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SYNCHRONIZATION AND INFORMATION FLOW IN EEG OF EPILEPTIC PATIENTS

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Abstract— An information-theoretic approach for studying synchronization phenomena in experimental time series is presented and demonstrated in analysis of EEG recordings of an epileptic patient. Two levels of synchronization leading to seizures are quantified and "directions of information flow" (drive-response relationships) are identified.

I. Introduction

Synchronization on various levels of organization of brain tissue, from individual pairs of 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. New hopes appeared in the field of synchronization of chaotic systems which has undergone very important development recently [1]. Various measures of synchronization have been proposed, however, the problem of synchronization detection is far from being trivial and some claims of successful detection of the causal relationships are based on contradictory assumptions [2, 3]. Also, measures of synchronization based on infinitesimal properties and well performing on artificial systems can fail when applied on noisy experimental data. We propose to study synchronization in such data using statistical, coarse-grained measures with basis in information theory which could provide an indication of synchronization as well as of causal relationships if present in the scrutinized systems.

II. Entropy and information rates

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

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

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

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

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

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

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

$$I(X;Y) = H(X) + H(Y) - H(X,Y). \qquad (4)$$

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

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

For Z independent of X and Y we have

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

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

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

where $H(X_1,\ldots,X_n)$ is the joint entropy of the n variables $X_1,\ldots, X_n$ with the joint PDF $p(x_1,\ldots,x_n)$, is a measure of "information creation" by the process

$\{X_i\}$, or a rate how quickly the process "forgets" its history. The entropy rate, in the case of dynamical systems called Kolmogorov-Sinai entropy (KSE) 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 [6]. Instead, Paluš [6] has proposed to compute "coarse-grained entropy rates" (CER's) 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 $\{X(t)\}$, $t = 1, 2, 3, \ldots$. 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 the 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 $h^1 = I(x, x_{\tau_0}) - ||I(x; x_\tau)||$. It has been shown that h^1 provides the same classification of states of chaotic systems as the exact KSE [6]. Since usually $\tau_0 = 0$ and $I(x; x) = H(X)$ which is given by the marginal PDF $p(x)$, the sole quantitative descriptor of the underlying dynamics is the mutual information norm (8) which we will call the coarse-grained information rate (CIR) of the proces $\{X(t)\}$ and mark 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 CIR's $i(X)$ and $i(Y)$. In order to characterize an interaction of the two systems, in analogy with the above CIR we define their symmetric mutual coarse-grained information rate (MCIR)

$$i(X, Y) = \frac{1}{2\tau_{max}} \sum_{\tau=-\tau_{max}}^{\tau_{max}; \tau \neq 0} I(x; y_\tau). \quad (9)$$

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 the quantitative answer to this question we propose to evaluate the conditional CIR $i_0(X|Y)$

$$i_0(X|Y) = \frac{1}{\tau_{max}} \sum_{\tau=1}^{\tau_{max}} I(x; x_\tau|y), \quad (10)$$

considering the usual choice $\tau_{min} = \Delta\tau = 1$ sample. Recalling (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 which vanishes for uncoupled system (though then it can acquire both positive and negative values), we define

$$i(X|Y) = i_0(X|Y) - i(X). \quad (11)$$

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

$$i_1(X, Y|X) = \frac{1}{\tau_{max}} \sum_{\tau=1}^{\tau_{max}} I(y; x_\tau|x), \quad (12)$$

and, in order to obtain the "net asymmetric" information measure, we subtract the symmetric MCIR (9):

$$i_2(X, Y|X) = i_1(X, Y|X) - i(X, Y). \quad (13)$$

Using a simple manipulation we find that $i_2(X, Y|X)$ is equal to $i(X|Y)$, defined in (11). By using two different ways we have arrived to the same measure which we will mark 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 the process $\{X\}$, or, in other words, the average rate of the net information flow by which the process $\{Y\}$ influences the process $\{X\}$.

