

Chapter 1

Intermittency-driven complexity in signal processing

In this chapter, we first discuss the main motivations that are causing an increasing interest of many research fields and the interdisciplinary effort of many research groups towards the new paradigm of *complexity*. Then, without claiming to include all possible complex systems, which is much beyond the scope of this review, we introduce a possible definition of complexity. Along this line, we also introduce our particular approach to the analysis and modeling of complex systems. This is based on the ubiquitous observation of metastability of self-organization, which triggers the emergence of intermittent events with fractal statistics. This condition, named *fractal intermittency*, is the signature of a particular class of complexity here referred to as *Intermittency-Driven Complexity (IDC)*. Limiting to the IDC framework, we give a survey of some recently developed statistical tools for the analysis of complex behavior in multi-component systems and we review recent applications to real data, especially in the field of human physiology. Finally, we give a brief discussion about the role of complexity paradigm in human health and wellness.

1.1 What is Complexity ?

1.1.1 Complexity as emergence of self-organization from cooperation

In the past, monitoring the activity of systems with many degrees of freedom was typically limited to a very small portion of it, and often only a single basic component could be observed or, on the contrary, the overall activity of the system itself (bulk measurement) could be measured, but without any knowledge about the detailed evolution of the single components of the system. In the last two decades or so, many research fields have seen the development of new experimental techniques opening the way to much more accurate and complete observations of multi-component systems. More precisely, in many research fields it has become possible to get simultaneous observations, with high time/space resolution, of all the single unit activities in the network. As an example, the spiking activity of many neurons linked through a network can nowadays be simultaneously observed by means of large arrays of electrodes [1] or by recording calcium fluorescence through a high-speed high-resolution camera mounted on a microscope [2,3]. In this example, the new experimental tools make it available a large set of neuron spiking data that are recorded in parallel from many units and with great accuracy (i.e., not bulk measurements).

These large datasets are nowadays available in many research fields: sociology and economy (e.g., social networks, internet data, GPS mobility data); biology and physiology with the “-omics” data (e.g., proteomics, genomics, metabolomics, connectomics) [4–9]. The details of a multi-component system are then known and typically represented as a complex network (graph) of interacting units, defined as a set of nodes and links among nodes, thus allowing for the analysis and modeling of different time and space scales of the system, ranging from the single unit to the global dynamics.

Many recent studies are unveiling some common features and behav-

iors (e.g., emergence of self-organization, multi-scaling, self-similarity) among data-sets collected from very different multi-component systems. A general opinion is taking momentum in the scientific community that these common features could be the signature of some “*universal*” behavior, which is generically denoted as *complexity*, while the systems displaying such behavior are denoted as *complex systems* [9–13]. This new paradigm of complexity is triggering many interdisciplinary research activities involving skill, expertise and ideas from different fields: statistical physics, probability theory and statistics, stochastic processes, nonlinear dynamical systems, network science, data mining, signal processing.

In spite of the extensive use of the term “*complexity*” in hundreds of papers regarding the study of multi-component systems, a definition of complexity that is universally accepted in the scientific community does not yet exist and a unified view of how Complexity should be defined is probably still far from being reached. However, some aspects that, as said above, are common to many multi-component systems, are recognized to be signs or clues of complexity [7, 8, 10–14]:

- A complex system is a multi-component system with many degrees of freedom: individuals, particles, single units. Each unit is a node in a network with a complex topology of links among nodes, representing the (nonlinear) interactions among single units.
- Multi-component and nonlinearity are not sufficient to define complexity. **Complexity** is associated with the **emergence of self-organizing behavior**, i.e., the spontaneous formation of self-organized structures that are triggered by some **cooperative** mechanism in the nonlinear dynamics. This emergent behavior is not related to a master driving the system in a given self-organized state but, on the contrary, the self-organizing behavior emerges, in some sense, “*spontaneously*” from the overall cooperation on the single units¹. A master can be some unit

¹Cooperative dynamics in multi-component systems always need an external

or hub in the network, or an external forcing, affecting directly all the units, or a great majority of the units, of the multi-component system, thus having a direct control over all the internal dynamics.

- **Non-reducibility:** self-organized states have features and space-time scales that are hardly obtained as a simple (linear) function of an external forcing or by means of linear coarse graining procedures (e.g., average or weighted sum over single components).
- The spontaneous emergence of self-organization by the cooperative behavior in a complex network and without a master is associated with **self-similar**, i.e., **mono-fractal** behavior, whose signature is seen in the power-law relationships among different physical quantities. A **multiscaling (multifractal)** behavior can also emerge in some physical observable quantities [15]. For example, self-organized states display **long-range** space and/or time correlation functions, given by slow **power-law** decays in space and/or time. Consequently, the correlation exponents are an important example of **emergent properties**. It is worth noting that the association between self-organization (without a master) and scaling is so ubiquitous that scaling exponents are often used as an indicator of complexity and self-organization itself.

The emergence of scaling exponents related to self-organizing behavior is a intriguing and crucial aspect of complexity. Critical phenomena are an example of complexity [16] where long-range correlations and mono- or multi-scaling are always observed in combination with the emergence of self-organized structures (e.g, clusters of different sizes

energy source to sustain self-organization, i.e., the formation of coherent structures from the disordered background. However, this does not mean that the external forcing, even if pumping energy into the system, can control the inner mechanisms triggering the emergence of self-organizing behavior. Thus, the external forcing is not a master explicitly controlling the parameter of self-organized states, such as time and space scales, but only an external energy supply.

in the Ising spin model). The origin of scaling behavior and long-range correlations is well understood in this case. However, to our knowledge, for a generic complex cooperative system without a master the underlying mechanism determining the emergence of scaling behavior is not yet clear. Heuristically, it is reasonable to suppose that emergence of self-similar behavior is related to the absence of a master (unit, hub or external forcing). In fact, when a master determines the dynamics of all the units, then the self-organized structure should be driven by the same parameters, e.g., time and space scales, of the master.

As an example, in the laminar motion of a liquid pumped in a pipeline, a rotation is observed immediately downstream of the pump whose angular velocity is related to that of the pump itself, with possible differences can be related to the friction of pipeline wall. No scaling behavior can be observed in this case. On the contrary, in cooperative dynamics without a master, whatever the scale of motion, self-organized structures emerge spontaneously and, in this case, long-range correlations and, in general, mono- or multi-scaling behavior, are always observed. Then, we can heuristically argue that the “spontaneous” emergence of a macroscopic, ordered structure from microscopic units requires a set of intermediate levels of organization, from a few units interacting over local domains and short time intervals (small scales) to the global level (large scales)². The need for intermediate levels of organization is essentially the reason why self-organizing behavior is usually related to a scale-free condition and, thus, to the emergence of self-similarity, mono-/multi-scaling and fractality.

From the above discussion about the general features of a complex system, we here propose a definition where the scaling features are

²Roughly speaking, the emergence of self-similarity is probably the most efficient way to carry information from the small to the large scales and this could be the reason for the emergence of this intermediate organizing levels filling the gap from the microscopic to the macroscopic scales. However, this intriguing problem is not well established and should deserve further investigations, which are beyond the scope of this chapter.

explicitly required, even if the simultaneous presence of cooperative dynamics and absence of a master should be sufficient to justify the emergence not only of self-organization, but also of the related scaling features.

Definition 1.1 (Complexity). *A multi-component, nonlinear, system is defined to be **complex** if*

(i) the dynamics are cooperative and trigger the emergence of self-organizing behavior;

(ii) there is not a master (unit or hub) whose features and parameters can be directly linked to the features and parameters of the emergent self-organized states.

(iii) The system's dynamics are monoscaling (self-similar) or multi-scaling.

We do not claim to give here a general definition of complexity. However, in the following we refer to systems satisfying the definition of complexity given above, a definition which seems to include many real multi-component systems spanning from socio-economic systems to biological networks. The self-organizing behavior associated with mono-/multi-scaling determines the ubiquitous emergence of power-law dependence of different physical quantities, such as: long-range time and/or space correlations; the scale-free distribution of the average degree of nodes in a complex network; the avalanche size distribution in self-organized critical systems; the cluster size distribution in percolation [16].

