FRACTAL ANALYSIS OF EPILEPSY

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ABSTRACT

A complex system has constituents interacting in a nonlinear way. A complex biological system is the human brain, which function is based on the communication between neurons, if there is a mistake in the communication between them, it can cause epilepsy. Epilepsy affects from 1% to 2% worldwide population.

Fractal Geometry is used to analyze electroencephalograms (EEG) from epileptic patients to determine where the epileptogenic region is located to make a surgery to the epileptic patient. In this work fractal geometry is applied (using four self-affine trace methods: R/S analysis, Roughness-Length, Variogram, and Wavelets), to study temporal series generated by EEG from data that refers to people that do not have epilepsy but have had a neurological problem and epileptic patients.

After doing the fractal analysis, it is concluded that for all complex signals (EGG) under studying, the best methods to analyze epilepsy are R/S and Variogram, because they were the solidest to every analyzed channel, in addition to be the nearest to the average values from the four self-affine trace methods.

Keywords: fractal analysis, complexity, epilepsy, complex system.

INTRODUCTION

Complex systems contain several constituents interacting nonlinear in such a way that their behaviour is a balance between non-stationary and stationary components. A complex system is capable of emerging behaviour that is usually responsible for power-laws which are universal and independent of the microscopic details of the phenomenon.

Complex systems can be physical, ecological, chemical, financial or biological. An example of a biological complex system is the brain. Human brain is a complex system made up of billions of nerve cells, called neurons, which transmit signals inside the brain, and between this and the rest of the body

Human brain controls a wide range of tasks, such as consciousness, awareness, movement and posture. The brain sends and receives messages to make these tasks happen, if there is a mistake in this communication a seizure can occur.

A seizure is a sudden surge of electrical activity in the brain that usually affects how a person feels or acts for a short time. Epilepsy is the tendency to have repeated seizures that began in the brain, due to clusters of neurons communicating abnormally.

As epilepsy can begin in all ages and it develops social problems (significant problems are often experienced by people with epilepsy in the areas of personal relationships, employment, psychological problems, sometimes legislation and lack of proper medical treatment), biomedical sciences look to predict the clinical onset from epileptic seizures so that a patient could have a surgery. Electroencephalograms (EEGs) and brain scans are common diagnostic test for epilepsy. To interpret the electroencephalographic strokes is done by visual way and it requires a high degree of knowledge and training. However, the exact time of electrographic clinical seizure onset is often controversial among clinical epileptologists, due to it is often difficult to determine, by visual inspection, and opinions frequently vary between individual experts.

An approach that has been important to study epilepsy is fractal geometry, used to analyze, describe, and model complex forms or curves found in nature, through fractal dimension, that serves as a quantifier of complexity. The study of complex systems in a unified fractal framework has become recognized in recent years as a new scientific discipline. Fractal dimension measures the rate of addition of structural detail with increasing magnification, scale or resolution.

The ability of fractal dimension to detect transitions and non stationarities in signals, suggest that this may be a useful tool to explore the beginning of seizures in electroencephalograms and to provide important help to the surgery process.

In this work, it was done a fractal analysis to time series, generated from electroencephalogram (EEG) from epileptic patients and non epileptic ones (but they had had a neurological problem as headache, stress or depression), in order to decide which method of self-affine methods can characterize statistical patterns from epilepsy.

This paper is the second part of Epilepsy as a Dynamic Complex System presented in The 50th Anniversary Meeting of the International Society for the Systems Sciences (Contreras, 2006), in which some concepts about epilepsy and some researches about mathematical characterization of epilepsy using fractal theory were mentioned.

DEVELOPMENT

Epilepsy is the tendency to have repeated seizures that begin in the brain, produced by an abnormal electric shock in brain wiring. It means that epilepsy is a symptom that the way a person's brain works is sometimes disrupted. It is not a sickness itself, it is a neurological disturbance that affects the brain and it is shown by seizures, in which neurons communicate abnormally. During de seizures there is a neuronal discharge of high frequency in a brain´s zone called focal seizure onset that is going to repeat over the time (Contreras *et al.*, 2006; Rocha *et al.*, 2005; Espinoza *et al.*, 2005; Contreras, 2007).

