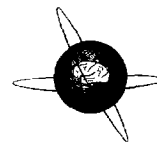




ELSEVIER

Electroencephalography and clinical Neurophysiology 99 (1996) 405–411



The evolution of complexity in human brain development: an EEG study¹

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Accepted for publication: 27 April 1996

Abstract

Analysis of the EEG as a signal from a deterministic non-linear system should, in principle, allow insights into the complexity of underlying brain activity. We examined the capability of this method to analyse the marked changes in brain activity during normal brain development. Resting EEGs of 54 healthy children (newborns to 14 years old) and of 12 normal adults were recorded digitally. The following parameters were calculated: correlation dimension, a measure of the complexity of the underlying system, and the first Lyapunov coefficient, indicating the system's 'unpredictability'. Analysis of variance (ANOVA) was performed with probands grouped by age. The subgroups of children older than 1 year was further examined by regression analysis. In all analysed epochs, Lyapunov coefficients were significantly positive ($P < 0.0001$, t test). The presence of non-linear dynamics was asserted statistically in 64–76% of examined epochs. A highly significant increase in correlation dimension with age was found in all examined leads ($P < 0.0001$, ANOVA). In all age groups, marked differences in correlation dimension in different brain regions became evident ($P < 0.01$ – 0.0001 , ANOVA). Evidence for the presence of non-linearity can be found even in newborns. Brain maturation was reflected in a marked and highly significant increase in correlation dimension (complexity). Our work indicates that non-linear dynamics analysis is suitable for measuring complexity of brain activity during maturation and provides age-dependent normal values as a basis for further study.

Keywords: Electroencephalography; Non-linear dynamics; Chaos theory; Lyapunov coefficient; Brain development

1. Introduction

Since a first report by Babloyantz and Salazar (1985), the analysis of the human EEG using methods from chaos theory and non-linear dynamics has emerged as an important advance in understanding the collective behaviour of cortical neurones. The presence of deterministic non-linear or chaotic behaviour in various physiological (e.g. sleep; Babloyantz and Salazar, 1985) and pathological states (e.g. epilepsy; Frank et al., 1992) has been postulated, but also disputed (Theiler, 1994). Since parameters characterising non-linear dynamic behaviour, such as correlation dimension or Lyapunov exponents, are fundamentally independent from parameters derived from spectral analysis (e.g. EEG power spectra), the information con-

tained in these measures represents a new line of study that is complementary to 'classical' EEG analysis.

The concept of the phase space is central to the analysis of non-linear dynamics (Peitgen et al., 1992; Pritchard and Duke, 1992). In a hypothetical system governed by n variables, the phase space is n -dimensional. Each state of the system corresponds to a point in phase space whose n coordinates are the values assumed by the governing variables for this specific state. If the system is observed for a period of time, the sequence of points in phase space forms a trajectory. This trajectory fills a subspace of the phase space called the system's attractor. The dimension of this attractor can be estimated. The dimension value, which will usually be much lower than the dimension of the phase space, is an estimate of the number of variables minimally needed to describe the system's behaviour and thus, a measure of its complexity. It will usually be non-integer in a system displaying non-linear chaotic dynamics (the attractor is a fractal).

In reality, the number n of governing variables and thus, the dimension of the phase space, are unknown. However,

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¹ Parts of the data have been presented at the 40th Jahrestagung der Deutschen Gesellschaft für klinische Neurophysiologie, in Bielefeld, Germany, on October 12th, 1995.

it is possible, by a method described by Takens (1981) using time-phase delays, to construct from a single time series, corresponding to the readout of a single EEG electrode, trajectories in 'embedding' spaces of increasing dimension.

In theory, attempting to construct the attractor also allows for detection of random behaviour of a system, since in this case the trajectory should fill the phase space and the method for dimension estimation does not converge to a finite number. However, it has been shown that 'filtered' variants of random systems, generating so-called brown noise, may nevertheless yield attractors with finite and non-integer dimension (Osborne and Provenzale, 1989). Thus, detection of a finite attractor dimension is in itself not sufficient to deduce a system's non-linear or chaotic behaviour. For this reason, methods have been devised to allow for statistical testing for non-linear behaviour. In the present study, we employed a method, further described below, that constructs random time series with the same power spectrum as the EEG examined (Theiler et al., 1992a).

