Detrended-Fluctuation-Analysis (DFA) and High-Frequency-Oscillation (HFO) Coefficients and their Relationship to Epileptic Seizures

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Abstract: We tested the applicability of methods based on Detrended Fluctuation Analysis and HFO detection to the analysis of EEG signals from patients diagnosed with epilepsy, in order to test how efficient these methods would behave in a seizure prediction application. We were able to statistically distinguish the coefficients estimated in the pre-ictal period from the coefficients obtained on the inter-ictal period, suggesting that the methods can be used to the development of seizure detection algorithms.

1 INTRODUCTION

1.1 EEG in Clinical Epilepsy

Epilepsy may be characterized by a diversity of pathological neuronal conditions leading to abnormal electric activity in a cortex region, thus causing epileptic seizures (Fisher et al., 2005). Such recurrent seizures impose harmful effects in life quality, and frequently are associated with irreversible damages in patient's cognitive capabilities (Brodie, 2005).

The EEG signal is widely used to study the brain clinical conditions, since it provides simple, costless and non-invasive tool to investigate the brain activity dynamics (Li et al., 2005).

For many years, the frequency band considered clinically significant for analyzing the EEG signal was lower than 70 Hz (Jacobs et al., 2012). But the identification of the patterns known as High Frequency Oscillations (HFO) are pointing out that biological relevant brain activity exceeds that frequency band.

1.2 High Frequency Oscillations

High frequency oscillation (HFO) is a term used to describe a high frequency EEG pattern including the frequency range from 70 up to 500 Hz.

The first register of HFO patterns occurring spontaneously in epileptic patients was obtained in 1999 (Bragin et al., 1999). Since then, several researchers are studying the potential link between the identification of HFOs and the occurrence of epileptic seizures.

Detecting HFOs enable to identify the location of the seizure onset zone in patients with normal magnetic-resonance images (Andrade-Valenca et al., 2012), and even non-invasive scalp EEG recordings may provide enough data to support the use of HFOs as biomarkers for the identification of the epileptic zone (Andrade-Valenca et al., 2011), provided that cerebral activity is carefully separated from muscular artifacts.

However, some issues tied to the identification of HFOs on healthy individuals suggests there is still too much work to be done in order to better understand and classify the high-frequency patterns in a effective way (Buzsaki, Silva, 2012; Engel, Silva, 2012).

1.3 Seizure Prediction

Seizure prediction may cause great benefit on investigations related to diagnosis and treatment of epilepsies. It enables pre-ictal SPECT exams (Li et al., 2005), medical intervention to avoid the occurrence of abnormal neuronal discharges and

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even the self preparation of patients for the seizure, making it easier and safer for those patients to execute basic tasks, thus improving their life quality (Quyen, 2005).

1.4 Goal

This article makes use of certain signal analysis methods to extract characteristics from scalp EEG signals of patients diagnosed with epilepsy, in order to investigate seizures with information prior to their occurrence. Consequently, we can evaluate the usefulness of such methods in order to fund seizure detection algorithms.

1.5 Signal Processing

1.5.1 Detrended Fluctuation Analysis

Detrended-Fluctuation Analysis (DFA) is a powerful tool capable of providing a simple parameter to represent the long-term power law correlation proprieties of a signal. One advantage of this method over the other fractal analysis methods is the capability of detecting the correlations even when the temporal series is not stationary (Chen et al. 2002). First described to analyze non-stationary cardiac beating series (Peng et al. 1995), it has already been successfully utilized in a variety of studies in many areas (Lin et al., 2010; Zheng et al., 2008; Lachowycz et al., 2013; Blesic et al., 2005).

Given a signal $x[i]$, $i = [0 \dots N]$, wherein x maybe the EEG recording, i represents the discrete time and N is the total amount of signal samples, the method consists of obtaining an integrate time series $x_{int}[j] = \sum_{i=0}^{j} x[i]$, so that the resulting signal is an unbounded time series. This integrate series is then divided in segments of size L samples, and each segment is approximated to a linear function of the form $p = ax + b$. The square root mean deviation between the integrated series and the linear approximations is calculated using the expression.

$$F[L] = \sqrt{\frac{1}{N}\sum_{i=1}^{N}(x_{int}[i] - p[i])^2} \quad (1)$$

One may conclude that $F[L]$ grows as L increases its amplitude, since using larger scales for linear approximation will often result in larger errors. In fact, it is given that the relation between $F[L]$ and L is given by the power law

$$F[L] \propto L^{\alpha} \quad (2)$$

A plot of $\log(F[L])\ vs\ log(L)$ will provide the coefficient α as the angular coefficient of the obtained line. Often, the log-log plot presents a *crossover phenomena* and the data may be better fitted if two angular coefficients, α_1 and α_2, are used, as depicted in Fig. 1.