III. Application on numerically generated data

Consider the unidirectionally coupled nonidentical ($b_1 = 0.1$ and $b_2 = 0.3$) Henon maps (defined in [2, 7]) where the drive is marked by $\{X\}$ and the response by $\{Y\}$. For 101 values of the coupling strength ϵ we iterate the systems, compute their Lyapunov exponents (LE) and CIR's, MCIR and TCIR's. The latter are computed using the simple box-counting based on marginal equiquantization, i.e., a partition with equiprobable marginal bins [6]. The results, obtained using 8 marginal bins, $\tau_{min} = \Delta\tau = 1$ and $\tau_{max} = 15$ samples are illustrated in Fig. 1. The positive LE (Fig 1a) of the drive is constant, while the largest LE of the response (LLE(Y)) decreases with increasing ϵ and becomes negative at $\epsilon = 0.38$. After $\epsilon = 0.6$ it rises and touches zero around $\epsilon = 0.62$ and then it falls again into negative values which define synchronized states. The CIR $i(X)$ (Fig. 1b) is constant, while

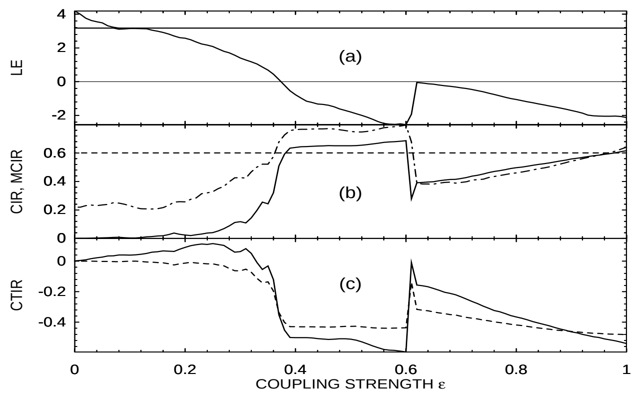

Figure 1: (a) The largest Lyapunov exponents of the drive $\{X\}$ (constant line) and the response $\{Y\}$ (decreasing line), (b) the CIR $i(X)$ of the drive (dashed line) and $i(Y)$ of the response (dash-and-dotted line) and the mutual CIR $i(X,Y)$ (full line), (c) the coarse-grained transinformation rates $i(X|Y)$ (dashed line) and $i(Y|X)$ (full line) for the unidirectionally coupled nonidentical Henon systems.

$i(Y)$ reflects the development of LLE(Y). The mutual CIR $i(X,Y)$ is zero for $\epsilon < 0.2$, then it rises with LLE(Y) approaching zero and then $i(X,Y)$ reflects the behavior of $i(Y)$ and the state of generalized synchronization [1, 2] is accompanied with $i(X,Y)$ rising into values $\min(i(X), i(Y)) \leq i(X,Y) \leq \max(i(X), i(Y))$. The CTIR's (Fig. 1c) indicate the correct causal relation of $\{X\}$ being a drive of $\{Y\}$ by their relation $i(X|Y) < i(Y|X)$, i.e., there is a larger flow of information from $\{X\}$ to $\{Y\}$ than vice-versa. This is, however, recognizable only before the synchronization threshold. Consider a state of identical synchronization, then one has two identical time series and it is impossible to infer a causal relation just from the data. This explanation can be generalized into time series related by a one-to-one nonlinear function as is the case of the generalized synchronization. In summary, the above introduced CIR, MCIR and CTIR can indicate synchronization and causal relation of drive and response (sub)systems. The latter is possible to establish only in states in which the (sub)systems are coupled, but not yet fully synchronized. For more details and other examples see [7].

