Inability of Lyapunov Exponents to Predict Epileptic Seizures

Ying-Cheng Lai,[1] Mary Ann F. Harrison,[2] Mark G. Frei,[2] and Ivan Osorio[2,3]

[1]*Department of Mathematics and Statistics, Departments of Electrical Engineering and Physics, Arizona State University, Tempe, Arizona 85287, USA*

[2]*Flint Hills Scientific L.L.C., 5020 15th Street, Lawrence, Kansas 66049, USA*

[3]*Department of Neurology, University of Kansas Medical Center, 3901 Rainbow Boulevard, Kansas City, Kansas 66160, USA*

(Received 3 April 2003; published 8 August 2003)

It has been claimed that Lyapunov exponents computed from electroencephalogram or electrocorticogram (ECoG) time series are useful for early prediction of epileptic seizures. We show, by utilizing a paradigmatic chaotic system, that there are two major obstacles that can fundamentally hinder the predictive power of Lyapunov exponents computed from time series: finite-time statistical fluctuations and noise. A case study with an ECoG signal recorded from a patient with epilepsy is presented.

DOI: 10.1103/PhysRevLett.91.068102 PACS numbers: 87.19.La, 05.40.Ca, 05.45.Tp

Increasingly, concepts from nonlinear dynamics such as Lyapunov exponents and fractal dimensions are being applied to biomedical time series for detection, prediction, or control of critical system states. In the area of epilepsy, nonlinear time series techniques have been utilized to analyze brain wave data collected through the electroencephalogram (EEG) or electrocorticogram (ECoG) [1–14] for early prediction of epileptic seizures [4,6,7,10], which affect about 1% of the population in the United States. This is one of the most important, yet still outstanding, problems in this field, requiring an interdisciplinary approach among biomedical and physical sciences, engineering, and applied mathematics. There has been much effort in this direction [4,6], with claims that seizures can be predicted minutes or tens of minutes in advance of their clinical onset by monitoring the evolution of the Lyapunov exponents. Our central concern is that there has been no systematic analysis about the *predictive power* of Lyapunov exponents from *nonstationary* time series such as ECoG in the existing literature. Without such analysis, any claim of prediction may be misleading. While Lyapunov exponents are fundamental invariant quantities characterizing a dynamical system, estimating them from time series is sophisticated and nontrivial. We thus devise an approach by which the evolution of the estimated exponents can be monitored and analyzed in a *controllable* way on nonstationary time series. Our idea in this Letter is to construct a paradigmatic deterministic dynamical system in which there is parameter drift through a crisis, in order to determine whether the finite-time Lyapunov exponents can detect this drift in advance of the crisis. Even for this low-dimensional chaotic system, our analysis indicates that statistical fluctuations due to finite-time computation and the presence of small additive noise have a significantly deleterious effect on the Lyapunov exponent's ability to detect or predict a critical system state. We then present results with a segment of ECoG containing a seizure, to illustrate how these fluctuations impair even the ability to detect the seizure itself.

We construct a model consisting of a deterministic chaotic system with parameter variations, in order to mimic nonstationary ECoG data with seizure. Our choice is the Ikeda-Hammel-Jones-Moloney (IHJM) map, which models the dynamics of a nonlinear optical cavity [15]: $z_{n+1} = 1 + 0.85 z_n \exp[i0.4 - ip_n/(1+|z_n|^2)]$, where $z = x + iy$ is a complex number and p_n is a time-varying parameter. We choose p from an interval about the nominal value $p_c \approx 7.27$, at which there is an interior crisis [16]. For $p \lesssim p_c$, there is a chaotic attractor of relatively small size in the phase space. At $p = p_c$, the small attractor collides with a preexisting, nonattracting chaotic set to form a larger attractor. For $p \gtrsim p_c$, a trajectory spends most of time in the phase-space region where the original small attractor resides, with occasional visits to the region in which the original nonattracting chaotic set lies. A typical time series then consists of behavior of smaller amplitude most of the time, with occasional random bursts of relatively larger amplitude (e.g., random motion of larger amplitude, as in the ictal phase in ECoG). To be concrete, we focus on a long time interval ($t_f = 50\,000$ iterations) and assume $p_n = p_0$, for $n < t_i = 20\,000$, $p_n = p_0 + n(p_1 - p_0)/5000$ for $t_i \leq n < t_m = 25\,000$, $p_n = p_1 - n(p_1 - p_0)/5000$ for $t_m \leq n < t_f = 30\,000$, and $p_n = p_0$ for $n > t_f$, where $p_0 = 7.25$ and $p_1 = 7.55$.

