

## Detection of nonlinear event-related potentials

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Received 11 November 2005; received in revised form 24 March 2006; accepted 30 March 2006

### Abstract

The methods used to evaluate event-related potentials (ERPs) are generally insensitive to nonlinear responses. Our goal was to show that nonlinear ERPs could be detected using recurrence analysis (RA). When fixed-phase sine signals were added to baseline electroencephalograms (EEGs), the added linear determinism was detected by signal averaging, as expected, and by RA. However, when nonlinear determinism was simulated by adding either random-phase sine or Lorenz signals, the added signals were detected only by RA. Auditory evoked potentials (AEPs) were studied in five subjects using RA. We detected not only the characteristic linear effects caused by onset and offset of the sound, but also nonlinear AEPs not previously reported; they occurred at 473–661 ms after onset, and 282–602 ms after offset, depending on the subject. In five other subjects we found nonlinear magnetosensory evoked potentials; they occurred at 209–354 ms after field onset, depending on the subject. RA was less sensitive than time averaging for detecting linear ERPs, but had the advantage of being able to detect nonlinear ERPs.

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**Keywords:** Event-related potentials; Nonlinear method; Auditory evoked potentials; Magnetosensory evoked potentials; Recurrence analysis; Time averaging; Magnetic field

### 1. Introduction

An event-related potential (ERP) is a change in the electrical state of the brain that occurs in response to a discrete sensory or cognitive event (Lopes da Silva, 1999). The change may arise from the addition of a signal to the electroencephalogram (EEG) (Ruchkin, 1988), or from processes that do not satisfy the principle of superposition such as stimulus-induced phase resetting of ongoing EEG rhythms (David et al., 2005; Graben and Frisch, 2004; Makeig et al., 2002; Penny et al., 2002). Whatever its origin, an ERP is always detected simultaneously with the totality of ongoing brain electrical activity and with signals due to eye movement, muscle activity, and nonbiological noise.

An ERP that arises by superposition on the baseline EEG can be extracted by averaging away the portion of the signal that is not time-locked to the stimulus onset. It has long been recognized, however, that the variability rejected by the

averaging process might itself be physiologically significant (Regan, 1975). The presence of nonlinear determinism in the EEG (dynamic changes governed by nonlinear differential equations) has been studied using Lyapunov exponents and fractal dimension (Stam, 2005), but neither method has been shown to be useful for detecting ERPs, perhaps because the methods require a stationary signal, which is a condition often not realized in practice. Presently, there are no established methods for verifying the presence of nonlinear event-related potentials.

In the absence of a priori knowledge regarding how an ERP is generated, the optimal detection procedure is one that makes minimal assumptions regarding the dynamical nature or statistical properties of the recorded signal, but yet affords a requisite sensitivity. Our purpose was to describe recurrence analysis (RA), a method that meets these conditions and appears to be particularly useful for detecting nonlinear ERPs. First, we describe the mathematical and statistical steps involved in using RA for detecting ERPs. Then, a mathematical model of ERPs created by adding segments of linear or nonlinear waveforms to baseline EEG signals is used to compare the ability of RA and time averaging to detect the added signals. Third, we apply RA to auditory

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evoked potentials and show that, in addition to the expected linear responses, nonlinear responses that were not detected by means of signal averaging also occurred after both onset and offset of the sound. Finally, we present another example that indicates RA reveals the occurrence of nonlinear evoked responses, namely the occurrence of magnetosensory evoked potentials.

## 2. Materials and methods

### 2.1. EEG measurements

EEGs were recorded from O<sub>1</sub>, O<sub>2</sub>, C<sub>3</sub>, and C<sub>4</sub> referenced to linked ears (International 10–20 system) using gold-plated electrodes attached to the scalp with conductive paste; the subjects were clinically normal. The signals were amplified using a multi-channel recording system (Nihon Kohden, Irvine, CA) filtered to pass 0.5–35 Hz, sampled at 10 kHz (to accurately characterize signal amplitude) and stored on a computer hard-drive.

A sound stimulus consisting of a binaural 454 Hz tone (10 ms rise and fall times) was presented to each of five subjects; the sound pressure at the location of the subject was 65 dB. A subliminal magnetic field stimulus was applied to five additional subjects. Uniaxial magnetic fields, 2 G, 60 Hz, uniform to within 5% in the region of the head, were applied in the coronal plane by means of two sets of three coplanar, coaxial coils; the coil sets were separated by 65 cm. Each set consisted of a circular coil (21 turns, radius of 21.6 cm), and two square coils (85, 120 turns, respective side length of 48.3 and 66 cm). The coil current was obtained using a function generator (Model 182A, Wavetek, San Diego, CA) and amplifier (Model 7500, Krohn-Hite, Avon, MA), and was applied by means of a zero-crossing switch controlled by a computer-generated timing signal.

The stimuli were applied for 2 s, with a 5 s inter-stimulus period (7 s trial); at least 80 trials were recorded for each subject. Trials that contained visible artifacts were discarded and the artifact-free trials were sub-sampled at 300 Hz (because the original 10 kHz rate proved unnecessary for the RA calculations), digitally filtered between 0.5 and 35 Hz, and then analyzed by RA and time averaging.

The Institutional Review Board at the LSU Health Sciences Center approved all procedures involving human subjects.

### 2.2. Modeling

A nonlinear event-related potential is defined here as a stimulus–response relationship in which the response is manifested in the EEG and is governed by nonlinear differential equations. Assessment regarding whether an EEG contains evidence of nonlinearity is made by determining whether the putative response (1) has zero mean and (2) can be detected by recurrence analysis. If the answer to both questions is yes, then the event-related potential is considered to be nonlinear.

To mimic determinism occurring in the EEG in response to a sensory stimulus, 300 ms segments of fully deterministic signals were added to baseline EEG trials. The added signals had an RMS value equal to that of the epochs to which they were added. Three model signals were considered: (1) a 10 Hz sine wave that

had a constant phase; (2) a 10 Hz sine wave whose phase varied randomly from trial to trial; and (3) a portion of a solution of the nonlinear system of Lorenz equations (Abarbanel, 1996; Lorenz, 1963); the parameters were chosen so that the system was in the chaotic domain. The augmented trials were analyzed using both RA and time averaging to assess their relative ability to reveal the added signals.

