Intermittency-driven complexity in the brain: towards a general-purpose event detection algorithm

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Abstract. In this work we first discuss a well-known theoretical framework for the analysis and modeling of self-organized structures in complex systems. These self-organized states are metastable and rapid transition events mark the passages between self-organization and background or between two different self-organized states. Thus, our approach focuses on characterizing and modeling the complex system as a intermittent point process describing the sequence of transition events.

Complexity is usually associated with the emergence of a renewal point process with power-law distributed inter-event times, hence the term fractal intermittency. This point process drives the self-organizing behavior of the complex system, a condition denoted here as intermittency-driven complexity.

In order to find the underlying intermittent birth-death process of selforganization, we introduce and discuss a preliminary version of an algorithm for the detection of transition events in human electroencephalograms. As the sequence of transition events is known, the complexity of the intermittent point process can be investigated by applying an algorithm for the scaling analysis of diffusion processes driven by the intermittent process itself. The method is briefly illustrated by discussing some preliminary analyses carried out on real electroencephalograms.

Keywords: signal processing, complexity, fractal intermittency, brain, electroencephalogram (EEG), disorders of consciousness

1. Introduction

The brain is composed of many elementary units, neurons and astrocytes, with an extremely complicated topology of the links among units (axon, dendrites, metabolic network)⁴ [1]. The links are characterized by strong nonlinear interactions among neurons (e.g., the chemically activated electrical discharges through the ionic channels) with very complicated feedback mechanisms. The overall picture is that of a complex network with a huge number of nodes (neurons and astrocytes) and links with a very complicated topology. The nonlinear dynamics of single neurons (i.e., the threshold mechanism for the electrical discharges generating spikes and bursts) are highly enhanced by the complex network topology, but at the same time some kind of ordering, or self-organizing, principle triggers the emergence of global cooperativity.

It is then not surprising that brain dynamics display a very rich landscape of different behaviors and a very efficient plastic behavior, characterized by a rapid and efficient capability of response to rapid changes in the external environment. Thus, a great interest is nowadays focused on a better understanding of the brain information processing, with the challenging goal of describing brain complexity by means of a relatively low number of parameters. This is not only a very fascinating problem and a very hot topic in brain research, but it also has important potential applications in several fields (e.g., clinical applications, new diagnostic indices).

In this general framework, the *complexity* approach [2, 3] is focused on the study of emerging self-organized structures in multi-component systems and complex networks. This general approach is nowadays gaining momentum in the field of biomedical signal processing. In order to extract useful information from large clinical datasets, storing many different physiological data and signals, algorithms for the reduction of data complexity are needed to derive reliable diagnostic indices. Then, a great interest is focused in defining, developing and testing statistical indices that can enclose the minimal information required to interpret the basic features of physiological signals. The availability of large datasets storing many different physiological data and signals is asking for reliable procedures of complexity reduction in large datasets. This is needed to extract useful information from the data themselves, which is of much relevance in clinical activity, such as in the diagnosis and treatment of disorders of consciousness (DOC) [4]. However, such indices are useful if they are able to describe the key features of the signals and if these features can be exploited by physicians in their clinical activity, e.g., in the evaluation of a medical condition or disease (diagnosis); in foretelling the course of a disease (prognosis); in the consequent choice of the proper therapy (decision making).

In this work we introduce and discuss an approach to the processing of ElectroEncephaloGrams (EEGs) that is based on the observation that, in many complex systems, such as the human physiology, the nonlinear dynamics of the

⁴ Astrocytes are responsible for the regulation of the neural metabolism and, thus, for the energy delivery and storage that neurons need for their electrical activity. The role of the substrate network of astrocytes is nowadays recognized to play a crucial role in brain information processing, as it has been recently found that the metabolic component of the brain is characterized by an intense cooperativity between astrocytes and neurons [1].

network trigger intermittent events, each one associated with the emergence or decay of self-organized structures and/or with the transition among different self-organized states [5–12]. Our approach to the modeling of such complex systems and, consequently, to the associated algorithms for data analysis and signal processing is based on the idea that intermittent events drive the complex (self-organizing) behavior of multi-component systems.

The paper is organized as follows. In Section 2 we present and discuss the concept of intermittency-driven complexity. After discussing the concept of fractal intermittency (FI), we give a brief review about the emergence of FI in the human brain. In Section 3 we sketch our proposal of a preliminary version of a general-purpose event detection algorithm. Finally, in Section 4, in order to illustrate the event detection algorithm, we briefly discuss an application to real EEG data by showing a few preliminary results.

