Quantitative analysis by renormalized entropy of invasive electroencephalograph recordings in focal epilepsy

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Invasive electroencephalograph (EEG) recordings of ten patients suffering from focal epilepsy were analyzed using the method of renormalized entropy. Introduced as a complexity measure for the different regimes of a dynamical system, the feature was tested here for its spatiotemporal behavior in epileptic seizures. In all patients a decrease of renormalized entropy within the ictal phase of seizure was found. Furthermore, the strength of this decrease is monotonically related to the distance of the recording location to the focus. The results suggest that the method of renormalized entropy is a useful procedure for clinical applications like seizure detection and localization of epileptic foci. [S1063-651X(98)11710-5]

I. INTRODUCTION

Focal epilepsies are characterized by seizures that originate from a distinct region of the brain. The identification of this so called epileptogenic focus is a prerequisite for surgical treatment. Thus much attention is paid to the characterization of invasive electroencephalograph (EEG) recordings of patients suffering from this disease. Competitive techniques like high-resolution positron-emission tomography or MRI using specific ligands or metabolites are used as alternatives to localize the epileptogenic focus in order to avoid invasive EEG recordings. For the time being no superiority of either method has been established yet [1–4]. Any method will be preferred that has a better spatial and timewise resolution than the other with acceptable validity. Within this scenario an approach in EEG analysis is described in this paper.

Since there is only little doubt about the nonlinearity of the dynamical system underlying the observed time series a broad range of nonlinear analysis techniques has been applied to these data. As one of the first results of nonlinear EEG analysis indication of low-dimensional chaos was reported by Babloyanz and Destexhe [5] who claimed a noninteger correlation dimension in the EEG recording of a petit mal seizure. Furthermore, Frank *et al.* [6] obtained positive Lyapunov exponents by analyzing two seizure recordings. Similar effects, giving indication of chaotic behavior in EEG data, were also described by Freeman and Skarda [7], Dvorak and Siska [8], Basar and Bullock [9], and Pijn *et al.* [10]. Windowed estimates of these measures for piecewise classification of EEG were used by Lehnertz and Elger [11], Tirsch *et al.* [12], Pritchard *et al.* [13], and Iasemidis and Sackellares [14]. Lehnertz *et al.* [11] analyzed the EEG recordings of 20 patients suffering form unilateral temporal lobe epilepsy. The variability of the correlation dimension, estimated for subsequent segments of the EEG, was found to be a good indicator of the lateralization of the epileptic focus. In a case study Lerner [15] found the correlation integral itself to be suitable to detect seizure activity in an EEG recording.

By now it is well appreciated that results, obtained by use of these measures, have to be interpreted with care. Several investigators [16–18] have especially shown that the value of the correlation dimension is influenced by computational as well as recording parameters. Theiler *et al.* [19] found no evidence for low-dimensional chaos when re-examining EEG data of 110 patients. The finite correlation dimensions, they obtained for the same data sets in an earlier study [20], were found to be caused by an artifact of the autocorrelation in the oversampled signals.

A methodologically different approach is based on the examination of neural spike trains that might be observed in the EEG of epileptic patients. In a basic implementation the statistical properties like mean, variance, or skewness of the interspike interval distribution are used to characterize the EEG. Although this method neglects the sequence of these intervals it is proven to be of practical use for some applications [21]. However, for analysis of epileptic seizures advanced methods seemed to be necessary, i.e., sequence-sensitive methods [22–25]. Using a sequence-sensitive complexity measure Rapp *et al.* found a decrease of nonrandom structure of these sequences in focal epileptic seizures induced in rats by application of penicillin [26].

