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Classification of Interictal EEG Data Based on Subdural Recordings

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Abstract: - The aim of this study is to develop an automated algorithm that determines patterns of dynamic brain behavior during monitoring of epileptic seizures. The goal is to interpret and characterize subdural EEG activities while focusing on behavioral patterns recorded from channels that lead to seizure. The software implemented would be general both in its implementation structure as well as in characterizing specific EEG patterns, in order to cope with what is expected to be a multitude of elusive brain behavioral characteristics. A main challenge is in the ability to provide meaningful assessments of such subdural EEG behaviors within the context of electrodes that do or do not lead to a seizure. The EEG interictal data recorded inside the brain can be processed to define similar patterns evident in those electrodes that lead to a given seizure to further facilitate surgical planning. The contributions of this study is in the implementation of a back-propagated neural network that automate the decision making process. This process is to exploit different parameters in order to assess relevant brain changes in the subjects during, at the onset, and after an epileptic seizure. This allows determining whether the patient has a consistent source of ictal activity with the most potential to lead to an epileptic seizure, so the epilepsy focus could be located with a higher degree of accuracy.

Key Words: - Epileptic seizures, subdural EEG, ictal activity, neural network

1 Introduction

Seizures are related to a malformed pathologic substrate that is more extensive than the lesion evident on MRI scans [1, 2]. The EEG interictal data recorded inside the brain can be processed to define similar patterns evident in those electrodes that lead to a given seizure to further facilitate surgical planning [3].

A mathematical framework is provided for the study of interictal EEG leading or not to an epileptic seizure. The EEG of epileptic subjects can be divided into two main categories, interictal and ictal. The interictal EEG is the EEG taken when the patient is not having seizures or in between seizures [2]. Interictal activity is considered to be abnormal if it can occur in a patient with epilepsy in the absence of an actual seizure. The ictal EEG activity on the other hand is when the actual seizure occurs.

The main objectives of this study, which are to elicit new patterns related to seizures, consist of the following steps: (1) to identify and formulate those patterns in EEG recordings that are inherent to those electrodes that lead to a seizure; (2) to extract features that best characterize those EEG electrodes that lead to an ictal activity; (3) to establish mathematical derivations that provide not only quantitative measures, but also describes and locates the focus of an ictal activity; (4) to correlate the clinical features with the EEG findings in order to determine whether the patient has a consistent source of ictal activity, which is coming from the location concerning the group of channels that present interictal activity; (5) to classify and to group those EEG channels that are known in advance to lead to seizures in order to extract similarities in their behavior, so a common behavioral pattern could be found; (6) to find the best suitable classifiers that separate in a new feature space the two classes of electrodes, leading and not leading to an ictal activity.

2 Method

In this study, eight children with medical refractory partial seizures that underwent pre-surgical evaluation have been analyzed. The subdural EEG data was recorded using XLTEK Neuroworks Ver.3.0.5 (equipment manufactured by Excel Tech Ltd. Ontario, Canada). Sampling frequency of 500Hz with 0.1-70 Hz bandpass filter settings and 12 bits

A/D conversion were used to obtain the digital EEG recordings. Figure 1 shows the intracranial recording strips placed on the brain of one patient for illustrative purposes and to highlight the clinical significance of such a preoperative process.

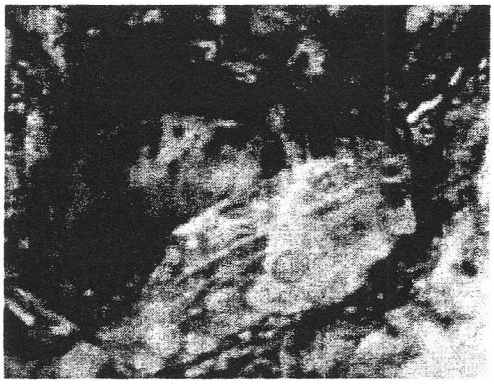

Fig. 1 Intracranial electrodes as placed during surgery (courtesy of Miami Children's Hospital).

