Correlation-dimension and autocorrelation fluctuations in epileptic seizure dynamics

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We focus on an anomalous scaling region in correlation integral $[C(\epsilon)]$ analysis of electrocorticogram in epilepsy patients. We find that epileptic seizures typically are accompanied by wide fluctuations in the slope of this scaling region. An explanation, based on analyzing the interplay between the autocorrelation and $C(\epsilon)$, is provided for these fluctuations. This anomalous slope appears to be a sensitive measure for tracking (but not predicting) seizures.

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An outstanding problem in biomedical sciences is to devise techniques to understand and, more importantly, to predict in advance of clinical onset, epileptic seizures that affect about 1% of the population in industrialized countries. Epileptic seizures are characterized electrographically by sudden simultaneous changes in power spectral density and increases in wave rhythmicity. These changes in brain activity, whether local or global, can be monitored via electrodes on the scalp (electroencephalogram, EEG), or intracranially (electrocorticogram, ECoG). These recordings provide a window, perhaps the only practically accessible window at present, through which the dynamics of epilepsy can be investigated. Analysis of EEG/ECoG has thus become the subject of renewed interest in this field.

An approach that is gaining increasing attention is the application to this problem of techniques from nonlinear dynamics and chaos, originally developed for the study of low dimensional, nonlinear, deterministic systems [1–11]. Preliminary results suggest that EEG/ECoG signals during the seizure state can be described by low-dimensional dynamical systems [1–3]. If this were true, there would be hope that detection or even prevention of epileptic seizures is within reach, because prediction [12] and control [13] of low-dimensional chaotic systems are achievable. However, reexamination of these early claims indicates a lack of low-dimensional dynamical structure in the EEG/ECoG [14,15]. Despite this finding, measures that are useful for characterizing low-dimensional chaotic systems, such as the correlation dimension and the Lyapunov exponents, have been and continue to be used to study the EEG/ECoG signals [4,5,7,8,11], resulting in various claims that epileptic seizures can be predicted up to several minutes or hours before their clinical manifestations [4,7,8,11]. In this paper, we make a reasonable assumption that EEG/ECoG has a significant stochastic component (with infinite dimensionality in both the seizure and nonseizure states), which should preclude detection of a dimension drop at seizure onset. In light of this, our position is that at the present, it is uncertain whether techniques based on nonlinear dynamics would perform better than conventional Fourier-based methods such as the autocorrelation function, which is the inverse Fourier transform of the energy spectral density by the Wiener-Khintchine theorem [16]. Prediction of seizures based on EEG/ECoG signals thus remains an open problem.

In this paper, we focus on the correlation integral $[C(\epsilon)]$, a measure originally proposed by Grassberger and Procaccia [17], which has become one of the most popular nonlinear dynamics based tools in the analysis of EEG/ECoG data. A previous study [8] has demonstrated that decreases in $C(\epsilon)$ are predictive of seizure onset. The driving force behind a large number of studies on dimension analysis of EEG/ECoG [1–3,7,8] is that epileptic seizures are regarded as emergent states with reduced dimensionality compared to nonepileptic activity. This concept finds support in the observations [18] that neuronal hypersynchrony underlies seizures, a phenomenon during which the number of independent variables required to describe the system is smaller than at other times. Thus, measures that detect reduced dimensionality of EEG/ECoG may allow for the prediction of seizures. However, recent results have suggested that these decreases in the $C(\epsilon)$ merely may reflect sudden increases in signal amplitude [19], which by themselves are nonspecific indicators of seizure onsets that can be more easily tracked through other available approaches. Our main result is that $C(\epsilon)$ has seizure discriminating (but not predictive) power in an amplitude-normalized signal, and that this information is contained in the scaling of $C(\epsilon)$ with an intrinsic length scale (ϵ). Specifically, during seizure, the slope of a linear scaling region is observed to undergo relatively large fluctuations compared to the preseizure and postseizure states. We focus on these fluctuations and give an argument for their dynamical origin based on monitoring the corresponding temporal variation in the autocorrelation of the data. We mention that there are existing works on comparing linear and nonlinear data-analysis techniques applied to EEG signals [20]. The unique feature of our work is the identification and analysis of the anomalous scaling region in the correlation integral from ECoG signals.

