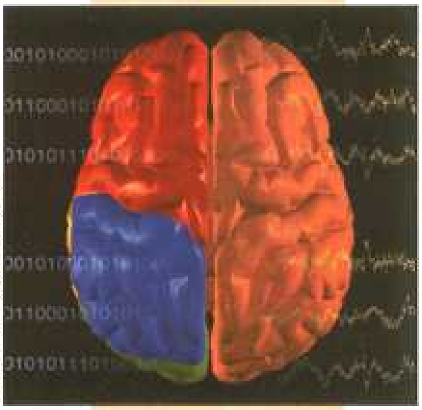

Synchronization and Information Flow in EEGs of Epileptic Patients

A Potentially Promising Method for Anticipating Epileptic Seizures

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Synchronization on various levels of organization of brain tissue, from pairs of individual neurons to much larger scales (within one area of the brain or between different parts of the brain) is one of the most important topics in neurophysiology. Some level of synchrony is usually necessary in order to attain normal neural activity, while too much synchrony may be a pathological phenomenon such as epilepsy. Detection of synchrony, or transient changes leading to a high level of synchronization, and identification of causal relations between driving (synchronizing) and response (synchronized) components is a great challenge, since it can help in anticipating epileptic seizures and in localization of epileptogenic foci. Standard linear statistical methods have brought only a little success in this area.

Recently, there has been considerable interest in the study of cooperative behavior of coupled chaotic systems [1]. Methods developed in the field of nonlinear dynamics and chaos have been successfully applied in studies of cardiorespiratory synchronization [2, 3] and synchronization of neural signals [4-7]. The problem of quantitative description of synchronization phenoma, however, is still far from being solved, and some claims of successful detection of causal relationships are based on contradictory assumptions [4, 5]. Also, measures of synchronization, based on infinitezimal properties and performing well on artificial systems, can fail when applied to noisy experimental data.

In this article we introduce nonlinear, statistical, coarse-grained measures based on information theory that could provide an indication of synchronization as well as of causal relationships if present in scrutinized systems. The introduced approach is applied in case studies of EEG recordings of epileptic patients. Two levels of synchronization leading to seizures are detected and "directions of information flow" (drive-response relationships) are identified.

Coarse-Grained Information Rates

Consider discrete random variables X and Y with sets of values Ξ and Υ, respectively, and probability distribution functions (PDFs) $p(x)$, $p(y)$ and joint PDF $p(x,y)$. The *entropy* $H(X)$ of a single variable, say X, is defined as

$$H(X) = -\sum_{x\in\Xi} p(x)\log p(x), \tag{1}$$

and the *joint entropy* $H(X,Y)$ of X and Y is

$$H(X,Y) = -\sum_{x\in\Xi}\sum_{y\in\Upsilon} p(x,y)\log p(x,y). \tag{2}$$

The *conditional entropy* $H(X|Y)$ of X given Y is

$$H(X|Y) = -\sum_{x\in\Xi}\sum_{y\in\Upsilon} p(x,y)\log p(x|y). \tag{3}$$

The average amount of common information contained in the variables X and Y is quantified by the *mutual information* $I(X;Y)$, defined as

$$I(X;Y) = H(X) + H(Y) - H(X,Y). \tag{4}$$

The conditional mutual information $I(X;Y|Z)$ of the variables X, Y given the variable Z is given as

$$I(X;Y|Z) = H(X|Z) + H(Y|Z) - H(X,Y|Z). \tag{5}$$

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CERs can be estimated with lower computational cost and are more robust against noise than estimates of Lyapunov exponents or exact entropies.

For Z independent of X and Y we have

$$I(X;Y|Z) = I(X;Y). \quad (6)$$

Now, let $\{X_i\}$ be a stochastic process; i.e., an indexed sequence of random variables. Its entropy rate [8]

$$h = \lim_{n\to\infty} \frac{1}{n} H(X_1,...,X_n), \quad (7)$$

where $H(X_1,...,X_n)$ is the joint entropy of the n variables $X_1,...,X_n$ with the joint PDF $p(x_1,...x_n)$, is a measure of "information creation" by the process $\{X_i\}$, or a rate of how quickly the process "forgets" its history. The entropy rate, in the case of dynamical systems called Kolmogorov-Sinai entropy (KSE) [9-11], is a suitable tool for quantification of dynamics of systems or processes; however, possibilities of its estimation from experimental data are limited to a few exceptional cases [8, 11, 12]. Instead, Paluš [12] has proposed to compute "coarse-grained entropy rates" (CERs) as relative measures of "information creation" and of regularity and predictability of studied processes.