### 2.3. Recurrence analysis

Recurrence analysis was developed by Webber and Zbilut to detect deterministic behavior in time series data, such as the EEG. The deterministic behavior may be linear or nonlinear; RA imposes no constraints on the stationarity or statistical characteristics of the time series (Webber and Zbilut, 1994).

Use of RA to detect actual or simulated event-related potentials involves phase space embedding of successive intervals of the EEG signal, calculation of the corresponding recurrence plots, and quantification of the plots using an appropriate nonlinear quantifier (Fig. 1). The time series of the quantifier is computed for each of a sufficient number of independent epochs, and the ERP is detected by time averaging or, if necessary, statistical comparison with the time series of the quantifier computed from control epochs.

The mathematical details of RA have been described elsewhere (Eckmann et al., 1987; Takens, 1981; Webber and Zbilut, 1994; Zbilut and Webber, 1992). Briefly, the method is based on the principle that the occurrence of deterministic changes in the EEG caused by a sensory or cognitive stimulus can be identified by analyzing the composite signal together with a number of time-lagged versions of the signal (Takens, 1981). After choosing an embedding dimension ( $M$ ) and a time delay ( $\tau$ ), the brain's electrical activity is represented by a series of  $M$ -dimensional vectors, the sequence of which corresponds to a trajectory in the phase space. The trajectory is represented in two dimensions by a recurrence plot (Eckmann et al., 1987), which can be quantified using any of a number of nonlinear quantifiers (Webber and Zbilut, 1994; Zbilut and Webber, 1992); the quantifier used here is percent recurrence ( $\%R$ ), defined as the ratio of the number of recurrent points to the total number of points in the recurrence matrix (Eckmann et al., 1987). Points in phase space are said to be recurrent if the distance between them in phase space is less than an adjustable parameter (here, chosen to be 15% of the maximum distance). For calculating the distances, we used the Euclidean norm (Zbilut and Webber, 1992).

A phase space can be constructed for an entire epoch of the EEG, leading to a single value of  $\%R$ . For example, if an EEG voltage,  $V(t)$ , is sampled at 300 Hz for 2 s (600 measurements) and embedded in a phase space (say,  $M = 5$ ,  $\tau = 5$ ), the result is a trajectory consisting of  $N - \tau(M - 1) = 580$  points, from which a recurrence plot can be computed (Fig. 1a,  $\%R = 15.5\%$ ). However, to detect the transient changes in the EEG produced by the ERPs, it was necessary to iterate the calculation, using a sliding window of points in  $V(t)$  to produce a corresponding time series,  $\%R(t)$ ; this process captured the dynamic activity (both linear and nonlinear) in the EEG occurring over small time intervals (Fig. 1b). For example, use of the first 30 points (100 ms) in  $V(t)$

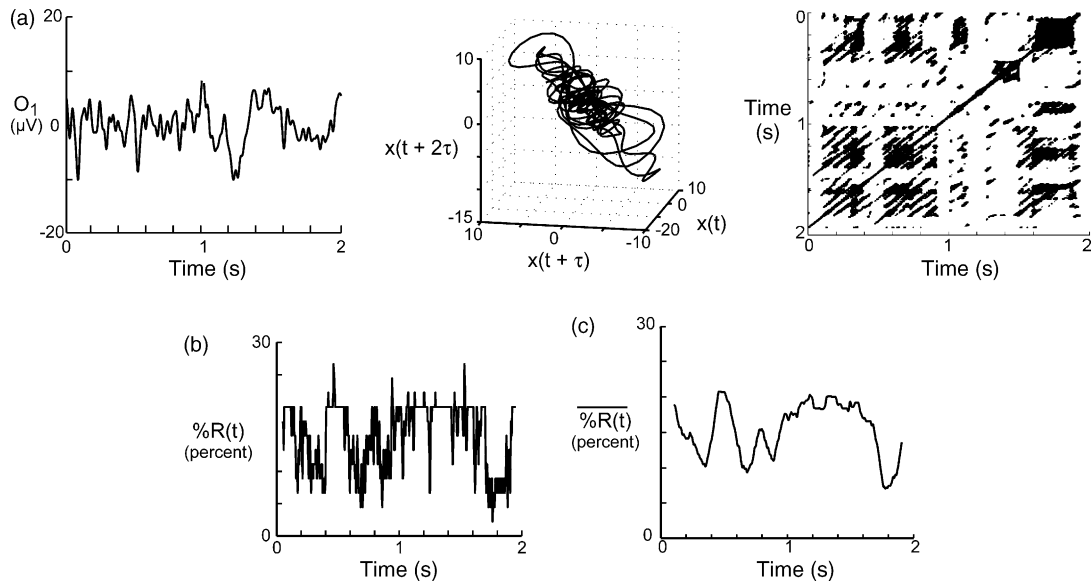


Fig. 1. Successive steps in the use of recurrence analysis for detection of an ERP. (a) General procedure: EEG measurement, phase space embedding, calculation of the recurrence plot, and computation of  $\%R$  (15.5%). (b) Calculation of  $\%R$  time series from the EEG, using a sliding window of 30 points (100 ms), with a shift of one point. (c)  $\overline{\%R}$  time series obtained from (b), using a 30 point averaging window, with a shift of one point.

resulted in a phase space of  $30 - 5(5 - 1) = 10$  points, and a corresponding recurrence plot leading to a specific value for  $\%R$ . The process was then repeated using points 2–31 to produce the next value of  $\%R$ ; successively shifting the window forward by one point results in  $\%R(t)$ , which consists of the same number of points as the  $V(t)$  epoch from which it was calculated, less the number of points chosen for the window. The changes induced in the EEG by the stimulus are more easily detected by analyzing  $\overline{\%R(t)}$ , a smoothed version of the  $\%R(t)$  produced by use of a sliding averaging window (Fig. 1c).