We compute the Lyapunov spectrum from time series by using the standard method [17]. When an m-dimensional embedding space is used on a d-dimensional invariant set, where $m > 2d$ [18], there will be $m - d$ spurious Lyapunov exponents. For convenience, we call λ_i^e $(i = 1, \ldots, m)$, all m exponents computed from the time series, the *pseudo-Lyapunov spectrum*. For low-dimensional dynamical systems in the absence of noise and with some specific choices of the embedding dimension, there are criteria for distinguishing the spurious exponents from the true

 0031-9007/03/91(6)/068102(4)$20.00

exponents [19]. In particular, for a one-dimensional chaotic map with a positive Lyapunov exponent λ, the $(m-1)$ spurious exponents are $2\lambda, \ldots, m\lambda$. For a two-dimensional map (or equivalently, a three-dimensional flow) with a positive and a negative exponent, $\lambda_1 > 0 > \lambda_2$. For $m = 5$ the pseudo-Lyapunov spectrum is $\lambda_1^e \approx 2\lambda_1$, $\lambda_2^e \approx \lambda_1$, $\lambda_3^e \approx \lambda_1 + \lambda_2$, $\lambda_4^e \approx \lambda_2$, and $\lambda_5^e \approx 2\lambda_2$ (three spurious exponents are then $2\lambda_1$, $\lambda_1 + \lambda_2$, and $2\lambda_2$). For instance, for stationary time series $\{x_n\}_{n=1}^{n=10\,000}$ from the IHJM map for $p = 7.25$, the two true exponents are $\lambda_1 \approx 0.357$ and $\lambda_2 \approx -0.568$. Using $m = 5$ and delay time $\tau = 1$ to reconstruct phase-space, our algorithm yields $\lambda_1^e \approx 0.712 \approx 2\lambda_1$, $\lambda_2^e \approx 0.331 \approx \lambda_1$, $\lambda_3^e \approx -0.176 \approx \lambda_1 + \lambda_2$, $\lambda_4^e \approx -0.586 \approx \lambda_2$, and $\lambda_5^e \approx 1.112 \approx 2\lambda_2$, which are the correct ones for two-dimensional maps [19]. For general systems, spurious exponents cannot be identified *a priori* in this manner, so we use the pseudo-Lyapunov spectrum for detecting or predicting seizures, regardless of whether or not a particular exponent is a true exponent.

It is necessary to use a moving window for detection or prediction of characteristic changes in the system. For a finite data set such as this, a key concern is statistical fluctuations of the pseudo-Lyapunov exponents. If the number of data points N in the moving window is small, the computed pseudo-Lyapunov exponents will have large fluctuations, as shown in Figs. 1(a)–1(f) for $m = 5$ and $N = 630$, where Fig. 1(a) shows the nonstationary time series and Figs. 1(b)–1(f) are the evolutions of λ_i^e $(i = 1, \ldots, m)$. The vertical dashed line indicates t_i, the time at which the control parameter p starts to change. Let Δt be the time from the beginning of the drift to the time the drift is detected. We see that the change in p is somewhat reflected in λ_1^e. For the change in λ_1^e to be statistically significant, it should be greater than the average amount of fluctuations. This occurs at about $\Delta t \approx 700$. Other exponents show no statistically discernible changes after t_i. Extensive numerical computations using many values of N indicate that Δt does not change appreciably as N is increased.

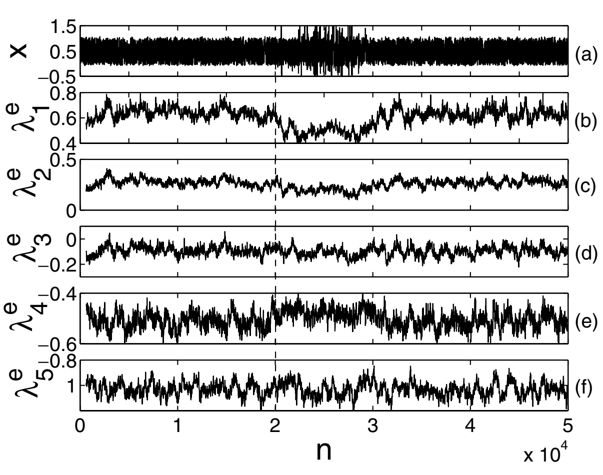

FIG. 1. For the Ikeda-Hammel-Jones-Moloney (IHJM) map, $m = 5$ and $N = 630$, (a) nonstationary time series, (b)–(f) temporal evolution of λ_i^e for $i = 1, \ldots, 5$, respectively.