From 16 to 30% from epileptic patients are resistant to epileptic drugs and they still have seizures although they have received high dose of epileptic medications. In some cases, a surgical resection from the brain damage or the brain location of seizure origin, that is responsible of epilepsy, can eliminate or decrease the incidence of epileptic seizures. But it is much more frequent a focal resection. When a patient is sent to a surgical intervention it is necessary a presurgical evaluation that requires input from many members of an integrated team, which includes neurologists, neurophysiologists, neuropsychologists, social workers, radiologists, nurses, and epilepsy neurosurgeons. Aspects of the presurgical evaluation include the patient's history and physical examination findings, social circumstances, seizure syndrome and severity, and diagnostic testing. When all presurgical information points to a unifying location and theory regarding focal seizure onset, then the patient may proceed directly to respective surgery. EEG and brain imaging, axial computerized tomography (cerebral scanner), magnetic resonance scanning and positron emission tomography are the most important test to diagnose epilepsy.

Electroencephalography is the neurophysiologic measurement of the electrical activity of the brain by recording from electrodes placed on the scalp or, in special cases, on the cortex. The resulting traces are known as an EEG and represent so-called brainwaves. This device is used to assess brain damage, epilepsy and other problems. The recording is obtained by placing electrodes on the scalp, each electrode is connected to an input of a differential amplifier (one amplifier per pair of electrodes), which amplifies the voltage between them (typically 1,000–100,000 times, or 60–100 dB –decibels- of voltage gain), and then displays it on a screen or inputs it to a computer. The amplitude of the EEG is about 100 µV when measured on the scalp, and about 1-2 mV when measured on the surface of the brain.

Biomedical science tries to predict the clinic onset of epileptic seizures, characterized by sudden changes in the power spectrum density and growing in the wave ritmicity; EGG/ECoG analysis provides a window through epilepsy dynamics can be studied.

Clinic and electroencephalographic evaluation of seizures allow to make a hypothesis about where the epileptic onset is, even more, it can be enough in some cases to determinate it surely, but in some other cases it is known that they can produced wrong conclusions. EGG interpretation requires a high knowledge and training to find the place where the onset (and its propagation) is in order to remove it. However, to observe the exactly moment of a epileptic seizure in an EGG is controversial among epileptologist (specialized neurologist in epilepsy), due to in some occasions it is difficult to determined it by simple inspection and opinions vary from one expert to another (Contreras, 2007; Alonso, 1999). This is the main reason to have a quantitative tool to complement the visual inspection in order to the neurosurgeon takes surgical decisions with more certainty and speed.

It has been done some studies using chaos theory and fractal geometry in the EEG analysis to characterized neurophysiologic transitions and it has been observed fractal structures in electroencephalograms: when increasing sections from it, it can be observed the same aspect, the same section (Contreras, 2007; Ying-Cheng, 2002). Next there are mentioned three studies of EEG using chaos theory and one analysis done by fractal geometry.

Torres (1991) indicates that he has observed chaotic dynamic in neuronal activity from advanced animals. Data from EEG shows that this activity is periodic in the case of an epileptic seizure or when periodicity is induced through external stimulus (motivation, inhalation). In regular condition (walking) it is not periodic and it does not exist in deep anesthesia. Studies done in human being show similar results. Some researchers have suggested that chaotic dynamic of brain is a way it has in order to globally process information that it picks up from its environment. The great sensibility of this dynamic gives it the capacity of discriminating sensorial information. In each case the dynamic is chaotic but it has different levels, depending on the state of awake of sleep. Just in case of epilepsy, periodicity is observed.

An electrographic seizure is the beginning of an observed crisis in the EEG, it has four stages:

- Pre-ictal: the period before the seizure,
- Ictal: it is the moment when the seizure takes place,
- Post-ictal: after the seizure
- Inter-ictal: period between crises.

Andreu *et al.* (1998) say through no linear analysis techniques it can be identified with some anticipate minutes the beginning of epileptic crisis. The EEG of a healthy brain is irregular; this activity experiments a drastic change when an epileptic seizure starts. When observing a recorded EEG during a seizure, it has been found that electrical activity is more violent in terms of amplitude but more regular in rithmicity. Before and during an epileptic seizure, the fractal dimension of the EEG, decreases: there is a “complexity loss” due to the coordination of neurons population. Thus, although it is paradoxical because of the appearance and condition of the crisis, the brain waves decrease their complexity (Contreras, 2007; Torres, 1991; Andreu *et al.*, 1998).