We begin by briefly reviewing the basic concepts in dimension analysis of nonlinear time series. Given a signal, we use the standard technique of delay-coordinate embedding [21] to reconstruct, with appropriate choice of the delay time [22], an m-dimensional phase space. An often computed dimension in nonlinear time series analysis is the correlation

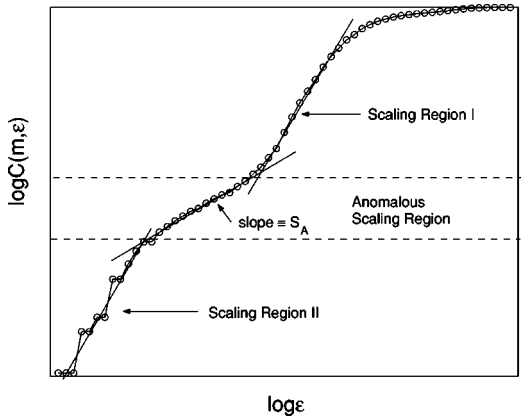

FIG. 1. Illustration of the anomalous scaling region in a typical plot of the correlation integral from a segment of ECoG time series. The commonly used base of the logarithm is 2.

dimension D_2. Grassberger and Procaccia show [17] that D_2 can be evaluated using the correlation integral $C(\epsilon)\sim\epsilon^{D_2}$, where $C(\epsilon)$ is the probability that a pair of points, chosen randomly in the reconstructed phase space, is separated by a distance less than ϵ. Let $\mathbf{x}(t)$ represent the reconstructed vector time series of length N. The correlation integral can be approximated by the following correlation sum: $C_N(m,\epsilon)=[2/N(N-1)]\Sigma_{j=1}^{N}\Sigma_{i=j+1}^{N}\Theta(\epsilon-|\mathbf{x}_i-\mathbf{x}_j|)$, where $\Theta(\cdot)$ is the Heaviside function given by: $\Theta(x)=1$ for $x\geqslant 0$ and 0 otherwise, and $|\mathbf{x}_i-\mathbf{x}_j|$ stands for the distance between points $\mathbf{x}_i$ and $\mathbf{x}_j$. For N large, we have $C_N(m,\epsilon)\approx C(\epsilon)$. The correlation dimension D_2 is usually estimated by examining the slope of the linear portion of the plot of $\ln C_N(m,\epsilon)$ versus $\ln\epsilon$ for a series of increasing values of m. For $m<D_2$, the dimension of the reconstructed phase space is not high enough to resolve the structure of the dynamical state and, hence, the slope approximates the embedding dimension. As m increases, the resolution of the dynamical state in the reconstructed phase space improves. For a low-dimensional dynamical system, the slope in the plot of $\ln C_N(m,\epsilon)$ versus $\ln\epsilon$ increases with m until it reaches a plateau; its value at the plateau is then taken as the estimate of D_2 [17,23]. For stochastic dynamics, the slope increases with m, never reaching a plateau.

Theiler points out [22] that for a finite, autocorrelated data set, the plot of $C(m,\epsilon)$ on a logarithmic scale can exhibit approximately linear regions with distinct slopes that do not increase with m. Assuming that we have a window of data $\{x_j\}_{j=1}^{N}$, the autocorrelation of the data, α, is computed through the following average: $\alpha=(1/M)\Sigma_{k=1}^{M}(\alpha_k)^{1/k}$, where we use $M=6$ in our computation and $\alpha_k=\langle x_j x_{j+k}\rangle/\langle x_j^2\rangle$. Theiler considers a Gaussian stochastic time series consisting of N data points with autocorrelation $0<\alpha\leqslant 1$ and argues that if N is large enough, or if α is small enough (near zero), then the effect of autocorrelation is negligible. However, if N is not sufficiently large (as in the case of ECoG analysis where a temporally moving window is slid through the time series) and/or if α is not close to zero, the effect of autocorrelation becomes noticeable, leading to an anomalous scaling region in the plot of $C(m,\epsilon)$. The slope of