For another descriptor of non-linear behaviour, Lyapunov exponents were calculated. This measure is defined as follows: two points close to one another in phase space are chosen and their evolution over time determined. In a chaotic system, the two trajectories will diverge rapidly, reflecting the sensitive dependence on initial conditions. The Lyapunov exponents are the mean exponential divergences of such trajectories calculated for each of the n dimensions of the phase space. They are ordered by descending size. If the first (biggest) Lyapunov coefficient is positive, the system exhibits chaotic behaviour (Peitgen et al., 1992).

The development of the healthy human brain leads, by synaptic sprouting and pruning and by myelination, to dramatic changes in inter- and intrahemispheric connectivity and in the functioning of the cortical neural network (Yakovlev and Lecours, 1967). Insofar as the intricacy of the electrical activity of the cortex is reflected in the scalp EEG, measures from non-linear dynamics, especially the attractor dimension, should, in principle, allow an insight into the evolution of complexity of underlying brain activity. Therefore, in this pilot study, we analysed the resting EEG of a group of healthy children of various ages and of adults to ascertain whether age-dependent changes can be found in non-linear EEG dynamics, measured by dimensional complexity and the first Lyapunov coefficient.

2. Methods

All children were examined by an experienced neuro-paediatrician and judged to be neurologically normal and developed appropriate for age. Newborns were born after uneventful labour. Adults were examined by a neurologist, had a normal neurological exam and mental status. A history of mental or neurological disease was not present in

any subject. No subject took regular medication or had received drugs prior to the EEG recording. Subject statistics are summarised in Table 1.

For the EEG recording, electrodes were placed in accordance with the 10–20 system. Newborns received a subset of all electrodes consisting of FP1, FP2, C3, C4, O1, O2, T3, T4. For comparability, only the readouts from these electrodes were evaluated for all subjects although all other recordings were made with a full array of 19 electrodes. Newborns and children less than 3 years old were recorded in a state of relaxed wakefulness as determined by behaviour monitoring by the recording technician and by polygraphy. Older children and adults were comfortably seated in a shielded room, asked to relax and the awake EEG recorded with alternating periods of opened and closed eyes. The EEG was recorded versus a reference at FPz with a bandpass filter of 0.16–70 Hz, using a 12 bit A/D-converting system (Walter Graphtec), with a sampling interval of 6 ms/s per channel. Data were written on hard disk. Raw EEG tracings were evaluated by an experienced physician and judged to be appropriate for age and not indicative of pathology. Three continuous 20 s epochs with eyes closed that were free of movement artifacts were selected. For newborns, selected epochs showed EEG either of the *activité moyenne* (low voltage irregular) or mixed pattern (Fisch, 1991). Ocular movement artefacts were suppressed by an autoregressive method as described in Krieger et al. (1995). Data were recomputed versus a central (Cz) reference and transferred to a SUN SPARC-station 20 minicomputer for further evaluation.

Vectors in phase space were computed by a time-delay method as described by Takens (1981). For calculating the time delay τ , the first zero crossing or the first local minimum of the autocorrelation function was used, whichever occurred earlier. Time delays were in the range of 12–60 ms.

For the calculation of the correlation dimension, we used a modified correlation integral algorithm (different from that first described by Grassberger and Procaccia, 1983) as found in Wackermann et al. (1993). Briefly, the correlation dimension was calculated as the mean of 200 analysis runs. In each run, 30 000 data point pairs x_i, y_i were randomly selected from the epoch. To correct for autocorrelation, selected point pairs were required to be at least 60 ms apart. The value

$$D^2(r) = \sum_{i=1}^{30000} \theta(r - \|x_i - y_i\|) \quad (1)$$

was then calculated for a range of r , where $\theta(x)$ is the heavyside function, defined as 1 if $x > 0$ and 0 if $x \leq 0$, and $\| \cdot \|$ denotes Euclidean norm. Thus, $D^2(r)$ counts the number of point pairs whose distance is smaller than r . Since, by the definition of the correlation dimension, the relation $D^2(r) \propto r^c$ holds for small r , where c is the correlation dimension, a plot of $\ln(D^2)$ versus $\ln(r)$ yields an approximately linear region of constant slope

