To Appear in *Phys. Lett. A* LA-UR-93-4471

On the evidence for low-dimensional chaos in an epileptic electroencephalogram

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September 7, 1994

Abstract: A variant of the method of surrogate data is applied to a single time series from an electroencephalogram (EEG) recording of a patient undergoing an epileptic seizure. The time series is a nearly periodic pattern of spike-and-wave complexes. The surrogate data sets are generated by shuffling the the individual spike-and-wave cycles, and correspond to a null hypothesis that there is no deterministic structure in the cycle-to-cycle variability of the original data. Using estimates of autocorrelation, correlation dimension, and Lyapunov exponent as discriminating statistics, the evidence for dynamical correlations between successive spike-and-wave patterns is evaluated both formally and informally.

Contents:

1 Introduction

Chaos provides an alluring explanation for erratic behavior, because it can be exhibited by systems that are both low-dimensional and deterministic. This means that the instantaneous state of the system can be described with only a few variables, and that the dynamical evolution can be understood and even predicted. Especially alluring is the hypothesis that the irregular fluctuations of the human electroencephalogram (EEG) reflect an underlying chaotic determinism. This idea has inspired a considerable effort to find evidence for chaos in the EEG data. The algorithm of Grassberger and Procaccia [1] for estimating correlation dimension has provided the basis for the bulk of these studies [2–15], though a few have augmented these calculations with estimates of the Lyapunov exponent [14–16]. A fuller list of references can be found in the recent review of Pritchard and Duke [17].

This initial surge of interest in chaos as a description of EEG has begun to ebb somewhat, as researchers realize that careful application of these algorithms to EEG data does not always lead to the conclusions of low-dimensional dynamics that were first reported [18]. Indeed, researchers are finding for normal EEG that there is scant evidence for substantial nonlinearity [19, 20] or nontrivial deterministic structure [21]. On the other hand, the spike and wave patterns characteristic of EEG during epileptic seizures continue to be cited as one example where the evidence for chaos is still suggestive. This issue will be addressed by reconsidering a single epileptic EEG time series (see Fig. 1) which had previously been reported to be chaotic. It is, of course, impossible to provide an absolutely definitive resolution of whether or not a given finite data set is chaotic. Statistics can provide some guidance in evaluating the evidence one way or the other, but ultimately, the question involves some judgment.

In this paper, I will present the view that testing against a null hypothesis provides a means of sharpening that judgement. In testing for chaos, in particular, it may not be enough to have the latest state-of-the-art correlation dimension or Lyapunov exponent estimator; one should also have a basis for calibration. In this case, the null hypothesis will be advanced that the that there is no dynamical correlation at all between successive spike-and-wave patterns. This hypothesis will be examined both formally, to determine whether there is adequate evidence in the data to reject the null hypothesis, and informally, to judge the evidence for chaos in the light of this null hypothesis.

It should be emphasized that this is not a test of the null hypothesis that the time series is linear, as is often the case with surrogate data studies. The time series is undoubtedly nonlinear. In fact, Pijn [22, 23] has found convincing evidence for nonlinearity in epileptic EEG, by comparing against a control signal obtained by randomizing the phases of the Fourier transform. It is clear that the dynamics that generates the individual spike-and-wave cycles exhibits deterministic structure; but it is the *cycle-to-cycle variability* that will be studied here.

2 The Data

A number of epileptic EEG data sets were analyzed by Frank *et al.* [15], but only two of these sets yielded evidence for low-dimensional chaos. It is the one set which gave the clearest evidence that was discussed in Ref. [15], and that is the data set shown in Fig. 1. This is data from an electrode at the right occipital site on the scalp (labelled O2 according to the standard 10-20 system). The patient is a 35 year old male undergoing a generalized state of absence myoclonic (*petit mal*) and tonic-clonic (*grand mal*) seizure events. We are grateful to the authors of Ref. [15] for making that data set available. A delay plot of a short but representative segment of the data is shown in Fig. 2. A correlation dimension of $\nu = 5.6 \pm 0.2$ and a Lyapunov exponent of $\lambda = 1.0 \pm 0.2$ were reported [15]. It bears remarking that this Lyapunov exponent indicates interesting dynamics over at least three or four periods.