To synchronize  $V(t)$  and  $\%R(t)$ , we adopted the convention that each point in  $\%R(t)$  was plotted in the middle of the time interval from which it was computed. For example, the value of  $\%R$  computed from points 1 to 30 of  $V(t)$  was plotted at  $t = 50$  ms. The same rule was followed to synchronize  $\%R(t)$  and  $\overline{\%R(t)}$ , so that the average value of points 1–30 in  $\%R(t)$  (the first point in  $\overline{\%R(t)}$ ) was plotted at 100 ms.

The presence of a transient deterministic change in the EEG (an ERP) was assessed by time averaging  $V(t)$  and by evaluating  $\overline{\%R(t)}$ , either by time averaging an appropriate number of independent epochs, or by statistical comparison of the stimulus epochs with the control epochs on a point-wise basis, using the  $T$ -test at a comparison significance level of  $P < 0.05$ . The ERP was considered to be nonlinear if it was detected in  $\overline{\%R(t)}$  but not in the time average of  $V(t)$ ; otherwise it was considered to be linear.

Recurrence analysis of experimental signals involves the choice of specific values for important parameters including embedding dimension ( $M=5$  used here), delay time ( $\tau=5$ , unless noted otherwise), scale for calculation of  $\%R$  (15%, Euclidean norm), EEG window for RA calculation (30 points), and averaging window for calculation of  $\overline{\%R(t)}$  (30 points). The optimal choice of each of these parameters has a deep but presently unknown relationship to the dynamics of the baseline

EEG and the ERP, and the rate at which the combined signals are digitized. For each stimulus, these parameters must be determined empirically by systematically varying their values and assessing the effect on the ability to detect an ERP. In what follows, the consequences of varying  $\tau$  are discussed, but our focus is on showing that nonlinear ERPs can be detected by means of RA, not on proving that we have identified optimal parameters for the detection of simulated and actual ERPs.

Calculations of  $\%R(t)$  were carried out using software provided by Webber (2006), and independently verified using a custom code (Matlab, Mathworks, Natick, MA).

### 3. Results

Fixed-phase sine voltage added to epochs of baseline EEG was detected by signal averaging and by RA (Fig. 2). When a 10 Hz sine wave was added at  $t=0.8$ –1.15 s to each  $V(t)$  epoch such that the added segment always had the same phase ( $0^\circ$  at 0.85 s), the sine was detected by time averaging, as expected (Fig. 2b), and also by RA (Fig. 2d).

The presence of random-phase sine voltage added to epochs of baseline EEG was detected by RA, but not by signal averaging (Fig. 3). A 10 Hz sine wave is linear (because it is governed by linear differential equations); however, when a deterministic response of a system is a random-phase sine (that is, the phase appears to be random in the time domain), then the stimulus–response relationship must be governed by nonlinear laws. Thus, addition of a random-phase sine mimics a nonlinear stimulus–response relationship. When the phase of the sine added at  $t=0.85$  s varied randomly from epoch to epoch (thereby simulating a nonlinear ERP), the added determinism could not be detected by averaging of the EEG signals (Fig. 3b), but was readily detected by time averaging multiple epochs of  $\overline{\%R(t)}$  (Fig. 3d).

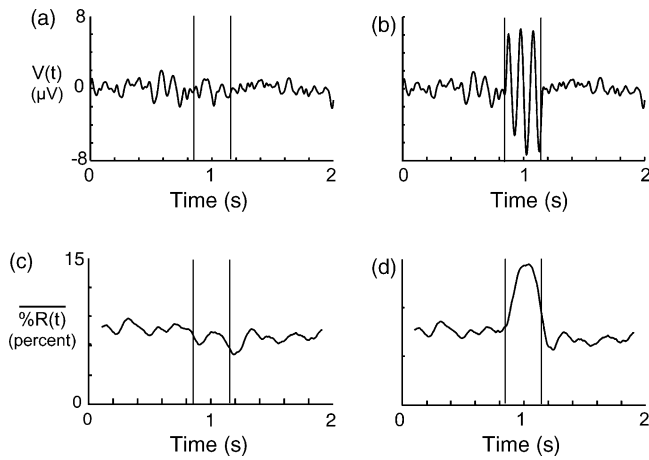


Fig. 2. Detection of fixed-phase ( $0^\circ$  at  $t=0.85$  s) 10 Hz sine signal added to epochs of baseline EEG. (a) Time average of baseline EEG from  $O_1$  ( $n=50$ ). (b) Effect of addition of the signal at 0.85–1.15 s (vertical lines) to each epoch. (c) Time average of  $\overline{\%R(t)}$  calculated from the epochs averaged in (a). (d) Time average of  $\overline{\%R(t)}$  calculated from the epochs averaged in (b).

The ability of RA to detect the presence of random-phase sine signals added to the  $V(t)$  epochs was proportional to the square root of the number of epochs averaged (Fig. 4).

The effectiveness of RA in detecting a nonlinear signal (random-phase sine) added to the EEG depended on the choice of delay time (Fig. 5). When the combined signals were unfolded at  $\tau=3$ , RA was less effective in detecting the added signal, compared with the result found using  $\tau=5$  (Fig. 5a and b); at  $\tau=1$ , the added signal could not be detected (Fig. 5c).

