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Nonlinear Analysis of Anesthesia Dynamics by Fractal Scaling Exponent

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Abstract—**The depth of anesthesia estimation has been one of the most research interests in the field of EEG signal processing in recent decades. In this paper we present a new methodology to quantify the depth of anesthesia by quantifying the dynamic fluctuation of the EEG signal. Extraction of useful information about the nonlinear dynamic of the brain during anesthesia has been proposed with the optimum Fractal Scaling Exponent. This optimum solution is based on the best box sizes in the Detrended Fluctuation Analysis (DFA) algorithm which have meaningful changes at different depth of anesthesia. The Fractal Scaling Exponent (FSE) Index as a new criterion has been proposed. The experimental results confirm that our new Index can clearly discriminate between aware to moderate and deep anesthesia levels. Moreover, it significantly reduces the computational complexity and results in a faster reaction to the transients in patients' consciousness levels in relations with the other algorithms.**

I. Introduction

ASSESMENT of the patient's brain state during the surgery has long been an objective of research in the field of automated electroencephalogram (EEG) analysis. Anesthesiologists need to manage the hypnotic state of their patients by administering anesthetics and sedatives. They make heuristic decisions on the depth of anesthesia and adjust the anesthetic dosage by integrating meaningful changes in vital signs with their experience. However, these signs may not always be readily available and may be unreliable. Therefore, overdosing, underdosing, and intraoperative awareness still complicate general anesthesia.

Different analysis methods such as higher order spectra, entropy, evoked potential, wavelet and statistical analysis have been proposed for monitoring the brain state during the anesthesia. Bispectrum as a higher order statistical analysis that examines the phase correlation among the frequency components is used to quantify the amount of synchronization in the EEG signal [1]. While the bispectral index provides a reliable index of hypnosis, its technology introduces a large inherent delay that reduces the performance expectations of any closed loop controller that relies on this feedback.

Nonlinear dynamical analysis has emerged as a novel method for the study of complex systems in the past few decades. In this investigation we have concentrated on the dynamic of the EEG signal generator which has a complex nonlinear structure. Our goal in this research is to quantify the dynamic of the system which is affected by anesthetic drugs. Here, we aim to find the effect of anesthetic agents on the rate of signal fluctuations. By translating these fluctuations with Detrended Fluctuation Analysis (DFA) algorithm to fractal exponent, we can analyze the dynamic of brain during anesthesia. Since the EEG signal is nonstationary and noisy, all such studies should be carried out with care and caution [2]. The main objective of this research is to find the optimum fractal scaling exponent by selecting the best box sizes in DFA algorithm which have meaningful changes with different hypnotic depths.

The organization of the rest of this paper is as follows. In section 2 we introduce the methodology of nonlinear signal processing with fractal dynamics and discuss why we have used detrended fluctuation analysis. The effect of the box sizes for optimal fractal scaling exponent estimation has been argued in section 3 and the experimental results on optimum box sizes are illustrated in section 4. Finally, section 5 discusses on the advantages of our new algorithm for depth of anesthesia quantification and the concluding remarks are made.

II. Nonlinear Dynamical Analysis

A. Methodology

The brain functionality studies show that the EEG dynamics can not be modeled exclusively by a specific random process. The nonlinear analysis method has been effectively applied to electroencephalogram (EEG) to study the dynamics of its complex underlying behavior [3]. Dealing with complex dynamic systems which produce the biological time series is an important consideration to select the best analysis techniques. The analysis of these biological signals is complicated due to their highly irregular and nonstationary properties.

In the analysis of EEG data, different chaotic measures

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such as correlation dimension, Lyapunov exponent and entropy have been used in recent years [4]. For a reliable estimation of the fractal dimension, a time series has to satisfy the requirements such as stationarity, a sufficiently large number of data points and a reasonable signal to noise ratio. It is very improbable that these requirements for the EEG are simultaneously met [5]. To overcome these limitations we have focused on the long-range power-law correlations which have been discovered in a wide variety of systems, including those of physiological [6]. The quantification of power-law correlations, with a critical exponent, may give useful information on understanding the properties of the nonlinear dynamic systems. In this paper, we have proposed an optimal nonlinear analysis algorithm for processing the EEG signals without being concerned about the nonstationarity and finite length of the signal. The fractal scaling exponents that quantify the power-law correlations are computed through the Detrended Fluctuation Analysis (DFA).