A qualitative characterization of epileptic seizures is given by van der Heyden *et al.* [27]. Their results, obtained by analyzing EEG data of patients suffering from mesial temporal lobe epilepsy, indicate that the property of reversibility of a time series can be used to discriminate between seizure and nonseizure activity. Casdagli *et al.* [28] report recurrent activity to occur in spatiotemporal patterns related
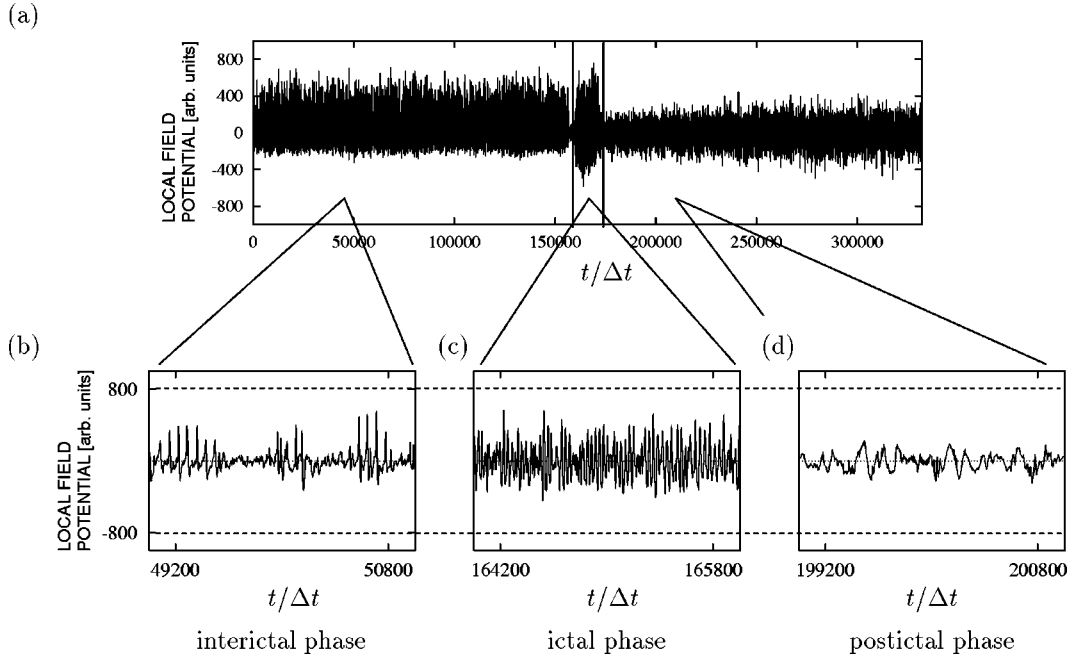
FIG. 1. Invasive EGG recording of an epileptic seizure (a): segments of the (b) interictal phase, (c) ictal phase, and (d) postictal phase. The vertical lines in (a) denote the beginning and the end of the ictal phase. The measured local field potentials are shown in arbitrary units.

to the location of an epileptic focus.

In the present paper a procedure is described that seems to be appropriate to classify the EEG of epileptic patients in an uniform way. The method of renormalized entropy, proposed in [29] for classification of the different states of a dynamical system, is applied to the EEG data of ten patients suffering from temporal lobe epilepsy. The method is tested for its ability to assign a given segment of an EEG time series to the corresponding neurophysiological state of the epileptic patient, i.e., interictal, ictal, or posictal phase, as well as its use for localization of an epileptic focus.

II. RENORMALIZED ENTROPY

Applying Klimontovich's S theorem [30] to Fourier spectra of scalar time series, Saparin *et al.* [29] introduced renormalized entropy as a complexity measure for the different regimes of a dynamical system. Here each regime is represented by the normalized Fourier spectrum $S_i(\omega)$ of one observable $x_i(t)$, which, in formal analogy to classical statistical physics, is viewed at as a distribution function of an open system.

Given a reference distribution $S_r(\omega)$, representing the system's state of equilibrium, the relative degree of order of the regime described by $S_i(\omega)$ is determined by comparing the entropies of these two distributions under the additional constraint of same mean energy in both states. To this end an effective Hamiltonian

$$H_{\text{eff}} = -\ln S_r(\omega) \qquad (1)$$

is introduced and the reference spectrum is renormalized ("heated up") into

$$\widetilde{S}_r(\omega) = C(T_i)e^{-H_{\text{eff}}(\omega)/T_i} = C(T_i)S_r(\omega)^{1/T_i}, \qquad (2)$$

so that the following holds:

$$\int \widetilde{S}_r(\omega)H_{\text{eff}}(\omega)d\omega = \int S_i(\omega)H_{\text{eff}}(\omega)d\omega \qquad (3)$$

