have the EEG signal (blue) with the moments of detection of spikes (green). In this figure, all spikes were detected.

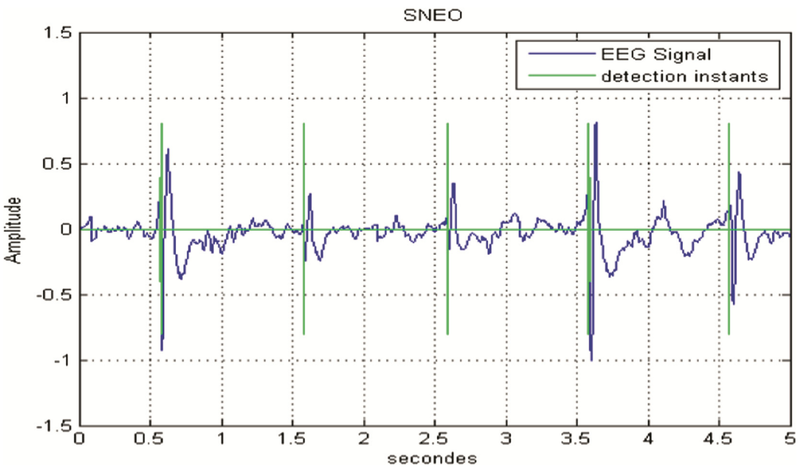

Fig. 3. IPE detected using adaptive SNEO (Color figure online)

We apply this method on all signals of the two databases. In more the execution time of the signals of one hour duration is approximately equal to 4.6 s. It is a very good time because we can detect hundreds of spike in a signal of duration one hour.

In addition, we represent in the ROC space [14] (Fig. 4) the performance indicators of SNEO for different morphologies. In Fig. 4, we have two curves of the two databases (databases BIG and GONT). It is noted that the two curves have points which are near to the ideal functioning point for a detector (point of coordinates (0%, 100%)). With this ideal point, the sensitivity and the selectivity are all equal to 100%. The curve of database GONT is above that database BIG. Consequently, it has the best point with sensitivity and selectivity equal respectively 100% and 98%.

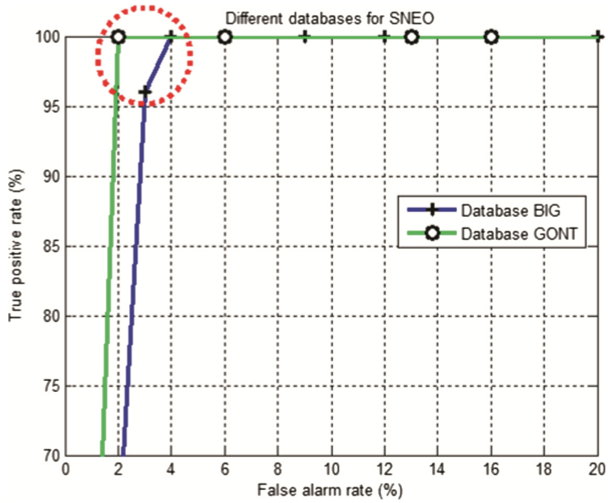

Fig. 4. Performances of spikes detection with different databases

Moreover, GONT presents for certain morphologies more false alarms than BIG. In these cases, BIG is more selective than GONT.

Consequently, the results of detection depend on the nature and the morphology of the spikes. This last depend on the state of vigilance of the patient: concentrate, light sleep, deep sleep etc.

5.2 Results Spikes Classification

Before classifying the spikes, we extract them by using a window from length 256 samples i.e. 1 s. The extracted spikes are recorded in a textual file to facilitate their loading under Matlab. Then, we apply wavelet filtering to the obtained matrix.

In addition, according to the experts, we meet in practice seldom more than 3 morphologies of IPE (spikes) on very different over one hour from recording. We will evaluate our classifier on mixtures of 3 types of IPE to the maximum.

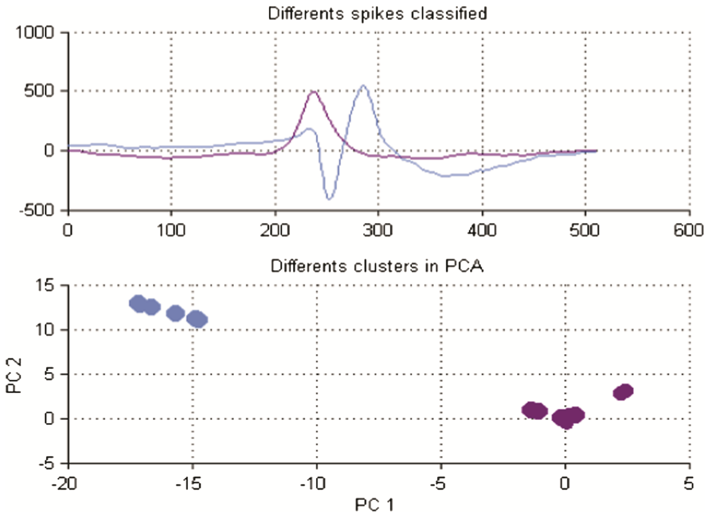

Fig. 5. Clustering and identification for mixture of two different spikes (P and NPW)