The dissipative chaos can cause local order through phase transitions. The waves in the EEG show that the brain, as system, is in a dissipative chaos zone. The stable stational waves characterize epileptic seizures (Torres, 1991; Andreu *et al.*, 1998).

Jing *et al.* (2003) measure the fractal dimension of human cerebellum in magnetic resonance images of 24 healthy young subjects (12 men and 12 women) using the box-counting method. The results indicate that the cerebellum is a fractal structure with a fractal dimension of 2.57 ± 0.01, and there is not significant differences between men and women. They mention that Thompson *et al.* (1996) measure in photos of human brain, the morphometric variance of several parts of the brain, and they found that fractal dimension was 2.10. The researches conclude that based on the low variability in the fractal dimension, exists a stable value for a regular brain, which can be used as a control in the patologic problems itself.

Esteller *et al.* (2002) determine the fractal dimension in cortex electroencephalogram

(IEEG, ECoG), using Katz algorithm. Their results said that an electrographic seizure in an ECoG occurs when there is an increasing in complexity in the system. Also they show a reproducible and quantifiable pattern that discriminates ictal period from pre-ictal one (figure 1). The tendency in the fractal dimension shows similar patterns for the four patients: (1) during the pre-ictal period the fractal dimension is low, (2) the fractal dimension presents an increasing during the beginning stage of ictal period, and (3) the fractal dimension decreases reaching the lowest level of complexity. Then, it seems the electrographic seizure can be identified with a better precision by the algorithm of fractal dimension instead of the epileptologist, as it can be observed in the little change in the waves of seizures from a patient to another, respect time 0.

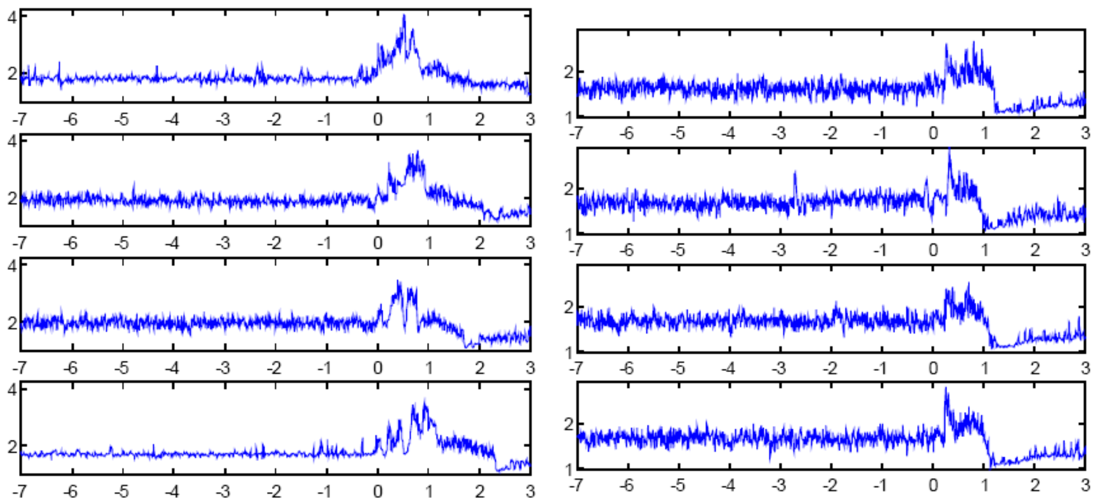

Figure 1. Fractal dimension in minutes. Stage pre-ictal (-7 to 0 minutes) and Ictal (0 to 3 minutes) for two patients.

Sackellares *et al.* (2002) found that temporal lobe epilepsy is characterized by episodic paroxysmal electrical discharges (ictal activity). These discharges consist of organized synchronous activity of mesial temporal neurons, particularly those of the hippocampus. The researches have postulated that epileptic brains, being chaotic nonlinear systems, repeatedly make the abrupt transitions into and out of the ictal state because the epileptogenic focus drives them into self-organizing phase transitions from chaos to order. When spatiotemporal chaos in the brain fails, the seizure represents a mechanism for returning brain dynamics to a more normal (chaotic). Thus the seizures are used as the recovery mechanism order-chaos.