To classify those electrodes that lead to an epileptic seizure, a program was developed in order to quantify the patterns that are inherent to those electrodes. Input data in this study was subdural EEG segments from 20 to 3600 seconds of duration of epileptic patients. The first step in the procedure involved identifying the pertinent electrodes in the overall interictal EEG recordings in which the seizures occurred. The physicians performed this task initially through visual inspection of the recorded data. A computer program was earlier [4,6] developed in order to detect automatically interictal spikes so as to provide more accurate and consistent input data to the proposed classification algorithm.

The classification algorithm consists of the following steps. Results obtained are revealed in the next section in order to assess both the validity of such steps and the merit of each step for identifying a suitable linear classifier.

Step 1- Obtaining an approximated input EEG matrix

In this preprocessing step, filtering was performed applying the Singular Value Decomposition (SVD), which is based on the eigenvalues decomposition [7,8]. The larger singular values were retained (in this case the first five were deemed sufficient for the analysis), so a better approximation is obtained, or equivalently, more information is contained in that approximation and the other values are set to zero, thus a new matrix was created. The approximated matrix, containing less noise was used in the subsequent steps. This implementation concluded the filtering preprocessing step.

Step 2- Applying different parameters to the EEG data

Since brain dynamics are nonlinear, this study investigated methods such as the calculation of correlation dimension integral, mobility and complexity.

The correlation dimension integral $R(r)$ given in equation (1) is a measure of spatial organization, where the space is occupied by a set of random points. It determines the degree of complexity in the EEG signal.

$$R(r) = \frac{1}{N^2} \sum_{j=1}^{N-1} \sum_{i=j+1}^{N-1} \theta\left(r - \left|X_i - X_j\right|\right) \quad (1)$$

Where, r is the threshold value used to evaluate the similarity between two reconstructed vectors X_i and X_j. N is the total number of points in the time series. The vector X_i is a point in the embedded phase constructed from the input EEG signal as a single time series according to the following formula:

$X_i = (X_i, X_i + \tau, X_i + 2\tau, \ldots X_i + (m-1)\tau)$, where m is the so called embedding dimension and τ is a time delay.

Additionally, the Hjorth's parameters, mobility and complexity were calculated using equations 2 and 3. Mobility (equation 2) gives a measure of deviation of the voltage changes with respect to deviation of the EEG voltage amplitude, while complexity (equation 3) provides a measure of excessive details with regard to the slightest possible signal's shape [9, 10]. The mobility is computed using the following formula.

$$M(y(t)) = (\sigma(y')/\sigma(y))^{2} \quad (2)$$

where σ is the variance and y' is the first derivative of the primary signal y. The complexity, $C(y(t))$ involves the first derivative of the mobility $M(y')$ and the mobility of the signal itself $M(y)$ and it is expressed as:

$$C(y(t)) = (M(y')/M(y))^{\frac{1}{2}} \quad (3)$$

Step 3- Extraction of the best features from the EEG data

The next step dealt with extracting features from the filtered EEG matrix using the aforementioned parameters of step 2 in order to discriminate between

the two groups of electrodes. All these three parameters were computed for each electrode separately using successive epochs or non-overlapping windows of 1 second for all the recorded subdural EEG data. By computing these parameters, a behavior for each feature over time was established for each electrode.

Step 4- Implementation of regression lines for each electrode and parameter

As all the different parameters were represented in time, regression lines for all of these parameters were calculated in order to keep a suitable track of the behavior of each electrode with respect to the computed parameter. This also helps in determining a linear classifier that separates in the parameter vs. time space the two different classes of electrodes. One condition to make this study more relevant from a clinical point of view was to require from these two classes of electrodes to be totally independent in terms of source location, and synchronicity of the spike firing. After obtaining regression lines for all electrodes, two groups of regression lines per parameter were created. These computed linear approximations were used for each electrode to facilitate visualization of the overall trend of each electrode.

Step 5- Applying a Neural network for linear classification

Establishing an artificial neural network (ANN) that is trained to extract seizure-leading features of interictal EEG is a significance outcome, since this ANN

(1) can help to overcome the subjective factor associated with human classification;
(2) can serve as a second expert for decision process validation; and
(3) can be used for fast automated seizure leading channels detection, even for on-line recordings, sparing EEG technicians the tedious task of long-term monitoring.