and

$$\int \widetilde{S}_r(\omega)d\omega = 1. \qquad (4)$$
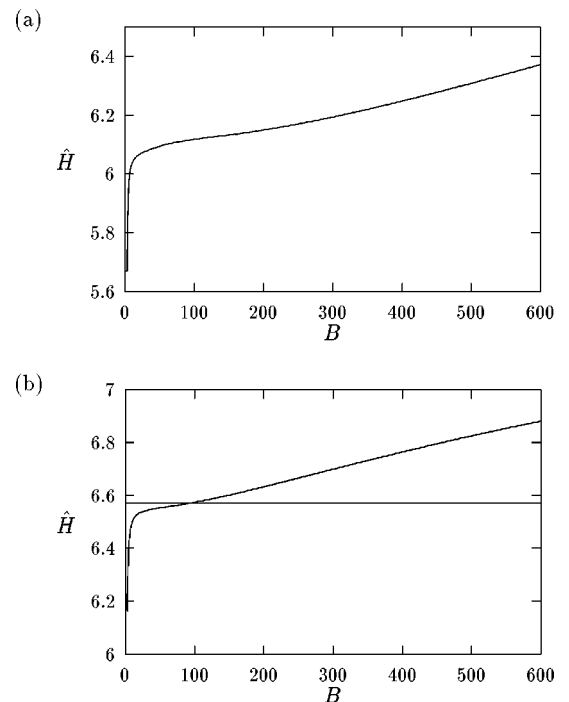

FIG. 2. Estimate $\hat{H}$ of spectral entropy vs width B of the smoothing window obtained for a segment of an EEG (a) and an AR(2) process (b) of length $N = 4096$. The horizontal line in (b) denotes the true value of spectral entropy.
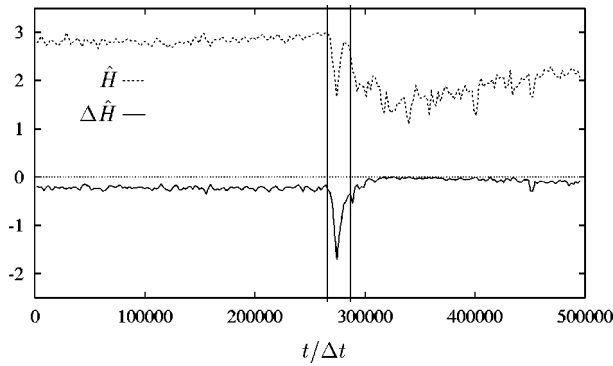
FIG. 3. Course of spectral entropy $\hat{H}$ and renormalized entropy $\Delta\hat{H}$ obtained for a recording location in the epileptogenic area. Vertical lines denote the beginning and the end of the ictal phase.

Here Eq. (3) ensures the equality of mean energies of the two states, Eq. (4) the normalization of the renormalized spectrum. $C(T_i)$ is a normalization factor depending on T_i. Renormalized entropy now is given by

$$\Delta H = \int \widetilde{S}_r(\omega)\ln \widetilde{S}_r(\omega)d\omega - \int S_i(\omega)\ln S_i(\omega)d\omega. \quad (5)$$

Applying this method to the different regimes of the logistic map, Saparin *et al.* [29] found renormalized entropy to clearly detect all transitions between the different types of periodic behavior as well as the different types of chaos. Kurths *et al.* [31] and Voss *et al.* [32] analyzed the heart rate variability of patients after myocardial infarction. They report renormalized entropy to be a suitable method for the detection of high risk patients threatened by sudden cardiac death.

Because of Eq. (1) the method can only be applied to processes that have a purely positive spectrum, i.e., chaotic or stochastic processes. Because spectra of such processes have to be estimated the spectrum chosen as reference should be of lower energy than each other state of the system to avoid ''temperatures'' T_i less than 1. ''Cooling down'' an estimated spectrum increases the variance of the estimate and therefore the variance of the estimated entropy.