Let $\{x(t)\}$ be a time series considered as a realization of a stationary and ergodic stochastic process $\{X(t)\}$, $t = 1,2,3,...$. In the following we will mark $x(t)$ as x and $x(t+\tau)$ as x_τ. For defining the simplest form of CER we compute the mutual information $I(x;x_\tau)$ for all analyzed datasets and find such τ_{max} that for $\tau' \geq \tau_{max}: I(x;x_{\tau'}) \approx 0$ for all datasets. Then, we define the norm of the mutual information

$$\|I(x;x_\tau)\| = \frac{\Delta\tau}{\tau_{max} - \tau_{min} + \Delta\tau} \sum_{\tau=\tau_{min}}^{\tau_{max}} I(x;x_\tau) \quad (8)$$

with $\tau_{min} = \Delta\tau = 1$ sample as a usual choice. The CER h^1 is then defined as

$$h^1 = I(x,x_{\tau_0}) - \|I(x;x_\tau)\|. \quad (9)$$

It has been shown that the CER h^1 provides the same classification of states of chaotic systems as the exact KSE [12]. Since usually $\tau_0 = 0$ and $I(x;x) = H(X)$, which is given by the marginal probability distribution $p(x)$, the sole quantitative descriptor of the underlying dynamics is the mutual information norm [Eq. (8)], which we will call the coarse-grained information rate (CIR) of the process $\{X(t)\}$ and denote by $i(X)$.

Now, consider two time series $\{x(t)\}$ and $\{y(t)\}$ regarded as realizations of two processes $\{X(t)\}$ and $\{Y(t)\}$, which represent two possibly linked (sub)systems. These two systems can be characterized by their respective CIRs $i(X)$ and $i(Y)$.

In order to characterize an interaction of the two systems, in analogy with the above CIR we define their mutual coarse-grained information rate (MCIR)

$$i(X,Y) = \frac{1}{2\tau_{max}} \sum_{\tau=-\tau_{max}}^{\tau_{max};\,\tau\neq 0} I(x;y_\tau). \quad (10)$$

Due to the symmetry properties of $I(x;y_\tau)$ the MCIR $i(X,Y)$ is symmetric; i.e., $i(X,Y) = i(Y,X)$.

Assessing the direction of coupling between the two systems, we ask how is the dynamics of one of the processes, say $\{X\}$, influenced by the other process, $\{Y\}$. For a quantitative answer to this question we propose to evaluate the conditional CIR $i_0(X|Y)$ of $\{X\}$ given $\{Y\}$:

$$i_0(X|Y) = \frac{1}{\tau_{max}} \sum_{\tau=1}^{\tau_{max}} I(x;x_\tau|y), \quad (11)$$

considering the usual choice $\tau_{min} = \Delta\tau = 1$ sample. Recalling Eq. (6) we have $i_0(X|Y) = i(X)$ for $\{X\}$ independent of $\{Y\}$; i.e., when the two systems are uncoupled. Since we prefer a measure that vanishes for uncoupled systems (though then it can acquire both positive and negative values), we define

$$i(X|Y) = i_0(X|Y) - i(X). \quad (12)$$

For another approach to a directional information rate let us consider the mutual information $I(y;x_\tau)$ measuring the average amount of information contained in the process $\{Y\}$ about the process $\{X\}$ in its future τ time units ahead (τ-future thereafter). This measure, however, could also contain information about the τ-future of the process $\{X\}$ contained in this process itself if the processes $\{X\}$ and $\{Y\}$ are not independent; i.e., if $I(x;y) > 0$. In order to obtain the "net" information about the τ-future of the process $\{X\}$ contained in the process $\{Y\}$, we need the conditional mutual information $I(y;x_\tau|x)$. The latter measure can also be understood as an information-theoretic formulation of the Granger causality concept [13]. Also, recently Schreiber [14] proposed a "transfer entropy" that is in special cases equivalent to $I(y;x_\tau|x)$.

Next, we sum $I(y;x_\tau|x)$ over τ as above

$$i_1(X,Y|X) = \frac{1}{\tau_{max}} \sum_{\tau=1}^{\tau_{max}} I(y;x_\tau|x), \quad (13)$$

and, in order to obtain the "net asymmetric" information measure, we subtract the symmetric MCIR [Eq. (10)]:

$$i_2(X,Y|X) = i_1(X,Y|X) - i(X,Y). \quad (14)$$

Using a simple manipulation we find that $i_2(X,Y|X)$ is equal to $i(X|Y)$, defined in Eq. (12). By using two different methods we have arrived at the same measure, which we will denote by $i(X|Y)$ and call the coarse-grained transinformation rate (CTIR) of $\{X\}$ given $\{Y\}$. It is the average rate of the net amount of information "transferred" from the process $\{Y\}$ to process $\{X\}$, or, in other words, the average rate of the net information flow by which the process $\{Y\}$ influences the process $\{X\}$.