We can argue theoretically that increasing the size of the moving window will in general not reduce the detection time Δt. We imagine choosing a large number of initial conditions and computing the Lyapunov spectra for all the resulting trajectories of length N, where N is large, for a system with a chaotic attractor. For trajectories on a chaotic attractor, the typical distribution of a finite-time Lyapunov exponent λ_N is [20] $P(\lambda_N, N) \approx [NG''(\bar{\lambda})/2\pi]^{1/2} \exp[-\frac{N}{2}G''(\bar{\lambda})(\lambda - \bar{\lambda})^2]$, where $\bar{\lambda}$ is the value of λ_N in the limit $N \to \infty$, $G(x)$ is a function that satisfies $G(\bar{\lambda}) = 0$, $G'(\bar{\lambda}) = 0$, and $G''(\bar{\lambda}) > 0$. Thus, for large N, the standard deviation of λ_N is $\sigma_{\lambda_N} \sim 1/\sqrt{N}$. If the moving time window is located completely in $t < t_i$, the average Lyapunov exponent is $\lambda_N = \frac{1}{N}\sum_{i=1}^{N} \lambda^{(1)}(i)$, where $\lambda^{(1)}(i)$ is the time-one Lyapunov exponent for $t < t_i$. Now consider a moving time window across the critical time t_i, where N_1 points are before t_i, N_2 points are after t_i, and $N_1 + N_2 = N$. The computed exponent is $\lambda'_N = \frac{1}{N}[\sum_{i=1}^{N_1} \lambda^{(1)}(i) + \sum_{i=1}^{N_2} \lambda^{(2)}(i)]$, where $\lambda^{(2)}(i)$ is the time-one Lyapunov exponent for $t > t_i$. Let $\bar{\lambda}^{(1)}$ and $\bar{\lambda}^{(2)}$ be the asymptotic values of the Lyapunov exponent for $t < t_i$ and $t > t_i$, respectively. If $N_1 \gg 1$, $N_2 \gg 1$, $N_1 \sim N$, and $N_2 \sim N$, we can write $\sum_{i=1}^{N} \lambda^{(1)}(i) = N\bar{\lambda}^{(1)} + \mathcal{O}(1/\sqrt{N})$, $\sum_{i=1}^{N_1} \lambda^{(1)}(i) = N_1\bar{\lambda}^{(1)} + \mathcal{O}(1/\sqrt{N_1}) \approx N_1\bar{\lambda}^{(1)} + \mathcal{O}(1/\sqrt{N})$, and $\sum_{i=1}^{N_2} \lambda^{(2)}(i) = N_2\bar{\lambda}^{(2)} + \mathcal{O}(1/\sqrt{N_2}) \approx N_2\bar{\lambda}^{(2)} + \mathcal{O}(1/\sqrt{N})$, where $\mathcal{O}(1/\sqrt{N})$ is a number on the order of $1/\sqrt{N}$. The change in the computed time-N exponent is thus $\Delta\lambda_N = \lambda_N - \lambda'_N \approx \frac{1}{N}(N\bar{\lambda}^{(1)} - N_1\bar{\lambda}^{(1)} - N_2\bar{\lambda}^{(2)}) + \mathcal{O}(1/\sqrt{N}) = \frac{N_2}{N}(\bar{\lambda}^{(1)} - \bar{\lambda}^{(2)}) + \mathcal{O}(1/\sqrt{N}) \sim \frac{N_2}{N}$. For the change in the Lyapunov exponent to be statistically significant and thus detectable, we require $\Delta\lambda_N \gtrsim \sigma_{\lambda_N}$, which gives the time required to detect the change: $\Delta t = N_2 \gtrsim \sqrt{N}$. We see that increasing the size of the moving window in fact increases the time required to detect a change in the Lyapunov exponent. This increase is, however, incremental compared with the increase in N and therefore may not be easily observed. This is why in numerical experiments we did not see an apparent increase in Δt when N was increased.