IV. An EEG case study

A 30 months old male patient has been 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, later myoclonic-astatic seizures appeared. Recently two long-term video/EEG monitoring sessions were performed, the first one 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 the synchronization analysis using the above CIR's, MCIR and TCIR's. The latter were estimated from a 1024-sample moving window (moving step 128 samples, sampling frequency 256 Hz), using 4 marginal equiquantal bins and $\tau_{min} = \Delta\tau = 1$ and $\tau_{max} = 50$ samples. Signals form reference and longitudinal (bipolar) montages have been analyzed. The latter have brought more clear results in establishing "directions of information flow", i.e. the drive-response relations using TCIR. From a segment with a short seizure, signals from the leads T_6O_2 (Fig. 2a) and F_4C_4 (Fig. 2b) are illustrated here. Before the seizure both $i(T_6O_2)$ and $i(F_4C_4)$ present occasional increases, however, develop independently and the mutual CIR $i(T_6O_2, F_4C_4)$ keeps on low values (Fig. 2c). At the edge of the seizure (time 32 sec.) CIR's 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) has been recently used for anticipating approaching seizures [4, 5]. For evaluating predictive properties of CIR's we do not have enough data yet, thus we proceed to the TCIR 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 same signals but from a segment in an interictal (i.e., far from seizures) recordings (Fig. 3). Both the CIR's $i(T_6O_2)$ and $i(F_4C_4)$ fluctuate on the same level, though the dependence of the signals, measured by $i(T_6O_2, F_4C_4)$ is low (Fig. 3c). The drive-response relation cannot be unambiguously defined, since the CTIR's $i(T_6O_2|F_4C_4)$ and $i(F_4C_4|T_6O_2)$ are either approximately the same or mutually exchange their dominance. These results suggest that transients to seizures are characterized by increasing level of synchronization (both local and between areas) and an

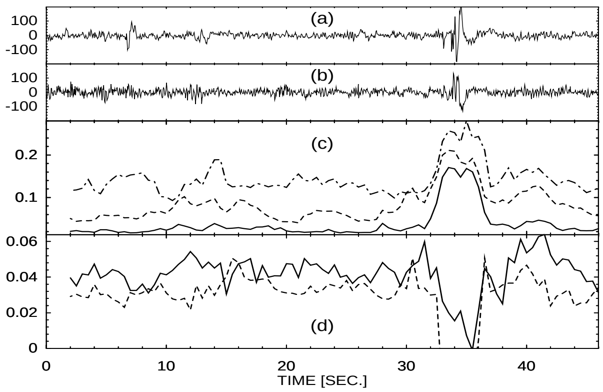

Figure 2: (a) An EEG segment with a short seizure, recorded from leads T_6O_2 (a) and F_4C_4 (b). (c): The CIR's $i(T_6O_2)$ (dashed line), $i(F_4C_4)$ (das-and-dotted line) and the mutual CIR $i(T_6O_2, F_4C_4)$ (full line). (d): The coarse-grained transinformation rates $i(T_6O_2|F_4C_4)$ (dashed line) and $i(F_4C_4|T_6O_2)$ (full line).

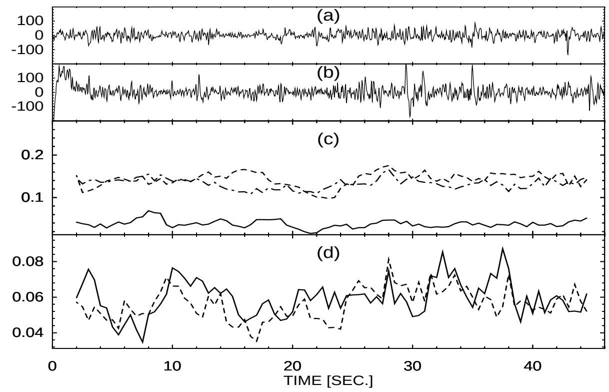

Figure 3: The same as in Fig. 2, but for an interictal EEG segment.

asymmetry in information flow emerges or is amplified. Considering the latter we have found that the signal T_6O_2 drove all signals from the right hemisphere and even some signals from the left central and frontal areas. 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 my 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 epileptogenic areas are the left temporal and occipital region, which drive the rest of the left hemisphere and the right temporal and occipital areas, which secondarily drives the rest of the right hemisphere. This is in accordance with MRI and PET scan results. The driving from left temporal/occipital to right central/frontal areas, and the symmetrical one, is probably a secondary interaction due to common dynamical components in the signals from the left and right temporal/occipital areas.

V. Conclusion

An information theoretic approach has been introduced for study of synchronization phenomena in experimental time series. Preliminary but promising results from analysis of EEG recordings of an epileptic patient have been presented. The method still requires further development on both theoretical and technical levels, however, we hope it will be helpful in neurology research and clinical practice.

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