B. *Detrended Fluctuation Analysis*

Detrended fluctuation analysis (DFA) is a scaling analysis method that provides a simple quantitative parameter to represent the correlation properties of a signal [7]. The advantages of DFA over other methods are that it permits the detection of long-range correlations embedded in apparently nonstationary time series, and also avoids the counterfeit detection of seeming long-range correlations that are an artifact of nonstationarity. Peng et al. (1994) have developed this algorithm to estimate scaling exponents with local-detrending to remove the nonstationary components [7]. This technique can be mapped into a self-similar process through simple integration. An EEG series as a time variant signal x(t) of finite length N, can be integrated to generate a new, self-similar series y(k) shown in (1) (The results are illustrated in Figures 1 and 2).

$$y(j)=\sum_{i=1}^{j}\left[x(i)-\langle x\rangle\right] \tag{1}$$

Where the average value of x, denoted by $\langle x\rangle$, is given by

$$\langle x\rangle=\frac{1}{N}\sum_{J=1}^{N}x(i), \quad i=1,...,N \tag{2}$$

After partitioning the entire range of y(k) into boxes of equal sizes, we fit an integrated time series by using a polynomial function, $y_{fit}(i)$, which represents the local trend within that box $y_n(k)$. After removing the trend in the root-mean-square fluctuation (Shaded area in Figures 1 and 2), the Detrended fluctuation, is given by:

$$F(n)=\sqrt{\frac{1}{N}\sum_{k=1}^{N}\left[y(k)-y_n(k)\right]^2} \tag{3}$$

The above computation is repeated for boxes of size n (different scales) to provide a relationship between $F(n)$ and n. A power-law relation between $F(n)$ and the size of the box, indicates the presence of power-law: $F(n) \sim n^{\alpha}$.

The parameter α, called the scaling exponent or the correlation exponent, represents the correlation properties of the signal. If $\alpha = 0.5$, there is no correlation and the signal is an uncorrelated signal (white noise); if $\alpha < 0.5$, the signal is anticorrelated and when $\alpha > 0.5$, there are positive correlations in the signal. $F(n)$ is the average fluctuation and usually increases linearly with n. The scaling exponent can then be approximated as the slope of log (F(n)) against log(n) (Fig. 3 and 4).

The scaling exponent (self-similarity parameter), α, should therefore be able to completely describe the significant correlation properties of the EEG signal. Since $F(n) \sim n^{\alpha}$ represents the scale transformation independent of n, then the exponent α provides a succinct measure of the dynamics across a range of box size, n. For purely fractal signals, such behavior persists without a limit in n. However, for real systems, its range is always finite, and may in addition be interrupted by dynamical mechanisms which introduce characteristic time scales into the data. In our investigation this limitation occurred and we had to select an optimal range of box sizes for different depth of anesthesia; otherwise the scaling exponent estimation on the non optimum region could not be used for meaningful quantification of the depth of anesthesia. In [9] we have used wavelet coefficients of the EEG signal instead of the raw EEG for fractal scaling exponent estimation, because we did not use the optimum margin of box sizes.

TABLE I: SCORING CRITERIA OF ANESTHESIA STATE LEVELS

Anesthetic Depth Levels			
	Deep Anesthesia	BIS Index : 0 -25	6
		BIS Index : 25 -40	5
	Moderate Anesthesia	BIS Index : 40 -50	4
		BIS Index : 50 -60	3
	Light Anesthesia	BIS Index : 60 -80	2
	Awake	BIS Index : 80 -100	1

C. *Data Gathering*

The BIS algorithm was introduced by Aspect Medical Systems to quantify the depth of anesthesia [1,8]. Several clinical studies and a growing body of evidence from routine users have shown the usefulness of the BIS Index to manage anesthesia. Therefore, we have used this Index as the most well known technology which has confirmed clinical evidence and FDA standards approval to compare the validity and accuracy of our algorithm. To prepare a database of raw EEG during anesthesia, the EEG signal was saved by BIS XP monitor (Aspect medical system Inc.) through contact electrodes placed on the patient's forehead. The noise free intervals were selected and only one channel of signal from cerebral cortex was used for further analysis. The database contains data from 45 patients which had been anesthetized with different anesthetic drugs (Gas and Intra

Venous (IV) agents). The main protocol in our research is the TIVA (Total Intra Venus Anesthesia) system with Propofol and Remifentanil.

III. Optimum Feature Selection

A. Fluctuation rate and box size

To investigate the effect of box size on detrended fluctuation analysis we have represented the integrated signal and fitted line in three different box sizes. Fig. 1 demonstrates the integrated signal (A0) which is related to deep anesthesia with BIS Index of 15 and fitted lines with box sizes of 50 in 'A1', 100 in 'A2' and 270 in 'A3'. As mentioned earlier, detrending is the process of subtracting a fitted line from the integrated line where the residue is a measure of fluctuation in each box (shaded area in figures). Fig. 2 demonstrates the rate of these fluctuations with box sizes of 4 in 'B1', 10 in 'B2', 57 in 'B3' and 80 in 'B4'. The increase in fluctuation is shaded for more clarity. When the box sizes increase, the fluctuations are increased too, but the rate of upward trend will not be equal in different signals from separate brain state activity during anesthesia (Fig. 3).