Numerical properties of the above-introduced coarse-grained information rates and their abilities to detect synchronization have been tested in an extensive study [20] using artificial data generated by numerical solutions of unidirectionally coupled chaotic systems. Typically, a system $\{X\}$ was an autonomous, independently evolving system that drove another system $\{Y\}$. The two systems were studied for a number of different values of coupling strength, from independency (no coupling) through weak coupling to fully synchronized states. In the case of identical systems, the state of identical synchronization is characterized by

$$i(X,Y) = i(X) = i(Y). \quad (15)$$

The CTIRs start at zero for uncoupled systems, then, with increasing coupling strength the CTIR $i(Y|X)$ increases into distinctly positive values while the CTIR $i(X|Y)$ remains zero, which indicates that the system $\{X\}$ drives the system $\{Y\}$, while $\{X\}$ evolves independently of $\{Y\}$. This distinction, however, ends shortly before the synchronization threshold, when both the CTIRs start to fall and reach the identical synchronization state with

$$i(X|Y) = i(Y|X) = -i(X) = -i(Y) = -i(X,Y).$$

With emerging synchronization we loose the possibility to establish the "direction of information flow," or the causal relationship between the systems $\{X\}$ and $\{Y\}$. It is understandable: in the identical synchronization the series $\{x(t)\}$ and $\{y(t)\}$ are identical and there is no possibility to establish the causal relationship between $\{X\}$ and $\{Y\}$ just from the data.

In the cases of generalized synchronization [1, 4, 15] of two nonidentical systems, the situation is more complex. Since the CIRs, similar to their inspiration CERs [12], are not dynamical invariants, in the case of generalized synchronization we cannot expect the equality [Eq. (15)]; however, the generalized synchronization is accompanied with $i(X,Y)$ rising into values

$$\min(i(X),i(Y))i(X,Y) \leq \max(i(X),i(Y)). \quad (16)$$

The CTIRs indicate the correct causal relations of $\{X\}$ being the drive of $\{Y\}$ by their relation

$$i(X|Y) < i(Y|X) \quad (17)$$

again only before the synchronization threshold. The above explanation of the impossibility to infer a causal relation from an identical time series in the state of identical synchronization can be generalized into time series related by a nonlinear function as is the case of the generalized synchronization.

Summary of the Mathematical Methods

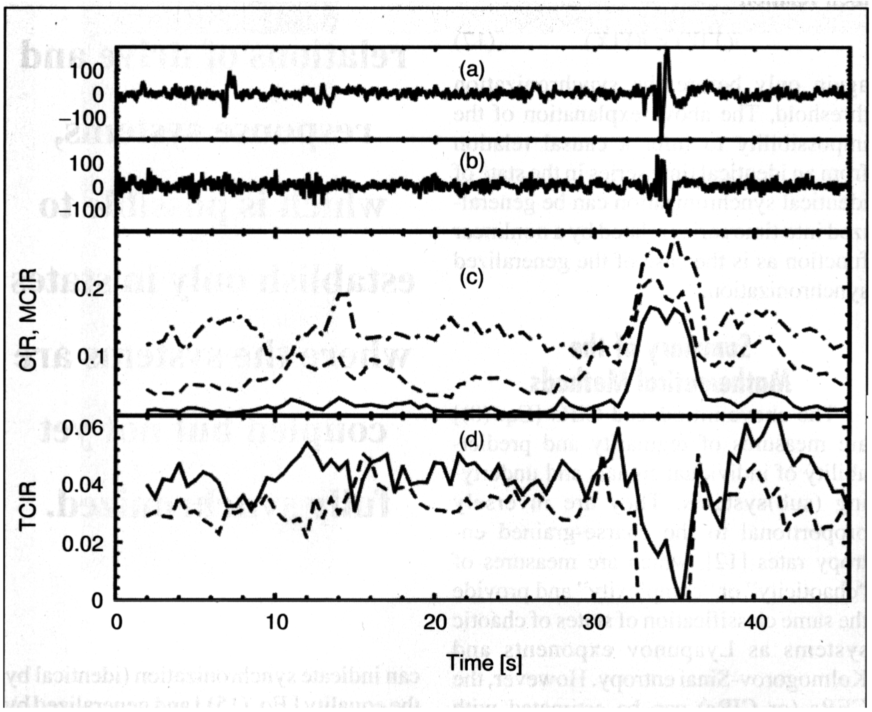
The above-introduced CIRs [Eq. (8)] are measures of regularity and predictability of individual signals and underlying (sub)systems. They are inversely proportional to the coarse-grained entropy rates [12], which are measures of "chaoticity" or "complexity" and provide the same classification of states of chaotic systems as Lyapunov exponents and Kolmogorov-Sinai entropy. However, the CERs (or CIRs) can be estimated with lower computational cost and are more robust against noise than estimates of Lyapunov exponents or exact entropies [12]. The mutual CIR [Eq. (10)], based on the mutual information [Eq. (4)], is a symmetric measure of mutual dependence of two time series, and thus it reflects the level of coupling of two (sub)systems and can indicate synchronization (identical by the equality [Eq. (15)] and generalized by the relation [Eq. (16)]). The mutual information [Eq. (4)] is a measure of general dependence between two variables: it is equal to zero for independent variables and positive otherwise. The CTIRs are based on the conditional mutual information, which quantifies influence of one system, say $\{X\}$, on a future of another

CTIRs are able to identify the causal relations of drive and response systems, which is possible to establish only in states where the systems are coupled but not yet fully synchronized.

