FRACTAL DIMENSION CHARACTERIZES SEIZURE ONSET IN EPILEPTIC PATIENTS

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ABSTRACT

We present a quantitative method for identifying the onset of epileptic seizures in the intracranial electroencephalogram (IEEG), a process which is usually done by expert visual inspection, often with variable results. We performed a fractal dimension (FD) analysis on IEEG recordings obtained from implanted depth and strip electrodes in patients with refractory mesial temporal lobe epilepsy (MTLE) during evaluation for epilepsy surgery. Results demonstrate a reproducible and quantifiable pattern that clearly discriminates the ictal (seizure) period from the pre-ictal (pre-seizure) period. This technique provides an efficient method for IEEG complexity characterization, which may be implemented in real time. Additionally, large volumes of IEEG data can be analyzed through compact records of FD values, achieving data compression on the order of one hundred fold. This technique is promising as a computational tool for determination of electrographic seizure onset in clinical applications.

1. INTRODUCTION

Clinical Background

The exact time of electrographic seizure onset on IEEG is often controversial among clinical epileptologists. This is because it is often difficult to determine, by visual inspection, exactly when low amplitude, high frequency fast activity, subtle rhythmic activity or bursts of epileptiform discharges which evolve into seizures, begin. It is also difficult to distinguish these seizure onsets from similar bursts of non-sustained activity that occur regularly between seizures (interictally). Opinions frequently vary between individual experts, and even over time in single experts. The need for a quantitative tool to supplement expert visual analysis is clear. The ability of the FD to detect transients or nonstationarities in signals suggests that this may be a useful tool for this application. It is possible that in the future, with validation of this method over a larger number of patients, clinical neurologists could use FD records as a method for rapid screening of IEEG for seizure onsets, before focusing on more cumbersome tracings of raw IEEG.

Mathematical Background

Since the origin of Euclidean geometry and trigonometry, the line has been used as a basic building structure to describe the objects around us. Fractal geometry, popularized over the last decade, is a new language used to describe, model, and analyze complex forms or curves found in nature. FD can be considered a relative measure of the number of basic building blocks that form a pattern. This particular feature has been used, with great success in a variety of applications in biomedical science for transient detection, waveform complexity estimation, pattern recognition, etc, [1]-[11]. One area in which FD analysis has been particularly useful is in the analysis of EEG to characterize neurophysiological states [5]-[7], [12]-[13].

FD is a measure of signal complexity that can characterize different pathophysiological conditions. It provides an alternative technique for assessing signal complexity in the time domain, as opposed to the embedding method of assessing this complexity by reconstructing the attractor in the multidimensional phase space [12], [14]-[16]. This innovation permits a direct connection between complexity variations and EEG changes over time, providing a fast computational tool to track nonstationarities in this signal. The FD also has the advantage of data volume reduction. It is calculated over time in an overlapping sliding window, which greatly reduces the number of data points stored. The exact amount of data depends upon the sliding window size and on the overlap used for the analysis.

A fractal curve in an n-dimensional space has topological dimension n, and a non-integer or fractional dimension called *fractal dimension*. It also possesses the characteristic that each portion of it can be considered a reduced-scale image of the whole for all time scales (i.e. its topological properties are preserved under magnification or reduction). If the scaling factor is the same for all time scales, then the curve is said to be self-similar. Many algorithms developed to estimate the FD are based on the assumption of self-similarity and independence of scaling.

2. METHODS

Intracranial EEG (IEEG) recordings were obtained from four patients with MTLE implanted with depth and strip electrodes at Emory University Hospital as part of their pre-surgical evaluation for medically refractory epilepsy. IEEG recordings provide a relatively artifact-free signal, and better signal to noise ratio (SNR), than is typically obtainable from conventional scalp EEG. The IEEG was sampled at 200 Hz and stored on compact discs. Time synchonized video of the patient's clinical condition throughout the monitoring period was also stored on video tape, for purposes of determining time of clinical seizure onset. The acquisition system had a built in bandpass filter with low and high cutoff frequencies of 0.1 and 100 Hz, respectively. 64 channel digital IEEG, with coincident surface EEG, was recorded referentially on a standard Nicolet 5000 video-EEG acquisition system. Ten minute segments of IEEG were analyzed. The channel where the first changes

signaling seizure onset were observed (focus channel) was used in the analysis in conjunction with a spatially adjacent channel.