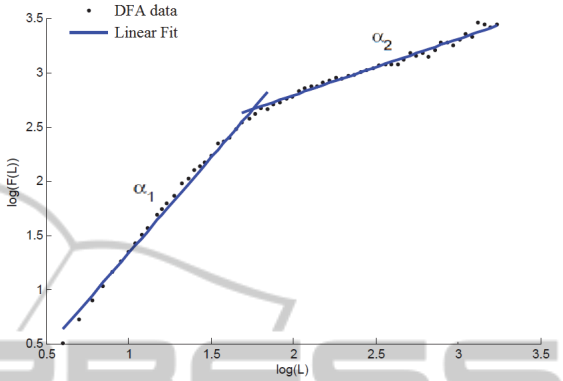

Figure 1: Illustration of the *crossover phenomena*. It is clear that the data is better adjusted by using two linear fits with different angular coefficients α_1 and α_2.

DFA method was already applied to studies regarding epilepsy. It was suggested that the coefficients obtained are capable of differentiate ictal from inter-ictal epochs (Yuan et al. 2011), but it is important to note that previous researches involving DFA only considers the conventional frequency band in EEG analysis and short time interval records, resulting in limited portion of the data (Parish et al. 2004; Yuan et al. 2011; Nikulin et al. 2005). In this study we considered all frequency bands available according to the Nyquist theorem. Further, we analyzed several hours of EEG records and considered both alpha coefficients provided by the *crossover effect*. Therefore, resulting in a better coverage for different frequency activities and better estimates for the statistical analysis.

1.5.2 HFO Detection

Most of HFO detection methods are based on detecting alterations on energy or power for various segments of the signal, which is filtered to show only the interest band of frequencies (Zelmann et al., 2012).

There are comparisons between different types of detectors, showing some algorithms may have better results under certain circumstances, such as the quantity of HFO in a small time interval (Zelmann et al., 2012).

The implemented method used in this study was based on the algorithm proposed by von Ellenriender

and collaborators (Ellenriender et al., 2012), which consists in a simple and functional method using a moving threshold value, to which the local power of the signal is compared to.

The original method consists in three steps.

- The EEG signal is filtered, so that to consider a few frequency bands of interest (high frequency bands). The resulting signal will be represented here by $y_k[i]$,wherein the index k will be associated to one single frequency band. Notice that one may consider more than one frequency band, resulting in more than one filtered signal for the same EEG signal.
- The moving threshold ($T_{hk}[i]$) and the Root Mean Square ($RMS[i]$) for a moving window of size $4N_k$ for each filtered signal $y_k[i]$ are calculated as shown in Equations (3) -(5), wherein N_k is the number of samples tied to one temporal cycle of the central frequency of the kth frequency band in consideration.

$$T_{hk}[i] = T_{hk}[i-1] + c\left(\frac{1}{N_b}(z_k[i-2N_k] - z_k[i-N_b-2N_k])\right) \quad (3)$$

$$z_k[i] = \min(T_{hk}[i], RMS[i]) \quad (4)$$

$$RMS[i] = \sqrt{\frac{1}{4N_k+1}\sum_{m=-2N_k}^{2N_k} y_k^2[i-m]} \quad (5)$$

Where $N_b = t_b f_s$, f_s is the sample frequency of the EEG signal and t_b being a fixed parameter. c is the proportionality constant,

- The RMS (5) is then compared to the moving threshold for each time sample i, as shown in (6). The result is a series with the same length of the input signal (for each kth frequency band), indicating the samples in which there was an increase of the high frequency signal power in reference to the basal activity.

$$detect[i] = \begin{cases} 0, & RMS[i] \le T_{hk}[i] \\ 1, & RMS[i] > T_{hk}[i] \end{cases} \quad (6)$$

The difference between the standard method of the literature (Ellenriender et al., 2012) and our proposition is related to the filtering of the signal prior to the detection step. These differences are noted in Section 2.2.