At this stage, a plot of the three selected features revealed well defined electrodes clusters. No other features produced class clusters so compact and separated from each other. But extrapolation of this mechanism of classification in time did not work as anticipated since the time dynamics of the parameters strongly changed from one recording to the other, despite visible class clustering. In a parameter vs. time plot, the separating points between the two electrode groups changed from one recording to another.

This is best illustrated in Figure 4. Note that each plot is represented only for 20 seconds in two different segments of the EEG data. The real time, where the data was taken, is displayed at the bottom of the two plots.

In order to consider this relative change and yet make real-time classification possible, time independent analysis was performed by computing for each feature three statistical parameters, namely the mean of the regression line that represents the feature behavior, the standard deviation of the parameter over time and the power of the frequency spectrum of the feature over time.

The average and the standard deviation for each regression line were computed for each group of electrodes. Also, the Fourier Transform was applied to the behavior of each parameter over time and its power frequency was calculated for each electrode. These statistical parameters were then inputted to an artificial neural network (ANN) in order to obtain a linear classifier for each feature [6]. Linear decision functions could then be established for classifying the electrodes based on these statistical parameters. One decision function was created exclusively for each of the three parameters (correlation, mobility, and complexity). These specific decision functions would find the optimum separating plane between the two classes of electrodes in a 3D space where the axis are represented by the statistical parameters used (mean, standard deviation, and frequency power).

The training and testing process was carried out using a cross validation training technique. The network was trained with a 25 percentage of the EEG data and tested in the remaining.

Establishing an artificial neural network (ANN) that is trained to extract seizure-leading features of interictal EEG is a significance outcome, since this ANN: (1) can help to overcome the subjective factor associated with human classification; (2) can serve as a second expert for decision process validation; and (3) can be used for fast automated seizure leading channels detection, even for on-line recordings, sparing EEG technicians the tedious task of long-term monitoring.

The network configuration used in this research consist of 3 input neurons that correspond to the mean, standard deviation, and frequency power (μ,σ,Φ) of the parameter analyzed. The output would be 1 or -1, which indicates if a given channel leads to seizure or not, respectively.

The output classifiers are three decision functions of the form:

$$f_\xi(X) = w_1 \cdot \mu_\xi(X) + w_2 \cdot \sigma_\xi(X) + w_3 \cdot \Phi_\xi(X) + w_4 \quad (4)$$

The subscript ξ is defined as follows:

$$\xi = \begin{cases} R & \text{for Correlation} \\ M & \text{for Mobility} \\ C & \text{for Complexity} \end{cases}$$

Where $\underline{X}$ is a vector containing the values of the specific parameter (correlation integral, complexity, or mobility) for all time windows; w_1, w_2, w_3, and w_4 are coefficients and $\mu_\xi(\underline{X})$, $\sigma_\xi(\underline{X})$ and $\Phi_\xi(\underline{X})$ are the mean, the standard deviation, and the frequency power of vector $\underline{X}$, respectively. Electrodes are classified as leading to seizure only if $f_\xi(\underline{X}) > 0$ for a specific feature.

The decision functions consisted of feed-forward ANNs trained via back-propagation. These ANNs are structured with 3 input neurons and 1 output neuron, with linear activation functions. This type of structure produces a linear classifier.

3 Results

The algorithm was tested with various types of interictal data. Results indicate that this EEG analysis technique allows defining two regions of electrodes, one for electrodes leading to an ictal state and another for the remaining electrodes that do not lead to such state. Also, using different parameters, characterization of the behavior of the interictal EEG over time is possible. The rate of missed detections as well as the rate of incorrect positive detections were extracted and are given in percentages in Table 1. As it can be observed, the complexity results are the best compared to the other two parameters. Two misclassification percentage rates are calculated: one for the group of electrodes leading to seizure (False Negative Rate) and the other for to the group of electrodes that do not lead to seizure (False Positive Rate).

It should be mentioned that making the ANN converges and yielding accurate classification results should be emphasized as well as that the separability is achieved because of the choices of the 3 discriminant features of mean, standard deviation, and frequency power. This in itself constitutes a mayor contribution of this dissertation.

In assessing the examples treated before, the complexity parameter produces the most consistent and reliable results across all 8 patients included in the study.