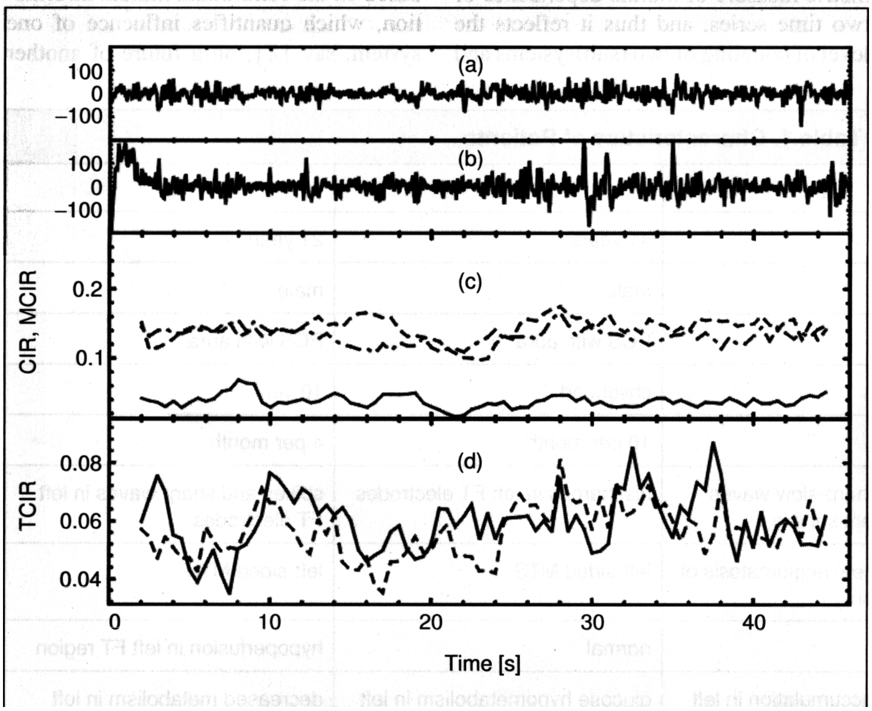
Table 1. Characteristics of Patients

Patient	I	II	III
Age	30 months	41 years	21 years
Sex	male	male	male
Type of Seizures	PCS	PCS with aura	PCS with aura
Age When Seizures Started	8 months	childhood	10 years
Frequency of Seizures	3-4 per day	10 per month	4 per month
Interictal EEG	sharp and sharp-slow waves over right hemisphere	discharges in left FT electrodes	spikes and sharp waves in left FT electrodes
MRI Scans	leptomeningeal angiomatosis of left TO region	left-sided MTS	left-sided MTS
SPECT	–	normal	hypoperfusion in left FT region
PET-FDG	decreased accumulation in left TO region	glucose hypometabolism in left medial T region	decreased metabolism in left T lobe

system $\{Y\}$, eliminating the influence of the history of $\{Y\}$ on its own future. Therefore, the CTIRs are able to identify the causal relations of drive and response (sub)systems (relation 17). This is, however, possible to establish only in states in which the (sub)systems are coupled but not yet fully synchronized [20].



1. An EEG segment with a short seizure, recorded from leads (a) T_6O_2 and (b) F_4C_4. (c) The CIRs $i(T_6O_2)$ (dashed line), $i(F_4C_4)$ (dash-and-dotted line), and the mutual CIR $i(T_6O_2,F_4C_4)$ (full line). (d) The coarse-grained transinformation rates $i(T_6O_2|F_4C_4)$ (dashed line) and $i(F_4C_4|T_6O_2)$ (full line) (Patient I).



2. The same as in Fig. 1 but for an interictal EEG segment of the same patient.

Materials and Methods

About 20-30% of patients with epilepsy are pharmacoresistant. Some of these patients are candidates for surgical resection of epileptogenic focus. The objective of presurgical evaluation is to identify the area of the brain responsible for generating seizures. In most cases, presurgical evaluation involves interictal EEG; long-term video EEG monitoring with noninvasive scalp, semi-invasive sphenoidal, and in few patients invasive (subdural or depth) electrodes; neuropsychological testing; neuroimaging (usually magnetic resonance imaging (MRI) scans); single-photon-emission computed tomography (SPECT); positron-emission tomography (PET); and magnetic resonance spectroscopy (MRS). In this article we present analyses of EEG recordings of three patients with medically refractory partial complex seizures. Their clinical, neuroimaging, and EEG data are listed in Table 1.