While our analysis suggests that the critical change of the system state can be detected through the pseudo-Lyapunov spectrum from time series, it is not clear whether the change can be *predicted* in advance. We thus ask whether any state change can be detected through the pseudo-Lyapunov exponents before the critical point. To address this question, we consider the following: suppose a critical event occurs in which the system bifurcates to a characteristically distinct state. Before the event, the parameter drifts toward the critical bifurcation, although not necessarily at the same rate as it passes through the critical point. We thus consider a scheme of parameter variation for the IHJM map, where initially the parameter p is fixed at a constant value (7.1) below the critical point p_c. As p passes through p_c at about $n \gtrsim 20\,000$ a critical event (interior crisis) occurs. Before this, we allow p to change at a slower rate for $10\,000 < n < 20\,000$. The entire time interval of interest is taken to be 40 000 iterations. If one examines a time series before the critical point, there is no apparent characteristic change, despite the slow change in parameter. We believe this setting represents a reasonable test bed for the predictive power of pseudo-Lyapunov exponents.

We proceed by choosing a moving window containing N data points and examining any changes in the pseudo-Lyapunov spectrum. When N is small, the large fluctuations in the exponents render undetectable the slow parameter changes preceding the onset of crisis. This indicates that the crisis cannot be predicted when N is small. As N is increased, the fluctuations are reduced so that the system change preceding the crisis can be detected, as shown in Figs. 2(b)–2(f) for $m = 5$ and $N = 3981$. The change can indeed be detected at time $n \gtrsim 10\,000$, which precedes the crisis. While this seems to indicate that the exponents have the predictive power for crisis, our key point is that *the presence of small noise can wipe out this power completely.*

To simulate noise, we add two terms $D\xi_n^x$ and $D\xi_n^y$ to the x and y equations of the IHJM map, respectively, where ξ_n^x and ξ_n^y are independent random variables uniformly distributed in $[-1, 1]$, and D is the noise amplitude. Figures 3(b)–3(f) show, for $m = 5$ and $N = 3981$, the temporal evolutions of the five pseudo-Lyapunov exponents for noise level $D = 10^{-2.0}$. Since the range of the time series is about 2.0, this noise level roughly corresponds to 0.5% of the variation of the dynamical variable. We observe a deterioration of the predictive power of the exponents, since the parameter change preceding the crisis can no longer be detected at the small noise level of about $D = 10^{-2.0}$. We find that for relatively larger noise such as $D = 10^{-1.0}$ (but still small in amplitude comparing with the size of the chaotic attractor) even the critical event (crisis) itself cannot be detected through the variation of these exponents. These results suggest that, in practical situations where small noise is inevitable, one should not expect Lyapunov exponents computed from time series to have any predictive power.

We now present results with a segment of ECoG signal containing a seizure to further illustrate our point. Our data were collected from patients with pharmacoresistant seizures who underwent evaluation for epilepsy surgery at the University of Kansas Comprehensive Epilepsy Center. The data were recorded via depth electrodes, sampled at the rate of 240 Hz, amplified, and digitized to 10 bit precision using commercially available devices (Nicolet, Madison, Wisconsin). For convenience, we normalize the data to the unit interval. The time delay used in the embedding was chosen to be $\tau = 1/12$ s, according to the autocorrelation criteria in Ref. [21]. The size of the linear neighborhood used in the Lyapunov exponent algorithm is about 2% of the signal amplitude. Fixing the embedding dimension at $m = 5$, we compute the five Lyapunov exponents versus time in Fig. 4 for windows of approximately 13.18 s long. Because of the large fluctuations before, during, and after seizure, there is little indication of any ability to even definitively detect this epileptic seizure. Similar behavior was found with systematic choices of the embedding dimension ranging from 5–25 and with various window sizes.

Our analysis and computations thus indicate that the Lyapunov exponents estimated from time series of low-dimensional and noisy chaotic systems cannot be effective for detecting critical events after they occur, let alone for predicting them in advance. The brain dynamical system responsible for the epileptic seizures is much more complicated than low-dimensional chaotic systems

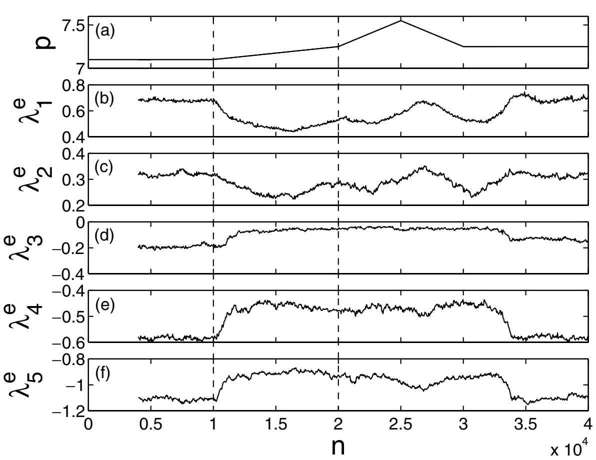

FIG. 2. (a) Scheme of parameter variation with time, (b)–(f) in the absence of noise, temporal evolutions of λ_i^e ($i = 1, \ldots, 5$) for $m = 5$ and $N = 3981$. In this case, the parameter change preceding the crisis can be detected through the pseudo-Lyuapunov exponents.