2 METHODS

2.1 Data Set Acquisition

All the EEG data used in this study was obtained from the CHB-MIT database, which was collected from epileptic patients on Children's Hospital Boston. All signals were obtained with sampling frequency of $256\,Hz$ and 16 bits resolution, using the standard 10-20 international system for electrode positioning.

All seizures observed during the recording of the patients were marked by specialists with two time markers, one for the start and one for the end of the seizure.

The data bank is better described on Shoeb's thesis (Shoeb, 2009) and is available on PhysioNet's data bank (Goldberger et al., 2000).

Our dataset consists of a selection of 10 patients from available data, including 54 epileptic seizures. The selection was performed in order to automate the algorithms to read and analyze the EEG signals, since some of the files from the original database contain extra channels, making some of the patients having non standardized channel names and distribution.

2.2 HFO Detection Parameters

For the pre-detection stage of the algorithm, the EEG data was filtered using a band-pass FIR filter designed based on the window method, considering a Hamming window with $\alpha = 0.54$. The cut-off frequencies were $f_1 = 80\,Hz$ - $f_2 = 128\,Hz$, and the frequency response presented a ripple of $0.02dB$, attenuation of $-56dB$ and transition band width of 9.5 Hz.

2.3 Data Pre-Processing

To assess the behaviour of the methods' results in a seizure prediction scenario, the methods were applied in order to obtain the results as a function of time.

The DFA method provides as result two coefficients, α_1 and α_2. To obtain a series of α_1 and α_2 in function of time, the original EEG signals were divided into segments of length $N = 5000$, and to each segment, the method was applied in order to obtain both alphas. This leads to a time series for each coefficient, and the time resolution of the series is $\Delta t = N/f_s$, where f_s is the sample frequency of

the EEG data. In the case of this study, $\Delta t = 19.53\ s$.

In order to provide comparison between both methods, the results from the HFO detection are summarized by a time series with the same time resolution of the time series generated from the DFA analysis. The result is a time series for the coefficients, indicating the rate of detected increases on high frequency activity for each segment (s) of length N, as a function of time.

$$HFO\ Rate[s] = \frac{\sum_{i=s.N}^{s.N+N-1} detect[i]}{N} \quad (7)$$

2.4 Statistical Analysis

The statistical analysis was based on the distribution of the coefficients obtained into four different groups. The segments containing any part of the signal belonging to a seizure are classified as the *seizure group* (S group). The segments before the occurrence of the seizure were classified as the *before-seizure group* (BS group). The segments after the occurrence of the seizure were classified as the *after-seizure group* (AS group). The segments distant to any seizure were classified as the *distant-seizure group* (D group).

Our goal is to distinguish each of the groups from the other ones, using a hypothesis test. We have employed a "t test", without the supposition that the variances for the two compared distributions are equal. This is also known as the "Welch t test". Hypothesis is that both groups under comparison are generated from the same distribution and with $p < 0.01$, this hypothesis is rejected with 5% confidence, meaning that the two compared distributions are statistically different at that confidence level.

2.5 Software

All steps of signal processing were developed using our own software, which was particularly implemented for visual analysis and processing of EEG data. The software results from the need of an efficient tool, including various processing methods and offering an easy way of viewing and selecting the EEG signal.

The software was written in C++, using Qt 4.8.5, and it is still undergoing revisions and improvements, so that to be released as free open source software for general use of EEG data processing.

All statistical analysis was made using scripts from Mathworks MATLAB.

3 RESULTS AND DISCUSSION

Figures 2 and 3 depicts results from the two methods.

These figures show are tied to data for only one seizure register of one single patient. For some recordings, changes in the coefficients time evolution near the occurrence of the epileptic seizure is very clear, but in some cases the changes are subtle or not present at all.