The video-EEG recordings were performed on a 32-channel Schwarzer system. Signals were sampled at 256 Hz using an analog-to-digital converter with 16-b resolution. Patient I is a 30-month-old boy suffering from epileptic seizures since the age of 8 months. The Sturge-Weber syndrome has been diagnosed because of congenital periorbital hemangioma and leptomeningeal hemangiomas in the left temporooccipital area revealed by the MRI scan. His first EEG showed spiking in the left temporooccipital area. In the beginning he had partial complex seizures, while later myoclonicastatic seizures appeared. Recently, two long-term video/EEG monitoring sessions were performed. The first session showed ictal onset in the left temporal lobe. The second monitoring, by scalp electrodes 1.5 years later, revealed mostly generalized spiking with a slight excess in the right temporooccipital lobe. Interictal PET showed glucose hypometabolism in the left temporooccipital lobe. A part of the most recent EEG recordings underwent synchronization analysis using the above CIRs, MCIR, and CTIRs. They were estimated from a 1024-sample moving window (moving step 128 samples, sampling frequency 256 Hz), using four marginal equiquantal bins and $\tau_{min} = \Delta\tau = 1$ and $\tau_{max} = 50$ samples. Signals from reference and longitudinal (bipolar) montages were analyzed. The latter brought more clear results in establishing "directions of information flow"; i.e., the drive-response relations using CTIR.

Patients II and III are adult (41 and 21 years old) men suffering from partial complex seizures due to medial temporal lobe epilepsy associated with left-sided mesiotemporal sclerosis revealed by the MRI scan. Hypoperfusion in the left frontotemporal region was found by SPECT and decreased metabolism in the left temporal lobe by PET-FDG in the case of patient III, while patient II had normal SPECT results and glucose hypometabolism in the left medial temporal region found by PET-FDG. In addition to standard scalp electrodes, the EEG signals of patients II and III were also recorded from sphenoidal electrodes (Sp_1, Sp_2). Therefore, we have analyzed only the data from the reference montage, using a window length of 4096 samples, a window step of 1024 samples, and eight marginal equiquantal bins. Other processing parameters were the same as in the case of patient I.

Results

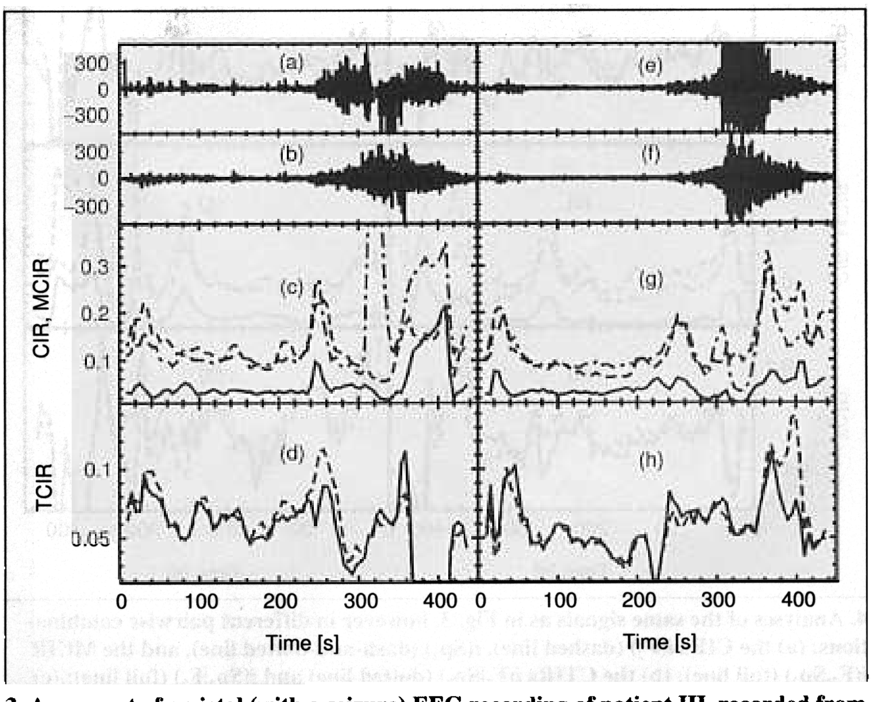
Patient I

From a segment with a short seizure, signals from leads T_6O_2 [Fig. 1(a)] and F4C4 [Fig. 1(b)] are illustrated here. Before the seizure both $i(T_6O_2)$ and $i(F_4C_4)$ present occasional increases; however, they develop independently and the mutual CIR $i(T_6O_2,F_4C_4)$ keeps low values [Fig. 1(c)]. At the edge of the seizure (time: 32 s) CIRs and MCIR rise sharply, reflecting an increase of both local synchrony (CIR) and synchronization between different areas of the brain (MCIR). The increased synchrony revealed by the increased information rates could also be indicated by decreased entropy rates or decreased "dimensional complexity" measures; e.g., by the correlation dimension. The latter and related dimensional and entropy measures (correlation integrals) have recently been used for anticipation of approaching seizures [18-19]. For evaluating predictive properties of CIRs, we do not have enough data yet, thus we proceed to the CTIR to find that in the presented segment $i(F_4C_4|T_6O_2) > i(T_6O_2|F_4C_4)$; i.e., the information flow from T_6O_2 to F_4C_4 dominates over the opposite flow, or the subsystem (brain area) represented by the signal from the lead T_6O_2 (signal T_6O_2 for short) drives that from F_4C_4.