Another aspect that has to be mentioned regards the transport properties, which are usually characterized by anomalous scaling, i.e., non-linear time dependence in the growth of the variance. This condition is also known as *anomalous diffusion* [13, 17–20]. Many authors refer to the tools of *fractional calculus* to develop models that are able to reproduce the the power-law behavior of different observable quantities and, in particular, the anomalous transport properties of a complex system [17, 21–25].

Z

1.1.2 Metastability of self-organizing states: intermittency-driven complexity

Another property is often observed in multi-component complex systems. This property concerns the stability of self-organized states, which typically do not emerge as asymptotic equilibrium states, but are characterized by *metastability*. In our opinion, this property, which is often neglected or considered as a side effect, it is, on the contrary, a crucial aspect deserving a great attention when dealing with the emergence of self-organization. In more detail, we have the following general observations [11, 12, 18, 26–32]: :

- (a) Self-organized states are usually **metastable** states, i.e., relatively long, but not infinite, **life-times** characterize these states. The life-time is defined as the time interval between some **birth** time (**emergence** of self-organizing behavior) and a **death** time (**decay** of the self-organized structure).
- (b) An ubiquitous observation in complex systems is that the transitions between a not-organized state to a self-organized one (birth) and *vice versa* (death) are very **rapid**, usually leaving a mark of their occurrence in some experimentally measured quantities (e.g., neuron spiking activity). The overall behavior is then given by an alternation of self-organized and not-organized conditions whose passages are marked by **fast transition events** among these two conditions. In some complex systems the rapid transition can also occur between two different self-organized states.
- (c) The fast transitions events often determines a **fast memory drop** in the dynamics, so that self-organized states, and the transition events themselves, are statistically independent from each other. This is known as **renewal** condition [33].

The mathematical description of the metastability described above refers to tools of probability theory and stochastic processes [13, 18–

20, 33–39]. In particular:

- (i) The sequence of fast transition events among self-organized states is described by a **intermittent birth-death point process** of self-organization (i.e., coherence): $\{t_n\}$; $t_{n+1} > t_n$; $t_0 = 0$; $n = 0, 1, 2, \dots$, being t_n the occurrence times of the n -th transition event.
- (ii) The life-times of coherent structures are defined by the time intervals between two successive transition events: $T_n = t_n - t_{n-1}$; $n = 1, 2, \dots$. These times, hereafter denoted as *Waiting Times* (WTs), are mathematically treated as random variables and studied through the tools of probability and statistics. An ubiquitous feature of WTs is the emergence of a **inverse power-law tail** in the Probability Density Function (PDF): $\psi(\tau) \sim 1/\tau^\mu$ [26–32], being $\psi(\tau) = \text{Prob}\{\tau \leq T < \tau + d\tau\}d\tau$.
- (iii) Due to the renewal condition, the sequence of transition events is mathematically described by a **renewal point process**, which is defined as a point process whose WTs T_n are mutually independent random variables [33]. Conversely, in the time interval (t_n, t_{n+1}) between two events, i.e., in correspondence of a self-organized state, the dynamics are strongly correlated³.

The inverse power-law tail in the WT distribution is the manifestation of a self-similar behavior in the cooperative dynamics of the complex system and is also a crucial emergent property, characterizing the capacity of the complex system to trigger self-organization. Below we will show how this emergent property can be exploited as a measure of complexity, at least for the class of complex systems displaying intermittency associated with metastable self-organized states.

Exploiting the above list, we can give the following

³Surprisingly, even in the presence of the renewal condition, a complex system can display long-range correlation functions, and the slow power-law decay of the correlation is connected to the inverse power-law decay in the statistical distribution of the random life-times [26].

Definition 1.2 (Fractal Intermittency). *Given a complex multi-component system, we define as **Fractal Intermittency (FI)** the condition emerging when the transition events between two metastable, self-organized states are described by the stochastic point process defined in the above Points (i),(ii) and (iii).*

We chose here to include also the renewal condition (i.e., statistically independent events and WTs) in Def. 1.2, as this is, sometimes implicitly, the definition applied in many theoretical and experimental studies [26,34–42]. However, the role of the renewal condition is not yet clear and would deserve further investigations⁴. FI is the signature of a particular class of complex systems [12, 13, 20, 30, 31]. This particular kind of complexity is defined by the following

Definition 1.3 (Intermittency Driven Complexity). *Let us consider a complex system, i.e., a multi-component system satisfying Def. 1.1. We define the **Intermittency Driven Complexity (IDC)** as the particular class or subset of complex systems displaying Fractal Intermittency, that is, the kind of metastability described in the above points (a)-(c) and mathematically represented in the above points (i)-(iii).*

In the following we will limit ourselves to the class of complexity given in Def. 1.3⁵.

⁴It is rather intuitive that the fast transition events should always be associated with a memory drop (low predictability) in the system itself, so that the events should always satisfy the renewal condition. However, this is not experimentally verified in all complex signals. In spite of this, we are convinced that FI typically involves renewal events and that the renewal process driving the complexity could be sometimes hidden below a mixture of different contributions to the intermittency generated by the system, including also the presence of noisy, secondary events. However, it is possible that an extension of the renewal condition to a slightly non-renewal condition could be necessary in order to derive more robust models and algorithms for data analysis based on the FI and IDC paradigms.

⁵This complex behavior is also known as *Temporal Complexity* [43–47], a term underlining the difference of the intermittency-based complexity, focused on the

1.1.3 How intermittent event are generated: a dynamical explanation of metastability

We do not claim here that all complex systems belong to the IDC class. However, it is also true that this kind of complexity seems to emerge in a great majority of complex systems. In fact, fractal intermittency is observed in many multi-component systems where cooperative dynamics triggers the emergence of self-organized structures, which are typically metastable and self-similar. Examples of complex systems displaying a fractal intermittent behavior are: ecological systems [51], neural dynamics [52], blinking quantum dots [40, 41, 53], social dynamics [54], brain information processing [26, 28, 30, 31, 48, 49, 55–59], atmospheric turbulence [19, 20, 22, 39], earthquakes [60], single particle tracking in cell biology [61–64], molecular biology [18].

In order to give a possible explanation of the dynamical origin of metastability and of associated complex transition events, we refer to the models discussed in Refs. [65–67]. These authors propose a dynamical model for the brain information processing, but the paradigm of metastability introduced therein can be used also as a general paradigm for complex transition events. The brain dynamics are here modeled through a dynamical nonlinear system living most of the time on a *stable heteroclinic channel*. This is essentially a set of trajectories in the vicinity of a heteroclinic skeleton, consisting of saddle points and unstable separatrices. As known, this determines a slow motion towards the saddle points. This slow motion in the neighborhood of the saddle point can be interpreted as a metastable state that maintains its coherence (i.e., self-organizing behavior) for a long time interval. As the dynamical system approaches the saddle point a critical time occurs when the motion suddenly changes from a slow to a fast one. In this passage, the system experiences a sudden acceleration and a consequent rapid motion towards another saddle point

study of the temporal structure of self-organization, with the more known approach focused on the topological and spatial features of complexity (e.g., the degree distribution in a complex network, the avalanche size distribution) [47–50].

1.2 Complexity in biology and human physiology

(i.e., another metastable state). This critical time corresponds to the fast transition event, also associated with a sudden decrease of predictability and, then, with the drop of self-organization and memory, thus corresponding to the renewal property.

This very simplified brain model also illustrates another important aspect of complexity, which is actually a crucial paradigm for living systems. From nonlinear dynamical systems theory it is known that the above situation is not really typical of so-called chaotic systems (existence of a *strange or fractal attractor*), neither of systems with well-defined stable points or structures, such as limit cycles giving rise to perfect periodic patterns. Complexity is neither totally disordered (completely random) nor totally ordered (completely deterministic). In fact, in the above model, complex behavior is given by an alternation of calm (laminar) and chaotic (turbulent) motions. Then, complexity is a particular condition emerging in an intermediate region between total disorder and total order, total randomness and total determinism.