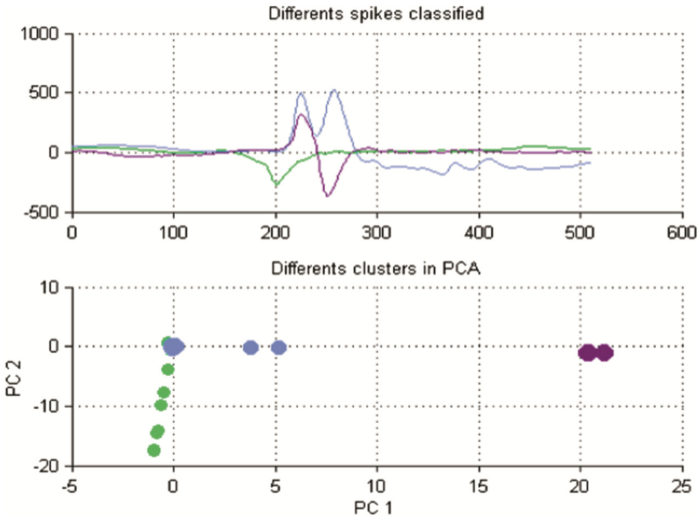

Fig. 6. Clustering and identification for mixture of three different spikes (N, PN and PP)

As explains it very well [15], "the evaluation of the pertinent of the groups formed in unsupervised classification remains an open problem. The difficulty comes mainly owing to the fact that the evaluation of the results of algorithms of clustering is subjective by nature because there are often various possible relevant regroupings for the same data file". Therefore, we use the indices of the confusion matrix [14] to evaluate the performances of our classification.

Figures 5 and 6 show the clustering of different spikes in a given mixture. In each figure, we can clearly identify clusters corresponding to each spike. These clusters give us principal components (PC) representation of various spikes. And we note that the position of the clusters is exactly the morphology of classified spikes.

The good distribution of clusters depends on the performance of the k-means algorithm. Consequently, these figures (Figs. 5 and 6) show that the mixed spikes were well classified with a small false alarms rate. These results are confirmed on Fig. 7.

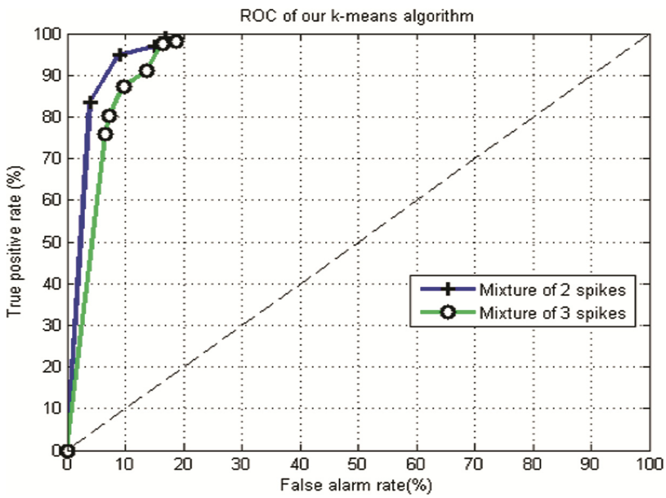

Fig. 7. Performances of unsupervised classification using k-means

In Fig. 7, the curve of the mixtures with 2 spikes is above that of the mixtures with 3 spikes. Moreover, the points of the curve with 2 spikes are more in the North-West (tending towards the ideal point of a classifier) in ROC that those of the 3 spikes. Consequently, the results in the case of the mixtures with 2 spikes are better than those of 3 spikes. That is due to confusion between spikes i.e. those which have identical morphological parts. Thus it is easier to make the separation of the spikes in a mixture of 2 IPE. In addition, the results of the mixtures with 3 spikes are also very satisfactory.

Indeed, our proposals applied to signals of duration lower or equal to one hour. We find hundreds spikes in these signals which could be classified correctly according to their morphology. Moreover, the average time of execution of the classification of the various mixtures is estimated at 30 s.

6 Conclusion

The biomedical signals are not easy to treat considering their complexity by nature. The tools for signal treatment developed can take part in the assistance with the diagnosis of the epilepsy. In this paper, we proposed adaptive spike detection based on SNEO. The results showed that detector SNEO gives us very satisfactory performances in terms of sensitivity, selectivity and time execution. Moreover, the median values of sensitivity and selectivity are respectively equal to 99% and of 92% on the tests carried out. And our detector appeared robust with morphological variability which can exist between spikes of the EEG signals for different patients. After the detection and the extraction spikes, the k-means algorithm associated with the principal components analysis gives us clusters which represent exactly the morphology of the concerned spikes. Moreover, the representation in ROC space gives us points near to the ideal point for a good classification. For the various mixtures, we obtain good rates of true positive. We could have respectively 94% and 88% in cases of mixtures with 2 spikes and 3 spikes. So our algorithm was able to distinguish different spikes extracted according to their morphology. Thus, combinations of detection and classification will enable us to conceive an assistance system with the diagnosis of the drug-resistance epilepsy.

To continue this work, we intend to use others methods of unsupervised and supervised classification in order to compare them. We will conceive a new model to detect the presence of slow wave in the interictal paroxystic event.

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