The total number of electrodes that presented interictal activity was 75, out of which 30 lead to seizure onset and 45 did lead to an ictal state. The following evaluation results were obtained.

$$Specificity = \frac{TN}{FP+TN} = 96\% \quad (5)$$

$$Sensitivity = \frac{TP}{TP+FN} = 97\% \quad (6)$$

$$\text{Precision} = \frac{TP}{TP+FP} = 94\% \quad (7)$$

The terminology used is explained as follows: FP (Not leading to seizure), FN (Leading to seizure), FN (Leading to seizure), and TN (Not leading to seizure).

Examples of the complexity outcome are given in Figures 5, 6 and 7. The electrodes represented in red (-) are the channels that lead to seizure and the electrodes in blue (+.) are the channels that do not lead to seizure. Note that the three features (μ,σ,Φ) have great potential for classifying electrodes leading to seizure, regardless on what type of classifier used with respect to the 3 parameters.

Key findings can be affirmed as follows: (1) it was found that at any window of time along the EEG signal (independent of time), acceptable classifiers could be obtained using just the complexity values; (2) A search for such decision functions across patients is ineffectual, because experiments reveal that such decision functions are patient dependent; (3) It is extremely important that when one is to search for such decision functions, electrodes should be analyzed only if they are localized in different locations and with recorded interictal spikes not happening simultaneously.

Table 2 Lower ⇓ or higher ⇑ values of the leading to seizure with respect to the not leading to seizure channels.

Patient	*Mobility (M)*	*Complexity (C)*	*Correlation (R)*
1	⇑	⇑	⇓
2	⇑	⇑	⇓
3	⇓	⇓	⇑
4	⇑	⇑	⇓
5	⇑	⇑	⇓
6	⇑	⇑	⇓
7	⇓	⇓	⇑
8	⇓	⇑	⇑

A summary of the results for of all the patients is provides in Table 2. The arrows indicate if for a given parameter, the values of the red group of

electrodes are higher or lower with respect to the blue group of electrodes. As can be observed, for 5 patients out of 8, the complexity values for those electrodes that lead to an ictal state are higher than the values of those electrodes that do not lead to seizure. Also, the mobility values for these five patients behave in the same manner. Two patients behave in a similar fashion, and their complexity and mobility values are reversed if we compare them with the other five patients.

A closer look at this table reveals the following conditions: If we assign a negative (-) to $\Downarrow$ and a (+) to $\Uparrow$, then, the following relations hold:

$$\begin{aligned} C * R &< 0 \\ M * R &< 0 \\ M * C &> 0 \\ M * C * R &< 0 \end{aligned} \tag{8}$$

These relations as established in equation 8 constitute another mayor observation in this study. It could be concluded that the integration of these 3 parameters could augment our results.

4 DYNAMICS OF CORRELATION INTEGRAL, MOBILITY, AND COMPLEXITY AS POTENTIAL SEIZURE PREDICTORS

In assessing the examples treated before, the complexity parameter produces the most consistent and reliable results across all 8 patients included in the study. Nevertheless, a detailed example is provided for a long event consisting of one hour of EEG recording prior to a seizure to see how these 3 parameters change as we approach an ictal state. For this particular example, we provide the behavior of one the 3 parameters in 2 distinct windows of time for visual appreciation. For each window of time, the behavior of the parameter itself is provided with respect to time as well as through regression line approximations corresponding to that behavior.

It can be observed, as illustrated in Figure 2, in this long event of 1 hour, how the mobility of the EEG signal can differentiate between the two groups of electrodes. Mobility remains the most reliable feature in this case. The regression lines corresponding to this parameter are separated in two well defined groups. The blue channels (--) do not lead to seizure and the red (-) lead to seizure as illustrated in Figures 2 and 3. Also correlation integral and complexity behave in a similar manner.

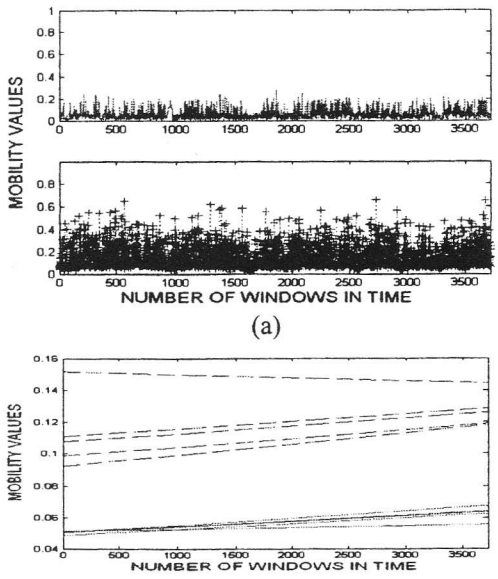

Fig. 2 Behavior of the mobility: (a) behavior of the parameter one hour before seizure; (b) regression lines one hour prior to a seizure.