Table 1

Descriptive data of proband sample				
	Mean (range)	SD		<i>n</i>
Newborns	39.6 (36–45)	3.0	(gestational week)	19
Age <1 year	3.9 (2.5–6)	1.3	(months)	14
Age >1 year	8.4 (1–14)	5.5	(years)	21
Adults	35.2 (26–61)	9.5	(years)	12

c. The linear region was numerically determined as the subset of no less than 60 plot points, with $r < 0.7$ of maximal distance, that exhibits the highest linear correlation (at least $r = 0.97$). The correlation dimension is estimated by a least-squares-fit of that linear region. This approach avoids the problem of selecting appropriate reference points on the attractor present in the original algorithm. The first Lyapunov coefficient was calculated by an algorithm by Frank et al. (1992) who modified the procedure of Wolf et al. (1985). An arbitrary data point is chosen. In each step another data point is sought whose distance to the reference point is less than a distance SCALMAX up to which dynamics are assumed to be linear but bigger than a distance SCALMIN below which noise is assumed to perturb data. The trajectories of the data points are followed for a time span EVOLV and the logarithm of the ratio of the distance of the evolved points to the original points distance calculated. A replacement point is then sought that is associated with minimum orientation change relative to the distance vector, and the procedure repeated until the data is exhausted. The sum of the logarithms of the distances, divided by the whole time elapsed, is the estimate of the first Lyapunov exponent. Algorithms of this kind depend heavily on the choice of the parameters, printed in capitals above. Estimates of Lyapunov exponents were found to differ up to 6-fold if parameters were varied. The values used in this analysis were: SCALMAX, 10% of maximum distance; SCALMIN, 160 μ V; and EVOLV, 0.48 s (2.08 Hz).

EEG data were statistically tested for non-linearity by using the method of surrogate data as described by Theiler et al. (1992a) and Prichard and Theiler (1994). The Fourier transform of the evaluated EEG epochs was calculated. From this, surrogate time series were calculated by randomising the phases of the complex amplitude at each frequency, accomplished by multiplying each complex amplitude by $e^{i\varphi}$, where φ is independently chosen for each frequency from the interval $[0, 2\pi]$, symmetrising phases by observing $\varphi(f) = -\varphi(-f)$, and taking the inverse Fourier transform. By construction, these time series have the same power spectrum as the original data (and thus the same mean frequency etc.), but non-linear relationships have been destroyed by randomisation. The attractor dimension is then calculated for the surrogate datasets, as described above. The results of 80 surrogate time series are compared to those obtained with the original EEG by independent t test. If the EEG has non-linear

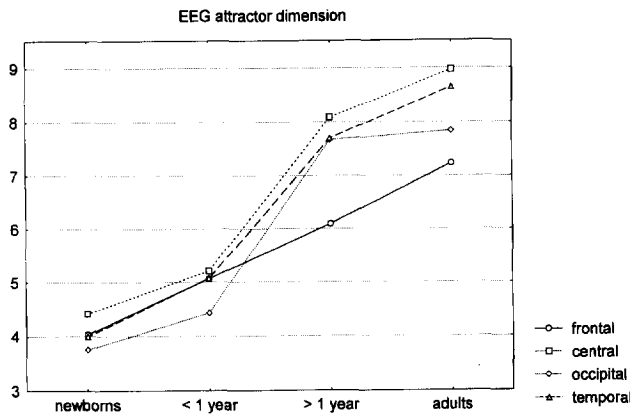


Fig. 1. Age-group dependency of the EEG attractor dimension in the 4 examined brain regions (averages from left and right side).

properties, its attractor dimension should differ significantly from those of the surrogate (randomised) datasets. This method, thus, allows for inferential statistical testing of a time series' non-linearity at the price of increasing computation time by a factor of >80 .

Results were examined statistically using analysis of variance (ANOVA) with age and location as factors. In addition, the subgroup of children older than 1 year was subjected to regression analysis with age as independent variable.

3. Results

The results of the dimensional analysis are shown in Fig. 1 and summarised in Tables 2 and 3. Since no significant left-right differences were found in this study (t test), averaged values both for attractor dimension and Lyapunov coefficients are reported for simplicity and designated frontal (average of FP1 and FP2), central (average of C3 and C4), occipital (average of O1 and O2) and temporal (average of T3 and T4), respectively.