For comparison we present the same analysis of the signals from the same leads but from a segment in an interictal (i.e., far from seizures) recording (Fig. 2). Both CIRs $i(T_6O_2)$ and $i(F_4C_4)$ fluctuate on the same level; however, the dependence of the signals measured by $i(T_6O_2,F_4C_4)$ is low [Fig. 2(c)]. The drive-response relation cannot be unambiguously defined, since the CTIRs $i(T_6O_2|F_4C_4)$ and $i(F_4C_4|T_6O_2)$ are either approximately the same or mutually exchange their dominance [Fig. 2(d)].

An evaluation of these results suggests that transients to seizures are characterized by an increasing level of synchronization (both local, i.e., among neurons of a particular brain area which causes the increased regularity of the registered EEG signals measured by the individual CIRs, and between different brain areas, which is reflected in increased mutual MCIR), and an asymmetry in information flow emerges or is amplified. Considering the latter, we have found in the (pre)ictal segment that the signal T_6O_2 drove all signals from the right hemisphere. Symmetrically, the same has been found about the signal T_5O_1; however, there was no distinction of causality between T_5O_1 and T_5T_3. In fact, the latter drove all the signals as T_5O_1 did. On the other hand, there was no distinction of the information flow direction (although there is a nonzero dependence indicated by MCIR) between laterally symmetrical leads such as C_3P_3-C_4P_4, with the one exception—T_5O_1 has been found to drive T_6O_2. This analysis suggests that the primary epilepto-

Transient phenomena leading to seizures have been characterized by increased synchronization (local and between areas) and asymmetry in information flow



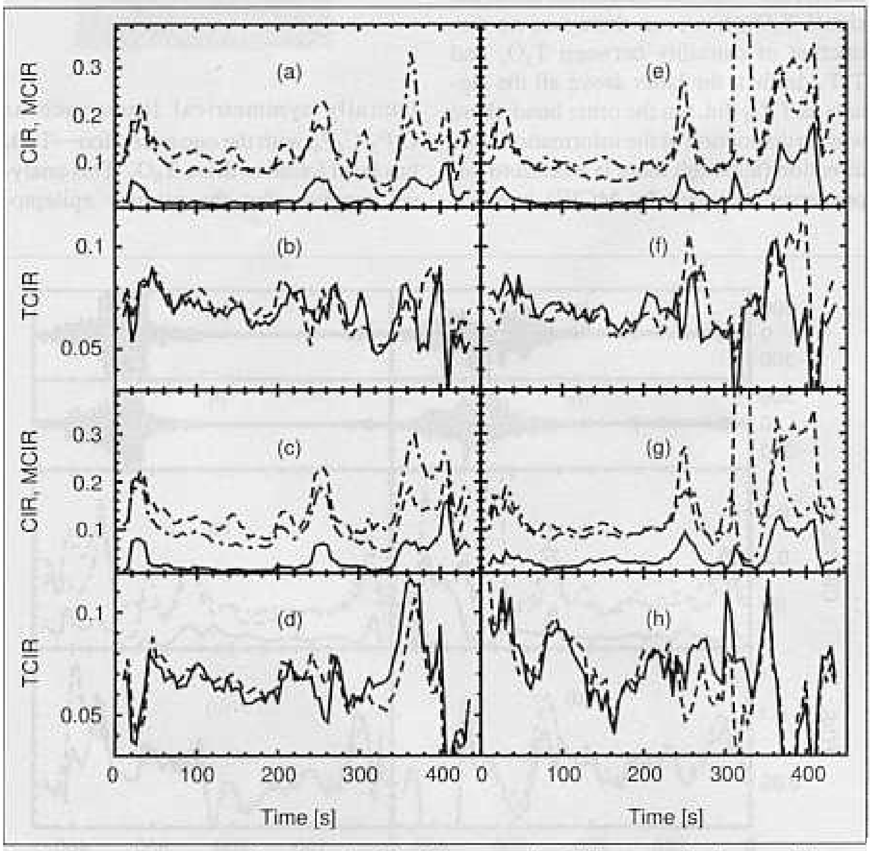
3. A segment of an ictal (with a seizure) EEG recording of patient III, recorded from (a) the leads F_7 and (b) Sp_1. (c) The CIRs $i(F_7)$ (dashed line), $i(Sp_1)$ (dash-and-dotted line), and the mutual CIR $i(F_7,Sp_1)$ (full line). (d) The coarse-grained transinformation rates $i(F_7|Sp_1)$ (dashed line) and $i(Sp_1|F_7)$ (full line). (e)-(h) The same as in (a)-(d), but for the signals from the laterally symmetrical leads F_8, Sp_2. (The leads F_7, Sp_1 belong to the left hemisphere, F_8, Sp_2 to the right hemisphere.)

genic area is the left temporal and occipital region, which drives the rest of the left hemisphere and also the right temporal and occipital areas, which secondarily drive the rest of the right hemisphere. This is in accordance with the MRI and PET scan results.