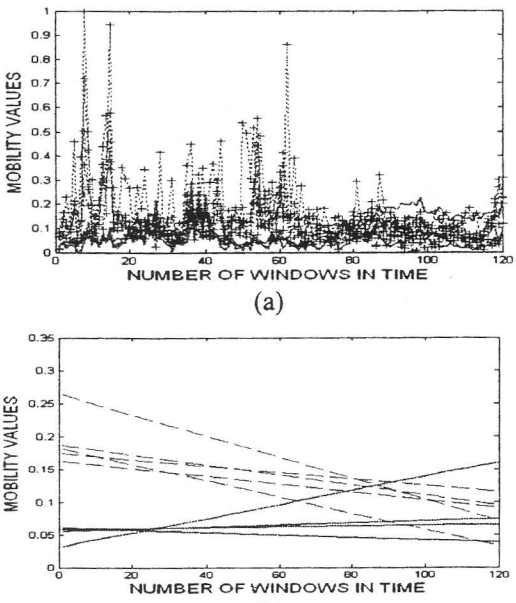

Fig. 3 Behavior of the mobility: (a) behavior of the parameter 2 minutes before seizure onset; (b) regression lines 2 minutes prior to a seizure.

As time approaches the onset of the seizure, the trend of the behavior of the measured parameters through time becomes similar for the two classes of electrodes. In other words, just prior to the seizure, the regression lines of the two groups of electrodes converge into one group; there is no clear separation between them as can be seen in Figure 3.

It can be concluded that even for a long event of interictal data, the aforementioned parameters succeed in discriminating the two classes of electrodes.

4 Conclusion

In this study, we presented a new quantitative technique for the classification of different electrodes from short and long duration EEG data. The unique contribution of our study is to understand better the characteristics of the different interictal epileptiform activities, so a better localization of the epileptic focus could be determined. The likelihood of the success of surgery is increased when all test results point to a single epileptogenic focus [11-14]. In all of these performance values of the 3 parameters implemented, it can be said that the results obtained show great promise in delineating electrodes that lead to seizure from those that do not. It is fitting to note that when our results failed to discriminate between these two sets of electrodes, a clinical analysis revealed that those electrodes were indeed situated in the same region and their interictal spikes were happening simultaneously. As this study will involve a higher number of patients as they become available, additional results will provide more credence to our findings.

The uniqueness of this algorithm is in the establishment of a mathematical foundation capable of extracting features from interictal EEG signals using the above mentioned parameters, which served as change indicators for our analysis. The integration of several parameters (correlation integral, mobility, and complexity) constitutes a unified method for assessing differences in the EEG channels.

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Table 1 Percentage of misclassification (results have been averaged across all EEG segments).

Patient	Correlation FNr	Correlation FPr	Mobility FNr	Mobility FPr	Complexity FNr	Complexity FPr
Patient 1	40.7 %	0.0 %	14.3 %	12.9 %	14.3 %	0.0 %
Patient 2	37.5 %	0.0 %	20.0 %	0.0 %	0.0 %	0.0 %
Patient 3	0.0 %	8.2 %	0.0 %	0.0 %	0.0 %	0.0 %
Patient 4	33.3 %	0.0 %	0.0 %	0.0 %	0.0 %	0.0 %
Patient 5	0.0 %	5.0 %	0.0 %	0.0 %	0.0 %	0.0 %
Patient 6	28.6 %	0.0 %	14.3 %	0.0 %	14.3 %	0.0 %
Patient 7	42.8 %	0.0 %	28.6 %	0.0 %	14.3 %	0.0 %
Patient 8	42.8 %	5.0 %	14.3 %	0.0 %	0.0 %	0.0 %