A marked increase in dimensionality with age group was found in all examined leads as shown in Fig. 1. Group means by region are reported in Table 2. Statistical ANOVA showed a highly significant age effect ($P < 0.0001$) for each examined region and overall. As shown in Table 3, the age effect predicted more than 95% of the variance of the attractor dimension. Within each age group, the dimensions measured at the different electrodes were not uniform but differed significantly by region

Table 2

Mean EEG attractor dimension versus age group				
	Frontal	Central	Occipital	Temporal
Newborns	4.0	4.4	3.8	4.0
Age <1 year	5.1	5.2	4.4	5.1
Age >1 year	6.1	8.1	7.7	7.7
Adults	7.2	9.0	7.8	8.7

Table 3

ANOVA results of EEG attractor dimension versus age group (Rao $R = 13.79$; $P < 0.0001$)

	Mean sq. effect	Mean sq. error	P -level
Frontal	29.02	1.26	0.0001
Central	77.31	0.90	0.0001
Occipital	76.75	1.26	0.0001
Temporal	76.69	1.20	0.0001

examined (ANOVA with location as factor: $P < 0.01$ – 0.0001 , details not shown).

Changes of the first Lyapunov coefficient with age are shown in Fig. 2 and Tables 4 and 5. The mean Lyapunov coefficients were highly significantly greater than 0 ($P < 0.0001$, one-tailed t test) at all age groups. Over the frontal region, the coefficient dropped significantly with increasing age ($P < 0.003$, Table 3). The other regions showed no change between age groups ($P > 0.3$ – 0.5). Overall, ANOVA shows a weak age effect on the first Lyapunov coefficient ($P < 0.05$) that is entirely due to the frontal region.

Regression analysis of the subgroup of children older than 1 year showed a significantly positive increase of attractor dimension with age over the central ($r = 0.73$, $P < 0.0001$) and occipital ($r = 0.70$, $P < 0.0002$) regions. The increase at the frontal and temporal regions failed to reach significance ($P > 0.1$). In this subgroup, no age-dependency of Lyapunov coefficients was found in any region ($r < 0.01$ – 0.05 , $P > 0.6$).

Table 6 shows the results of the surrogate data analysis. At a significance level of $P = 0.05$, non-linearity could be demonstrated by inferential statistical testing in between 63.6 and 75.8% of examined EEG epochs. This ratio was about the same in all age groups. When epochs in which non-linearity could be shown were compared with those that did not differ significantly from surrogate data in this respect, no significant differences in attractor dimension and Lyapunov coefficients were found (t test).

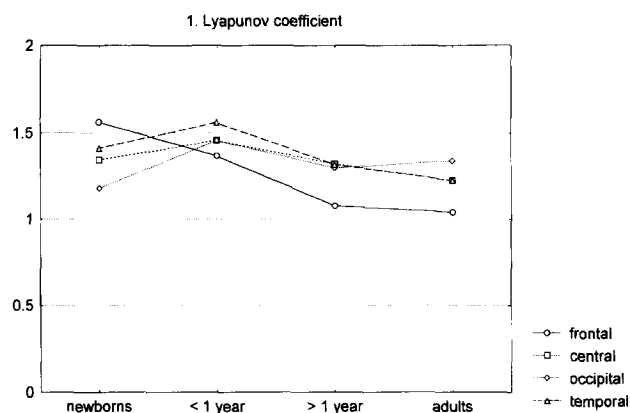


Fig. 2. Age-group dependency of the first (largest) Lyapunov coefficient in the 4 examined brain regions (averages from left and right side).

Table 4

Mean first Lyapunov exponent versus age group

	Frontal	Central	Occipital	Temporal
Newborns	1.56	1.34	1.18	1.41
Age <1 year	1.37	1.46	1.46	1.56
Age >1 year	1.08	1.32	1.30	1.32
Adults	1.04	1.22	1.34	1.22

4. Discussion

In this pilot study, we have shown that the marked increase in complexity that is found in human brain development is reflected by parameters of non-linear EEG analysis. Before the implications of this result can be discussed, it will be necessary, in view of the methodological diversity present in this field of study at this time, to address several technical issues.