Addition of Lorenz signals to baseline EEG was detected by RA, but not by signal averaging (Fig. 6). When Lorenz segments (Fig. 6a) were added to each of 50 baseline epochs of EEG, the added determinism was averaged away in  $V(t)$  (Fig. 6b), as expected, because of the nonperiodic nature of the Lorenz signal. Also as expected, when the number of epochs was increased to 500, the cancellation effect of the averaging procedure was even

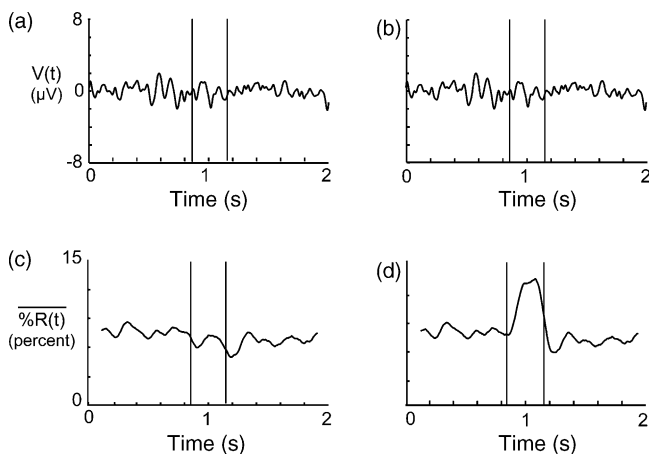


Fig. 3. Detection of random-phase ( $0-360^\circ$  at  $t=0.85$  s) 10 Hz sine signal added to epochs of baseline EEG. (a) Time average of baseline EEG from  $O_1$  ( $n=50$ ). (b) Effect of addition of the signal at 0.85–1.15 s (vertical lines) to each epoch. (c) Time average of  $\overline{\%R(t)}$  calculated from the epochs averaged in (a). (d) Time average of  $\overline{\%R(t)}$  calculated from the epochs averaged in (b).

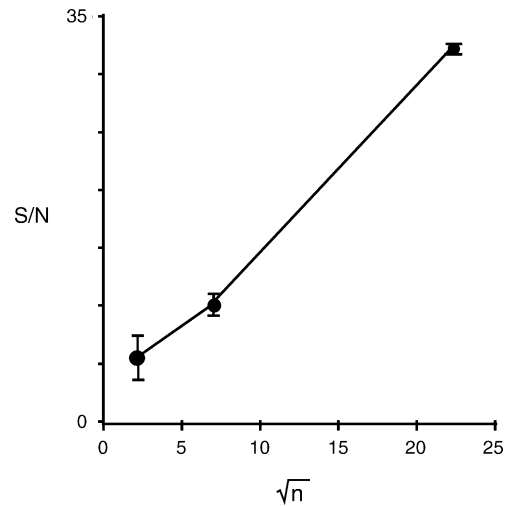


Fig. 4. Signal-to-noise ratio (S/N) in the model system as a function of number of trials ( $n$ ) containing a random-phase 10 Hz sine signal added to baseline EEG. Mean  $\pm$  S.D., averaged over 10, 100, and 500 trials.

more dramatic (Fig. 6c). In contrast to these results, when the added determinism was captured using  $\overline{\%R(t)}$  prior to averaging, its presence was detected with sensitivity proportional to the number of epochs analyzed (Fig. 6d and e).

The modeling results shown in Figs. 2–6 were repeated six times, using six different sets of EEG baseline data, and identical results were obtained (not shown).

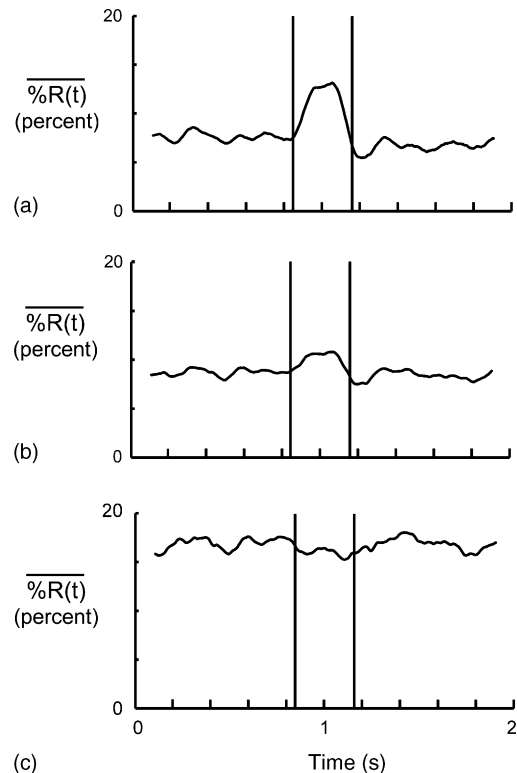


Fig. 5. Effect of time delay ( $\tau$ ) on detection of random-phase 10 Hz sine signals. The signals were added to baseline EEG (vertical lines), and  $\overline{\%R(t)}$  was calculated for 50 epochs and averaged, after the augmented EEG epochs were unfolded in five dimensions. Time delay for the unfolding,  $\tau=5$  (obtained from Fig. 3d),  $\tau=3$ , and  $\tau=1$  in a–c, respectively.