III. ANALYSIS OF THE EEG

The EEG data analyzed in this study were recorded using chronically implanted subdural and intrahippocampal electrodes measuring the local field potential. The obtained signals were passed to a multichannel amplifier system with
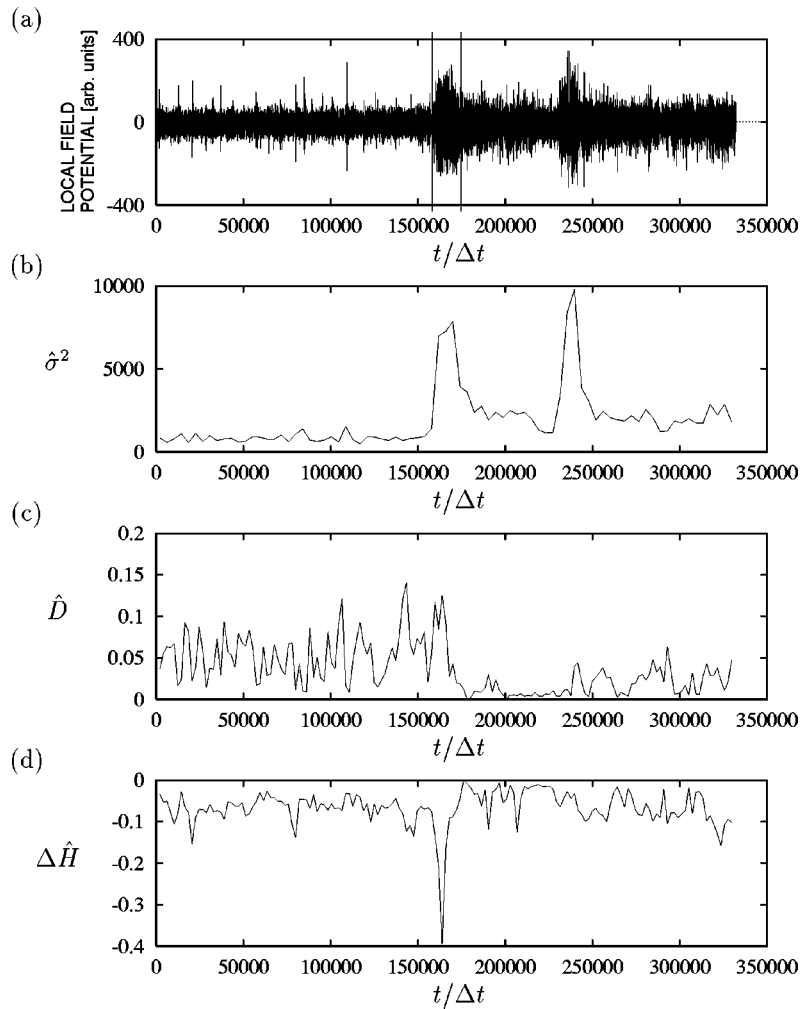

FIG. 4. Course of (b) estimated variance $\hat{\sigma}^2$, (c) Euclidean distance $\hat{D}$, and (d) renormalized entropy $\Delta\hat{H}$ obtained for the EEG shown in (a). Vertical lines in (a) denote the beginning and the end of the ictal phase.

band-pass filter settings of 0.53–85 Hz and were written to a digital storage device with a sampling interval of $\Delta t = 5.76$ ms per channel. Figure 1 displays representative samples of the obtained time series for different phases of an epileptic seizure. For each recording the identification of the different phases was done by experienced clinicians by visual inspection of the time series.

For analysis the data of each channel were divided into consecutive segments x_i of length $N = 4096$ with a 50% overlap. The length corresponds to a duration of 24 s per epoch and was chosen to achieve at least quasistationarity for each segment according to [33].

To apply the method described above to these data the spectrum of each segment has to be estimated and for each channel a reference spectrum has to be found. To estimate the spectra S_i the periodograms

$$Per_i(\omega_k) = 1/N \left| \sum_{j=1}^{N} x_{i,j} e^{i\omega_k j \Delta t} \right|^2 \qquad (6)$$

were smoothed:

$$\hat{S}_i(\omega_k) = \sum_u w_u Per(\omega_{k-u}). \qquad (7)$$

As smoothing kernel w_u the Bartlett-Priestley window was chosen [34]:

$$w_u = \begin{cases} C[1 - (u/b)^2], & |u| \leq b \\ 0, & |u| > b. \end{cases} \qquad (8)$$

Variance and bias of the estimator depend on the width $B = 2b + 1$ of the smoothing window and the structure of the true spectrum. To find an appropriate value for the window width the spectral entropy

$$\hat{H} = -\sum_k \hat{S}(\omega_k) \ln \hat{S}(\omega_k) \qquad (9)$$

was calculated as a function of B for different segments. Figure 2(a) shows the plot obtained for one segment of an EEG. The graph can be divided into two regions. For small values of B the fluctuations of the periodogram are suppressed insufficiently: because each summand in Eq. (9) is a convex function of $S(\omega_k)$ the spectral entropy is underestimated. In this region the estimated spectral entropy increases fast with increasing B. For large values of B there is an area of small increase where the periodogram is oversmoothed. Since information about the structure of the spectrum is lost, in this region the spectral entropy is overestimated. Figure 2(b) shows the corresponding plot for one realization of an AR(2) process