For clarity, we state the following definitions:

- ***Ictal period***: time when the seizure takes place and develops.
- ***Preictal period***: time preceding the ictal period.
- ***Clinical onset***: the time when a clinical seizure is first noticeable to an outside observer who is watching the patient from whom the EEG is recorded.
- ***Electrographic onset***: the beginning of a seizure as marked by the current "gold standard" of expert visual analysis of the IEEG.

In all four patients analyzed, electrographic seizure onset clearly preceded clinical onset. This should always be the case, provided that implanted electrodes are placed near or in the region from which seizures first arise (ictal onset zone).

As a pre-processing step, the spatial difference of the EEG signal over time was obtained by subtracting the focus channel from the adjacent channel selected (bipolar montaging). This was done to remove any noise common to both channels. As a result, any common mode cortically generated signals were also eliminated. This was not felt to adversely affect the detection of seizure onset, however, as the seizure onset patterns were highly localized to the focus channel. IEEG data were processed both with and without channel subtraction. Results demonstrated better detection with channel subtraction. This shows that the spatial separation between the electrodes inside the brain is short enough to cancel the common noise in that region, and long enough to capture a voltage difference between the focus and its adjacent electrode. Of note, each of these electrodes records the global activity of many thousands of neurons.

After this, a notch filter was run over the preprocessed data to minimize the 60 Hz line effects. Subsequently, a sliding window of 250 points length (1.25 seconds) was shifted along the IEEG sequence with 160 points (0.8 s) of overlap. The methodology is summarized in figure 1. Over each IEEG segment obtained from the sliding window the FD of a curve was computed by the algorithm of Katz [13].

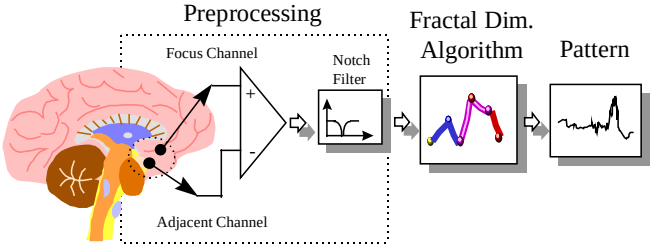

Figure 1: Methodology Diagram

The FD of a curve can be defined as:

$$D = \frac{\log_{10}(L)}{\log_{10}(d)} \qquad (2)$$

where L is the total length of the curve or sum of distances between successive points, and d is the diameter estimated as the distance between the first point of the sequence and the point of the sequence that provides the farthest distance. Mathematically speaking, d can be expressed as:

$$d = \max\left(\text{distance}(1,i)\right) \qquad (3)$$

Considering the distance between each point of the sequence and the first, point i is the one that maximizes the distance with respect to the first point.

The FD compares the actual number of units that compose a curve with the minimum number of units required to reproduce a pattern of the same spatial extent. FDs computed in this fashion depend on the measurement units used. If the units are different, then so are the FDs. Katz's approach solves this problem by creating a general unit or yardstick: the average step or average distance between successive points $\underline{a}$. Normalizing distances in Equation (2) by this average results in:

$$D = \frac{\log_{10}(L/\underline{a})}{\log_{10}(d/\underline{a})} \qquad (4)$$

Defining n as the number of steps in the curve, then $n = L/\underline{a}$, and (4) can be written as:

$$D = \frac{\log_{10}(n)}{\log_{10}(\frac{d}{L}\frac{L}{\underline{a}})} = \frac{\log_{10}(n)}{\log_{10}(\frac{d}{L}n)}$$

$$D = \frac{\log_{10}(n)}{\log_{10}(\frac{d}{L}) + \log_{10}(n)} \qquad (5)$$

Expression (5) summarizes Katz's approach to calculate the FD of a waveform.

3. RESULTS

Sixteen seizures from four patients with MTLE were analyzed. The FD was computed as stated in (5). Figures 2 through 4 show the FD over time for the preictal and ictal of all records from three of the patients analyzed.