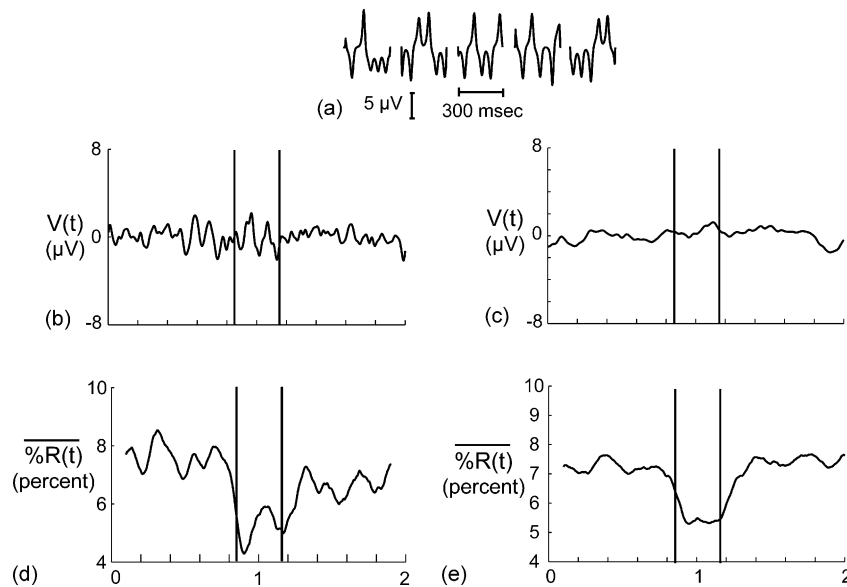


Fig. 6. Detection of Lorenz signals added to epochs of baseline EEG. (a) Representative 300 ms Lorenz signals. (b) Time average of baseline EEG from  $O_1$  after addition of Lorenz signals at 0.85–1.15 s (vertical lines) to each of 50 epochs (no two added Lorenz segments were identical). (c) Time average of 500 augmented epochs. (d and e) Time average of  $\overline{\%R(t)}$  calculated from the epochs averaged in (b) and (c), respectively. The Lorenz model parameters ( $\sigma$ ,  $r$ , and  $b$ , respectively) were 10, 28, and 2.67 (Abarbanel, 1996); the signals were obtained by choosing different initial conditions.

Using RA, both linear and nonlinear auditory evoked potentials (AEPs) induced by sound onset were found in all subjects (Fig. 7). Following presentation of the stimulus, typical linear AEPs were detected after averaging  $V(t)$  from 50 onset epochs (first column). When  $\overline{\%R(t)}$  was computed for the onset and control epochs and the results compared at each time point, the linear AEPs were detected at about 200 ms after onset. In addition, nonlinear AEPs (transient changes in the EEG voltage not observed in the time average of  $V(t)$ ) were detected in each subject around  $t = 600$  ms. The latency of the nonlinear AEPs (black bars along the time axes) was relatively constant but the duration varied from subject to subject. The nonlinear AEPs consisted of a reduction ( $P < 0.05$ ) in  $\overline{\%R(t)}$  in the onset epochs (last column). When sham onset epochs were analyzed, no false-positive results were seen in any subject (data not shown).

Nonlinear AEPs induced by offset of the sound were found in all subjects (Fig. 8). Linear offset AEPs were observed in the  $V(t)$  and  $\overline{\%R(t)}$  signals from the central electrodes (data not shown). Linear AEPs were not present in the occipital electrodes, however, nonlinear AEPs were found from these derivations around  $t = 400$  ms in each subject (Fig. 8). In comparison with nonlinear response to sound onset (Fig. 7), the response to offset exhibited greater inter-subject latency, but the direction and magnitude of the effect was comparable (Fig. 8). When sham offset epochs were analyzed, no false-positive results were seen in any subject (data not shown).

Onset of the magnetic field induced nonlinear magnetosensory evoked potentials (MEPs) in all subjects (Fig. 9). Time averaging of  $V(t)$  for 1 s following field onset revealed no effect due to application of the field. However, when  $\overline{\%R(t)}$  was computed for each onset epoch, a transient effect (an MEP) was seen in each subject; the statistical reliability of the observations were confirmed by means of point-by-point tests between

the onset and control epochs. The nonlinear MEPs triggered by application of the field occurred at 209–354 ms, depending on the subject (Fig. 9). When sham onset epochs were analyzed, no false-positive results were seen in any subject (data not shown).

#### 4. Discussion

The assumption underlying the use of time averaging for detecting ERPs is that the induced potentials are more or less reproducible in independent trials. In other words, time averaging entails the assumption that linear differential equations govern the system consisting of (1) the sensory or cognitive event, (2) the resulting electrical activity in the brain, and (3) the time-dependent voltages measured on the scalp. It is possible, however, that some event-response systems may be nonlinear (governed by nonlinear differential equations). In those cases, the deterministic response produced by the event would probably not be detected by the commonly used methods because of the mismatch between the mathematical properties of linear methods and the nonlinearity of the response. For example, a deterministic response that was positive in half the trials (increase in  $V(t)$  at  $t = t_0$ , compared with the control) and negative in the other half (decrease at  $t = t_0$ ), which is entirely lawful behavior for a nonlinear system but cannot occur in a linear system, would be completely obscured if  $V(t)$  were analyzed using the method of time averaging. It would be useful, therefore, to have an analytical method that could reveal the existence of both linear and nonlinear ERPs. Our aim was to show that RA is such a method, and to discuss its strengths and weaknesses.

Recurrence analysis revealed the presence of previously unreported transient change in brain electrical activity at 500–600 ms following the onset of a sound stimulus, as manifested by a reduction in  $\overline{\%R(t)}$  (Fig. 7). Several lines of evidence indicated