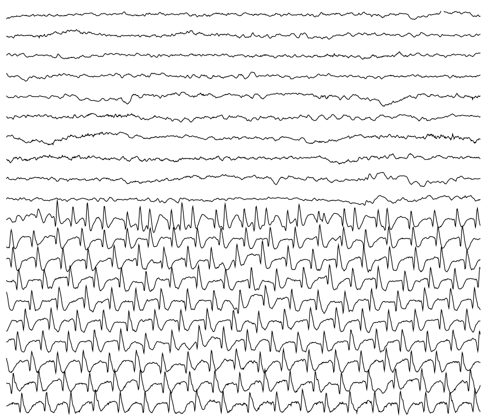

Fig. 1. This shows the full data set, from before the seizure, through onset, and during the seizure. Each horizontal segment is 1000 data points, which at a sample rate of 200 Hz corresponds to 5 seconds. Only the last 9000 points, after the onset of the seizure, are analyzed here. The frequency of the dominant oscillations in this region is about 3.5 Hz, which is about 50 data points.

3 The Null Hypothesis

The null hypothesis is that there is no dynamical correlation at all from one spike-and-wave pattern to another. A variant of the method of surrogate data (see Ref. [24] and citations therein) was used to test this hypothesis. The surrogate data was generated by separating out the individual spike-and-wave patterns and scrambling them. Fig. 3 is a pedagogical figure, showing a segment of the real data, and a surrogate of that segment, composed of shuffled periods from the original. Fig. 4 shows a longer segment.

The method of scrambling the order of the *intra*-cycle patterns while keeping the patterns themselves intact should be applicable to a variety of systems which are nearly periodic. What is also required is that there be a natural place to cut the periods so that they can be pasted together in any order. The epileptic EEG signals have a spike which serves this purpose. Another possibility is a signal which takes some waveform then falls to zero for a finite amount of time before rising again to the next wave. Here, one can always cut where the signal is both zero and flat. The celebrated Wolf sunspot series comes to mind as a possible example [25].

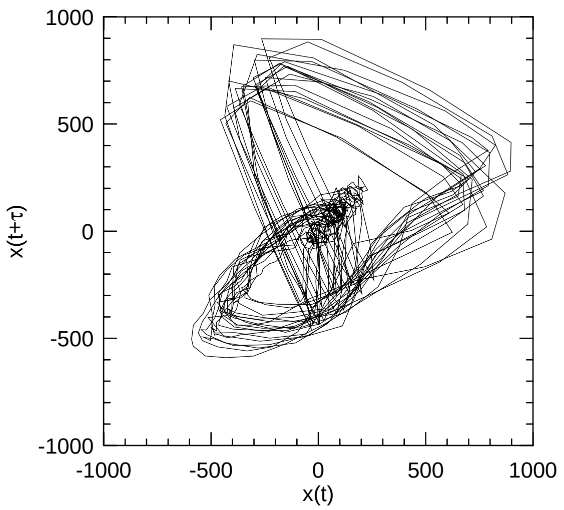

Fig. 2. Time delay plot of one segment (1000 points, or 5 seconds) of the spike-and-wave data. Here the lag time τ is 3 sample times, or about 0.015 sec.

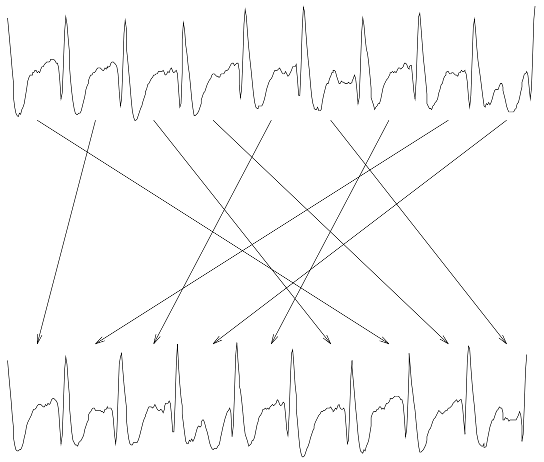

Fig. 3. Surrogates are obtained by shuffling the periods of the original data set. The top time series is (a very short segment of) the original data, and the bottom time series is a typical surrogate of the top segment.