1.2 Complexity in biology and human physiology

The emergence of self-organization in biological systems is nowadays well established [12, 18, 43, 64, 68–70]. There is a lack of general leading principles, which is a very old problem of theoretical biophysics with respect to other fields where the theoretical research can refer to guiding principles (e.g., the postulates of classical mechanics). Even though, the search of complexity in biology and physiology is increasing very rapidly, attracting the interest of many research groups, as it can be seen from the rapid increase in the rate of publications dedicated to these topics. For example, systems biology is a very fascinating research field where the paradigm of complexity could have deep implications. The meaning and the role of the complexity paradigm in systems biology is deeply discussed in Ref. [71], a in-

interesting paper facing the recent epistemological questions arising in biology and reviewing the historical debate between the reductionist and the holistic view in systems biology

The research activity in biology is very active since many years. Novel experiments are continuously carried out and new experimental data are often available, so that new findings are obtained and published very rapidly. Biology research is nowadays so active that it is not rare that some unexpected experimental findings determines the failure of existing paradigms and models, thus triggering the search of new paradigms, interpretations and models. An important example comes from cell biology and, in particular, the important finding of anomalous transport behavior in the cell environment, such as the motion of lipids or proteins in the cytoplasm and on the cell membrane [18, 61–64]. An interesting debate about the best modeling approach to describe anomalous transport in the cell is taking momentum in the field of statistical biophysics, as it is not yet clear which one of two modeling approaches is the best candidate: (i) a intermittency-based transport model (Continuous Time Random Walk, CTRW) or (ii) a long-range correlated model (Fractional Brownian Motion, FBM; Generalized Langevin Equation, GLE) [25, 64, 72].

1.2.1 The challenge of physiological complexity

The idea that an integrated view of the different physiological functions is becoming more and more necessary to better characterize the healthy condition of a subject (positive or negative) is taking momentum in the scientific community. Making reference to the availability of *-omics* data, many research groups are focusing on the development of complex network models. The goal is not only linking the functions of different tissues and organs, but also trying to fill the gap between molecular biology and the physiology of human body by means of theoretical tools and instruments taken from different fields such as: network theory, statistical physics, data mining, information science,

signal processing [73, 74].

In the following we give a brief survey of brain and heart physiology in the framework of the complexity paradigm.

Brain

The brain is an important example and prototype of complexity. The nodes of the brain network are the neurons, which are basic units of information transport by means of electro-chemical activity, and the astrocytes, mainly responsible for the nutrient supply [75], while the (anatomical) links are given by synapses (connecting axons and dendrites) and the metabolic pathway involving both astrocytes and neurons. In recent years the role of astrocytes is being reconsidered. Many studies are finding that astrocytes could play a more active role in brain dynamics, including the secretion or absorption of neural transmitters and the propagation of intercellular Ca^{2+} waves over long distances in response to stimulation [75–77]. In summary, the topology of brain network is very branched and inhomogeneous, while brain dynamics are very rich and span over many temporal and spatial scales. Many research groups are focusing their attention on understanding the basic self-organizing mechanisms of the neural information processing. This is done through the characterization of different signals measured in the brain, such as the functional magneto-resonance imaging (fMRI), measuring indirectly the neural activity through the oxygen supply by the blood flow, and electroencephalography (EEG), measuring the electrical neural activity.

In the last two decades, the Fingelkurts brothers deeply investigated the brain dynamics and developed a conceptual multi-scale model of the brain, the Operational Architectonics [58, 59, 78]. This is a model of the brain information processing that is based on the emergence of neural assemblies and operational moduli that are self-organized and metastable. Information processing in the brain is probably the most important example of IDC, as fast transition events and fractal intermittency were found to characterize the brain collective behavior [26, 28, 78, 79]. In Operational Architectonics neural assemblies are

associated with transient information flow. The temporal evolution of an assembly is given by a fast self-organizing event (*birth*), a relatively long quasi-stationary period, and a critical time when the self-organizing behavior suddenly decays. These sudden changes can be detected through the EEG signal, thus qualitatively clarifying the relationship between Operational Architectonics, Fractal Intermittency and IDC.

Heart

The heart activity is usually recorded through the electrocardiogram (ECG), which, similarly to the EEG, is the measure of an electrical activity [80]. However, at variance with the EEG, the ECG has a well-defined counterpart in autorhythmic features of the myocardial heart activity, which is driven by a small set of cells having a *pace-maker* function, denoted as the sinus-atrial node. This corresponds to the master hub, controlling directly the heart rhythm, discussed in the FI and IDC definitions 1.2-1.3. The ECG in a healthy subject is given by the normal sinus rhythm (NSR), given by a well-known sequence of waves: P, QRS complex and T. As known, the R wave is given by a sharp peak in the ECG, which is so easily identified that is used to define the heart beating as the sequence of RR time distances, which are exactly the time intervals between two successive R peaks. Thus, the heart rate is given as number of R waves (beats) per minute. The NSR is identified through a set of reference ranges for some given features of these waves, mainly time intervals such as, e.g., the time between the beginning of the P wave and that of the QRS complex (QR interval, about 0.12 – 0.20 seconds) Then, standard criteria commonly used in the clinical practice to evaluate the healthy/unhealthy cardiovascular status of a patient are given by the mean morphological parameters of the P-QRS-T sequence.

Another important diagnostic parameter is given by the heart rate variability (HRV), which involves variations in the RR sequence [81]. At variance with the mean morphological parameters, the HRV is strictly connected with the correlation features of the ECG. This does

1.2 Complexity in biology and human physiology

not only add further information to the evaluation of the subject's health condition, but it has also a potential predictive capability. At a first sight the R peaks, being rapid transitions in the ECG signal, could be considered as good candidates for a event-based description of heart dynamics and the RR distances as the WTs in the IDC framework. However, the RR time distances have slow variations from one beat to the next, so that there is a strong correlation among R peak events due to the quasi-periodicity of the RR time distances. This violates the renewal condition and the inverse power-law distribution of WTs in the FI and IDC definitions 1.2-1.3.

It is also worth noting that the well-defined sequence of waves P-QRS-T, which is the manifestation of the controlling *pacemaker* function, is not compatible with power-law correlations in the original ECG signal. Thus, the RR peaks are not genuine complex events compatible with the IDC description. In fact, in HRV there are two kind of superposed dynamical systems. The first one is related to the sinus-atrial pacemaker, is strongly synchronized, generates the RR sequences, and is associated with the mechanics of the heart pump. The second, hidden, one is responsible for the HRV, operates through the modulation of heart beating by other physiological systems, mainly the autonomic nervous system (sympathetic and parasympathetic), and is associated with the adaptability of the heart rhythm to internal and environmental changes [81]. The non-complexity of the first dynamics, even if producing the very coherent and self-organized structure of heart pumping, is due to the presence of a master or control hub, i.e., the pacemaker. On the contrary, the second, hidden, dynamics is responsible for the complexity features of HRV. This concept is also denoted as *memory beyond memory* [82] and involves a proper definition of events marking the variations in the RR frequency. These genuine complex events are mutually independent and, at the same time, responsible for the emergence of long-range, power-law, correlations in the HRV.

1.3 Measuring IDC in signal processing: a survey of statistical tools and algorithms

In the complexity field, the main goal of many research groups working on complex systems is nowadays the development of algorithms, and associated models, for the extraction and interpretation of useful information from the big bunch of available data. Then, the main focus is on the development and testing of reliable and synthetic statistical indices (e.g., data mining, network analysis [7, 9, 14]). Following Def. 1.1, we recall that the complexity paradigm is essentially based on the concept of emergence. In particular, we mean here emergence of self-organized structures from cooperative dynamics. The main idea is that self-organized structures are the main contributors to different features of the complex system: transport properties; relaxation curves; response to external stimuli, this last one involving the adaptability to environmental changes (e.g., homeostasis in biology and physiology).

Consequently, in the development of models and statistical tools for data analysis and signal processing the main focus is on the characterization and simulation of emerging self-organized structures. In this framework, the statistical indicators extracted from the data analysis usually refer to some global property associated with the dynamical evolution of coherent, self-organized structures. Along this line, a *complexity measure* should characterize the ability of the system to trigger self-organization from overall cooperation among units without a master.

Coming back to Def. 1.1, point (iii) suggests the main direction in the development of complexity indices, that is, the self-similarity (mono-scaling) or multi-scaling, multi-fractal behavior of several observable quantities. In practice, this leads us to exploit the power-law behavior of several functions, such as, for example, the correlation function or the power spectrum, as a measure of complexity. In the recent

1.3 Measuring IDC in signal processing: a survey of statistical tools and algorithms

literature many complexity measures were proposed and applied in different contexts and, in particular, in the processing of physiological signals. The most involved research fields are probably network theory (network analysis) and data mining, involving information science and statistics [5, 7, 9, 14, 83]. These measures are usually focused on the topological or spatial structure of the complex network, involving concepts such as metrics and distances (e.g., connectivity measures). We refer the reader to the cited literature for the above measures, while we focus here on the intermittency driven complexity (IDC). The IDC class can usually be described in terms of the above topological measures, but other measures can be introduced in this case. These measures essentially focus on the temporal structure of the complex system, are clearly inspired to the metastability of the self-organized states and, thus, exploit the intermittency measures and other indices related to intermittency.