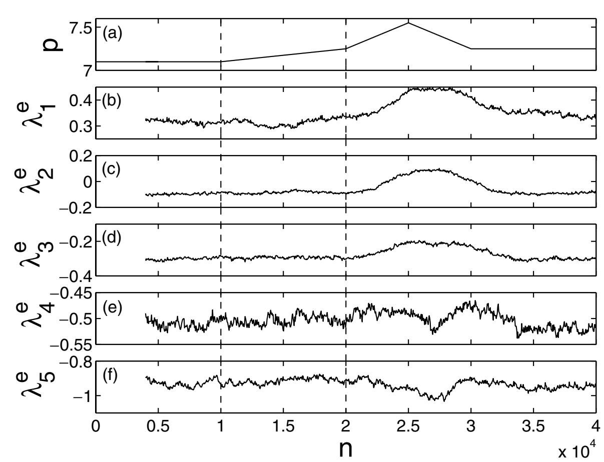

FIG. 3. (a) Scheme of parameter variation with time, (b)–(f) temporal evolutions of λ_i^e ($i = 1, \ldots, 5$) for $m = 5$, $N = 3981$, and noise amplitude $D = 10^{-2.0}$ (corresponding to about 0.5% of the amplitude of the measured data). At this noise level the crisis cannot be predicted in advance because the parameter change preceding the crisis cannot be detected.

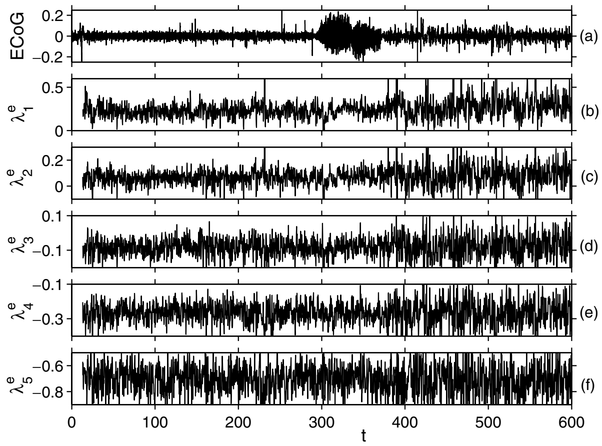

FIG. 4. (a) A segment of electrocorticogram (ECoG) time series containing a seizure which starts at approximately $t = 300$ s and lasts for about 80 s, (b)–(f) for $m = 5$ and $\Delta t \approx 13.18$ s (corresponding to $N = 10^{3.5} = 3162$), the five computed Lyapunov exponents versus time.

or even idealized high-dimensional systems such as coupled map lattices. In epilepsy, all information is from a few dozen probes, each sensing approximately 10^5–10^8 neurons [22], into the corresponding neuron ensemble in the brain about which relatively little is known. The signals so obtained (ECoG) are inevitably noisy. These considerations suggest that it should be reasonable that the Lyapunov exponents do not appear to have any predictive or detective powers for epileptic seizures.

In summary, we have addressed the inability of the Lyapunov exponents computed from time series to predict or detect critical events. Our analysis and computations indicate that there are two major factors that can prevent the exponents from being effective tools to predict characteristic system changes: statistical fluctuations and noise. The basic message is that for low-dimensional, deterministic chaotic systems the predictive power of Lyapunov exponents holds only in noiseless or extremely low-noise situations. In realistic situations where an appreciable but reasonable amount of noise is present, the utility of Lyapunov exponents is questionable, especially in a system as high dimensional and noisy as the brain's. We feel that this is an important point to keep in mind in light of repeated claims in the literature of seizure prediction with Lyapunov exponents [4]. It is also clear that our result is relevant to many other applications where the temporal evolutions of the Lyapunov exponents estimated from time series are intended for prediction or detection.

This work was supported by NIH under Grant No. 1R43NS43100-01. Y. C. L. was also supported by NSF under Grant No. PHY-9996454.

[1] A. Babloyantz and A. Destexhe, Proc. Natl. Acad. Sci. U.S.A. **83**, 3513 (1986).