Patients II and III

In general, the temporal evolution of the synchronization phenomena leading to seizures is similar to the previous case; however, "information flows" in the case of these patients are much less pronounced than in the previous one. In particular, the drive-response relationships cannot be determined for most pairs of the analyzed signals. Only the signals recorded in areas close to the epileptic focus are the exemption; e.g., in the case of patient III the signal from the left sphenoidal electrode Sp_1 drives the signals from the left frontal area, which then drive the signals from the left central area. No directions of the information flow can be established in the right hemisphere.

These phenomena in the results of patient III are illustrated in Fig. 3, where the signals from leads F_7 [Fig. 3(a)], Sp_1 [Fig. 3(b)], F_8 [Fig. 3(e)], and Sp_2 [Fig. 3(f)] are displayed together with their synchronization analysis in a 7-min recording segment containing a seizure. The local synchrony measured by the CIR $i(.)$ increases at the edge and during the seizure in all cases, as well as the interarea synchrony measured by the MCIR $i(.,.)$. The latter, however, is greater on the left (focus) side than on the right side; i.e., $i(F_7,Sp_1) > i(F_8,Sp_2)$ in its peaks. Note that during a part of the developed seizure the condition [Eq. (16)] for the generalized synchronization is fulfilled on the left side when $i(F_7) < i(F_7,Sp_1) < i(Sp_1)$, while the ictal increase of $i(F_8,Sp_2)$ is considerably lower than that of $i(F_8)$ and $i(Sp_2)$ [Fig. 3(c) and (g)]. Also, the emergence of preictal asymmetry in the information flow can be observed only on the left side when the TCIR $i(F_7|Sp_1)$ became greater than $i(Sp_1|F_7)$ in a time of approximately 160 s from the segment beginning [Fig. 3(d)], while no such asymmetry can be observed on the right side; i.e., between $i(F_8|Sp_2)$ and $i(Sp_2|F_8)$ [Fig. 3(h)].



4. Analyses of the same signals as in Fig. 3, however in different pairwise combinations: (a) the CIRs $i(F_7)$ (dashed line), $i(Sp_2)$ (dash-and-dotted line), and the MCIR $i(F_7,Sp_2)$ (full line); (b) the CTIRs $i(F_7|Sp_2)$ (dotted line) and $i(Sp_2|F_7)$ (full line); (c) the CIRs $i(F_7)$ (dashed line), $i(F_8)$ (dash-and-dotted line), and the MCIR $i(F_7,F_8)$ (full line); (d) the CTIRs $i(F_7|F_8)$ (dotted line) and $i(F_8|F_7)$ (full line); (e) the CIRs $i(F_8)$ (dashed line), $i(Sp_1)$ (dash-and-dotted line), and MCIR $i(F_8,Sp_1)$ (full line); (f) the CTIRs $i(F_8|Sp_1)$ (dotted line) and $i(Sp_1|F_8)$ (full line);(g) the CIRs $i(Sp_1)$ (dashed line), $i(Sp_2)$ (dash-and-dotted line) and the MCIR $i(Sp_1,Sp_2)$ (full line); and (h) the CTIRs $i(Sp_1|Sp_2)$ (dotted line) and $i(Sp_2|Sp_1)$ (full line).

Further pairwise analyses of the signal from the same leads and segment are presented in Fig. 4. The ictal increase of the mutual CIR $i(F_7,Sp_2)$ [Fig. 4(a)] is considerably lower than that of $i(F_7,Sp_1)$ and there is no clear asymmetry in the information flow between F_7 and Sp_2 [Fig. 4(b)]. On the other hand, the ictal increase of $i(F_8,Sp_1)$ is higher; however, $i(F_8,Sp_1)$ is still lower than both $i(F_8)$ and $i(Sp_1)$; i.e., the condition [Eq. (16)] is not fulfilled [Fig. 4(e)]. There is also a slight increase of information flow asymmetry reflecting the active role of the signal from Sp_1 [Fig. 4(f)]. The ictal increase of the MCIR between the laterally symmetrical leads F_7 and F_8 [Fig. 4(c)] and Sp_1 and Sp_2 [Fig. 4(g)] is again clearly visible, although lower than that between F_7 and Sp_1 [Fig. 3(c)}. There is no clear distinction of the direction of the information flow between F_7 and F_8 [Fig. 4(d)], while a slight excess in the direction from Sp_1 to Sp_2 can be seen [Fig. 4(h), from 220 s].