2. Intermittency-driven complexity

Following the paradigm of *emerging properties*, the complexity approach focuses on the analysis and modeling of self-organized large-scale structures or states emerging from the cooperative dynamics of complex networks. The main idea is that self-organized structures are the essential actors in the global dynamics of complex systems and play a crucial role in many aspects, such as the transport properties and the way the system respond to external stimuli. As a consequence, also the statistical indicators extracted from complex data analysis usually refer to some global property associated with the dynamical evolution of large-scale, global, self-organized states.

2.1. Complexity and fractal intermittency

As far as we know, a general agreement on the definition of complexity does not yet exist. However, we refer here to a class of complex systems displaying the following properties:

- (1) a complex system is multi-component with a large number of degrees of freedom, i.e., many functional units or nodes. As said above, these units interact with each other and their dynamics are strongly nonlinear:
- (2) non-linearity and multi-component is not enough to define complexity: the dynamics are cooperative and trigger the emergence of self-organized structures, being self-organization not related to the presence of a internal master or to an external ordering force;
- (3) self-organized states display long-range space-time correlations (slow power-law decay) and self-similarity (mono- or multi-scaling);
- (4) self-organized states are metastable, with relatively long life-times τ and fast transition events between two successive states.

In summary, the cooperative dynamics determine an alternation of strongly correlated self-organized structures and a background characterized by short-term

correlations, or an alternation among different self-organized states. The passages are marked by fast transitions that can be considered quasi-instantaneous events. The n-th event occurs at a random time t_n . The sequence of transition events is an emergent property described as a an intermittent birth-death point process of self-organization: $\{t_n\}_{n=0}^N$; $t_0 = 0$. Then, in the above list the feature (4) is a crucial one as it allows for a description of complexity in terms of intermittent events.

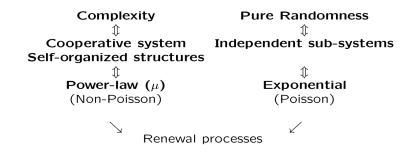
Due to the fast memory drop occurring during the fast transitions, each selforganized state is often independent from each other, as such as the crucial transition events and the inter-event times, also named Waiting Times (WTs): $\tau_n = t_n - t_{n-1}; n = 1, 2, \dots$ This is denoted as renewal condition. In this case, the sequence of crucial events is described by a renewal point process. A complex (cooperative) system is characterized by metastable self-organized states whose life-times τ_n are statistically distributed according to a inverse power-law function. This condition, i.e., the triggering of fast transition events that are renewal and with inverse power-law WT distribution, is denoted as fractal intermittency (FI) [9, 13–16]. The term intermittency-driven complexity (IDC) is here used to indicate both the associated complex behavior and the class of complex systems displaying FI. In this case the birth-death point process of self-organization is given by a non-Poisson process (renewal or not). The departure from the Poisson reference condition is a signature of complexity. In fact, a Poisson (renewal) point process is typically associated with the lack of cooperation and self-organizing behavior. A Poisson process does not generate neither long-range correlation or memory nor fractal intermittency, being the WT distribution given by an exponential decay [13, 15, 16]. Despite the presence of renewal events, the autocorrelation function of the intermittent signal can be long-range, i.e., with a slow power-law decay in the tail: $C(t) \sim 1/t^{\beta}$ [5].

The correlation exponent β is an important example of *emergent property* that can be used as a synthetic indicator of the cooperative dynamics in the complex system. For a complex system in the IDC class, β is related to the power index μ of the inverse power-law in the WT distribution:

$$\psi(\tau) \sim \frac{1}{\tau^{\mu}} \ . \tag{1}$$

Analogously to β , also $\psi(\tau)$ and μ are emerging properties and, thus, a signature of complex behavior. The parameter μ , denoted as complexity index, is an example of a statistical index that can quantify the presence of IDC in a system, thus evaluating the ability of the complex system to trigger self-organization. Other indices, depending on μ , can also be used as IDC indices [9, 13–16]. In particular, complexity is identified with a condition of very slow decay in $\psi(\tau)$, corresponding to the range $1 < \mu < 3$ (see Refs. [13, 16] for details). In Fig. 1 we sketch a synthetic scheme qualitatively explaining the connection between self-organization, cooperation and non-Poisson renewal processes. Poisson renewal processes always emerge in the case of independent systems, whatever the microdynamics of the single nodes. As a consequence, a departure from the Poisson statistics reveals some kind of cooperation among the nodes of the network.