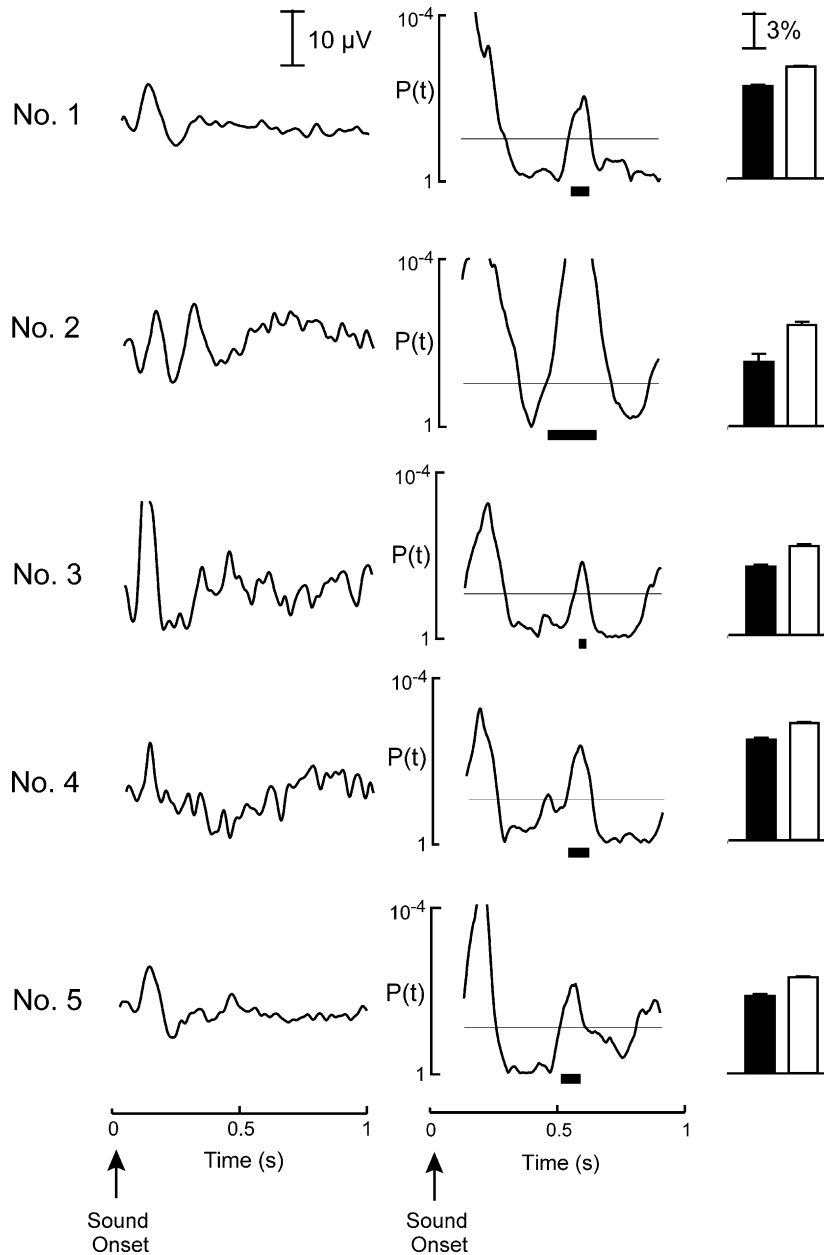


Fig. 7. Auditory potentials evoked by stimulus onset. Measurements from  $C_3$  in five subjects. First column, time average of  $V(t)$  from 50 onset epochs. Second column, probability for rejecting the null hypothesis that the mean of  $\%R(t)$  in the onset and control epochs at time  $t$  were identical (264  $T$ -tests). Horizontal line,  $P=0.05$ . Horizontal bars, latency, and duration of the nonlinear effect of sound: 545.8–615.1, 473.2–661.3, 565.6–6.109, 526.0–611.8, and 509.5–588.7 ms, in subjects 1–5, respectively. Third column, mean  $\pm$  S.D. of onset and control epochs of  $\%R(t)$ , averaged over times corresponding to  $P < 0.05$  (black bars in second column).  $\tau = 4$ .

that the observed changes were true nonlinear AEPs. First, they were observed in each subject tested and occurred with latencies that were similar from subject to subject. Second, their existence was established on the basis of statistical comparisons with appropriate control epochs. Third, when sham-stimulus epochs were compared with the controls, comparable regions of statistical significance were not found, indicating that the results (Fig. 7) were not produced by the analytical procedure itself. Fourth, RA, a method designed to detect both linear and nonlinear deterministic activity, detected the linear AEPs revealed by time averaging. Thus, the reliability of RA was confirmed in the area where an alternative method of analysis was avail-

able. Fifth, the AEPs around 500 ms detected by RA were not detected by time averaging.

Sound offset did not result in linear auditory potentials from the occipital derivations, but did result in transient nonlinear changes (Fig. 8). This may mean that the nonlinear and linear AEPs are not causally linked, but rather that both species of transient electrical changes are facets of ongoing brain processing of the stimulus. Alternatively, the pattern of appearance of the potentials (in the occipital derivations, nonlinear but not linear AEPs were seen in all five subjects) may simply reflect the nature of electrotonic propagation in the brain or the nonstimulus-related activity in the region of each electrode. Whatever the