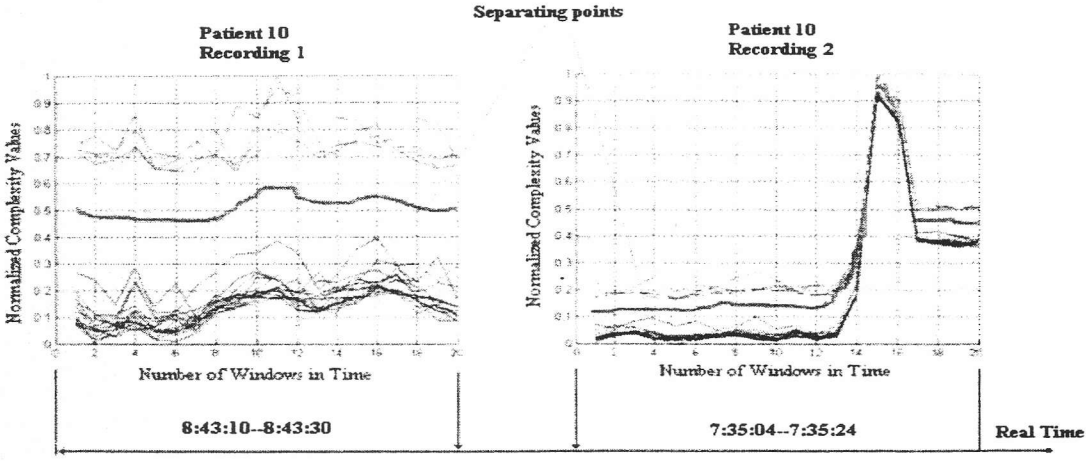
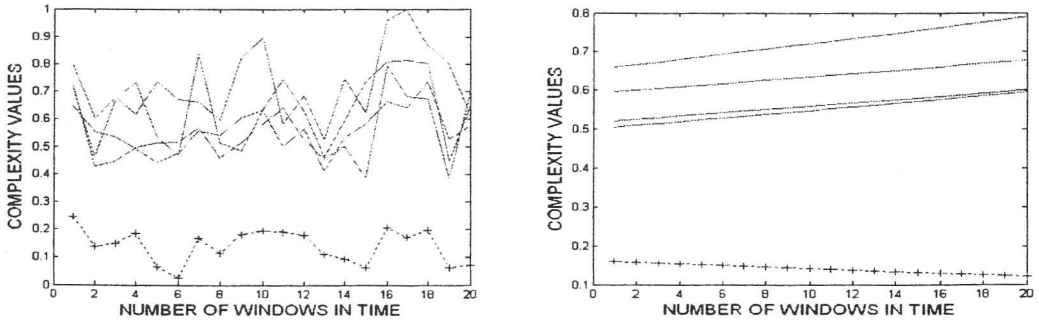


Fig. 4 Electrode clusters changing their relative location in the feature vs. time plot.



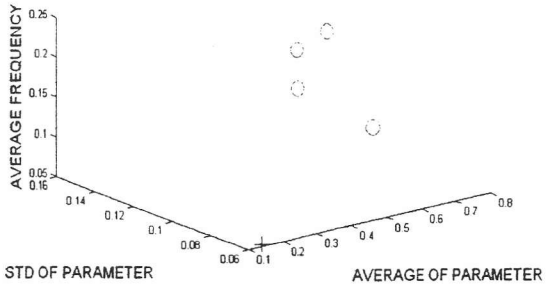


Fig. 5 Complexity results for patient 2.