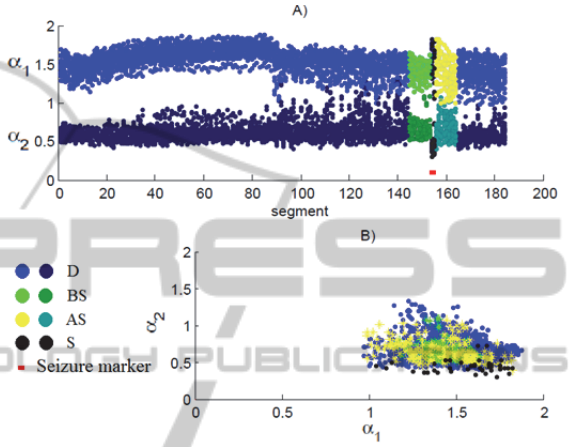

Figure 2: One-patient record example for: (A) the DFA coefficients $\alpha_1$and α_2 presented as a function of the segment number; (B) as α_2 vs α_1 dispersion plot. Notice the abrupt change on the behavior of α_1 occurring around segment 90. This change is not related to any marked fact, but may be occurring due to changes on brain state or muscular artifacts.

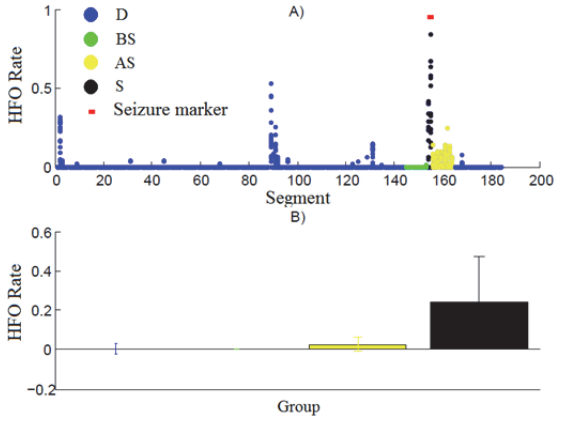

Figure 3: One-patient record example for: (A) HFO detection rate, presented as a function of the segment number; (B) mean and standard deviation for each one of the segment groups within this record. One can note an increased detection of high frequency activity around segment 90 that is not related to any marked event, but may be occurring due to changes on brain state or muscular artifacts. This change is correspondent to the behavior change visualized on Figure 2.

There are some ruptures in both the DFA coefficients and in the HFO rate coefficient time course that are not related to any identified epileptic activity, as seen in Figure (3A). These changes may be due to muscular artifacts or even due to patient's brain state changes (*i.e,* moving from sleep to awake state).

In order to assess the consistency of the method, we applied the statistical processing on all data, including all patients and all seizures. Tables (1) and (2) present the mean and standard deviation for the four groups, following the classification of all data. Figures 4 and 5 presents a better way of considering the results respectively from Tables (1)-(2).

Table 1: Mean and standard deviation (SD) values of DFA coefficients for each of the groups, considering all recordings of the study (Section 2.4).

Group	α_1		α_2	
	Mean	S.D.	Mean	S.D.
D	1.3587	0.3493	0.6165	0.1918
BS	1.3383	0.2913	0.6626	0.1675
AS	1.4234	0.3041	0.7105	0.1823
S	1.4061	0.2850	0.5107	0.1863

It is indeed clear that there are changes in the mean for each group, even if the difference from one group to another is small, also including huge standard deviations. The α_2 coefficient is increased for both BS and AS groups, whereas for the S group, the value of α_2 coefficient is smaller when compared to D group. Meanwhile, the α_1 coefficient is smaller for the BS group, but is increased for AS and S groups, when compared to D group.

The HFO rate coefficient follows a more logical and expected behavior, showing increased means for BS and AS groups, and even higher mean for the S group, when compared to the D group.

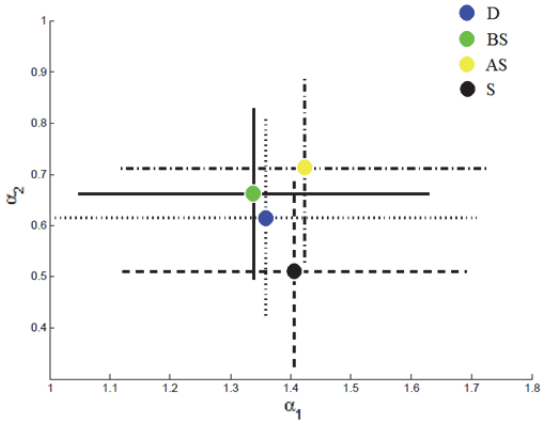

Figure 4: Mean and standard deviation for both DFA coefficients, for each one of the four groups, considering all recordings of the study (Section 2.4 and Table(1)).