Further, the emergence a fractal renewal process, i.e., a renewal process with inverse power-law WT distribution (fractal intermittency), means that cooperation is complex, i.e., associated with complex self-organized structures.



 $\textbf{Fig. 1.} \ \, \textbf{Comparison of Poisson (non-complex) and non-Poisson (complex) renewal processes.}$

2.2. Fractal intermittency in the brain: a brief survey of results

Metastability is a basic feature of the information processing in the brain neural network. Fingelkurts and Fingelkurts recognized that rapid changes in EEG records, called Rapid Transition Processes (RTPs), mark passages between two quasi-stationary periods, each one corresponding to different neural metastable assemblies, and are the signature of brain self-organization [17, 18]. Neural assemblies are associated with transient information flow among different neurons with the goal of developing a specific brain function and/or the response to external stimuli (e.g., Event Related Potentials). RTPs and neural assemblies are then a prototype of crucial events and meta-stable self-organized states, respectively. The algorithm for the automatic detection of RTP events in EEG data was developed in Ref. [18] and exploited by the authors of Refs. [5, 7, 6, 8–11] to characterize the complexity of the intermittent events. By exploiting a scaling detection method, the Event-Driven Diffusion Scaling (EDDiS) algorithm (see [13] and references therein), these authors found that brain dynamics display fractal intermittency. In particular, it was shown that the fractal intermittency approach is able to reveal the integrated (Rapid Eye Movement, REM) and segregated (Non-REM) stages during sleep, thus in agreement with the consciousness state of the subjects [9–11]. This important result proves that the IDC concept and the associated IDC measures could be good candidates for the characterization of DOCs.

In the intermittency-based analysis here proposed, a key aspect is the definition of events, which needs to be further studied in order to extend the above analysis to different experimental and clinical conditions.

3. Intermittency-based processing of complex physiological signals

The results obtained by applying the algorithms cited above, the RTP event detection algorithm [18] and the EDDiS algorithm [5, 16, 15, 13], are very promising in the perspective of potential applications in the clinical activity of neurological disorders. However, RTP events are defined only for some experimental conditions.

In this work we investigate the key aspect of the event definition. We propose an algorithm involving a more general definition of event and being able to detect and discriminate events with different neuro-physiological origins. The proposed method essentially extends the technique introduced and applied in Refs. [19–21], which allows to extract different kind of events marking the sudden increase of activity in given frequency bands.

We assume that the signals were already pre-processed for the artifact cleaning. Then, the event detection algorithm works as follows:

- (1) Splitting of the single EEG channel into different frequency bands. The following band ranges are usually considered: (a) δ band (0.5 4 Hz); (b) θ band (4 8 Hz); (c) α band (8 12 Hz); (d) σ band (12 16 Hz); (e) β band (16 35 Hz); (f) γ band (35 64 Hz).
- (2) For each frequency band, the component amplitude (the absolute value) is considered. Then, two moving-window time averages are computed at different time scales, a short and a long one, being this last one used to evaluate the signal envelope⁵.
- (3) Calculation of non-dimensional descriptors $A_k(t)$ for each frequency band $k = \delta, \theta, ...$: (short-time average long-time average)/long-time average. Then, the global average \overline{A}_k (or some local average) of $A_k(t)$ is computed and subtracted to $A_k(t)$ itself: $S_k(t) = A_k(t) \overline{A}_k$.
- (4) Identification of high- and low-activity epochs and of transition events between epochs. This is done for each frequency band by using a thresholding technique, whose details and parameters can also be changed depending on the specific events that must be detected. The most simple method, which be applied in the next section, is given by the zero crossings of the $S_k(t)^6$.
- (5) Storing in a database (spatio-temporal event maps). Extraction of specific kinds of events from the event maps.

⁵ In the original applications of the method [19–21] typical chosen values of the averaging times were 2 and 64 sec., as these values were the most suitable to detect macroscopic epochs of high intensity in the given frequency band.

⁶ The particular definition of event remain the most subtle point of the IDC approach. As an example, if we are interested in characterizing the epochs with substantially increased activity in a given band, and the associated transition events from/to these same epochs, usually two thresholds are used, a low and a high one. This is the standard approach used to automatically detect the waveforms that could be investigated also by visual inspection [19–21].