It is worth noting that these IDC-specific measures, involving the temporal structure of the complex system, can be related with some topological measures, but the two kind of measures could be also independent from each other. It is quite obvious that the existence of these relationships (e.g., correlation) depend on the observed features and on their dynamical evolution. As an example, let us consider the motion of a random walker over a scale-free complex network [4], being the motion given by random jumps between connected nodes. As known, the complex network is characterized by a scale-free degree distribution with a given power-law decay. We expect that the temporal features of the walker, such as diffusivity or return times, can be related to some topological measure of the complex network. This was proven by the authors of Ref. [84], who found that the scale-free property of the network is inherited by the random walker, showing a power-law decay in the PDF of the return times and they also found an explicit relationship between the power exponents of the return time PDF and of the degree distribution. This is a simple example where temporal and topological measures can be related. However, we again underline that this depends on the particular system under

consideration and on its dynamical behavior.

In the following we give a brief survey of some IDC-specific complexity measures, some of which were developed and/or applied by our research group.

1.3.1 The search for critical events in signal processing

According to Def. 1.3, IDC system dynamics trigger fast transition events occurring at some critical time instant when it is almost probable that also a sudden drop of memory occurs, a mechanism that is related to the passage from two different self-organized states. Then, IDC-specific measures are based on the existence of these *critical events* and on the possibility of extracting these events, i.e., their intensities and, especially, their occurrence times, from the experimental time series. In many complex systems (see, e.g., the fluorescence intermittency in Blinking Quantum Dots, BQDs, [40,41]) the emergence of self-organized states is quite evident and the definition of critical event is also clear and unambiguous. In these cases a well-defined event detection algorithm can be easily implemented.

This is not always the case, as it happens in brain dynamics or in turbulence, where more evident transitions are mixed with many ones that are much less evident. Even worse, the genuine complex events can be hidden by the presence of more evident fast transitions in the signal that, however, are not complex, which is the case of R peak events in HRV [82]. Up to our knowledge, there is no general event detection algorithm that can work for every system, but different methods can be applied depending on the particular kind of complex system considered. Different algorithms were in fact developed and applied to BQDs [29, 40–42], atmospheric turbulence [39], HRV [82, 85–87] and human EEGs [26–28, 57, 78, 79].

Brain events

The search for critical brain events is based on the Operational Ar-

1.3 Measuring IDC in signal processing: a survey of statistical tools and algorithms

chitectonics model by Fingelkurts and Fingelkurts [57,78] and on the associated event detection algorithm [79]. As said above, the concept of metastable neural assemblies correspond to the existence of crucial birth/death events. Neural assemblies and crucial events have a direct manifestation in EEG records by means of an alternation of relatively long-time quasi-stationary periods (neural assemblies) and quasi-instantaneous fast transitions between a self-organized neural assembly and a not-organized condition (death event) or *vice versa* (birth event). In the not-organized condition the majority of neurons near the EEG electrode is not firing (hyper-polarization) or, in any case, the local neural activity is not coordinated or synchronized. Consequently, the fast transition can be detected in the signals recorded by the nearest EEG electrodes. In Ref. [79] these fast transition events are denoted as Rapid Transition Processes (RTPs). After the usual artifact removal, the event detection algorithm for RTPs is applied to the single EEG channels according to the following steps: (i) a Hilbert transform is applied to the EEG signal; (ii) a moving average is applied to the resulting transformed signal to obtain a sort of local mean signal. (iii) The crossings between the transformed signal and its local mean are computed and the associated crossing times stored. These crossing events are candidates to become the critical transition events that we are looking for. (iv) A local derivative is evaluated. This can be done by just taking the two nearest sampling times, let's say t_n and t_{n+1} , and evaluating the corresponding local derivative of the EEG signal: $(\text{EEG}(n+1) - \text{EEG}(n))/(t_{n+1} - t_n)$. To avoid noisy effects, a local mean of the derivative is evaluated. (v) The distribution of the local derivative (absolute values) at the crossing times is computed. (vi) Finally, the RTPs are selected from the totality of the crossing times considering only the extreme values of the distribution, thus retaining only the crossing times with the steepest derivative. In our applications, we chose to retain the 99th percentile of the derivative distribution⁶. In the case of brain data,

⁶For further details about the RTP detection algorithm, we refer the reader to Ref. [79] and to Refs. [26,28] where our implementation is explained.

RTPs represent the prototype of complex events that we are looking for.

Heart events

The main goal of HRV analysis is characterizing the modulation of heart beating by the autonomic nervous system. This is the main focus of complexity studies as well, as HRV was found to display long-range, power-law, correlations and, thus, fractal or multifractal features [82, 88–91].

As discussed in Section 1.2.1, the R peaks are the wave of ECG that are most used to evaluate the heart beating. In order to detect the R peaks, and the associated QRS complexes, the algorithm are often divided into two main steps: (i) ECG signal preprocessing; (ii) decision rule for the QRS detection. The techniques used for Step (i) usually include a bandpass filtering to reduce noise coming by several sources, such as power line noise and muscle noise. The range 5 – 30 Hz usually covers most of the frequency content of the QRS complex [92]. Being Q, R and S sharp cusps, Step (i) can also include the evaluation of the signal derivative and/or even the squaring of the filtered signal, or of its derivative, in order to enhance the extremal values corresponding to local maxima/minima time points. The decision rule in Step (ii) is usually given through an amplitude threshold, which is often determined with some adaptive procedure. The reference time point is generally selected to be the R-wave, and the sequence of R peak occurrence times $\{t'_n\}_{n=1}^N$ is given as the output of the detection algorithm.

The associated RR time distances are then easily computed from the sequence of R time points t'_n and represent the basic feature exploited for the estimation of HRV in terms of complexity measures [82, 88, 90]. We recall that, at the end of Section 1.2.1, we showed that the R peak events are not complex events and do not satisfy the IDC definition 1.3, as they do not satisfy neither the renewal condition nor the emergence of fractal WT statistics (inverse power-law WT distribution). We again underline that this aspect is strictly connected to the pres-

1.3 Measuring IDC in signal processing: a survey of statistical tools and algorithms

ence of a control or master hub (the pacemaker) and indicates the lack of a spontaneous emergence of self-organization from cooperation in the heart.

Even though, the sequence of R peak events remains the basic feature used to characterize the HRV, even in the IDC framework. Roughly speaking, we can say that the dynamics of the single heart beat is not complex, while the variability in the heart beating (HRV) is complex, at least in healthy subjects [74, 81]. For this reason, the authors of Ref. [82] focused on a different kind of event involving the variations of RR distances. The algorithm works as follows:

- (i) A coarse graining procedure is applied by approximating the ideally continuous values of the RR distances by a set of discrete values with some given step ΔT . More precisely, let us consider the sequence of discrete values: $\tilde{T}_i = i \cdot \Delta T$. Then, the n -th WT is approximated by the nearest \tilde{T}_i :

$$T_n \rightarrow \tilde{T}_i \quad \text{if} \quad \tilde{T}_i - \frac{\Delta T}{2} \leq T_n < \tilde{T}_i + \frac{\Delta T}{2} \quad (1.1)$$

- (ii) The selection rule is given by selecting the time t_n when a jump between two different \tilde{T}_i occurs, usually: $\tilde{T}_i \rightarrow \tilde{T}_{i+1}$ or $\tilde{T}_i \rightarrow \tilde{T}_{i-1}$

The event detection algorithm was shown to be robust in a neighborhood of $\Delta T = 1/30$ seconds.

It is worth noting that the heart events extracted with the above algorithm are a prototype of the hidden complex events discussed at the end of Subsection 1.2.1 and driving the heart pacemaker. However, even this sequence of events contains both genuine complex events and pseudo-events and this is probably due to the unavoidable presence of false positives in the event detection algorithm [82].