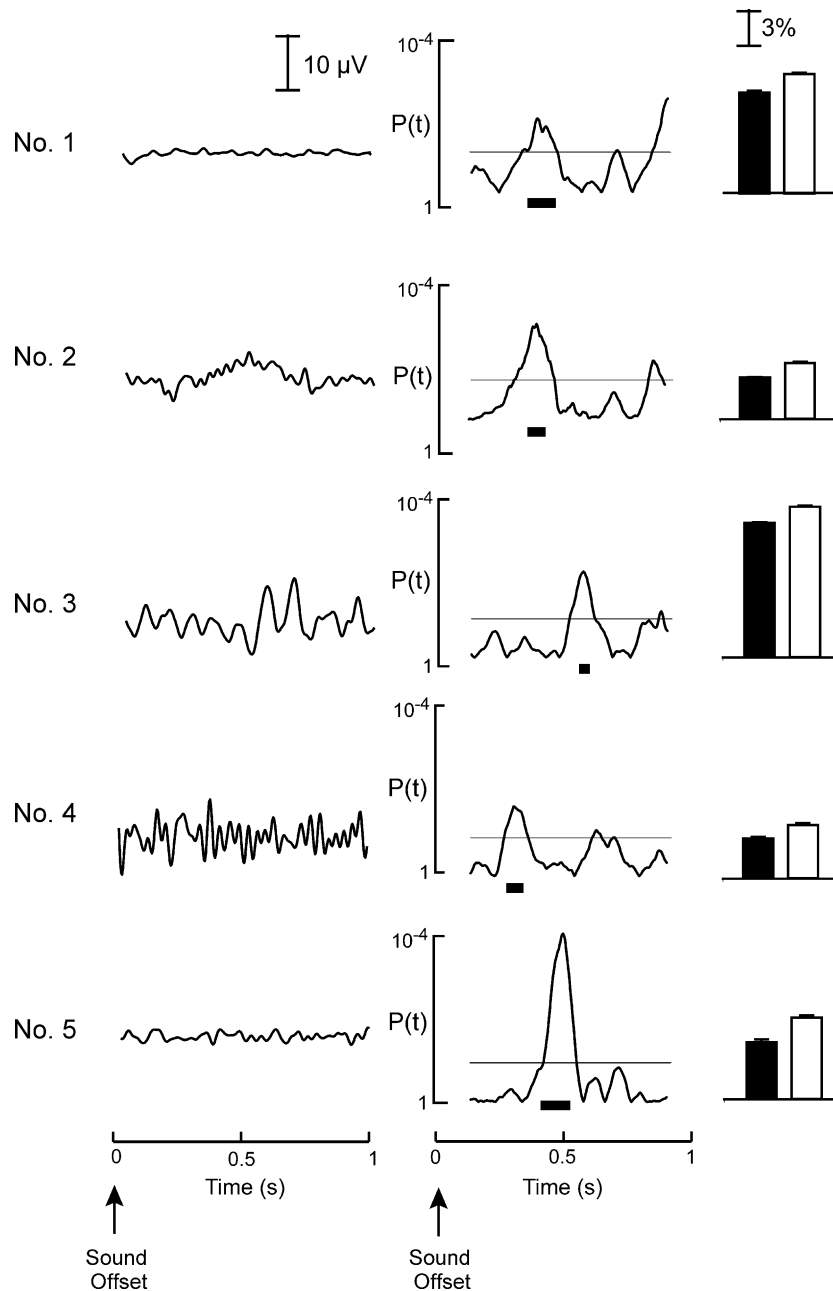


Fig. 8. Auditory potentials evoked by stimulus offset. Measurements from  $O_2$  in five subjects. First column, time average of  $V(t)$  from 50 offset epochs. Second column, probability for rejecting the null hypothesis that the means of  $\%R(t)$  in the offset and control epochs at time  $t$  were identical (270  $T$ -tests). Horizontal line,  $P=0.05$ . Horizontal bars, latency, and duration of the nonlinear effect of sound: 367.7–436.9, 361.0–473.7, 555.7–601.9, 281.8–337.9, and 423.7–535.9 ms, subjects 1–5, respectively. Third column, mean  $\pm$  S.D. of offset and control epochs of  $\%R(t)$ , averaged over times corresponding to  $P < 0.05$  (black bars in second column).  $\tau=4$ .

explanation, the results in Figs. 7 and 8, taken together, indicated that it is possible to detect a nonlinear ERP even when a linear ERP is not detected.

Further evidence that linear and nonlinear ERPs are in some sense independent was provided by our discovery of magneto-sensory potentials evoked by onset of a magnetic field (Fig. 9). In this case, time averaging of  $V(t)$  failed to reveal an effect due to the field in the occipital, central, or parietal electrodes, but a nonlinear effect with latency of 200–350 ms was observed in at least one of the occipital electrodes in each of the five subjects studied.

The demonstrated advantage of RA is its ability to detect nonlinear ERPs due to sensory stimuli; future studies may show that it is similarly useful for studying the consequences of cognitive events. The method also detects linear determinism (Figs. 7 and 8), but with far less time resolution, compared with time averaging, because a calculation of a single point in  $\%R(t)$  requires data for  $V(t)$  over a time interval. Thus, a point in  $V(t)$  could differ from its control, and thereby manifest an ERP as brief as 3.3 ms (assuming a sampling frequency of 300 Hz). In contrast, a statistically significant comparison at one point in  $\%R(t)$  has the physical meaning that the deterministic change

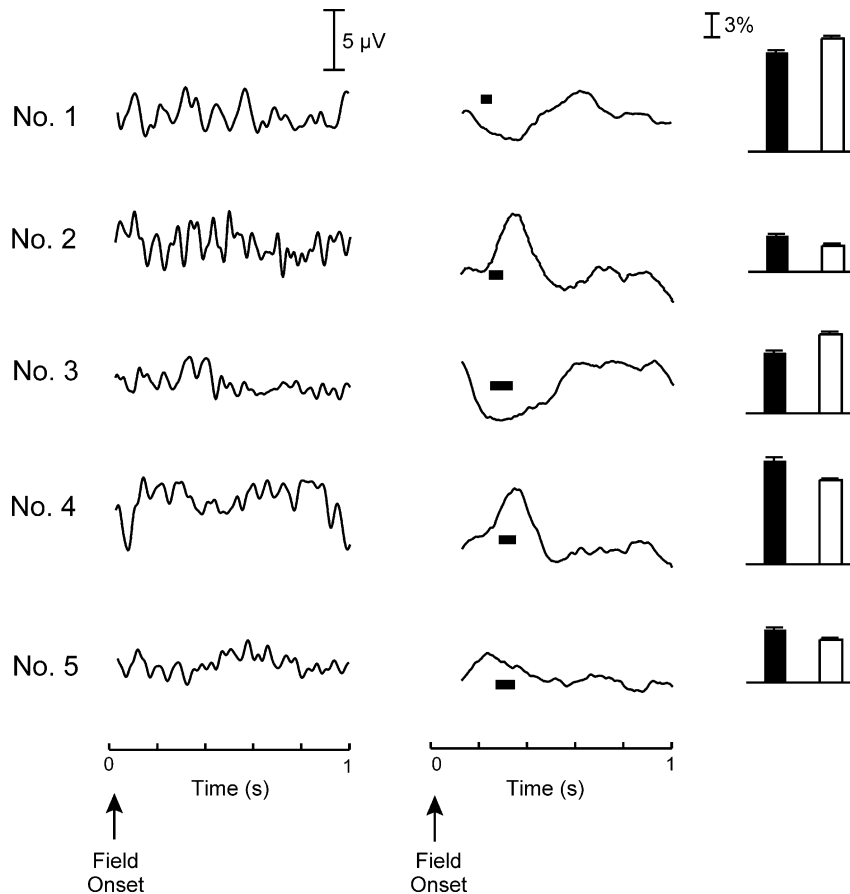


Fig. 9. Magnetosensory potentials evoked by stimulus onset. First column, time average of  $V(t)$  from 50 onset epochs. Measurements from  $O_2$ , except  $O_1$  for subjects 4 and 5. Second column, the average of  $\%R(t)$  computed from  $V(t)$  showing the location of the MEP (black bar) as assessed by statistical comparison with the controls. Location of the MEP (black bar): 209.2–255.4, 238.9–298.3, 248.8–337.9, 278.5–354.4, and 268.6–354.4 ms, nos. 1–5, respectively. Horizontal bars indicate the location and duration of the MEP. Third column, mean  $\pm$  S.D. of onset and control epochs of  $\%R(t)$ , averaged over times corresponding to  $P < 0.05$  (black bars in second column).

occurred somewhere within a larger interval (for the conditions employed here, 200 ms). RA is therefore useful in conjunction with linear methods for ascertaining the existence of nonlinear ERPs but it does not appear to be an alternative for studying linear ERPs.