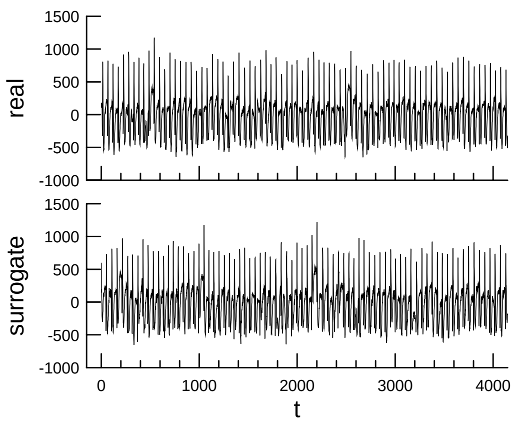

Fig. 4. A longer segment, about 20 sec, of the real and period-shuffled surrogate time series. Visual inspection does not readily distinguish them.

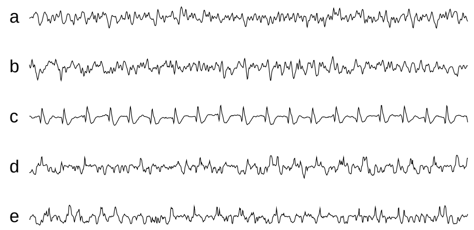

Fig. 5. A segment of the actual data is shown as (c), with two ordinary phase-randomized FT surrogate data sets shown in (a,b), and two amplitude-adjusted FT surrogate data sets shown in (d,e).

This method is contrasted with the more conventional implementation of surrogate data, which is based on randomizing the phases of a Fourier transform. The idea in that case is to create surrogate data which have the same Fourier power spectrum (and therefore the same autocorrelation function) as the original data. The null hypothesis being tested here is that the data arise from a stochastic linear process. (See Ref. [24] for further discussion.) Visual inspection of Fig. 5 indicates that that is not the case; the original data set is noticeably different from the surrogates.

4 Analysis

4.1 Autocorrelation

Based on examination of the autocorrelation curve, the authors in Ref. [15] argue that there is an "average rate of information dissipation" of about $k = 2.0\ \mathrm{sec}^{-1}$ [26]. Fig. 6 shows that the surrogate data (in which all of the relevant information is lost after a single period, about 0.28 sec) exhibit virtually identical autocorrelation curves as the original data. At least for the surrogate data, the "information" that is being dissipated is just the phase information; if the oscillator period were precisely constant (even though the fluctuations in amplitude in one period would be independent of those in another period), then subsequent peaks in the autocorrelation curve would be of equal height. Since there is some variation in the periods, the phase essentially drifts in a random walk fashion, leading to a slow loss of coherence which is manifested in the decreasing peak size of the autocorrelation curve.

Careful examination of the autocorrelation curves of the original and surrogate data sets shows that the peak heights of the original data appear to be decreasing slightly more rapidly than those of the surrogates; the effect is noticeable by the seventh peak. To test whether this effect was significant, thirty-nine surrogates were generated and the autocorrelation $A(\tau)$ was computed for each data set at $\tau = 375$ (this corresponds to about 1.9 sec). The value of $A(375)$ ranged from 0.208 to 0.389 for the surrogates, and was 0.197 for the original data. Since the probability of being on one extremum or another of a set of forty numbers is $2/40 = 0.05$, we can reject the null hypothesis at the 5% level.

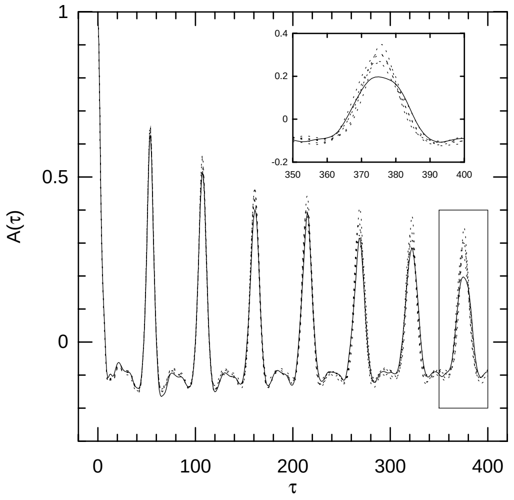

Fig. 6. Autocorrelation for the original and period-shuffled surrogate time series. The delay time τ is in units of sample time; so the temporal range on this figure is two seconds. Even though subsequent spike-and-wave periods are independent in the surrogate data set, there is still significant autocorrelation over several periods. The original and surrogate time series are nearly indistinguishable on this plot, but the inset shows that the difference, though not substantial, is significant. (Dotted lines represent the surrogate data, while the solid line indicates the original.)