1.3.2 Complexity measures for the IDC class

Let us recall that, according to Def. 1.1, a reliable measure of complexity should be able to estimate the ability of the system to trigger

self-organization. Always from Def. 1.1 we guess that the best approach is to evaluate the scaling features, i.e., the power exponents (e.g., the critical exponents in critical phenomena). Complexity measures are often developed in the context of network science [5,9] or in critical phenomena [8,16,93] and usually refer to the topology of the link structure or to concept associated with information transfer.

Before considering the IDC class, let us give two examples of topological measures of complexity. The most simple property that can be evaluated in a complex network is probably the covariance matrix. This can be used to give a first estimation of the connectivity (without causality relationships among nodes) and it is often used to define an adjacency matrix by a thresholding technique applied to the covariance matrix [50,94]. An important topological measure is given by the degree distribution, which is defined as the distribution of the number of link is whatever node of the network. In other words, if we randomly choose a node, the probability distribution of the links of this same node is defined as the degree distribution. A crucial result is that, in scale-free complex networks, the degree distribution is a inverse power-law function, thus revealing some kind of self-organization characterized by a self-similar behavior among different scales in the network structure.

From now on we refer only to complex systems in the IDC class. We are interested in the temporal complexity generated by the sequence of intermittent transition events, which, as already said, is modeled through a birth-death, stochastic, point process of self-organization. After the application of the event detection algorithm, we get the experimental sequence of events:

$$\{t_n\}; \quad n = 0, 1, 2, \dots; \quad t_0 = 0, \quad (1.2)$$

being t_n the occurrence time of the n -th event. The process is equivalently defined by the sequence of WTs $\{T_n\}$ with $\{T_n = t_n - t_{n-1}; n = 1, 2, \dots\}$.

Then, the formal definition of the birth-death *stochastic point process* of self-organization, associated with the above event sequence, is given

1.3 Measuring IDC in signal processing: a survey of statistical tools and algorithms

through the following counting process:

$$N(t) = \max \{n \in \mathbb{N} : t_n \leq t\} . \quad (1.3)$$

being \mathbb{N} the set of positive integer numbers. The IDC indices must refer to the statistical features of the point process $N(t)$. However, in the general case, the complete characterization of the point process $N(t)$ from an experimental dataset is practically impossible. In fact, the process $N(t)$ is rigorously and completely defined when all the k -order statistical distribution of the sequences $\{t_n\}$ and/or $\{T_n\}$ are given⁷:

$$\begin{aligned} P_1(\tau) &= \text{Prob}\{T_n < \tau; n = 1, 2, \dots\} \\ P_2(\tau_1, \tau_2) &= \text{Prob}\{T_{n_1} < \tau_1; T_{n_2} < \tau_2; n_1, n_2 = 1, 2, \dots\} \\ P_3(\tau_1, \tau_2, \tau_3) &= \text{Prob}\{T_{n_1} < \tau_1; T_{n_2} < \tau_2; T_{n_3} < \tau_3\} \\ P_4(\tau_1, \tau_2, \tau_3, \tau_4) &= \dots\dots\dots \end{aligned}$$

The numerical estimation of these distributions from the data is not only very demanding, but also clearly limited by the size of the statistical ensemble. For finite statistical samples it is also well known that the accuracy of the k -point distributions rapidly decreases as the order k increases. Even the development of theoretical models with general k -order statistics is a very difficult task.

However, in many models the WT-PDF $\psi(\tau) = P_1(\tau)$ and the 1|1 conditional probability:

$$P_{1|1}(\tau_1|\tau_2) = \text{Prob}\{T_{n_1} < \tau_1 | T_{n_2} < \tau_2\}$$

are sufficient to characterize, at least approximately, the point process $N(t)$. This is exactly true for a Markovian sequence of WTs, and it is even more true for renewal point processes, whose conditional probabilities do not depend on the previous history [33]:

$$P_{1|n}(\tau_{n+1} | \tau_n, \tau_{n-1}, \dots, \tau_2, \tau_1) = P_1(\tau_{n+1}) = \psi(\tau_{n+1}) .$$

⁷It is also possible to characterize the point process $N(t)$ by using directly the k -point statistical distribution of $N(t)$ itself. The statistical features of $N(t)$ and $\{T_n\}$ are clearly linked to each other.

Being the WTs mutually independent variables, a renewal point process $N(t)$ is uniquely defined by the WT-PDF $\psi(\tau)$.

Let us now recall that, as given in Def. 1.3, the IDC of a complex system is associated with the emergence of FI, which is defined in Def. 1.2. By this definition, FI is described by a renewal process with self-similar WT statistics, i.e., FI is associated with the emergence of a power-law tail in the WT-PDF:

$$\psi(\tau) \sim \frac{1}{\tau^\mu}, \quad (1.4)$$

which is, as said above, the signature of a self-organization with self-similarity and, thus, without a master. As a consequence, the signature of IDC emergence is associated with:

- (i) the occurrence of the renewal condition (at least approximately) and
- (ii) a power-law tail in the WT-PDF.

The power exponent μ is then a fundamental feature of the self-organizing behavior of the system that has been denoted as *complexity index* in recent literature [12,20,29,30]. With a more precise meaning, we here denote μ as **IDC index** and we claim that it can evaluate the capacity of the dynamics to trigger intermittent, complex events and, thus, self-organized, metastable structures whose self-similar behavior is not directly driven by a master.

The evaluation of the renewal condition and the computation of the IDC index requires some specific algorithms of statistical data analysis and signal processing. In the following we give a brief list of some algorithms developed and/or applied by our group to evaluate the renewal condition and the IDC index μ or scaling exponents related to μ itself. For further details about these algorithms, we refer the reader to the cited literature.

Analysis of Renewal Aging

Let us assume to observe a statistical ensemble of independent renewal processes with same fractal WT distribution. Suppose that the

1.3 Measuring IDC in signal processing: a survey of statistical tools and algorithms

system's preparation (i.e., initial condition) is made at $t = 0$ and that the starting time of experimental observation is some t_a . Then, when the WT-PDF $\psi(\tau)$ of the single renewal process has a slow inverse power-law (i.e., $\mu < 3$), the ensemble averages depend on the *aging time* t_a . In particular, the WT-PDF derived from the ensemble $\psi_{t_a}(\tau)$ depends on t_a and it is different from the WT-PDF of the single renewal process, which corresponds to the WT-PDF for $t_a = 0$ and is denoted as brand new WT-PDF: $\psi(\tau) = \psi_0(\tau)$. The departure of $\psi_{t_a}(\tau)$ from $\psi_0(\tau)$ in a renewal process is a statistical feature that was named *renewal aging* [35, 36, 38–42, 95, 96]. In general, aging is a property of many complex systems associated with the very slow relaxation of the initial conditions, also determining a departure from the ergodic condition (e.g., weak ergodicity breaking [64]).

The above feature can be exploited to give an indication about the “*renewal content*” of a time series or, in other words, if a point process is also renewal. Usually only a single sequence of events is experimentally available, so that the method has to start with the building of a statistical ensemble. Then, given the series of event occurrence times $\{t_n\}$, the renewal aging algorithm works as follows:

- (1) M sequences of *aged* events are built in the following way: the first sequence is the original one; the second sequence is given by the first one by removing the first WT; the third sequence is obtained from the second one by removing the first WT of the second sequence itself; and so on.
- (2) A time window of duration t_a is superposed to all sequences and the first available event with $t_n > t_a$ is taken, i.e., $t_n < t_a < t_{n+1}$.
- (3) The *aged* WTs are computed: $\text{WT}_m(t_a) = t_n - t_a$; $m = 1, M$.
- (4) Given the sequence $\{\text{WT}_m(t_a)\}$, the experimental aged WT-PDF $\psi_{t_a}^{exp}(\tau)$ is evaluated. The brand new WT-PDF $\psi_0^{exp}(\tau)$ is also evaluated.

-
- (5) In order to derive the aged WT-PDF in agreement with the renewal condition, we apply a random shuffling to the experimental WT sequence. The new sequence has exactly the same brand new WT-PDF $\psi_0^{exp}(\tau)$ of the original WT sequence, but the possible presence of inter-WT dependence has been destroyed, thus the shuffled WT sequence is renewal. Then, we repeat the steps from (1) to (4) to evaluate the renewal aged WT-PDF: $\psi_{t_a}^{ren}(\tau)$.