Gutiérrez (2001) developed an algorithm to extract some characteristics of the electrocorticographic signal, in order to classify the wave forms as epileptic waves. He used the wavelet method and the correlation function to establish the localization of the epileptogenic focus and its spread. Gutierrez concludes that both methods simulate the analysis that electroencephalographist does to determine if the waves are epileptic ones. This result is very important because the neurosurgeon can have a clinic tool to allow him to take faster decisions to remove the focus.

Fractal dimension ability to detect transitions and non stationarities in signal, suggest that fractal geometry is a quantitative useful tool to explore the seizures onset in the EEG.

Fractals

A fractal is an object made up of similar parts to the object as a whole. The fractal word (irregular, fragmented) is used to talk about objects in the space or temporal fluctuations that possess a self-affine form and they cannot be described in a single absolute scale (Balankin, 2003).

In the human body exists fractal structures, as bronchial ramifications, vascular system, and neuronal connections. These structures allow to optimize the systems function because in the minimal space there is a great surface.

Koch said that fractal theory could be considered as a valid and useful tool to study dynamic phenomena in the human body or in nature and it allows an approximation to complexity and the absence of linearity existent in those processes (Barabási, 1995).

In 1975 Benoit Mandelbrot called fractals a collection of forms that, generated throuhg a repetition process, is characaterized by having detail in every scale, having an infinity lenght, not being differential and exhibing a fractional (fractal) dimensión. Natural fractals tend to be irregular and they are self-similar just in a statistical way, it means, they are self-affine fractals, and their fractal dimension is obtained by doing average over their values in several parts and several bodies of the same type. When increasing one of the parts of a natural fractal the property of generating the same structure or similar has low and upper limits, in this case, fractals are just an excellent approximation to the strucutral parts of the nature (Balankin, 2003; Barabási, 1995; Morales, 2004; González *et al.*, 2001).

In order to obtain the dimensión of a rough curve (or whichever object) fractal dimension known as Hausdorff-Besicovitch is used. It is based on the idea of covering an object with little sets from the same object.

Hausdorf dimension is an integer to the classic geometric objects: points (*D=0*), lines (*D=1*), surfaces (*D=2*) and volume (*D=3*); and it takes non integer values (or fractional) to fractals. Every single geometric object and every natural object has a level of irregularity or fragmentary; fractal dimension (*D*) is the real number to quantify irregularity. Opposite Euclidean dimension, fractal dimension is equipped of continuity, accepting any value between 0 and 3. Fractal dimension allows measure the roughness of a curve, besides, measures the structural detail when increasing magnification, scale or resolution and it is a quantifier of complexity (Contreras, 2007; Balankin, 2003; Barabási, 1995; Morales, 2004).

A self-affine fractal is a set that remains invariant under a scale (statistical) of anisotropic transformation. If there is a magnification from one of the parts, one of the axis transform itself in a facto $b, x \rightarrow bx$, the rest of the axis must be rescaled in a factor b^{α_i}, $x_i \rightarrow b^{\alpha_i} x_i$, in order to preserve the set invariant. The exponents α_i are called roughness exponents or

Hurst exponents. For self-affine structures, fractal dimension just can be defined locally (Balankin, 2003).

Hurst exponent (H) is used to describe a fractal self-affine object, because it indicates the level of roughness of curves. H is used to determine if a temporal series has a fractal behavior and it measures the intensity of dependence. It is said that an analyzed phenomena is random (Brownian motion) when $H=0.5$; it is persisten when $0.5<H<1$ (invariance scale is asociated to positive correlations in long range, it means an increasing period is follow by a similar one), and finally it is antipersistent when $0<H<0.5$ (invariance in the scale asociated to negative correlations in long range, it means an increasing period is follow by a decreasing one).

For time series Hurst exponent is related to fractal dimension with the expression $H=2-D$, where D is the fractal dimension.

Data Analysis

The collected data was from EEG´s on the scalp. The results that are shown are from data that refers to five people with a neurological problem like depression, headache, and stress but epilepsy, and data from three epileptic patients. Each data represents voltage from neuronal activity, expressed in micro-volts per second ($\mu v/s$). This data was given by Neurologist and Clinic Neurophysiologist Noel Isaías Plascencia Álvarez (Centro Medico Nacional 20 de Noviembre Hospital, ISSSTE).

In this work it would be understood as non epileptic patients, but with neurological problems, people that suffer from headaches, depression and stress.