(6) Feature extraction from the event sequences and maps, such as: number of events per time unit for each band and/or EEG trace; covariance matrix based on events; estimation of complexity index, both for single EEG channels and global events (temporal coincidences among different EEG channels).

Despite its apparent simplicity, this algorithm is very flexible and powerful. Being based on the classical Fourier approach and on splitting the EEG signal into standard frequency bands, this approach allows for a more clear link between the event detection algorithm and its neuro-physiological interpretation. In this sense, a particular kind of brain events should be recognized to be a neural correlate of some increased or decreased neurophysiological activity.

4. An application to EEG data: preliminary results

In this final section we briefly illustrate an application of the event detection algorithm to real EEG records. The EEG data were collected during a study performed in the Brain Injury Unit, Department of Neuroscience, Cisanello Hospital, Pisa, Italy [22]. A few unconscious patients were treated with a drug (Zolpidem)⁷, with the working hypothesis that Zolpidem might increase the brain activity in a rapid way (i.e., within 30 minutes). The general objective of this pilot study was to stimulate a rapid recovery of the patient's consciousness. Clear clinical evidence was not obtained and it would be desiderable to get some kind of indications that the single treatment had some kind of effect on the brain electrical activity.

Here we show a preliminary analysis on one patient, whose EEG was recorded according to the international 10-20 configuration system. The EEG was

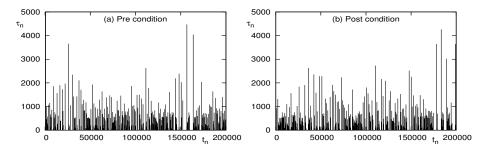


Fig. 2. Waiting Times τ_n vs. the occurrence times t_n of transition events (zero crossings) for the α band of the O_2 electrode. *Pre* condition in Panel (a) refers to the EEG baseline before the Zolpidem treatment, while *Post* condition in Panel (b) refers to the EEG measured 30 minutes after the Zolpidem treatment.

⁷ The hospital ethical committee approved the study and Informed written consent was obtained from the guardians or relatives of the patients.

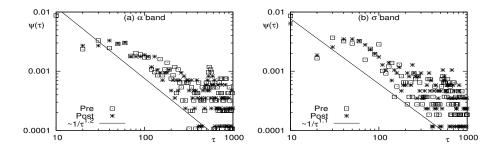


Fig. 3. Histograms $\psi(\tau)$ of the WTs extracted from the electrode O_2 for the bands α (Panel (a)) and σ (Panel (b)). The bin size is 10. The Pre and Post conditions are compared in each panel. The inverse power-law functions are reported as a guide-to-the-eye.

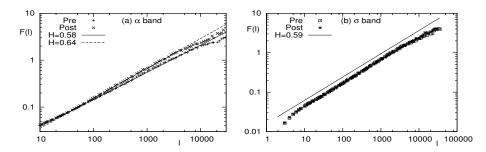


Fig. 4. DFA function F(l) as a function of the time lag l for the O_2 electrode. Panel (a) α band; Panel (b) σ band. The *Pre* and *Post* conditions are compared in each panel. The estimated index μ is also reported.

recorded before (baseline) and 30 minutes after the Zolpidem treatment. The sequence of zero crossing events and the associated WTs are derived for each frequency band. In Fig. 2 we report the sequence of WTs τ_n extracted from the α band of the O₂ electrode. WTs are plotted as a function of the event occurrence times t_n . Pre and Post conditions are reported in Panels (a) and (b), respectively. In Fig. 3 we show the histograms of WTs extracted from two different bands, α (Panel (a)) and σ (Panel (b)), of the same electrode (O₂). For each frequency band the Pre and Post conditions are reported and compared.

As a general observation, we can say that no qualitative and/or quantitative difference between the Pre and Post conditions is clearly stated and the WT distributions appear to be almost identical for the two conditions. This situation is also seen in the other electrodes and frequency bands. However, as said above, IDC is investigated by estimating the anomalous scaling behavior of diffusion processes that are built in a proper way using the transition events extracted from the signals. The EDDiS algorithm is applied to the WT sequences in order to obtain one or more (event-driven) diffusion scaling indices and/or the complexity index μ (see Ref. [13] for a review of the EDDiS algorithm). Here we

limit ourselves to derive a single diffusion process, which is defined by allowing a random walker to make a unitary jump ahead (+1) in correspondence of each transition event. This walking rule is known as Asymmetric Jump (AJ) and it has been proven to be an efficient and reliable method for the scaling evaluation (see Ref. [13] and references therein, in particular Ref. [23]). Applying the AJ rule we get a diffusing variable X(t). The IDC is estimated through the second moment scaling H, corresponding to the Hurst exponent, which is defined by the following power-law behavior:

$$F(l) \sim l^H; F^2(l) = \langle \left(X^(l) - \overline{X}(l)\right)^2 \rangle .$$
 (2)