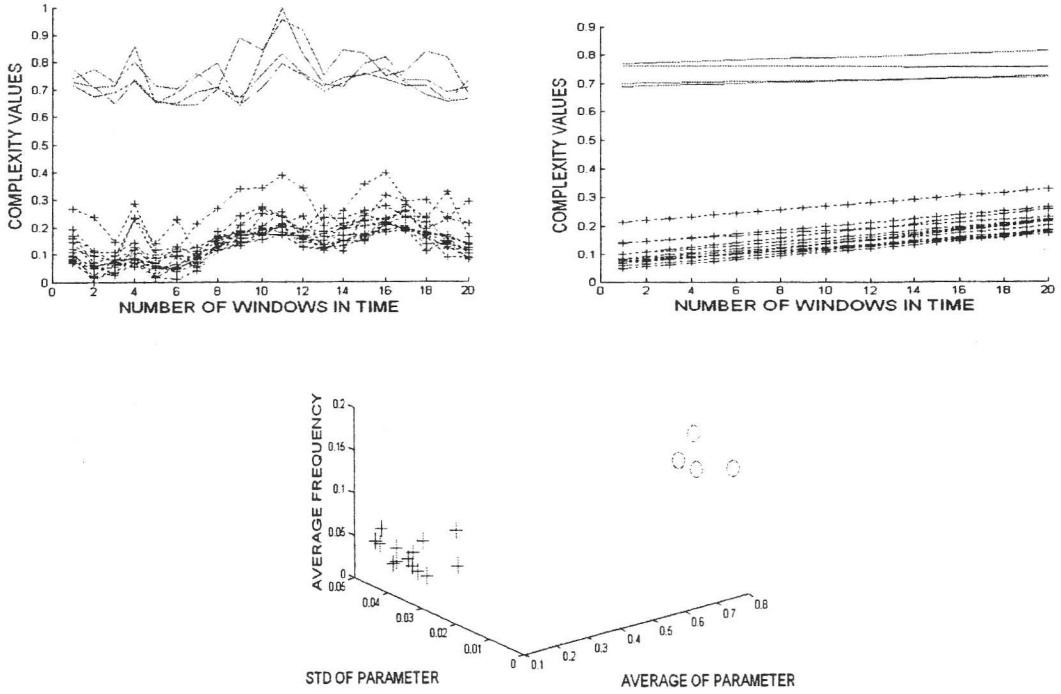


Fig. 6 Complexity results for patient 4.

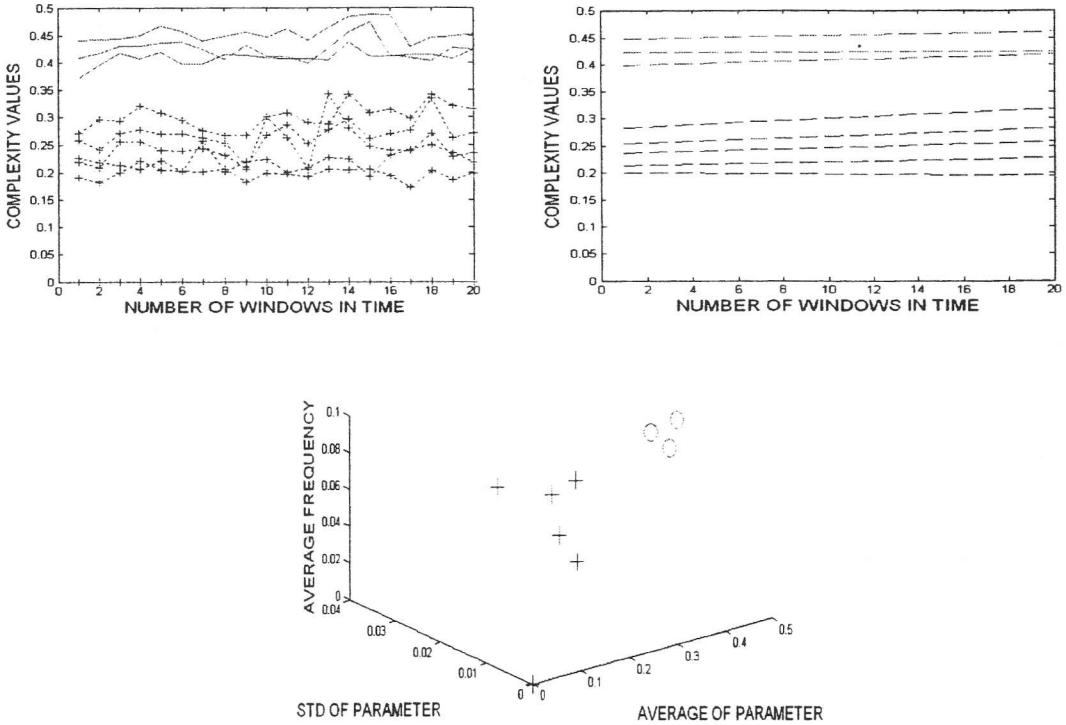


Fig. 7 Complexity results for patient 6.