The comparison of the two WT-PDFs can be used to establish if the experimental WT sequence is renewal or, if not, how it departs from the renewal condition. The renewal aging analysis was implemented also by using the corresponding Survival Probability Functions (SPFs), which are defined by:

$$\Psi(\tau) = \text{Prob}\{WT > \tau\} = \int_{\tau}^{\infty} \psi(\tau) d\tau = 1 - \int_0^{\tau} \psi(\tau) d\tau . \quad (1.5)$$

Renewal, IDC index and diffusion scaling: the EDDiS algorithm

The analysis of Event-Driven Diffusion Scaling (EDDiS) is based on the building of event-driven random walks, also named Continuous Time Random Walks (CTRWs) [97–99], and on the estimation of the scaling exponents associated with the resulting diffusion process. In the case of fractal intermittency, the relationships among the different diffusion scaling exponents and the IDC index μ are known. Then, it is possible to derive independent estimations of the IDC index μ that can be compared with each other. When the differences between the values of μ so obtained are inside the statistical errors, we can reasonably argue that the process is renewal and we also get a robust estimation of the IDC index μ .

The EDDiS algorithm collects a number of different methods for scaling analysis and several theoretical results from the theory of CTRWs that are well known in literature by many years (for a review, see [13, 26] and references cited therein). However, the joined

1.3 Measuring IDC in signal processing: a survey of statistical tools and algorithms

exploitation of these methods and results with the scope of evaluating both the renewal condition and estimating the IDC index was carried out by our group for the first time in Refs. [26–28] and the first application was on ElectroEncephaloGram (EEG) data.

We give here a brief explanation of the algorithm and refer the reader to Refs. [13, 20] and references cited therein for further details. The EDDiS algorithm works as follows:

- (1) Given the experimental sequence of events, three different event-drive random walks are built by applying three walking rules for the instantaneous velocity $\xi(t)$:
 - (i) Asymmetric Jump (AJ) walking rule: the walker makes a unitary step ahead at every event occurrence time: $\xi(t_n) = +1$; $\xi(t) = 0$ if $t_n < t < t_{n+1}$.
 - (ii) Symmetric Jump (SJ) walking rule: similar to the AJ rule, but the walker can make positive or negative jumps: $\xi(t_n) = \pm 1$, being the sign \pm chosen with a coin tossing prescription: $\text{Prob}\{+1\} = \text{Prob}\{-1\} = 1/2$.
 - (iii) Symmetric Velocity (SV) walking rule: the walker moves with constant velocity in a given direction, until a new random direction is chosen in correspondence of an event by a coin tossing prescription: $\xi(t) = \pm 1$; $t_n \leq t < t_{n+1}$. This walking rule is also known as *telegraph signal*.
- (2) For each walking rule, the associated CTRW is given by the diffusion variable:

$$X(t) = X_0 + \int_0^t \xi(t') dt' \quad (1.6)$$

- (3) We estimate two different scaling exponent of the diffusion process $X(t)$:

(a) the self-similarity index δ of the PDF of $X(t)$:

$$P(x, t) = \frac{1}{t^\delta} F\left(\frac{x}{t^\delta}\right) . \quad (1.7)$$

The scaling δ is computed by applying the Diffusion Entropy (DE) analysis [100] (see Appendix A).

(b) the scaling exponent H of the second moment:

$$\sigma^2(t) = \langle (X(t) - \bar{X})^2 \rangle \sim t^{2H} , \quad (1.8)$$

where \bar{X} denotes the the mean value of $X(t)$. The scaling H is computed by applying the Detrended Fluctuation Analysis (DFA) [101] (see Appendix A).

The scaling exponents δ and H are theoretically exactly known in the case of fractal intermittency with index μ (see Ref. [13] for and references therein) and can be used as reference values for the estimation of the system's IDC. In fact, as said above, these scaling exponents can be jointly used to estimate the renewal condition and, indirectly, the index μ [20]. However, δ and H can be also used directly as indicators of IDC, as they were built on the basis of the sequence of events extracted from the experimental times series.

The functional relationships $\delta = \delta(\mu)$ and $H = H(\mu)$ are summarized in Figs. 1.1 and 1.2. Normal scaling is defined by $\delta = H = 0.5$ and is the signature of absence of cooperation and memory, a condition compatible with the central limit theorem and the emergence of Gaussian PDF and markovian exponential correlations. On the contrary, $\delta \neq 0.5$ and/or $H \neq 0.5$ is associated with cooperation and spontaneous emergence of self-organization, and the distance from the reference value 0.5 is a measure of complexity. It is clear from ?? that the interesting range is $1 < \mu < 3$, where anomalous diffusion scalings are observed (for the SJ rule this occurs only in the range $1 < \mu < 2$), whereas normal diffusion ($H = \delta = 0.5$) emerges in the range $\mu \geq 3$.

1.3 Measuring IDC in signal processing: a survey of statistical tools and algorithms

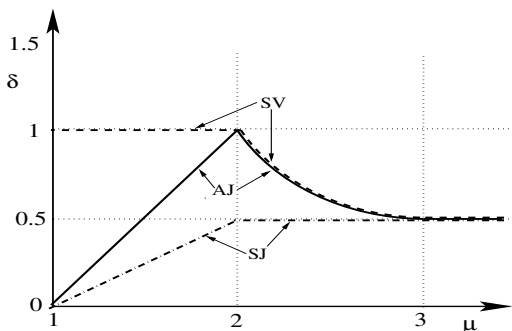


Figure 1.1: Scaling δ vs. complexity index μ for the three walking rules: AJ (continuous line), SJ (dotted-dashed line) and SV (dashed line).

The problem of noise and the PANDORA algorithm

The application of the EDDiS method was originally thought (i) to obtain a second check about the renewal condition in combination with the renewal aging method and (ii) to get a reliable estimation of the IDC index μ [26]. However, we later understood that the EDDiS method allows also to take into account the possible presence of noisy secondary events in the experimental sequence in the estimation of the IDC index μ . In fact, during the application of the EDDiS method, a surprising normal diffusion regime was seen in the long-time behavior of the SV-CTRW, even if the AJ-CTRW showed superdiffusion ($H > 0.5$) [26, 27]. This observation was explained by assuming the presence of noisy non-complex events generated by a Poisson process with event rate r_p , thus generating normal diffusion, mixed with the genuine complex events, thus generating fractal intermittency. This model is called Time Mixed Model (TMM). From this assumption, we found that the long-time normal diffusion in the SV rule was related to the exponential cutoff emerging in the WT-PDF of the mixed events.

This first result allowed us to explain the divergence among our findings, based on the EDDiS method, and those of other authors, based

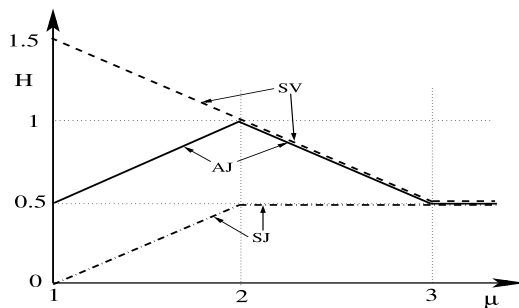


Figure 1.2: Scaling H vs. complexity index μ for the three walking rules: AJ (continuous line), SJ (dotted-dashed line) and SV (dashed line).

on a best fit applied to the WT-PDF (see, e.g., [102]). In fact, the presence of noisy events does not only introduce an exponential cutoff in the tail of the WT-PDF, but can also affect its power-law decay, as an apparent power exponent, completely different by the genuine IDC index of the complex process, can also appear in the WT-PDF [13,27]. This makes the application of the EDDiS method a very reliable statistical tool for the estimation of μ , a feature that is related to the capacity of the event-driven diffusion processes, especially the AJ rule, to separate the effect of noisy events from that of the genuine complex point process [19, 20].