Table 2: Mean and standard deviation values (SD) of the HFO rate, estimated for each of the groups, considering all recordings of the study (Section 2.4).

Group	Mean HFO rate	S.D.of HFO rate
D	0.0134	0.0503
BS	0.0201	0.0613
AS	0.0247	0.0585
S	0.0747	0.1638

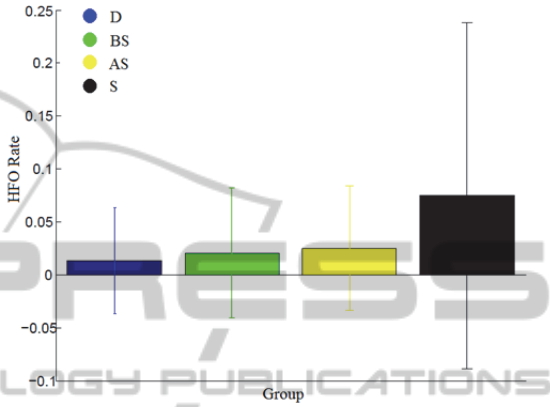

Figure 5: Mean and standard deviation of HFO detection rate, for each one of the four groups, considering all recordings included in the study (Section 2.4 and Table (2)).

The SD is pretty high during the seizure.

After the statistical Welch t test was applied in order to distinguish the different groups, it turned out that, for any of the three coefficients, all the groups are statistically different from one another. All tests led to $p < 0.01$, which means that each data group present a different statistical distribution of coefficients, with 5% confidence margin.

While the HFO detection rate provides a very high amplitude difference for each of the groups, it is not the case for the DFA method, which presents smaller differences between the mean of the different groups. One of the explanations for how it is possible to distinguish the groups is the fact that, since the four groups contain data of all patients, the number of segments in each distribution is very large, as shown in Table 3.

Table 3: Total number of segments in each one of the four groups, considering all recordings included in the study.

Group	Number of segments
D	322161
BS	10395
AS	10353
S	4221

Using a segment length of $N = 5000$ is indeed a good choice, since it leads to enough time resolution for the time analysis of the coefficient changes. Smaller segment sizes should be used carefully, since the DFA method needs large number of signal samples for the accurate estimation of the alpha coefficients.

It should be pointed out that the practical clinical framework of our article involves the application of neuroprosthesis or continuous monitoring of critical neurological patients. In both applications the neurologist will not access the whole EEG data for visually detecting HFOs, just because in the first case recordings are not available to the external environment, and in the second case the huge amount of data prevents continuous visual analysis. Consequently, data for the HFO detector was not visually reviewed by a neurologist. In this context, we can only assure that the detections pointed by the HFO method depicts local increase in high frequency activity of the brain, and may not be directly related to the definition of pathological HFO, used in most recent studies. Muscular artifacts may also have been included as false positives for high frequency brain activity, since they were not treated in any specific way.

4 CONCLUSIONS

All classification groups were statistically distinguished from one another. Notice that the ability to separate the BS group from the D group is really important as it suggests that it may be possible to detect changes in HFO rate and long-term power correlation of the EEG signal before the occurrence of the epileptic seizure. The results also reinforce previous researches, showing that the detection of local increases on high frequency activity is related to the occurrence of epileptic seizures (Engel, 2012).

Consequently, methods based on the Detrended Fluctuation Analysis and HFO detection may contribute to the development of seizure detection algorithms. DFA methods may be even helpful to locate the epileptogenic zone, through coefficient variation maps generated along with MRI images.

Although there are previous studies characterizing DFA analysis in identifying epileptic seizures, this studies is novel in the scene of analyzed frequency band and considered time length. Therefore, target phenomenon are other than in previous studies.

It is also worth noting that the methods are fairly quick to run on current computers. Notice that the HFO detection is slightly demanding in terms of computational complexity than the DFA technique. So algorithms based on these methods may be applied in real time, enhancing the practical capabilities provided by a seizure detector.

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