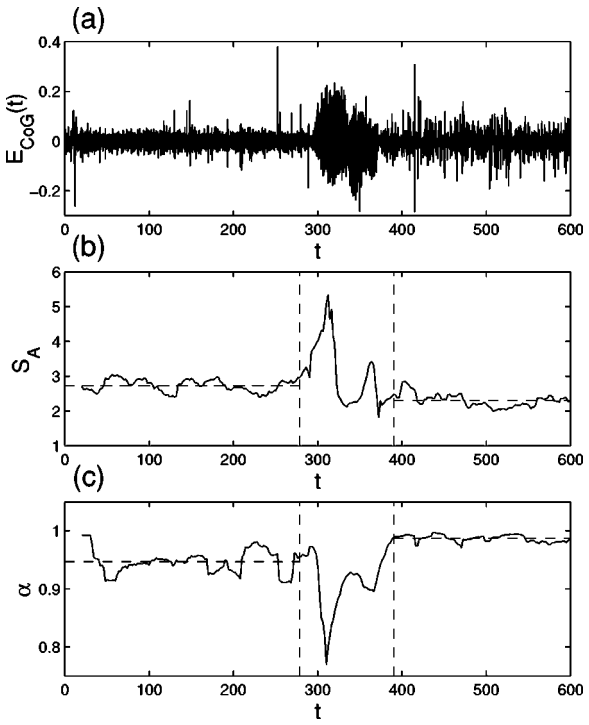

FIG. 2. (a) Original ECoG time series containing a seizure, (b) time-dependent value of the anomalous slope averaged over the embedding dimensions in the range $10\leqslant m\leqslant 20$, (c) time-dependent autocorrelation in each 2 s window of the ECoG segment shown in (a).

the plot in the anomalous scaling region is not dependent on the embedding dimension, and as such it does not reflect on the stochastic nature of the underlying process.

For instance, we show, in Fig. 1, a typical plot on a logarithmic scale of $C(m,\epsilon)$ obtained from a preictal segment of an ECoG time series. We notice three distinct regions with approximately linear scaling: regions I and II with a higher slope than that of a third region in-between them. In the cases that we have studied, the slopes extracted in regions I and II are close to that of the embedding dimension m, indicating that in these scales of ϵ, the ECoG time series are stochastic. The region of smallest slope reflects an appreciable amount of autocorrelation in the data: it is the anomalous scaling region. As we will show, the value of the slope in this region remains relatively constant in the preictal and postictal phases, but typically exhibits large fluctuations in the ictal phase.

Our data have been collected from patients who underwent evaluation for epilepsy surgery at the University of Kansas Comprehensive Epilepsy Center, and is recorded via depth electrodes (Ad-Tech), implanted stereotaxically into each amygdalo-hippocampal region. Signals are filtered (0.5–70 Hz), amplified, and digitized (240 Hz; 10 bits precision) using a commercially available device (Nicolet, Madison, WI). All recordings have been deemed of good technical quality and suitable for analysis. Each data set contains a number of seizures, captured over several days of continuous recording (mean duration of 100 h). Given a single ECoG time series, we utilize a moving window of