Data from five non epileptic patients was analyzed, there were 16 electrodes (channels) placed on the scalp of a patient, and each channel gave different numeric data (figure 2).

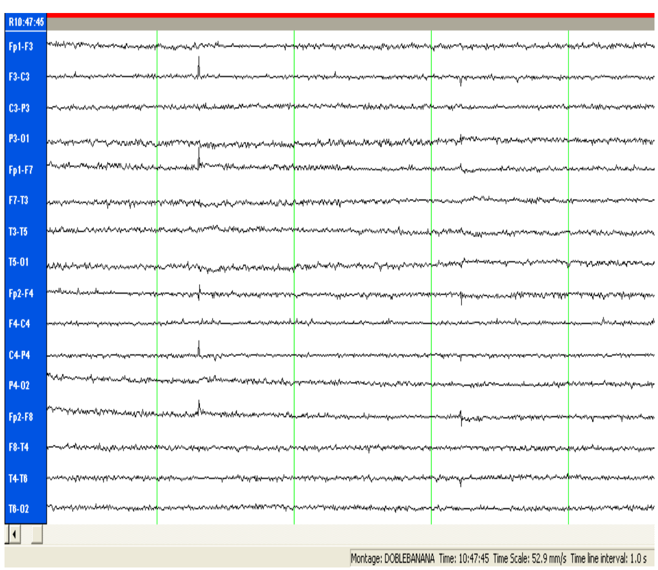

Figure 2. Electroencephalogram with 16 channels of a non epileptic patient.

First, numeric data from each channel was transformed into time series (16 per patient), each one with 32,000 rows; after that, from each channel it was obtained standard deviation (fluctuations) for 100 time horizons (from $n = 2$ to $n = 101$), then time series fluctuations were obtained; in total there were generated 1,616 time series (16 form original data and 1,600 with fluctuation data) per each patient; so there were obtained 8,080 temporal series for non epileptic patients.

Epileptic patients under study were sent to a surgeon, due to they have resistant temporal lobe epilepsy.

In this case, there were obtained a total of 18 time series of 450,000 data each one. There were done windows of 2^{15}=32,768 data per each channel, so there were generated 417 temporal series per channel. Thus, for each patient there are 435 time series (18 original series and 417 for each window of size 2^{15}=32,768). So, in total there were 1,035 temporal series of epileptic patients.

Fractal analysis

Fractal analysis consisted to determine the Hurst exponent to each time series under study. All temporal series were run in Benoit software (Scion Corporation) in order to obtain the Hurst exponent, which determines if a phenomena or a time series has a fractal behavior. There were used four self-affine trace methods from Benoit: R/S analysis, Roughness-Length, Variogram, Wavelets: Truncate Data, and Zoom. And finally it was done an average from the four methods applied to each time horizon or window, respectively. There was used data from epileptic and non epileptic people in order to know which method can be used in both cases. These results are presented on graphics of *H* values per method and average of each one of study signals.

There were studied the EEG of five non epileptic patients, it is shown just one graphic of H values for an original signal (without statistical treatment) of one patient (figure 3). H values are different to each method, and it is necessary to determine which one of them produce similar values and they are the nearest to the average. In this case, the R/S (curve 1) and Zoom-Wavelets (curve 4) present consistent values. The same way, the curves generated by these methods have a similar behavior to the average (6). Then, for this case, the elected methods to analyze complex signals are the R/S and the Zoom-Wavelets.

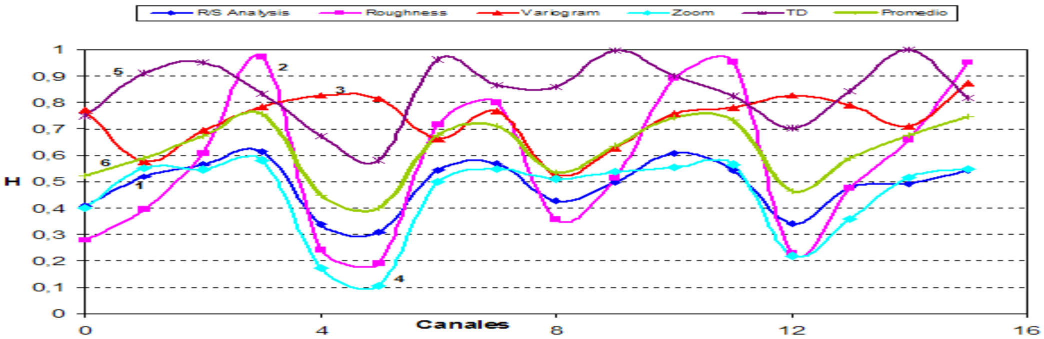

Figure 3. Graphic of Hurst values of a non epileptic patient (original signal).