Regarding TMM, we also found an interesting scaling law for the long-time diffusivity coefficient for the SV-CTRW:

$$D(\mu, r_p, T) \propto T^{\mu-2} r_p^{\mu-3}; \quad \mu > 2, \quad (1.9)$$

being r_p the Poisson rate of event occurrence and T the WT scale after which the complex behavior, marked by the passage to the power-law decay $1/\tau^\mu$, emerges in the WT-PDF. This scaling is valid for $\mu > 2$ and in the limit of small ratios between Poisson and complex events. In Ref. [13] we suggested a possible algorithm of time series analysis that, exploiting Eq. (1.9), could be used to evaluate both the IDC

1.3 Measuring IDC in signal processing: a survey of statistical tools and algorithms

index μ and the contribution of noisy events. This algorithm is here denoted as *Poisson Added Noise DiffusiOn Rescaling Analysis (PANDORA)*. Given the experimental sequence of event occurrence times $\{t_n\}$, the PANDORA algorithm works as follows:

- (1) Let us generate N random sequences of Poisson events $\{t_j^k\}$, $j = 1, 2, 3, \dots$ with the constrain that the occurrence time of the last Poisson event must be less than the total duration time of the experimental sequence. Each sequence has a different Poisson rate r_k , $k = 1, \dots, N$.
- (2) Then, for each k , let us build sequences that are given by the superposition of the experimental sequence $\{t_i\}$ and of the artificially generated Poisson sequence with rate r_k .
- (3) For each k , we apply the SV rule on the generated sequence of events (real+artificial Poisson) and we evaluate the long-time diffusivity coefficient $D_k = D(r_k)$. In this way we obtain a set of couples (D_k, r_k) that can be plotted to get the graph of the numerical function $D_k vs. r_k$.
- (4) It is known that the superposition of two Poisson processes with rates r_p and r_k results in a global Poisson process with total rate given by the sum of the single rates: $r_{\text{tot}} = r_p + r_k$. When the experimental sequence is affected by a Poisson noise with rate r_p , the Eq. 1.9 can be rewritten substituting the rate r_p with the total rate r_{tot} :

$$D_k = \tilde{D}(r_k; \mu, r_p, T) \propto T^{\mu-2} (r_p + r_k)^{\mu-3} . \quad (1.10)$$

A best fit procedure can now be used to evaluate the three parameters of the function $\tilde{D}(r_k)$, i.e., the IDC index μ , the rate r_p of the noisy (Poisson) events and the *complexity emergence time* T . It is also possible to apply a best fit with respect to only two parameters: r_p and T . In this case, μ is evaluated from the EDDiS method.

In order to validate the PANDORA algorithm, we simulated a sequence of complex events according to a fractal renewal process with $\mu = 2.3$. Then, we generated several TMM sequences where different Poisson processes with rates r were superposed to the simulated sequence. The long-time diffusivity coefficients $D(r)$ of the SV-CTRWs were estimated for each r and the resulting function $D(r)$ has been reported in Fig. 1.3 (circles). The dashed line is a best fit with a power-law function $r^{3-\mu}$, whose power exponent is in agreement with that predicted by the theoretical result given in Eq. (1.10), thus confirming the validity of our approach.

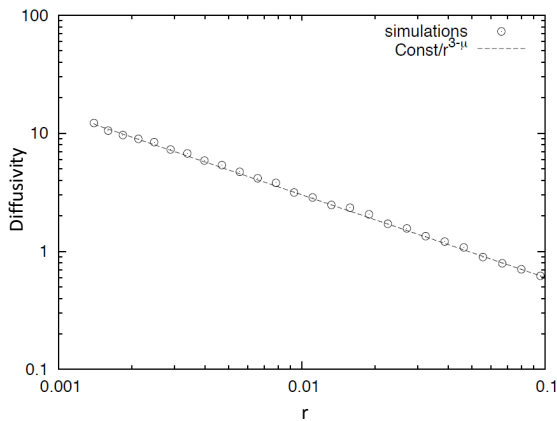


Figure 1.3: Simulation study showing the application of the PANDORA algorithm to an artificially generated sequence of complex events with $\mu = 2.3$. The diffusivity $D(r)$ has been plotted with respect to the rate r of the added Poisson noise (circles).

1.4 Applications to real physiological signals

The above algorithms (Renewal Aging, EDDiS and PANDORA), which are based on the FI and IDC paradigms given in Defs. 1.2 and 1.3, were applied to different experimental datasets, spanning from BQDs [40, 41] and turbulence [19, 20, 39] to ECGs and EEGs. In the following we give a brief survey of the applications carried out in the processing of two physiological signals, the EEG and the ECG, underlining the main results that were found within the IDC approach.

1.4.1 EEG complexity

As explained above, the Operational Architectonics model [78] includes concepts such as neural assemblies and operational moduli that are in agreement with the paradigm of emerging metastable self-organized states given in the IDC paradigm (Defs. 1.2 and 1.3). Through the definition of RTP events that mark sudden changes in the EEG traces and are associated with the fast transition events among self-organized states, a RTP event detection algorithm was also developed [79]. A version of this algorithm was implemented and applied by our group to extract RTP events from observed human EEG records collected in two different experimental conditions: the resting state condition and the sleep condition. Below we give a brief survey of the main findings.

Resting state

As known, the *resting state* condition, or is obtained when the subject is relaxed with closed eyes. This condition is typically characterized by the simultaneous emergence of α -waves in several EEG channels. From the RTP events of the single channels it is possible to define global events as the simultaneous occurrence of a given minimum number of single EEG events. Both the single channel and the global RTP events were analyzed through the EDDiS method to characterize

the complexity and, in particular, to estimate the IDC of the human brain during the resting state condition. The main experimental findings regarding IDC are [26–29]:

(1)

The sequences of global RTP events are compatible with a renewal fractal process for the global brain dynamics. The values of the global IDC index are in the range 2.05 – 2.4, while the values of the global diffusion scaling exponents span over the interval 0.8 – 1.

(2)

The probability of a EEG channel to be recruited into a global RTP event is higher for EEG channels belonging to the Default Mode Network (DMN) [103,104]. (3)

The EEG channels with high probabilities of being recruited into a global event are also those with the most complex behavior, with high values of the diffusion scaling δ that are compatible with superdiffusion. As said above, these channels belong to the DMN. On the contrary, the EEG channels with low δ (less complex or non-complex) have low probabilities to be recruited in a global complex brain event.

(4)

The variability among subjects of the δ scaling indices is much smaller for the EEG channels that are more complex (inside the DMN) with respect to the EEG channels that are less complex (outside the DMN).

(5)

The IDC indices of single EEG channels in the DMN have almost the same values of the global IDC index.

From these findings we can argue that the DMN drives the global complex behavior of the brain in the resting state condition. The small inter-subject variability suggests a sort of universal behavior of the DMN during the resting state, a result in agreement with previous findings, being the DMN the most active brain sub-network during the resting state condition [103,104].

Sleep condition: conscious vs. unconscious

The EDDiS analysis was also applied to EEG data collected during

1.4 Applications to real physiological signals

sleep. 29 nights have been analyzed, focusing on the first cycle that is usually the longest one [30–32]. As known, sleep is divided into cycles, typically 4 or 5 per night, and each cycle is divided into four main stages, defined on the presence of different waves, or graphoelements, and specific rhythms: N_1 , N_2 , N_3 (also called Slow Wave Sleep, SWS) and Rapid Eye Movement (REM) [55]. We focused on the first cycle, and we considered also the pre-sleep WAKE condition, approximately collecting the 30 minutes before the beginning of stage N_1 . Passing through stages N_1 , N_2 and N_3 the subject goes from a shallow sleep in the N_1 stage to the deep sleep in the N_3 stage (SWS). The SWS stage is a unconscious state, as the brain dynamics are segregated during this stage. On the contrary, during the REM stage, when dreaming occurs, the brain is segregated and a global conscious state emerges similarly to the WAKE conscious condition [55].

The main results regarding the IDC paradigm in the sleep condition are reported in Fig. 1.4, where the diffusion scaling exponents H , associated with the global brain events, are compared for different sleep stages. The pre-sleep WAKE and REM stages show an anomalous diffusion scaling $H = 0.75$, which corresponds, in the renewal condition, to $\mu = 2.5$. On the contrary, the SWS (N_3) stage reaches the asymptotic normal scaling $H = 0.5$ after a short-time transient. The N_2 stage also reaches an asymptotic normal scaling, but this occurs at times much longer than the SWS stage. In fact, it is evident an extended short-time range with an anomalous diffusion behavior. All these results are in agreement with the concept of segregation-integration in the brain network, associated with emergence of unconscious-conscious states. This confirms that the global IDC index and/or the related diffusion scaling exponents can be used to estimate the connectivity features of the brain neural network. Then, μ , H or δ can be used as indicators of consciousness.