[2] A. M. Albano, J. Muench, C. Schwartz, A. I. Mees, and P. E. Rapp, Phys. Rev. A **38**, 3017 (1988); P. E. Rapp, T. R. Bashore, J. Martinerie, A. M. Albano, and A. I. Mees, Brain Topog. **2**, 99 (1989); P. E. Rapp, I. D. Zimmerman, E. P. Vining, N. Cohen, A. M. Albano, and M. A. Jimenezmontano, J. Neurosci. **14**, 4731 (1994).

[3] G. Mayer-Kress and S. P. Layne, Ann. N.Y. Acad. Sci. **504**, 62 (1987).

[4] L. D. Iasemidis, J. C. Sackellares, H. P. Zaveri, and W. J. Williams, Brain Topog. **2**, 187 (1990); L. D. Iasemidis, J. C. Sackellares, R. L. Gilmore, and S. N. Roper, Epilepsia **39**, 207 (1998); L. D. Iasemidis, J. C. Sackellares, Q. Luo, S. N. Roper, and R. L. Gilmore, Epilepsia **40**, 165 (1999); J. C. Sackellares, L. D. Iasemidis, D. S. Shiau, R. L. Gilmore, and S. N. Roper, Epilepsia **40**, 176 (1999); Neurology **52**, A106 (1999);L. D. Iasemidis, P. Pardalos, J. C. Sackellares, and D. S. Shiau, J. Comb. Optim. **5**, 9 (2001); J. C. Sackellares, D. S. Shiau, L. D. Iasemidis, P. M. Pardalos, W. Chaovalitwongse, and P. R. Carney, Ann. Neurol. **52**, S65 (2002).

[5] M. L. V. Quyen, J. Martinerie, C. Adam, and F. J. Varela, Phys. Rev. E **56**, 3401 (1997).

[6] K. Lehnertz and C. E. Elger, Phys. Rev. Lett. **80**, 5019 (1998); C. E. Elger and K. Lehnertz, Eur. J. Neurosci. **10**, 786 (1998).

[7] J. Martinerie, C. Adam, M. L. V. Quyen, M. Baulac, S. Clemenceau, B. Renault, and F. J. Varela, Nature Medicine **4**, 1173 (1998).

[8] S. J. Schiff, Nat. Med. **4**, 1117 (1998).

[9] L. Diambra and C. P. Malta, Phys. Rev. E **59**, 929 (1999).

[10] L. M. Hively, V. A. Protopopescu, and P. C. Gailey, Chaos **10**, 864 (2000).

[11] R. Quian Quiroga, J. Arnhold, K. Lehnertz, and P. Grassberger, Phys. Rev. E **62**, 8380 (2000).

[12] R. G. Andrzejak, K. Lehnertz, F. Mormann, C. Rieke, P. David, and C. E. Elger, Phys. Rev. E **64**, 061907 (2001).

[13] R. Porcher and G. Thomas, Phys. Rev. E **64**, 010902 (2001).

[14] I. Osorio, M. A. Harrison, Y.-C. Lai, and M. Frei, J. Clin. Neurophys. **18**, 269 (2001); Y.-C. Lai, I. Osorio, M. A. Harrison, and M. Frei, Phys. Rev. E **65**, 031921 (2002).

[15] S. M. Hammel, C. K. R. T. Jones, and J. V. Moloney, J. Opt. Soc. Am. B **2**, 552 (1985).

[16] C. Grebogi, E. Ott, and J. A. Yorke, Physica (Amsterdam) **7D**, 181 (1983).

[17] J.-P. Eckmann, S. O. Kamphorst, D. Ruelle, and S. Ciliberto, Phys. Rev. A **34**, 4971 (1986).

[18] F. Takens, in *Dynamical Systems and Turbulence*, Lecture Notes in Mathematics, edited by D. Rand and L. S. Young (Springer-Verlag, Berlin, 1981), p. 366.

[19] T. D. Sauer, J. A. Tempkin, and J. A. Yorke, Phys. Rev. Lett. **81**, 4341 (1998); T. D. Sauer and J. A. Yorke, Phys. Rev. Lett. **83**, 1331 (1999).

[20] E. Ott, *Chaos in Dynamical Systems* (Cambridge University Press, Cambridge, 2002), 2nd ed., Chap. 9.

[21] J. Theiler, Phys. Rev. A **34**, 2427 (1986).

[22] See, for instance, P. Nuñez, in *Neocortical Dynamics and Human EEG Rhythms*, edited by P. Nuñez (Oxford University Press, Oxford, 1995), pp. 3–133.