4.2 Correlation dimension

The algorithm used for estimating dimension was similar to that of Frank *et al.* [15], but no attempt was made to duplicate it in every detail. For instance, the data was not converted to SVD coordinates, since this is merely a rotation in state space, and provides no important difference from the point of view of dimension estimation. (However, for other purposes, such as reducing the dimension of an embedding for the purpose of nonlinear forecasts, the SVD filter can make a big difference.) The analyzed data set included 180 waveform cycles (about 9000 points) taken well after the onset of the seizure. The embedding dimension varied from $m = 4$ to $m = 9$, and the delay time was chosen to be the first zero of the autocorrelation; that is, $\tau = 8$ sample times [27]. The correlation integrals $C(N, r)$ were computed for $r = 0.5, 1.5, 2.5, \ldots, 199.5$, avoiding pairs of points closer together in time than $W = 200$ sample times [28]. The slopes were estimated by a simple chord method [29], though similar experiments with Takens' estimator [30] gave essentially the same results.

Fig. 7 shows the correlation integrals and slopes estimated for the original data and for five surrogate data sets. The slopes do not converge with increasing embedding dimension as neatly as they did in Ref. [15], and although there is a detectable difference between the curves for the surrogates and the actual data, this difference occurs only at large r and large m.

A formal test for significance was not carried out at these large r and large m values, since the null hypothesis has already been formally rejected. The difference may well be significant at these values, but (in the judgement of this author) it is not large enough to imply that the data are low-dimensional.

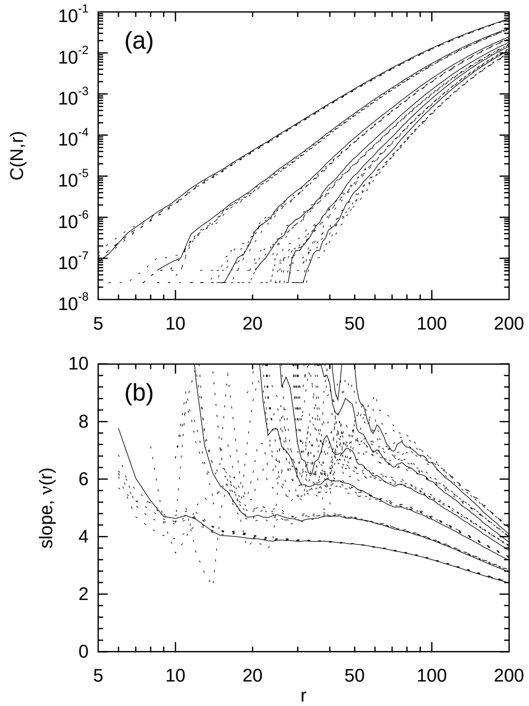

Fig. 7. **(a)** Correlation integral and **(b)** log-log slope of correlation integral (estimated dimension), for the original time series (solid) and for five surrogate data sets (dotted).

4.3 Lyapunov exponent

As well as the computed value of the correlation dimension, Frank *et al.* [15] base their "definitive indication" of chaos on a positive estimate of the Lyapunov exponent. They report $\lambda \approx 1.0$ sec^{-1} based on a fairly elaborate modification of the Wolf *et al.* algorithm [31]. This approach requires determining an evolution time over which separation of nearby trajectories remains relatively small. After such an evolution time, a replacement must be found as the new nearby trajectory. Interestingly, the average evolution time was reported to be 0.3 sec, which corresponds to just about one period.

Algorithms based on direct estimates of the Jacobian do not share this difficulty [32–34]. When one such algorithm [35] was applied to the data set of Frank *et al.* [15], only negative Lyapunov exponents could be obtained. Furthermore, comparison of these Lyapunov exponents with the values computed for the surrogates (see Fig. 8) did not show a substantial difference. For this reason, one should not interpret these estimates as true Lyapunov exponents.

As with the dimension estimates, these numbers will depend on the details of the embedding, and other input parameters of the program. Again, the reader should be reminded that this algorithm is not the same one that was used by Frank *et al.* [15]; it cannot be construed as a contradiction of those results. What is relevant about these computations is that they illustrate how comparison with the surrogates affects their interpretation.