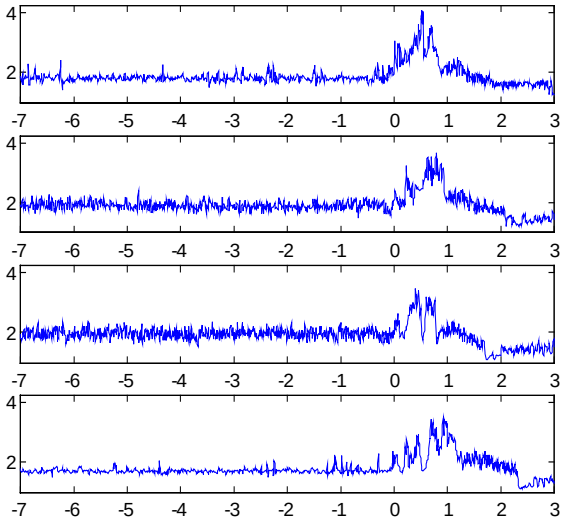

Figure 2: Fractal dimension over time (min) for patient 1, preictal (from –7 to 0 min) and ictal (from 0 to 3 min) periods.

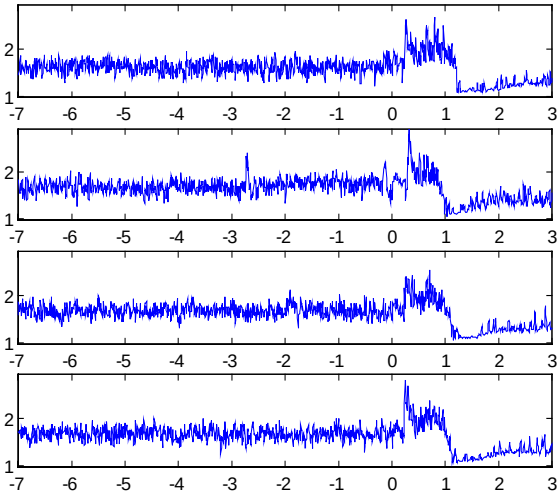

Figure 3: Fractal dimension over time (min) for patient 2, preictal (from –7 to 0 min) and ictal (from 0 to 3 min) periods

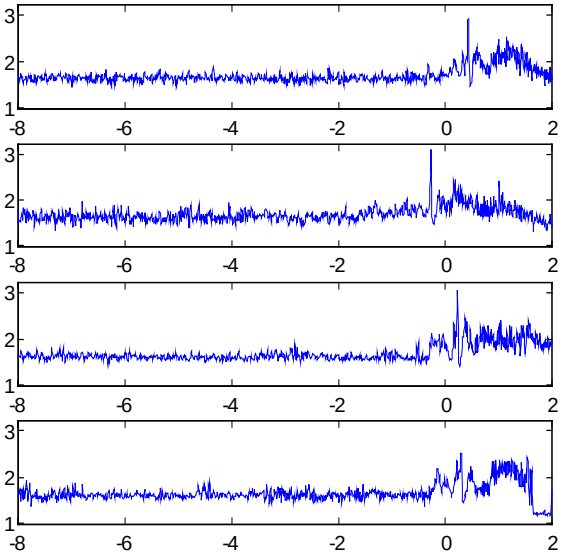

Figure 4: Fractal dimension over time (min) for patient 3, preictal (from –8 to 0 min) and ictal (from 0 to 2 min) periods

Electrographic seizure onset time, as marked by an expert reader is marked as time = 0 on these graphs. The FD in the fourth patient (not shown) demonstrated similar behavior.

A repetitive ictal pattern can be observed in each record, unique to each patient, and differing somewhat from one patient to another. The trend in FD from seizure onset to resolution is similar patterns across patients. The most remarkable aspects of these trends are: (1) during the preictal period the FD is relatively low, (2) the FD exhibits an increment during the initial stage of the ictal period, and then (3) it decreases again usually reaching the lowest complexity level of the recording. The mean and variance of the FD were calculated for two intervals in each seizure: (1) for the entire preictal period up until the first indication of the rise associated with ictal onset, and (2) for the entire ictal period (from the onset of the ictal rise in FD until the point at which the FD began its descent toward its minimum). Comparing the mean of FD for preictal and ictal epoch by student two-tailed t-test, demonstrates that these epochs can be easily distinguished from each other ($p = 5 \times 10^{6}$), and the time of seizure onset clearly identified. Figure 5 shows the variance for each record computed during the preictal periods (S1) and during the initial phase of the ictal portion (S2).