$$X(t) = a_1 X(t-1) + a_2 X(t-2) + \epsilon(t) \qquad (10)$$

with

$$a_1 = 1.3, \quad a_2 = -0.75, \quad \text{and} \quad \epsilon(t) \in \mathcal{WN}(0,1)$$

of length $N = 4096$. This process describes a damped linear oscillator driven by white noise [35]. The functional relation-

ship between the parameters a_1, a_2 and the frequency ω and relaxation time τ of the oscillator is given by

$$a_1 = 2 \cos \omega e^{-1/\tau}, \qquad (11)$$

$$a_2 = -e^{-2/\tau}. \qquad (12)$$

Because this process is linear its spectral entropy can be calculated analytically:

$$H = -\sum_k S(\omega_k) \ln S(\omega_k) \qquad (13)$$

with

$$S(\omega_k) = \frac{C}{|1 - a_1 e^{i\omega_k} - a_2 e^{i2\omega_k}|^2}, \qquad (14)$$

C a normalizing constant. As the plot shows the true value of spectral entropy, denoted by the horizontal line in Fig. 2(b), is reached in the area of transition from high to low increase of spectral entropy. Therefore, a value of $B = 33$ from this region in Fig. 2(a) was chosen for the analysis of the EEG.

To calculate the renormalized entropy of the EEG spectra for each channel a reference $S_r(\omega_k)$ has to be chosen. As mentioned before this state should be of lower energy than each other state of the system. Because

$$-\sum_k S_j(\omega_k) \ln S_r(\omega_k) \geq -\sum_k S_r(\omega_k) \ln S_r(\omega_k) \quad (15)$$

holds for every j if

$$-\sum_k S_j(\omega_k) \ln S_j(\omega_k) \geq -\sum_k S_r(\omega_k) \ln S_r(\omega_k) \quad (16)$$

the spectrum of lowest spectral entropy [Eq. (9)] was chosen as reference. If the postictal phase of an epileptic seizure differed from the interictal phase the corresponding segment was found in the beginning of the postictal phase resulting in a course of renormalized entropy shown in Fig. 3. Otherwise the reference was found in the interictal phase. Figure 3 also shows that the conventional spectral entropy as given by Eq. (9) does not serve as a feature characterizing the ictal phase.

To test and compare the behavior of the renormalized entropy in an epileptic seizure, EEG data of all patients were analyzed using the method of renormalized entropy as well as simple features like the variance

$$\hat{\sigma}_i^2 = \frac{1}{N-1} \sum_j \left(x_{i,j} - \frac{1}{N} \sum_l x_{i,l} \right)^2 \qquad (17)$$