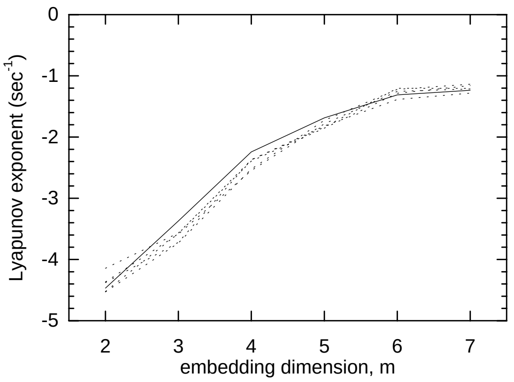

Fig. 8. Estimated Lyapunov exponent for different embeddings. The solid line is for the original data, and dotted lines are for the five surrogates. In this case all estimates of the Lyapunov exponents were negative; those for the original data are only slightly less negative at intermediate embedding dimensions.

4.4 Inter-spike variation

If there is dynamics on a time scale longer than the spike firing rate, then this should be manifested in a time series in which each time step corresponds to a single period, and the value at that time is some measure of the signal over that period. In the spirit of the dripping faucet [36], for example, one might consider a time series of inter-spike intervals. No evidence for deterministic structure was found in this time series, though this may not be the best inter-spike time series to use, since the variation in the inter-spike intervals is quite small. A faster sampling time (500 Hz is not uncommon) would improve the dynamic range in the variation of inter-spike intervals, and this might permit the use of statistics originally developed for analysis of single neuron spike trains [37–39].

5 Conclusion

A variant of the method of surrogate data was introduced and applied to an epileptic EEG time series. The method is based on shuffling blocks of data instead of individual data points as, for instance, was done in Ref. [40]. This randomization scheme should also be applicable to other nearly periodic data sets where the periods are easily shuffled.

The null hypothesis suggests a description of the dynamics as a nonlinear oscillator, with "noise" of some kind, either observational or dynamical (or both), which is uncorrelated over the timescale of a single oscillation. This description cannot be strictly valid, however, because it was possible to formally reject the null hypothesis with a confidence level of 95% by looking at a specific value of the autocorrelation. On the other hand, it may be regarded as a useful approximation, since the measured features of the original data (autocorrelation, and estimated dimension and Lyapunov exponents) were closely matched by the surrogate data.

For the epileptic EEG data, it was found that the estimated correlation dimension and Lyapunov exponent was essentially the same for the original and surrogate data sets. There was no qualitative difference in the scaling (with r) or saturation (with m) of these statistics, which suggests that one should be wary of interpreting the dimension as a number of active degrees of freedom, or the Lyapunov exponent as a rate of divergence of nearby trajectories in a deterministic phase space.

The analysis presented here does not indicate whether "chaos" occurs on a time scale smaller than the spike-and-wave period. However, one would expect such chaos to have a much larger Lyapunov exponent than was reported in Ref. [15]. A Lyapunov time on the order of one second is suspect, since it implies dynamical correlations over several periods.

Finally, it should be remarked that this analysis is limited to a few statistical techniques (autocorrelation, correlation integral and correlation dimension, and a particular algorithm for estimating Lyapunov exponent) and a single scalar time series. It is certainly possible that a more efficacious analysis, or another epileptic EEG time series (perhaps with more spike and wave periods, or with multiple channels), will provide the evidence for interesting dynamical structure that was not found here.

Acknowledgements

Although this Letter criticizes some of the conclusions drawn in the article by Frank *et al.*, I have found the authors of that work to be extremely cooperative. I am particularly grateful to Turab Lookman, for generously supplying the data set, and for discussing details of their algorithms. This work was supported by a grant from the National Institute of Mental Health (1-R01-MH47184) and performed under the auspices of the Department of Energy.