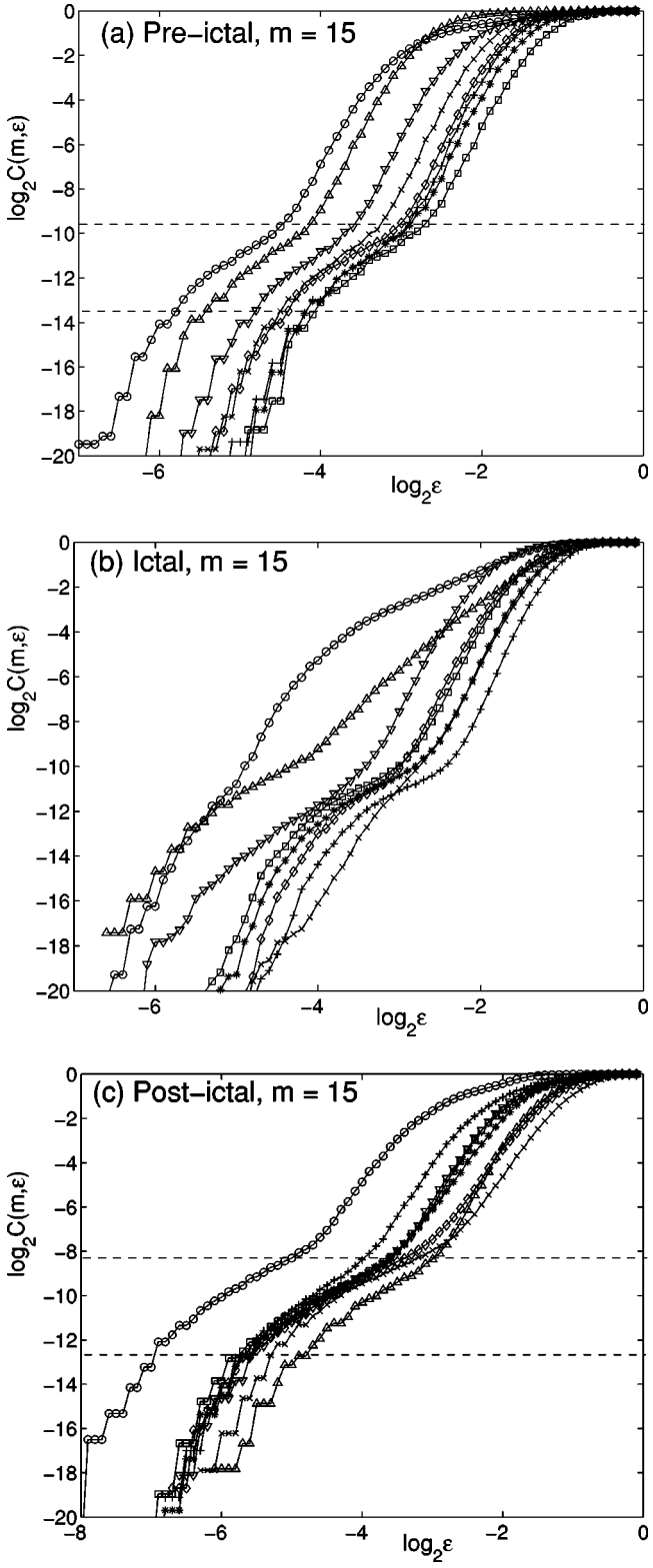

FIG. 3. For $m=15$, and eight time windows in the preictal (a), ictal (b), and postictal (c) phases, $\log_2 C(m,\epsilon)$ versus $\log_2 \epsilon$ on a logarithmic scale.

20(s). Nearby windows are overlapped with a time separation of 2(s). Thus, if the first window spans the time interval [0,20](s), then the second window is in [2,22](s), and so on. We then compute the amplitude-normalized correlation integral as a function of time (chosen to be the right-hand side of the window). The computation is performed for embedding dimension in the range $5 \leqslant m \leqslant 25$. The computation of $C(m,\epsilon)$ is made efficient by assigning a number of bins in the counter, each corresponding to a specific distance range. The delay time is chosen to be $\tau = 1/12$(s), which is a fraction of a typical oscillating period of the ECoG time series.

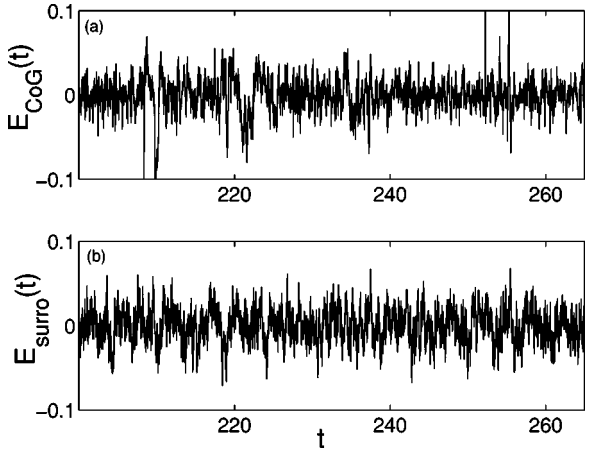

FIG. 4. A 65 s segment of data in the preictal phase: (a) the original ECoG time series and (b) the surrogate time series.

A typical ECoG time series containing a seizure is shown in Fig. 2(a). Our main result is represented by Fig. 2(b), which shows the time evolution of the anomalous slope averaged over a range of values of the embedding dimension ($10 \leqslant m \leqslant 20$). Figure 2(c) shows the autocorrelation for the same segment of ECoG. Some representative plots of the correlation integral $C(m,\epsilon)$ are shown in Figs. 3(a)–3(c) for the preictal, ictal, and postictal phases, respectively. We observe the following: (1) in almost all analyzed data windows (whether preictal, ictal, or postictal), an anomalous scaling region exists, which allows for the mean slope to be estimated, (2) in both the preictal and postictal phases, the plots in the anomalous scaling regime at different times tend to be parallel to each other, indicating that the slopes remain roughly constant (but with small fluctuations), with the plots in the preictal phase being steeper than the postictal phase, and (3) in the ictal phase, there is an apparent lack of an approximately ''constant'' slope in the anomalous scaling regime [as illustrated by the lack of parallelism in the lines in Fig. 3(b)], indicating that the value of the anomalous slope tends to fluctuate significantly. These behaviors can be understood through examination of the interplay between the autocorrelation of the ECoG time series and the correlation integral. It has been known [22] that, for a Gaussian random process, the ''flatness'' of the plot of $\log_2 C(m,\epsilon)$ versus $\log_2 \epsilon$ in the anomalous scaling regime depends on the value of the autocorrelation α. In particular, a closer-to-unity autocorrelation tends to generate smaller slopes in the anomalous scaling regime, than when the autocorrelation is farther away from 1. We have observed the following from numerical experiments: (1) in the preictal phase, the autocorrelation is relatively low, thereby generating relatively large values of the anomalous slope [about 2.8, as in Fig. 2(b)]; (2) in the postictal phase, the values of α are closer to 1, as compared