or the squared Euclidean distance

$$\hat{D}_i = \sum_k [\hat{S}_i(\omega_k) - \hat{S}_r(\omega_k)]^2 \qquad (18)$$

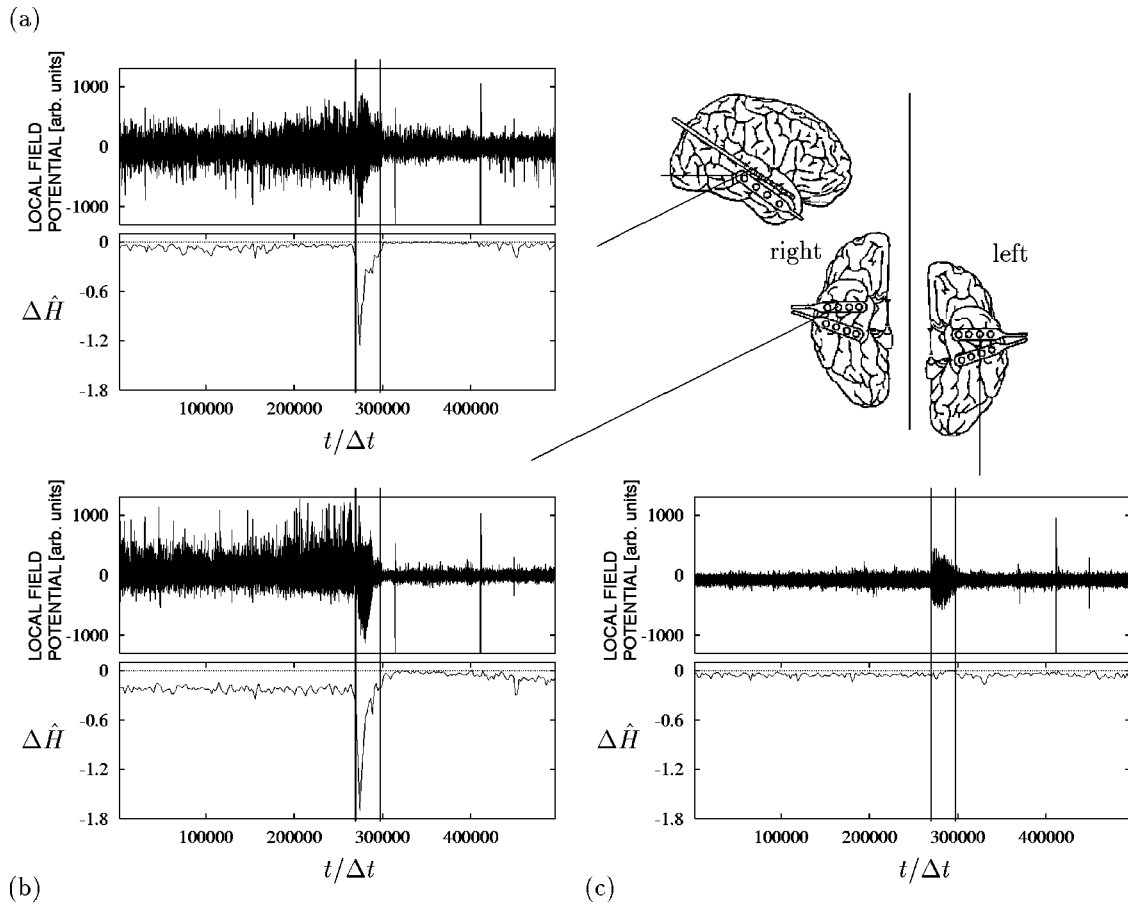of spectra. For determination of the Euclidean distance the

FIG. 5. EEG and course of renormalized entropy obtained for recording locations of different distance to the epileptic focus: (a) location nearby the epileptic focus, (b) location of smallest distance to the epileptic focus, (c) location on the contralateral hemisphere. Vertical lines denote the beginning and the end of the ictal phase.

spectra were calculated in the same way as were done for calculation of renormalized entropy. Also the distance was calculated with respect to the same reference spectrum to achieve results comparable to these obtained by use of renormalized entropy. A representative sample is given in Fig. 4. In Fig. 4(a) the EEG recording, in Fig. 4(b) the course of the estimated variance and in Fig. 4(c) the course of the squared Euclidean distance obtained for this recording are shown. By means of these simple characteristics a reliable identification of the different phases (interictal, ictal, and postictal phase) of an epileptic seizure is not possible. The squared Euclidean distance, which was chosen as an alternative and more elementary distance measure of spectra, fails to distinguish between the different phases. The variance detects the ictal phase but misclassifies a later postictal segment of the EEG. By way of contrast, the course of renormalized entropy reveals a temporary strong decrease only within the ictal phase.

To investigate the spatial behavior of renormalized entropy, for each patient up to eight channels, corresponding to recording locations of different distance to the epileptic focus, were analyzed. In all patients the value of renormalized entropy within the ictal phase was found to decrease with decreasing distance of the recording location to the epileptic focus, as shown for a representative example in Fig. 5. Thus, a technical device for localizing epileptic foci, based on the concept of renormalized entropy, is imaginable.

IV. CONCLUSIONS

The method of renormalized entropy, formally introduced to quantify the complexity of the different regimes of a dynamical system, has been applied to invasive EEG recordings of ten patients suffering from temporal lobe epilepsy.

In all patients the course of renormalized entropy obtained for recording locations nearby the epileptic focus shows a strong decrease in the ictal phase of an epileptic seizure with respect to the interictal or postictal phase. Because the strength of this decrease depends on the distance of the recording location to the focus not only a discrimination between the different phases but also a localization of the focus seems to be possible. The method makes exclusive use of the spectral properties of the time series under consideration and therefore human interaction is restricted to the choice of the spectral estimator to be used. Putting it all together the concept of renormalized entropy seems to be a promising candidate for clinical applications like seizure detection or localization of epileptic foci.

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