In figures 4-6 there are the obtained curves of Hurst values (H) corresponding to 100 the time horizons (⍰=2,3,4,...,100,101). It is necessary to mention that each H value represents a time series of standard deviation; so, there are 100 H values (100 hundred temporal series of standard deviation). There were obtained similar H values with Wavelets: Truncate data (curve 4) and Zoom (curve 5); also H values are similar with Variogram (curve 3) and Roughness-Length (curve 2).

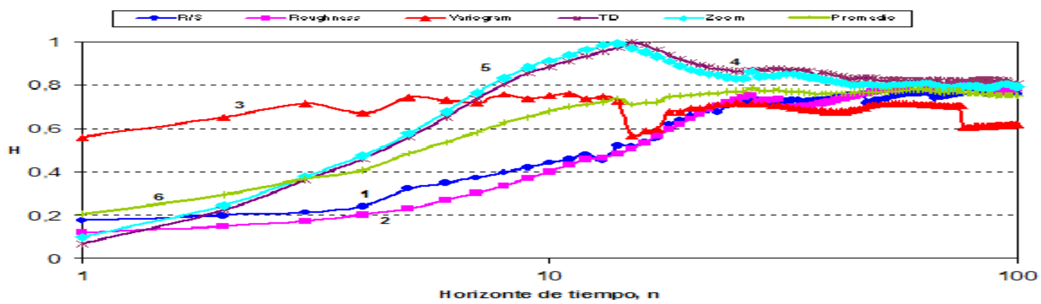

Figure 4. Curves with H of different time horizons (n), generated from the 100 time series of standard deviation. Channel 2.

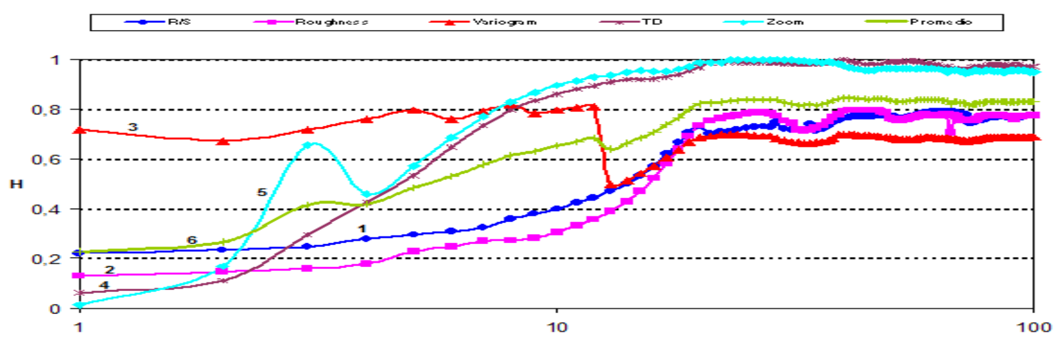

Figure 5. Curves with H of different time horizons (n), generated from the 100 time series of standard deviation. Channel 13.

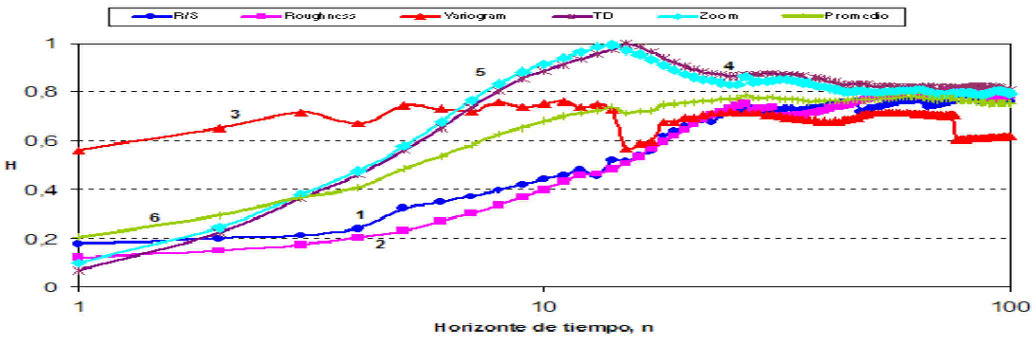

Figure 6. Curves with H of different time horizons (n), generated from the 100 time series of standard deviation. Channel 16.