References

1. P. Grassberger and I. Procaccia, "Characterization of strange attractors." *Phys. Rev. Lett.* **50**, 346–349 (1983).
2. A. Babloyantz, C. Nicolis, and M. Salazar, "Strange attractors in the human cortex." In *Temporal Disorder in Human Oscillatory Systems*, L. Rensing, U. an der Heiden, and M. Mackey, eds. (Springer Verlag, New York, 1985), pp. 48–56.
3. A. Babloyantz and A. Destexhe, "The Creutzfeld-Jakob disease in the hierarchy of chaotic attractors." In *From Chemical to Biological Organization*, M. Markus, S. C. Müller, and G. Nicolis, eds. (Springer-Verlag, Berlin, 1988), pp. 307–316.
4. A. Destexhe, J. A. Sepulchre, and A. Babloyantz, "A comparative study of the experimental quantification of deterministic chaos." *Phys. Lett. A* **132**, 101–106 (1988).
5. I. Dvořàk and J. Šiška, "On some problems encountered in the estimation of the correlation dimension of the EEG." *Phys. Lett. A* **118**, 63–66 (1986).
6. G. Mayer-Kress and J. Holzfuss, "Analysis of the human electroencephalogram with methods from nonlinear dynamics." In *Temporal Disorder in Human Oscialatory Systems*, L. Rensing, U. an der Heiden, and M. C. Mackey, eds. (Springer-Verlag, New York, 1987), pp. 57–68.
7. G. Mayer-Kress and S. Layne, "Dimensionality of the human electrocephalogram." *Ann. N. Y. Acad. Sci.* **504**, 62–87 (1987).
8. G. Mayer-Kress, F. Yates, L. Benton, M. Keidel, W. Torsch, S. Pöppl, and K. Geist, "Dimensional analysis of nonlinear oscillations in brain, heart and muscle." *Math. Biosci.* **90**, 155–182 (1988).
9. P. E. Rapp, I. D. Zimmerman, A. M. Albano, G. C. deGuzman, N. N. Greenbaum, and T. R. Bashore, "Experimental studies of chaotic neural behavior: cellular activity and electroencephalographic signals." In *Nonlinear Oscillations in Biology and Chemistry*, H. G. Othmer, ed. (Springer-Verlag, Berlin, 1986), pp. 175–205.
10. P. E. Rapp, "Oscillations and chaos in cellular metabolism and physiological systems." In *Chaos*, A. V. Holden, ed. (Princeton University Press, 1986), pp. 179–208.
11. A. M. Albano, L. Smilowitz, P. E. Rapp, G. C. deGuzman, and T. R. Bashore, "Dimension calculations in a minimal embedding space: low dimensional attractors for human electroencephalograms." In *Physics of phase space*, Y. S. Kim and W. W. Zachary, eds. (Springer-Verlag, New York, 1987), pp. 15–17.
12. P. E. Rapp, T. R. Bashore, J. M. Martinerie, A. M. Albano, I. D. Zimmerman, and A. I. Mees, "Dynamics of brain electrical activity." *Brain Topography* **2**, 99–118 (1989).
13. N. Xu and J. Xu, "The fractal dimension of EEG as a physical measure of conscious human brain activities." *Bull. Math. Bio.* **50**, 559–565 (1988).
14. A. Babloyantz and A. Destexhe, "Low-dimensional chaos in an instance of epilepsy." *Proc. Natl. Acad. Sci. USA* **83**, 3513–3517 (1986).
15. G. W. Frank, T. Lookman, M. A. H. Nerenberg, C. Essex, J. Lemieux, and W. Blume, "Chaotic time series analysis of epileptic seizures." *Physica D* **46**, 427–438 (1990).
16. D. Gallez and A. Babloyantz, "Lyapunov exponents for nonuniform attractors." *Phys. Lett. A* **161**, 247–254 (1991).
17. W. S. Pritchard and D. W. Duke, "Measuring chaos in the brain: a tutorial review of nonlinear dynamical EEG analysis." *Int. J. Neuroscience* **67**, 31–80 (1992).
18. P. E. Rapp, "Chaos in the neurosciences: cautionary tales from the frontier." *Biologist* **40**, 89–94 (1992).
19. M. Paluš, "Testing for nonlinearity in the EEG." In *Nonlinear Dynamical Analysis of the EEG*, B. H. Jansen and M. E. Brandt, eds. (World Scientific, Singapore, 1993), pp. 100–115.
20. J. Theiler and P. Rapp. Manuscript in preparation.
21. L. Glass, D. T. Kaplan, and J. Lewis, "Tests for deterministic dynamics in real and model neural networks." In *Proceedings of the Second Annual Conference on EEG and Nonlinear Dynamics*, B. H. Jansen and M. E. Brandt, eds. (World Scientific, Singapore, 1993), pp. 233–249.
22. J. P. M. Pijn, *Quantitative evaluation of EEG signals in epilepsy: nonlinear associations, time delays and nonlinear dynamics.* PhD thesis, Universiteit van Amsterdam Amsterdam, (1990).
23. J. P. Pijn, J. V. Neerven, A. Noest, and F. H. Lopes da Silva, "Chaos or noise in EEG signals: dependence on state and brain site." *Electroencephalography and clinical Neurophysiology* **79**, 371–381 (1991).
24. J. Theiler, S. Eubank, A. Longtin, B. Galdrikian, and J. D. Farmer, "Testing for nonlinearity in time series: the method of surrogate data." *Physica D* **58**, 77–94 (1992).
25. G. U. Yule, "On a method of investigating periodicities in disturbed series with special reference to Wolfer's sunspot numbers." *Philos. Trans. R. Soc. London A* **226**, 267–298 (1927).
26. Actually, the autocorrelation curve plotted in Fig. 2 of Ref. [15] is incorrect, as it is based on the full time series, including the part before the seizure (T. Lookman, personal communication; assurances have been made that a similar error was not made for the dimension calculations); a fit to the correct curve in Fig. 6 would give something more like $k = 1.0$ sec^{-1}, though it should be noted that the fit to an exponential is not particularly good.
27. Experiments with $\tau = 16$, 24, and 32 yielded similar