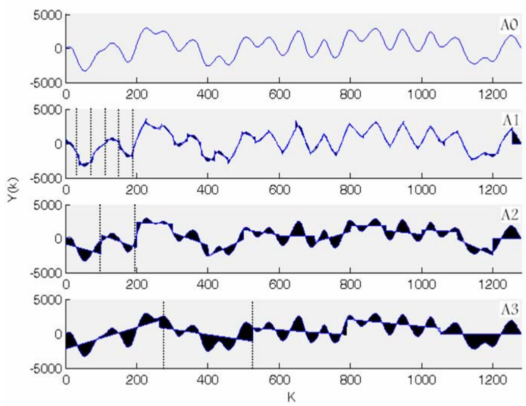

Figure 1: Integrated signal and fitted lines in three box sizes for a very deep anesthetized case (BIS=15). 'A0' is the integration signal and fitted with box sizes of 50 in 'A1', 100 in 'A2' and 270 in 'A3'.

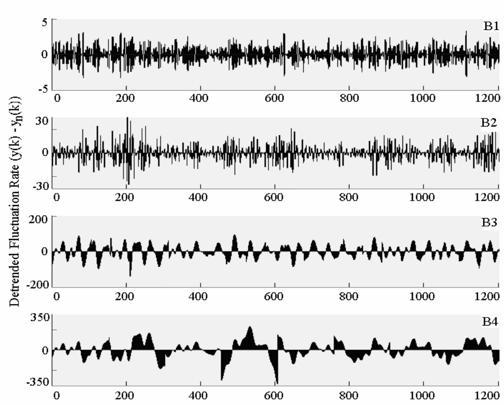

Figure 2: Detrended fluctuation rate for a moderate anesthetized case (BIS=45) with box sizes of 4 in 'B1', 10 in 'B2', 57 in 'B3' and 80 in 'B4'.

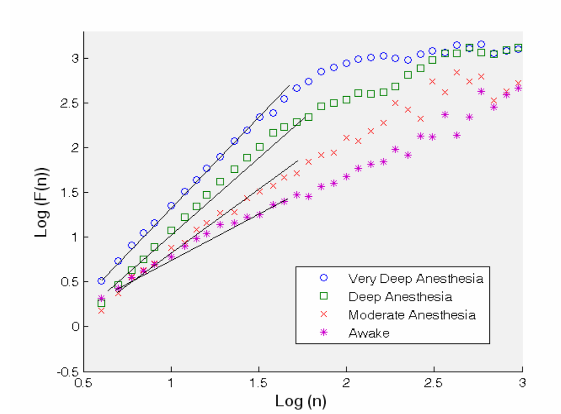

Figure3: Fluctuation versus Box size in logarithmic scale

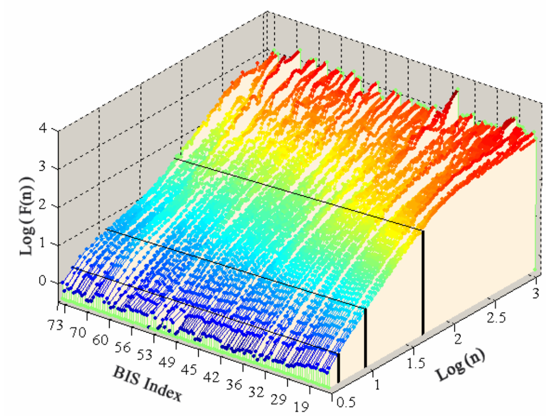

Figure 4: Detrended fluctuation analysis versus different anesthesia depth from very deep anesthesia to moderate and light levels which indicated with BIS Index.

B. Optimal box size

Although the algorithm is simple but the process of optimal feature selection on large amount of data, is not a straightforward problem. In this section, we discuss the optimal fractal scaling exponent estimation by selecting the best box sizes which have meaningful changes at different depths of anesthesia. To achieve this goal, we have randomly selected several epochs from different patients with wide anesthetic depth levels from light to very deep anesthesia levels, in our database to estimate the fractal scaling exponent. It is important to note that the selected data were gathered from different persons, so the optimal selected boxes would have enough robustness and will be case independent. But the effect of specific drug on special case will bring the precise results and become important in anesthesia researches.