To establish what pair of methods would be used in the analysis of EEG, there are going to be selected those which H values are closer to the average of both (curve 6); however, the resultant curves of each pair of methods are pat the same distance of the average, so, the pair of selected methods will depend on the chosen methods of epileptic patients, due to there is important to compare the EGG behavior of patients with neurological problems and epileptic people.

In the case of the generated signal from Variogram method (curve 3) there is a special behavior: although H values are not similar to the others, it has a nearly stationary behavior: from *n=2* to *n=11*, with a jump between *n=12* and *n=15*, to be stational from *n=20*, so this method must be considerated to analyze the EEG.

There were studied the EEG of three epileptic patients. In figure 7 there are H values from the original signal of an epileptic patient. As it can be seen the methods that have consistent values are R/S (curve 1) and Variogram (curve 3), these curves have a similar behavior to the one from the average (curve 6). It is concluded that for this case, the chosen methods are the R/S and the Variogram.

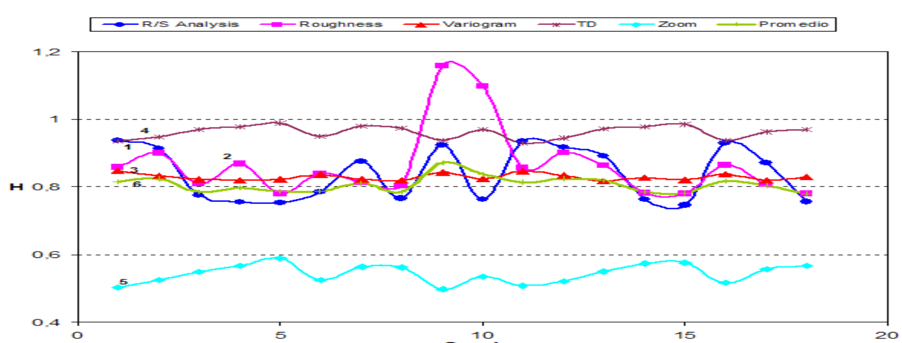

Figure 7. Graphic of Hurst values of an apileptic patient (original signal).

In figures 8-10 are shown the obtained curves of H values of the windows of size 2^{15}=32,768 (there are shown three out of 18 graphs). Each H value represents a time series generate from each window, thus, there are 417 H values.

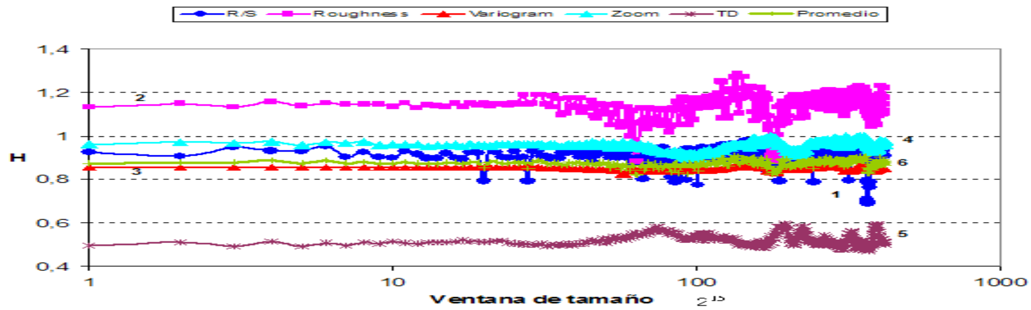

Figure 8. Curves of H values of different windows of size 2^{15}. Channel 1.

In this case, there were obtained similar H values with Wavelets-Zoom (curve 4), Variogram (curve 3) and Roughness-Length (curve 1). As the last two methods were selected to analyze complex signal of epileptic patients in original series, then, the chosen methods are R/S and Variogram.