As pointed out in Section 1, the reconstruction of a system's attractor in phase space should in principle allow a distinction between random, or noisy, behaviour on the one hand and deterministic behaviour on the other (Elbert et al., 1994). Deterministic behaviour, again, may be according to linear or non-linear laws, and non-linear systems may or may not behave chaotically. While it is not possible to discuss here the various approaches devised to distinguish between these 4 options (noise, linear, non-linear non-chaotic, non-linear chaotic), and their pitfalls (Theiler et al., 1992a), we want to draw attention to two issues that are of relevance to the previous discussion. Firstly, if attractor dimension is to be interpreted as a measure of a system's complexity, it is not necessary to assume that the system behaves chaotically; dimension is also a valid descriptor of complexity if a system follows linear laws, or behaves in a non-linear, but not chaotic, fashion. If the examined time series, however, represents a form of filtered noise, dimension is a misleading parameter as the usually high numerical value derived in this situation will be taken to reflect high complexity, whereas in reality it means noisy behaviour (Osborne and Provenzale, 1989). Secondly, if the computation-intensive procedure of non-linear EEG analysis shall be justified, it is desirable that the system under study is non-linear (chaotic or not), for if it behaves linearly, no new information will be obtained in addition to that accessible by classical EEG

Table 5

ANOVA results of first Lyapunov exponent versus age group (Rao $R = 1.83$; $P < 0.0475$)

	Mean sq. effect	Mean sq. error	P -level
Frontal	1.01	0.20	0.003
Central	0.11	0.17	0.582
Occipital	0.18	0.24	0.510
Temporal	0.26	0.22	0.313

Table 6
Results of surrogate data analysis

	% non-linear	<i>n</i> non-linear
Frontal left	75.8	50
Frontal right	63.6	42
Central left	66.7	44
Central right	71.2	47
Occipital left	71.2	47
Occipital right	69.7	46
Temporal left	74.2	49
Temporal right	71.2	47

Table shows percentage and absolute *n* of statistically significant ($P < 0.05$, *t* test) non-linear behaviour.

analysis, which is based on the examination of linear relationships within the data, e.g. those derived from the Fourier transform such as power spectra etc.

In our data, we could assert by inferential statistical testing, using a surrogate data method, that in about two-thirds to three-quarters of the examined epochs, non-linear behaviour was present. For the larger part of our data we could therefore positively show that they are: (1) not filtered noise, so that the attractor's dimension can be expected to be a measure of the systems complexity, and (2) not linear, so that, by non-linear EEG analysis, additional information is obtained that is not accessible by, and not dependent on, the power spectrum of the epoch under study. Our data should not be interpreted to infer that in the remaining one-third to one-quarter of EEG epochs, non-linear or chaotic behaviour was absent. The results only show that such behaviour could not be positively demonstrated. Indeed, it has been shown, for the statistical algorithm used in this report, that an increase in the complexity of a chaotic time series leads to a decrease in the ability to distinguish it from linearity, especially if only a limited number of data points is available to study (Theiler et al., 1992b). Depending on how complex the system behaves and how limited the data is, it is therefore to be expected that non-linearity is not assertable by statistical inference in a proportion of cases. The observation that in our data the attractor dimensions and Lyapunov coefficients were not significantly different between the two groups leads us to conjecture that the EEG dynamics are non-linear in these cases also.

In the calculation of Lyapunov exponents, the choice of proper parameters was found to be essential. Depending on their selection, absolute numerical values were found to vary widely. This is also reported in the literature (Frank et al., 1992; Fell et al., 1993). However, it can be stated that the Lyapunov exponents were almost always positive. Thus, the qualitative value of the method did not seem to be influenced as much by methodological issues. However, the wide variability of absolute numerical values must be borne in mind when comparing results from different studies. A problem common to all methods in non-linear dynamics is the large number of data points required

to reliably construct the attractors, resulting in long epoch times. Since it is probable that the brain state during a time of (as used in this study) 20 s is not constant, the attractor measured might actually represent a superimposition of attractors corresponding to several brain states sequentially assumed by the subject during the epoch. While this does not invalidate measures from chaotic dynamics, it will certainly contribute to inter- and intraexperimental variability.