The fluctuation diagram in Fig. 4 starts from a small box size n, in which the data is fully matched by detrending step and therefore the output value, is so small. On the extreme of the diagram, when n becomes large, there are some box sizes in which detrending is saturated and no meaningful increase in fluctuation is gained with an increase in the box size. Thus, the slope estimation must be performed on a limited region, where most of the discrimination takes place. Fig. 4 illustrates this hypothesis.

IV. RESULTS

By adaptively checking different margins, we observed that it could be possible to chose the minimum best boxes which the fluctuation rate statistically has the best meaningful relation to the BIS Index instead of many boxes in the DFA algorithm. The best box sizes for applying the slope estimation are indicated as three lines in Fig. 4, which are 3, 9 and 52. For quantifying the results of our algorithm and checking the validation, we define Fractal Scaling Exponent (FSE) as a new index for depth of anesthesia estimation:

$$FSE = Log\left(\frac{F(n_2)}{F(n_1)}\right) \tag{4}$$

Which F(n) is the detrended fluctuation rate in DFA algorithm on boxes with size of n_i.

Figure 5 represents the correlation between BIS Index and the Fractal Scaling Exponent (FSE) Index which have been extracted from only tow box sizes (n_1=3 and n_2=9) of DFA algorithm. The correlation coefficient (R=0.953) represents the optimal selection of box sizes for awake to moderate anesthesia levels. Figure 6 represents the same results between BIS Index and the FSE Index which have been extracted from only tow box sizes (n_1=3 and n_2=52) of DFA algorithm form deep to light anesthesia levels (R= 0.954). As shown in the figures, when BIS is high, the FSE is low and vice versa. This result validates our claims where an inverse relation between the FES index and well known BIS Index exists. When the patient cerebral state changes from awake to moderate levels the FSE index increase from 0.6 to 1 (Fig. 5) whereas the FSE index increases up to 2.2 for moderate to deep anesthesia (Fig.6). These ranges of fractal scaling exponent indicate long-range power-law correlations and the change in self-similarity properties of the signal related to the effect of anesthetic drugs on the brain.

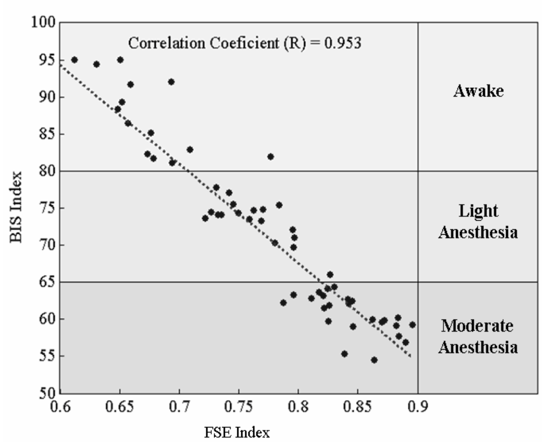

Figure 5: Correlation between BIS Index versus Fractal Scaling Exponent (FSE) for optimum box sizes (n_1=3 and n_2=9). Correlation coefficient R=0.954.

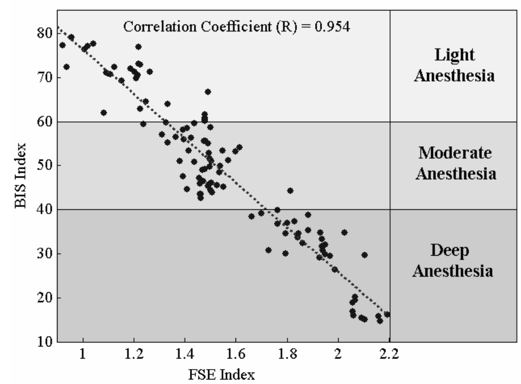

Figure 6: Correlation between BIS Index versus Fractal Scaling Exponent (FSE) for optimum box sizes (n_1=3 and n_2=52). Correlation coefficient (R=0.954).

V. CONCLUSION

In this paper we have presented a new algorithm based on the optimum fractal scaling exponent by selecting the optimum box sizes in the DFA algorithm which have meaningful changes with the different depth of anesthesia. The increase in the fractal behavior and self-similarity properties of the signal from awaked state to deeper anesthesia depth is based on the number of brain active sites in awake and anesthetized situation. In the awaked state, the numbers and the levels of activity of these operational sites are high, thus the entropy of signal is high and the observation of signal is more random like. But when the anesthetic drugs are becoming effective, the entropy increases and the self-similar properties of the signal can be notable. The experimental results of new FSE index offers significantly reduced computational complexity and a faster reaction to transients in patients' consciousness levels compared to the other known algorithms and technologies.

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