results in that differences in $C(N, r)$ between the original and surrogates were never very large. But where the biggest differences for $\tau = 8$ are large m, the biggest differences occur at smaller embeddings for $\tau = 16$ and 24. At $\tau = 32$, no significant differences were seen at all.
28. J. Theiler, "Spurious dimension from correlation algorithms applied to limited time series data." *Phys. Rev. A* **34**, 2427–2432 (1986).
29. J. Theiler and T. Lookman, "Statistical error in a chord estimator of correlation dimension: the 'rule of five'." *Int. J. Bif. Chaos* **3**, 765–771 (1993).
30. F. Takens, "On the numerical determination of the dimension of an attractor." In *Dynamical Systems and Bifurcations, Groningen, 1984*, B. L. J. Braaksma, H. W. Broer, and F. Takens, eds. vol. 1125 of *Lecture Notes in Mathematics*, (Springer-Verlag, Berlin, 1985), pp. 99–106.
31. A. Wolf, J. B. Swift, H. L. Swinney, and J. A. Vastano, "Determining Lyapunov exponents from a time series." *Physica D* **16**, 285 (1985).
32. J.-P. Eckmann and D. Ruelle, "Ergodic theory of chaos and strange attractors." *Rev. Mod. Phys.* **57**, 617–656 (1985).
33. M. Sano and Y. Sawada, "Measurement of the Lyapunov spectrum from chaotic time series." *Phys. Rev. Lett.* **55**, 1082 (1985).
34. J.-P. Eckmann, S. O. Kamphorst, D. Ruelle, and S. Ciliberto, "Liapunov exponents from a time series." *Phys. Rev. A* **34**, 4971–4979 (1986).
35. The program that was used is called "eck;" it is an implementation of the algorithm described by Eckmann *et al.* [32, 34] and written by Eric Kostelich. It is available by anonymous ftp from `saddle.la.asu.edu` in the file `pub/lyapunov.tar.Z`.
36. R. S. Shaw, *The Dripping Faucet as a Model Dynamical System.* (Aerial Press, Santa Cruz, CA 95060, 1984).
37. A. Longtin, "Nonlinear forecasting of spike trains from sensory neurons." *Int. J. Bif. Chaos* **3**, 651–661 (1993).
38. P. E. Rapp, G. Goldberg, A. M. Albano, M. B. Janicki, D. Murphy, E. Niemeyer, and M. A. Jiménez-Montaño, "Using coarse-grained measures to characterize electromyographic signals." *Int. J. Bifurcation Chaos* **3**, 525–541 (1993).
39. P. E. Rapp, I. D. Zimmerman, E. P. Vining, N. Cohen, A. M. Albano, and M. A. Jiménez-Montaño, "The algorithmic complexity of neural spike trains increases during focal seizures." *J. Neurosci.* **14**, 4731–4739 (1994).
40. J. A. Scheinkman and B. LeBaron, "Nonlinear dynamics and stock returns." *J. Business* **62**, 311–338 (1989).