For patient II similar phenomena have been observed, namely the lateral asymmetry in the level of synchronization when the ictal increase of both the local and interarea synchronization is very high in the left frontal, temporal, and central areas, while considerably lower on the right side [Fig. 5(c) and (g)]. The focus seems to be located closely to the left central area, since the signal from C_3 drives that from F_7 [Fig. 5(d)] and also that from Sp_1. No driving (asymmetry in the information flow) can be detected on the right side [Fig. 5(h)].

Conclusion

The above-introduced information-theoretic approach suitable for studying synchronization phenomena in experimental time series has been applied in analysis of EEG recordings of epileptic patients. Transient phenomena leading to seizures have been characterized by increased synchronization (local and between areas) and asymmetry in information flow (the area of the epileptogenic focus drives and synchronizes adjacent areas). Although the results should be regarded as preliminary, they suggest that the method has a promising potential for localization of epileptic foci and anticipation of approaching seizures.

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Milan Paluš was born in Bojnice, Slovakia, in 1963. He studied mathematical physics at the Charles University in Prague where he received the RNDr degree (an M.Sc. equivalent) in 1986. In 1992 he received his C.Sc. degree (a Ph.D. equivalent) in computer science from the Czechoslovak Academy of Sciences in Prague. In 1992 he was a visiting fellow at the Center for Complex Systems Research, Beckman Institute, University of Illinois, Urbana-Champaign, Illinois, USA, in 1992-1994 a postdoctoral fellow in the Santa Fe Institute (Santa Fe, New Mexico, USA), supported by the International Research Fellowship from the Fogarty International Center (National Institutes of Health, Bethesda, Maryland, USA); and in 1996 he was a visiting scholar at the School of Mathematics, Queensland University of Technology, Brisbane, Australia. Currently, he is with the Department of Nonlinear Modelling, Institute of Computer Science, Academy of Sciences of the Czech Republic, Prague. His research interests include nonlinear dynamics, chaos, and synchronization phenomena (especially in relation to time-series analysis); information theory (especially in relation to nonlinear dynamics and statistics); identification and characterization of nonlinearity; and nonlinear prediction and classification, with applications in physics, physiology, medicine, meteorology and climatology, economy, and finance.

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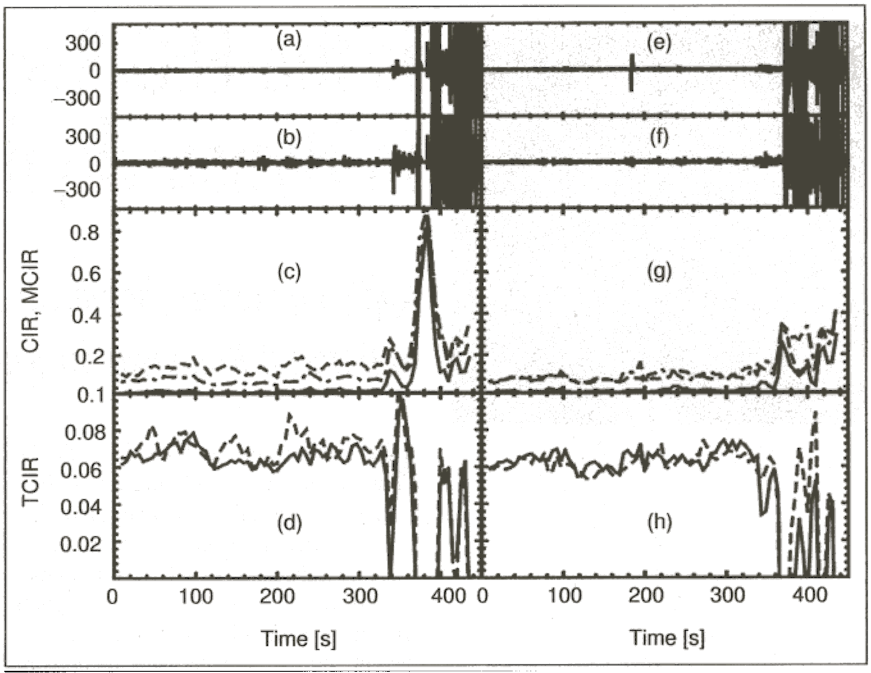

5. A segment of an ictal (with a seizure) EEG recording of patient II, recorded from (a) the leads F_7 and (b) C_3. (c) The CIRs $i(F_7)$ (dashed line), $i(C_3)$ (dash-and-dotted line), and the mutual CIR $i(F_7, C_3)$ (full line). (d) The coarse-grained transinformation rates $i(F_7 | C_3)$ (dashed line) and $i(C_3 | F_7)$ (full line). (e)-(h) The same as in (a)-(d) but for the signals from the laterally symmetrical leads F_8, C_4. (The leads F_7, C_3 belong to the left hemisphere, F_8, C_4 to the right hemisphere.)

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