Here l is the length of the time window that is moved along the time series in order to carry out the time average. In fact, the statistical analysis of time signals can be only carried out by means of time averages. For any l, the signal is divided into time windows of length l. Each segment is a pseudo-trajectory of a statistical ensemble of path of total duration l. The second moment $F^2(l)$ of properly detrended fluctuations is computed by averaging over this statistical ensemble.

In our specific application, the second moment scaling H is computed by using the Detrended Fluctuation Analysis (DFA) [24], which is a scaling detection algorighm based on a proper evaluation of the trend $\overline{X}(l)$. The value H=0.5, named normal diffusion scaling, indicates the absence of long-range correlations and of network connectivity. Then, the neurons whose electrical activity contribute to the electrode signal (O₂ in this case) do not cooperate each other. Values around H=0.5 indicate low levels of cooperation, so the departure from the normal diffusion scaling is a measure of network cooperativity. When applied to single EEG electrodes this feature can be exploited as a signature of the functional connectivity, i.e., cooperative behavior, of the particular brain region affecting the electrode potential.

In Fig. 4 we show the results of the DFA applied to the diffusing random walk X(t) computed applying the AJ rule to the WTs whose distributions are given in Fig. 3. The diffusion scaling of the σ band (Panel (b)) does not change significantly before and after the Zolpidem treatment. On the contrary, the α band (Panel (a)) shows a small, but net difference between the two conditions. In particular, the IDC index H changes from H=0.58 to H=0.64, which correspond to a small increase in the complexity of the brain dynamics, at least in the region corresponding to O_2 . Interestingly, the values of H here estimated for a DOC patient are, as expected, much smaller that the typical values found in conscious healthy subjects, that is, $H \sim 0.75 - 0.95$ [5, 9–11]. Further, it is worth noting that the difference Pre-Post cannot be appreciated from the comparison of WT distributions, as it is clearly seen in Fig. 3.

This preliminary analysis and discussion is far from being conclusive and needs further investigations. In particular, a global analysis of the brain network will be carried out. However, in previous papers it has been shown that the IDC indices can characterize the kind of brain connectivity determining the emergence of consciousness [9–11]. Thus, we are convinced that the use of event-driven

diffusion scaling analysis (EDDiS) for the investigation of the brain IDC can have potential applications in the field of neurological diseases.