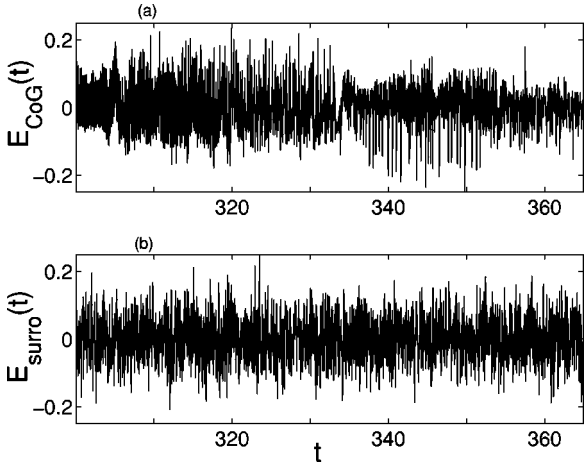

FIG. 5. A 65 s segment of data in the ictal phase: (a) the original ECoG time series and (b) the surrogate time series.

with those in the preictal phase, leading to a drop in the mean value of the anomalous slope; and (3) in the ictal phase, the autocorrelation varies widely in the range between α_0 and 1 ($\alpha_0<1$), hence the significant fluctuations [24] in the slope of the plot of the correlation integral in the anomalous scaling regime. While the specific interplay between α and anomalous slope S_A varies interindividually, all analyzed seizures (16 from four patients) have been characterized by significant fluctuations in the anomalous slope [25].

To be more confident that the anomalous scaling region is due to autocorrelations in the time series, we compute the correlation integrals for surrogate data derived from the ECoG time series. Figures 4, 5, and 6 show a segment of EcoG data of 65 s (a) and the corresponding surrogate one (b) for preictal, ictal, and postictal phases, respectively. The surrogate data are obtained via the standard procedure [26], i.e., by Fourier transforming the data, randomizing the phases of the Fourier components, and then performing inverse Fourier transform. Figures 7(a)–7(c) show the correlation integrals for eight windows of 20 s from the surrogate date in the preictal, ictal, and postictal phases, respectively, where the parameters are $m=15$ and $\tau=1/12$ s. The existence of the anomalous scaling region in the correlation integral from the surrogate date is evident. Due to the randomizing effect in the surrogate procedure, the fluctuations in the slope of the linear fit between $\log_2 C(m,\epsilon)$ and $\log_2 \epsilon$ in the anomalous scaling region are much smaller than those from the original data, which is apparent particularly for the ictal phase.

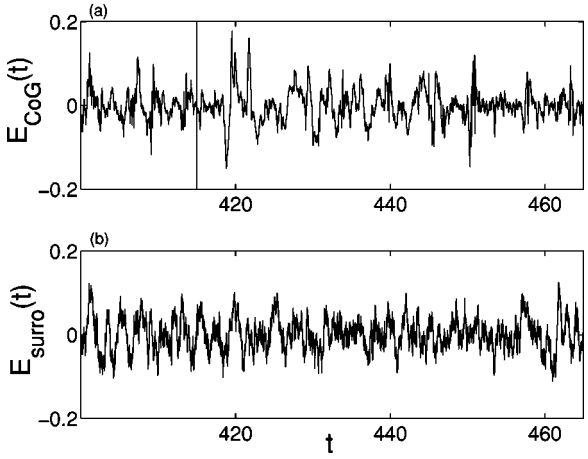

FIG. 6. A 65 s segment of data in the postictal phase: (a) the original ECoG time series and (b) the surrogate time series.