The FD algorithm implemented ran in 2.1410s over records of 12,000 points (10min), on a 400 MHz Pentium II computer. It required 3,351,461 floating point operations for each 10 minute record analyzed, as estimated using Matlab.

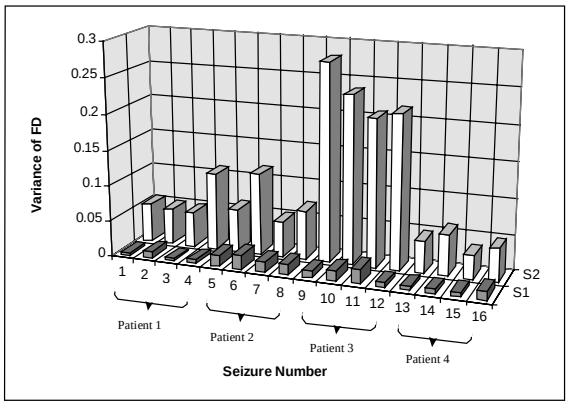

Figure 5: Variance of the fractal dimension for each record during preictal (S1) and ictal period (S2).

4. DISCUSSION

Our preliminary results indicate that electrographic seizure onset in IEEG occurs at the beginning of an increment in system complexity. Of note, the FD algorithm appeared to determine time of seizure onset with greater precision and reproducibility than our expert reader, as evidenced by the small relative shift in waveforms from one seizure to another, with respect to time = 0, in figures 2-4. This method, if quantified and validated on a larger number of patients, may prove useful to clinicians as they identify times of seizure onset and spread throughout the brain on the IEEG. In addition, the application of this FD algorithm might be useful as part of an automated seizure detection device.

To the best of our knowledge, only [5]-[6] have reported using this FD algorithm on EEG data, both with limited results. This appears to be due to the lack of a statistically reliable sample, and in some cases to the short length of the sequences analyzed. Much of the previous work using these techniques is based upon only one or very few EEG records [2], [6]-[13], [15]-[17].

Other algorithms to compute the FD have been proposed and applied to experimental data [3], [17]-[19]. Petrosian used a quick estimate of the FD. However, it turns out that this estimate is really the FD of a digital sequence. Since the EEG is an analog signal, a digital signal was derived by subtracting consecutive samples in this study [17]. From this sequence of subtractions, a binary sequence is created assigning +1 or –1 if the subtraction is positive or negative respectively. The FD is computed then as:

$$D = \frac{\log_{10} n}{\log_{10} n + \log_{10}\left(\frac{n}{n + 0.4\, N_{\Delta}}\right)} \qquad (1)$$

where n is the length of the sequence (number of points), and N_Δ is the number of sign changes (number of dissimilar pairs) in the binary sequence generated. We tested this algorithm on our data, but the distinctness of the patterns decreased in three of the patients.

Besides, the FD in (1) seems to be highly related to the mean frequency of the signal derivative, due to the nature of the digital signal considered. Note that the number of dissimilar pairs N_Δ can also be considered the number of zero crossings when the dc level is removed, and hence its relation to the frequency becomes apparent. For practical values of n and N_Δ Equation (1) is simply a straight-line relation between D and N_Δ.

In contrast to this method, our FD calculation is slightly slower than that of Petrosian, but it is derived directly from the IEEG, eliminating one step of preprocessing, and any bias introduced by linkage of the FD to the mean frequency of the signal derivative.

5. CONCLUSION

This study suggests that the FD is a useful, practical tool for identification of seizure onset in the IEEG. Results presented here show that each patient has a characteristic FD "fingerprint" during ictal epochs. Trends in FD during seizures were similar across patients. A complexity increment was observed in all patients at the beginning of the ictal stage followed by a reduction of system complexity. These complexity changes may provide insight into the underlying dynamics of this unknown system.

In addition, the method applied in this study opens the possibility of designing an intelligent system for detecting and warning of seizures in real time. Further studies, over a bigger database are required to provide statistical power to validate this method and compare it with the current "gold standard" of expert visual analysis of electrographic seizure onset.

6. REFERENCES

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