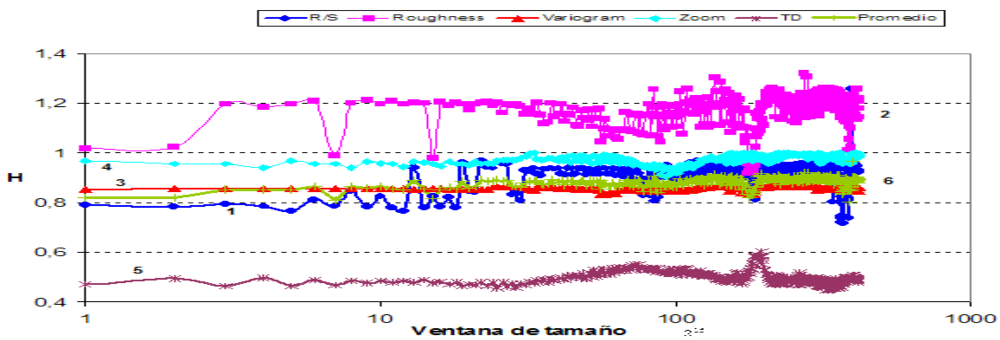

Figure 9. Curves of H values of different windows 2^{15} size. Channel 3.

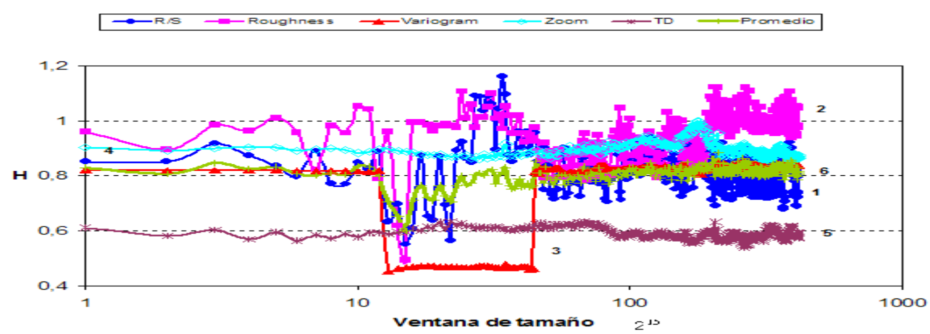

Figure 10. Curves of H values of different windows 2^{15} size. Channel 5.

It is important to mention that the curve generated from Variogram method presents a stationary behavior in every single channel, but in channel five (figure 10), in which it shows stationarity from *n=1* to *n=12* (H≈0.8), but it decreases in *n=13* (H=0.45) and has similar values up to *n=44* (H=0.47), since *n=45* (H=0.81) it goes back to be stational in that rank of values. There is not another signal with this behavior.

CONCLUSIONS

In this work epilepsy was considered as a biological complex system, so that it was possible to use fractal geometry in order to analyze the fluctuations in the observed electric signals in electroencephalograms (EGG) of epileptic and non epileptic (with neurological problems) patients, it is concluded:

- From the four used self-affine methods (R/S analysis, Roughness-Length, Variogram and Wavelets) the most consistent to analyze and characterize the EEG of patients with neurological problems and epileptic patients are R/S and Variogram, with both methods H values are very similar between them and the average from the four applied methods.

- As it was observed in figure 12, the generated curve with the Variogram method (curve 3) presents a stationary behavior "persistent" from *n=2* to *n=12* (H=0.80); after this point it presents a sudden jump *n=13* (H=0.45) kipping "antipersistent" up to *n=44* (H=0.47); and since *n=45* its behavior "persistent" is constant (H=0.80) until *n=101*.

- The behavior of the generated Variogram curve indicates that fluctuations of cannel 5 have an abrupt transition from a persistent state (positive correlation) to an antipersistent one (negative correlation but nearly random) to go in an abrupt way from an antipersistent state to another persistent.

- Based on points 2 and 3, it can be said that fluctuations of electric discharges among neurons that cause epilepsy, have a multifractal behavior because they have, at least, three different H values (0.80, 0.45 and, again, 0.80)

The transition from a persistent state to another antipersistent and vice versa, has been observed in a variety of complex systems, (sand piles avalanche, fluids turbulence and price volatility of crude oil), from this it can be established the idea of doing predictions (statically) over the changes in electrical signal among neurons in different scales, in order to say in a precise way, where the epileptogenic focus is and its propagation and the stage of the crisis is occurring during the process.

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