With these qualifications in mind, our finding of a marked and highly significant increase in dimensionality with subject age can be taken to show an increase in complexity of the brain's electrical activity. We are not aware of other studies examining brain development using methods of non-linear EEG analysis. However, our results fit well with previous studies showing that diminished dimensions are found in diseases or brain states that can be assumed to be associated with diminished complexity of brain activity such as sleep (Babloyantz and Salazar, 1985), epilepsy (Babloyantz and Destexhe, 1986) or schizophrenic negative syndrome (Meyer-Lindenberg, submitted). The study of Lutzenberger et al. (1992), demonstrating a positive correlation of intelligence with dimension, could also be interpreted in a similar manner. Seen in this context, our results point to the clinical utility of the non-linear dimensional measure as an indicator of the overall complexity of brain activity. A word of caution is needed, however. If a system of high complexity, such as the brain, is described by a single measure, such as dimension (or in a mathematical sense, if one projects the *n*-dimensional phase space onto a one-dimensional), it is obvious that many brain states with very different functionality will have similar correlation dimension (Wackermann et al., 1993). Thus, it cannot be expected offhand that ordering all brain states according to their dimension will also result in a meaningful hierarchy of other psychophysiological variables of interest.

Since age was such a strong predictor of dimensional complexity (explaining more than 95% of the variance) in our group of developmentally and neurologically normal subjects, it could be hoped that dimensional complexity might be a worthwhile parameter against which delays and aberrations in brain maturation might be tested. We are currently conducting an EEG study of developmental dyslexia to examine this possibility further. A further point of note in our data was that even in the newborn, significant regional differences in dimension were apparent, indicating that even at this early age brain mechanisms also differ topographically in their complexity. While the highest dimensions were always found over the central region, the lowest values were obtained occipitally for newborns and small children, whereas in older children and adults the smallest dimensions were measured over the frontal region. This topographical dimension should be examined further with a full array of electrodes. The possibility might thus arise to analyse delays and aberrations in

brain maturation in terms of topographical differences in complexity, also, since age was a very strong predictor of dimension not only overall, but also for each specific region studied.

A large number of classical studies demonstrate marked age-dependent changes in linear EEG measures (such as alpha rhythm frequency maturation) from 1 to 15 years (Petersén and Eeg-Olofsson, 1970; Fisch, 1991). Although, as demonstrated above, the results of the non-linear analysis are not explained by spectral measures, this subgroup of children was examined further by regression analysis. The results support the conclusions from the ANOVA by showing an increase of complexity with age within the subgroup over the central and occipital region. The age effect may have failed to reach significance in the other two regions because of the smaller subsample size ($n = 21$).

The first Lyapunov coefficients were found to vary with age over the frontal brain region only. The significance of this finding is difficult to interpret. Since we were recording from newborns, it was not possible, in our study, to exclude epochs with eye movements present. While these were suppressed (see Section 2), it cannot be completely excluded that remaining artifact in the frontal leads not detectable by visual inspection could cause the observed frontal decrease with age. Although limited by smaller subsample size, the fact that no age-dependency of Lyapunov coefficients was demonstrable in the subgroup of children older than 1 year might also point in this direction. In our experience, however, eye movement artifact that is not removed leads to a decrease of the first Lyapunov coefficient, contrary to the effect seen here. It might therefore well be that the observed decrease reflects a local change in non-linear dynamics with age. Speculatively, this finding might be linked to the large body of research demonstrating that the maturation of the frontal lobe differs from other regions with respect to duration of myelination and synaptic pruning (Yakovlev and Lecours, 1967; Hüttenlocher, 1979).

While the first Lyapunov coefficient and attractor dimension are related (see Peitgen et al., 1992), the exact nature of the relationship is unproven, but it is obvious that both parameters measure different aspects of a system's dynamics. Decreases in the Lyapunov coefficient have been observed in other instances, e.g. in sleep (Fell et al., 1993) and in studies of epileptic foci where they were found to be indicative of epileptic discharges (Frank et al., 1992; Iasemidis and Sackellares, 1991). The issue requires further study. We suggest that in further studies Lyapunov exponents and correlation dimension should both be determined as complementary measures of chaotic dynamics.

Acknowledgements

Sincere thanks are extended to Dr. Bernd Bätz, formerly

head of the EEG department, Allgemeines Krankenhaus Celle, and his staff, who recorded the majority of the EEGs on which the data presented here are based and whose generous support has made this study possible. Bettina Burghardt, Bernd Gallhofer, an anonymous reviewer, and John Gruzelier are thanked for helpful discussion.

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