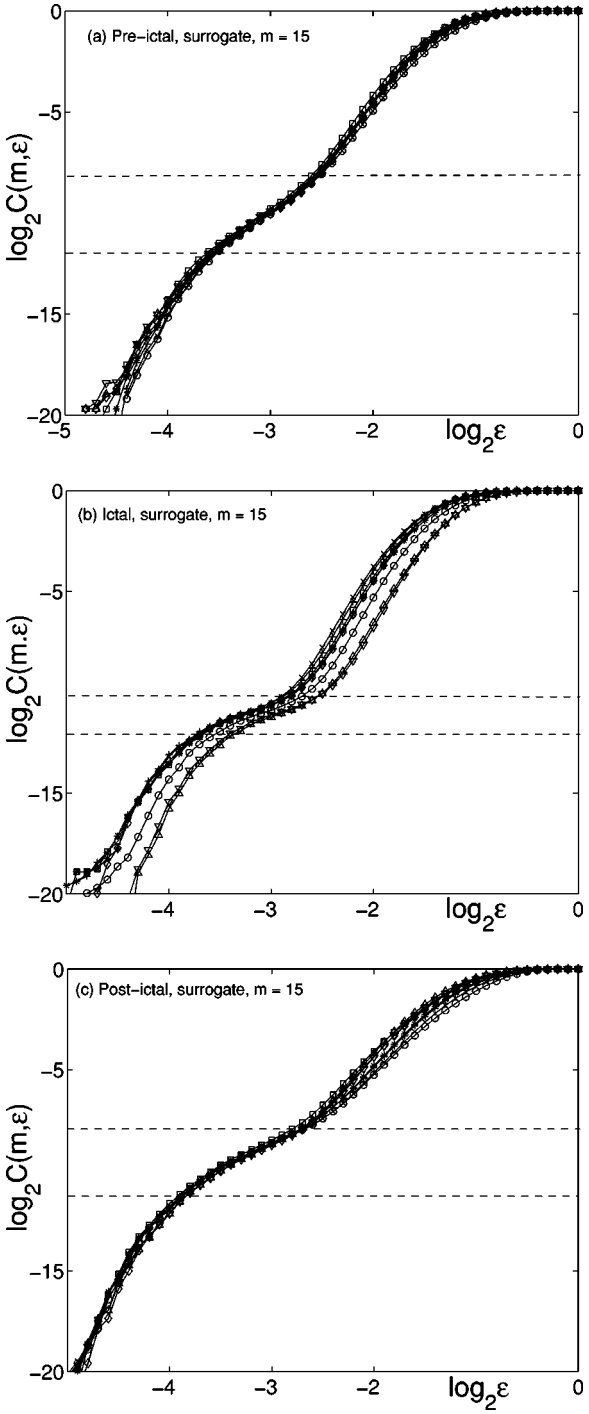

FIG. 7. For surrogate data, $m=15$, and eight time windows in the preictal (a), ictal (b), and postictal (c) phases, the plots of the correlation integral on a logarithmic scale. The existence of the anomalous scaling region is evident.

Our detailed and systematic analysis of the scaling with ϵ of the correlation integral, a concept from nonlinear dynamics that has been applied most commonly in the area of EEG/ECoG analysis, further suggests that the underlying dynamical process contains a significant stochastic component. Though epileptic seizures are characterized by fluctuations in the value of the anomalous slope, the fluctuations correspond to those of the autocorrelation, a more computationally efficient measure for seizure tracking. Thus, it is questionable whether any correlation integral based techniques can be more effective at predicting seizures than traditional signal processing methods. This is apparently in sharp contrast to the recent claims that such techniques are powerful for prediction of seizures [7,8].

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[24] Increase of fluctuations close to critical points is a classical signature of nonequilibrium phase transitions. In the case of epileptic seizures, evidence so far suggests that they are due to synchronization between neurons [27]. From this standpoint, the onset of a seizure is in fact a transition to synchronization of the underlying neural network in a generalized sense. While such a synchronous state typically possesses a lower dimensionality and can indeed be detected by tools from linear or nonlinear analysis, as we argue in this paper, it is difficult to *predict* such a transition in advance, due to the apparently stochastic nature of ECoG signals.

[25] Fluctuations in the autocorrelation correspond to changes in the time-frequency distributions of the signal. Variations such as these changes typically are used to visually score seizures, thus the anomalous slope detects signal variations identifiable through alternate means in contrast to claims that the correlation integral detects visually ''hidden'' information about the signal.

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