References

- M. Bélanger, I.Allaman and P.J. Magistretti: Brain Energy Metabolism: Focus on Astrocyte-Neuron Metabolic Cooperation, Cell Metabolism 14, 724-738 (2011).
- 2. R. V. Solé, J. Bascompte: Self-organization in Complex Ecosystems. Princeton University Press, Princeton (2006).
- 3. D. Sornette, Critical phenomena in natural sciences. Springer-Verlag, Berlin (2006).
- 4. , A.A. Fingelkurts, A.A. Fingelkurts, S. Bagnato, C. Boccagni and G. Galardi: Do we need a theory-based assessment of consciousness in the field of disorders of consciousness?, Front. Hum. Neurosci. 8(402), doi: 10.3389/fnhum.2014.00402 (2014).
- P. Allegrini, D. Menicucci, R. Bedini, L. Fronzoni, A. Gemignani, P. Grigolini, B.J. West, P. Paradisi, Spontaneous brain activity as a source of ideal 1/f noise, Phys. Rev. E 80 (2009), 061914.
- P. Allegrini, D. Menicucci, R. Bedini, A. Gemignani, P. Paradisi, Complex intermittency blurred by noise: Theory and application to neural dynamics. Phys. Rev. E 82 (2010) 015103.
- 7. P. Allegrini, P. Paradisi, D. Menicucci, A. Gemignani, Fractal complexity in spontaneous EEG metastable state transitions: new vistas on integrated neural activity. Frontiers in Physiology 1, 128 (2010).
- 8. P. Allegrini, P. Paradisi, D. Menicucci, R. Bedini, A. Gemignani, L. Fronzoni, Noisy cooperative intermittent processes: From blinking quantum dots to human consciousness. J. Phys.: Conf. Series 306 (2011) 012027.
- 9. P. Paradisi, P. Allegrini, A. Gemignani, M. Laurino, D. Menicucci, A. Piarulli, Scaling and intermittency of brain events as a manifestation of consciousness, AIP Conf. Proc. **1510** (2013), 151-161.
- P. Allegrini, P. Paradisi, D. Menicucci, M. Laurino, R. Bedini, A. Piarulli, A. Gemignani, Sleep unconsciousness and breakdown of serial critical intermittency: New vistas on the global workspace. Chaos, Solitons and Fractals 55 (2013) 32-43.
- 11. P. Allegrini, P. Paradisi, D. Menicucci, M. Laurino, A. Piarulli, A. Gemignani, Selforganized dynamical complexity in human wakefulness and sleep: Different critical brain-activity feedback for conscious and unconscious states, Phys. Rev. E **92**, (2015) 032808.
- 12. P. Grigolini and D.R. Chialvo (Eds.): Emergent Critical Brain Dynamics (Special Issue), Chaos Sol. Fract. **55**, 1-120, Elsevier, Amsterdam (2013).
- 13. P. Paradisi, P. Allegrini, Scaling law of diffusivity generated by a noisy telegraph signal with fractal intermittency, Chaos, Solitons and Fractals 81 (2015), 451462.
- P. Paradisi, G. Kaniadakis, A.M. Scarfone, The emergence of self-organization in complex systemsPreface, Chaos, Solitons and Fractals 81 (2015) 407411.
- 15. P. Paradisi, R. Cesari, A. Donateo, D. Contini, P. Allegrini, Scaling laws of diffusion and time intermittency generated by coherent structures in atmospheric turbulence. Nonlinear Processes in Geophysics 19 (2012) 113-126; P. Paradisi et al., Corrigendum, Nonlinear Processes in Geophysics 19 (2012) 685.
- P. Paradisi, R. Cesari, A. Donateo, D. Contini, P. Allegrini, Diffusion scaling in event-driven random walks: an application to turbulence. Rep. Math. Phys. 70 (2012) 205-220.

- A. A. Fingelkurts, A. A. Fingelkurts, Brain-Mind Operational Architectonics Imaging: Technical and Methodological Aspects. Open Neuroimag. J. 2 (2008) 73-93.
- 18. A.Y. Kaplan, A.A. Fingelkurts, A.A. Fingelkurts, B.S. Borisov, B.S. Darkhovsky, Nonstationary nature of the brain activity as revealed by EEG/EMG: methodological, practical and conceptual challenges. Signal Process. 85 (2005) 2190-2212.
- C. Navona, U. Barcaro, E. Bonanni, F. Di Martino, M. Maestri, L. Murri, An automatic method for the recognition and classification of the A-phases of the cyclic alternating pattern, Clin. Neurophysio. 113 (2002), 1826-1833.
- U. Barcaro, E. Bonanni, M. Maestri, L. Murri, L. Parrino, M.G. Terzano, A general automatic method for the analysis of NREM sleep microstructure, Sleep Med. 5 (2004), 567-576.
- M. Magrini, A. Virgillito, U. Barcaro, L. Bonfiglio, G. Pieri, O. Salvetti, M.C. Carboncini, An automatic method for the study of REM sleep microstructure, Int. Workshop on Computational Intelligence for Multimedia Understanding (IWCIM 2015), Prague, 29-30 October 2015, DOI: 10.1109/IWCIM.2015.7347066 [IEEE Xplore Digital Library]
- 22. G. Valenza, M.C. Carboncini, A. Virgillito, I. Creatini, L. Bonfiglio, B. Rossi, A. Lanatá and E.P. Scilingo, EEG complexity drug-induced changes in Disorders of Consciousness: a preliminary report, Proceedings of the 33rd Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC2011), 3724-3727 (2011) [Website: embc2011.embs.org/].
- 23. P. Grigolini, L. Palatella, G. Raffaelli, Asymmetric anomalous diffusion: an efficient way to detect memory in time series. Fractals 9 (2001) 439-449.
- C.-K. Peng, S. V. Buldyrev, S. Havlin, M. Simons, H. E. Stanley, A. L. Goldberger, Mosaic organization of DNA nucleotides. Physical Review E 49 (1994) 1685.