The idea that a lawful response must be consistent or exactly reproducible in independent trials may seem like a bedrock scientific principle, but we have known at least since the work of Lorenz (1963) that, for nonlinear systems, there is a sense in which this is not the case. For example, nonlinear MEPs were manifested by a reduction in the nonlinear quantifier used to characterize the response ( $\%R(t)$ ) in some subjects, but a significant increase in others (Fig. 9). Thus, the observation that indicated the existence of a deterministic change in brain electrical activity was not uniquely an increase or decrease in the nonlinear quantifier, but rather the occurrence of a statistically significant *change* in the quantifier. This characteristic of RA was also demonstrated in our modeling studies; the addition of nonlinear ERPs to baseline EEGs could produce either an increase or decrease in  $\%R(t)$  (compare Fig. 3d and Fig. 6e). Although this property of recurrence analysis is clearly established, the underlying physiological significance remains unknown. In particular, there is presently no model by which to understand whether the

added determinism will result in an increase or decrease in the nonlinear quantifier.

The nonlinear ERPs were detected using a specific set of values for the adjustable parameters in the calculation and analysis. We showed that with regard to  $\tau$ , the ability to detect the ERPs was critically dependent on the choice of the parameters used (Fig. 5); it can be anticipated that other parameters will also strongly influence the sensitivity of RA in particular cases. The point is that nonlinear ERPs detected using RA are more properly conceptualized as views or perspectives on the dynamical activity of the system, rather than as a unique characterization of that activity (which is more or less how linear ERPs are viewed). In other words, it is possible that a different set of parameters could result in the detection (with appropriate statistical certainty) of deterministic changes in brain electrical activity in time intervals other than those identified in the present analysis. In the case of sound, for example, it is certain that the brain electrical activity differed throughout the entire 2 s epoch following onset (because the subject had a continuous physiological sensation of hearing the sound), although our present methods of analysis do not permit objective verification.

We defined a nonlinear relationship between the stimulus and response as an inconsistent deterministic output that occurs upon



repeated applications of the stimulus. An inconsistent deterministic output might be related to modulation of brain sources other than those responsible for the deterministic influence of the stimulus. Possible examples include alpha desynchronization following stimulus presentation or induced gamma rhythms. These types of events could fit our definition of nonlinearity. The essential nonlinearity of these phenomena has already been pointed out (Breakspear, 2002; David et al., 2005; Tass, 2003). It might also be argued that only some of these effects are examples of nonlinear determinism. We have not addressed the issue of the relationship between recurrence analysis, alpha desynchronization, and gamma rhythms because that was not part of our objective.

In summary, nonlinear ERPs could be detected by embedding the EEG in phase space, computing the time series for percent recurrence, smoothing the time series, and then either time averaging it or comparing it statistically with corresponding results from control epochs.

## References

- Abarbanel HD. Analysis of observed chaotic data. New York: Springer-Verlag; 1996.
- Breakspear M. Nonlinear phase desynchronization in human electroencephalographic data. *Hum Brain Mapp* 2002;15:175–98.
- David O, Harrison L, Friston KJ. Modelling event-related responses in the brain. *Neuroimage* 2005;25:756–70.
- Eckmann J-P, Kamphorst SO, Ruelle D. Recurrence plots of dynamical systems. *Europhys Lett* 1987;4:973–9.
- Graben P, Frisch S. Is it positive or negative? On determining ERP components. *IEEE Trans Biomed Eng* 2004;51:1374–82.
- Lopes da Silva FH. Event-related potentials: methodology and quantification. In: Neidermeyer E, Lopes da Silva F, editors. *Electroencephalography*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 1999.
- Lorenz EN. Deterministic, nonperiodic flow. *J Atmos Sci* 1963;20:130–41.
- Makeig S, et al. Dynamic brain sources of visual evoked responses. *Science* 2002;295:690–4.
- Penny WD, Kiebel SJ, Kilner JM, Rugg MD. Event-related brain dynamics. *Trends Neurosci* 2002;25:387–9.
- Regan D. Evoked potentials in psychology, sensory physiology and clinical medicine. London: Chapman and Hall; 1975.
- Ruchkin DS. Measurement of event-related potentials: signal extraction. In: Picton TW, editor. *Human event-related potentials*. New York: Elsevier; 1988.
- Stam CJ. Nonlinear dynamical analysis of EEG and MEG: review of an emerging field. *Clin Neurophysiol* 2005;116:2266–301.
- Takens F. Detecting strange attractors in turbulence. *Dynamical systems and turbulence*. Berlin: Springer; 1981.
- Tass PA. Stochastic phase resetting of stimulus-locked responses of two coupled oscillators: transient response clustering, synchronization, and desynchronization. *Chaos* 2003;13:364–76.
- Webber Jr CL. Recurrence quantification analysis. <http://homepages.luc.edu/~cwebber>; 2006.
- Webber Jr CL, Zbilut JP. Dynamical assessment of physiological systems and states using recurrence plot strategies. *J Appl Physiol* 1994;76:965–73.
- Zbilut JP, Webber CL. Embedding and delays as derived from quantification of recurrence plot. *Phys Lett A* 1992;171:199–203.