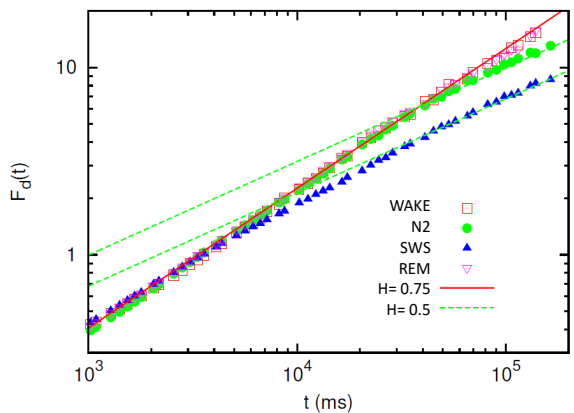


Figure 1.4: Comparison of the scaling H for different sleep stages

1.4.2 ECG complexity

HRV is recognized to be a useful clinical tool for the evaluation of cardiac autonomic changes. The relationship of HRV with the mortality risk following myocardial infarction is well established since many decades [105, 106]. More precisely, HRV is reduced in patients recovering from an acute myocardial infarction and, further, the mortality risk increases as the HRV decreases [107]. This important result was found by time and frequency methods, such as the estimation of signal variance, usually applied to the RR distance sequence. Clearly, a small variance indicates low HRV. However, it is well-known that HRV is affected by the parasympathetic and the sympathetic autonomic systems. Further, even if these relationships are still not completely understood and quite controversial, it is well established that the heart-autonomic system interactions are strongly nonlinear, and the overall coupled heart-autonomous system is reminiscent of a globally cooperative, complex system. Consequently, it seems quite natural to characterize the HRV in terms of complexity features extracted

1.4 Applications to real physiological signals

from the sequence of RR distances in order to improve the prognosis of different clinical conditions and, in particular, the distinction between health and disease. These methods do not strictly estimate the amplitude of HRV, but its complexity by means of scaling exponents and long-range correlation features associated with self-similarity, i.e. fractality.

Following this idea, the authors of Refs. [86, 87] compared several complexity measures, also denoted as nonlinear indexes, to investigate the prognostic potentiality in patient with chronic heart failure (CHF), thus highlighting the importance of HRV complexity measures in the prognostic stratification of CHF patients. Among others, also the δ index, computed from the R sequence through DE (see Appendix A), was evaluated. The DE and the δ scaling were used also in Refs. [82, 85] to evaluate the complexity and, thus, long-range correlations, of RR distances. As said at the end of Subsection 1.2.1, these authors assumed that the hidden dynamics, related to the autonomic system and driving the heart pacemaker, is associated with the heart events extracted with the algorithm discussed at the end Subsection 1.3.1. The main results of their analysis were:

- (i) The comparison between δ , estimated with the DE, and μ , estimated by the WT-PDF, makes evident the existence of hidden dynamics, as the DE is able to detect the genuine scaling δ of the hidden dynamics themselves.
- (ii) The scaling δ can be used a measure of complexity.
- (iii) Subjects with congestive Heart Failure (cHF) were compared with healthy subjects and it was found two well disting regions in the plane (δ, ϵ) , being ϵ the rate of pseudo-events.

Another powerful complexity measure extensively applied to HRV through the analysis of RR distances is given by the detrended fluctuation analysis (DFA), evaluating the second moment scaling H and whose algorithm and meaning is discussed in Appendix A. DFA

quantifies long-range correlations and, thus, the presence of (fractal) power-law memory in the signal. The first application to HRV proved the existence of universal fractal properties in healthy subjects and loss of fractal, complex, self-organization in heart failure patients [108]. In particular, it was found a general distinction between a short-time and a long-time behavior:

- (i) In the range $L < 11$ beats, a short-term scaling exponent H_1 , also denoted as α_1 , can be seen. Typical values for healthy subjects are $H_1 \sim 1$.
- (ii) In the range $L > 11$ beats, a long-term scaling exponent H_2 , also denoted as α_2 and different from α_1 , is evident.

Many authors found evidence that the short-term scaling H_γ of heart beating are related to the subject condition (health status, aging) and can have prognostic capability better than that obtained by more conventional measures of HRV (e.g., variance, power spectrum). Decrease in the H_1 scaling was shown to be associated with activation of both vagal and sympathetic outflow, thus resulting in a more random behavior, i.e., lower complexity, of heart beating [109]. Healthy elderly subjects display changes in the long-range correlation features of HRV [110]. The authors of Ref. [111] found that altered short-term DFA scaling in HRV precedes the onset of atrial fibrillation in patients without a structural heart disease. Similarly, changes in the short-term scaling are observed in ectopic tachycardia associated with disturbances in the autonomic system or in ectopic atrial pacemakers [112]. The application of DFA to patients with acute myocardial infarction (AMI) showed that lower values of short-term scaling H_1 are associated with a greater mortality [113]. DFA was observed to have a prognostic value even in the case of patients taking beta-blockers after acute myocardial infarction [114].

In general, all these studies indicate that, in subjects with several heart diseases, fractal or complexity measures change towards values indicating the presence of more random fluctuations and, thus, less

1.5 A brief discussion about wellness, health and complexity

complex behavior in HRV with respect to healthy subjects. Nonlinear, complexity, indexes have some advantages over the conventional measures of HRV in risk stratification purposes, such as (i) less dependency on heart rate, (ii) less inter-individual and intra-individual variations and (iii) smaller relative changes of individual values over time [86,87,115,116] (see Ref. [117] for a review).

1.5 A brief discussion about wellness, health and complexity

We conclude this chapter discussing an open issue in physiology, biomedicine and physiological signal processing that will probably attract the interest of the scientific community in the next years.

Diagnostic methods are based on chemical and physical analyses and on evaluation of symptoms. When there are no symptoms and the chemico-physical analyses give results within the normative values, the subject is considered to be in a healthy condition. However, it is very usual that the general health equilibrium of a subject with a good general diagnosis could be affected by some subtle, hidden stress working silently, i.e., much under the threshold of both subject self-perception and medical analyses. This silent external stress can work for years without any evidence, especially if it is almost continuous in time (daily) and relatively weak in intensity. In fact, human physiology is able to respond to a silent and weak stress factor by means of homeostatic mechanisms determining a shift in the general physiological equilibrium. This subtle, prolonged condition is probably the most hard to be detected when looking at single physiological parameters, which are usually associated with the functioning of single organs or tissues or with some cell metabolic process

The above discussion highlights the need for a integrated view of the human physiology [74,118] and, thus, for a model coupling the single physiological systems defined in the standard biomedical analyses. This coupled model surely requires ideas and concepts taken from the

complexity paradigm, as it is based on the emergence of self-organizing behavior with scaling and self-similarity. Following this holistic view ("the whole is more than the sum of its parts"), but without neglecting the complementary reductionist, analytic approach [71], future work and effort will be probably devoted to the development of a integrated model based on complexity paradigm. We expect that this is the best approach to derive a reliable *wellness* index, which should be the signature of a general healthy condition. The wellness index could be considered a sort of pre-nosological global parameter, able to reveal possible departures from a healthy physiological equilibrium. In this view, the overall self-organization of the human body is the central aspect to be understood, and we believe that wellness will probably refer to some kind of global *physiological complex self-organization* or *physiological complex integration*

An example of a physiological coupling, which is attracting the increasing interest of many research groups [119–122], is given by the heart-brain coupling, where self-similarity and scaling indices seem to play a crucial role [91]. The findings in this new challenging issue indicate that the IDC class of complex systems could play a crucial role in the study of this integrated view in human physiology, both through the theoretical development of IDC-based physiological models and the applications of related signal processing tools.

Diffusion Entropy and Detrended Fluctuation Analysis

Given a diffusive variable $X(t)$; $t = 1, 2, \dots$ (e.g., the event-driven random walks of the EDDiS algorithm, Eq. (1.6)), we are interested in evaluating the self-similarity index δ of the PDF, defined in Eq. (1.7), and the second moment scaling H , defined in Eq. (1.8). δ and H are evaluated by means of the Diffusion Entropy (DE) analysis [13, 20, 100] and of the Detrended Fluctuation Analysis (DFA) [101], respectively.

Diffusion Entropy

Given the PDF $P(x, t)$, the DE is defined as the Shannon entropy of the diffusion process:

$$S(\Delta t) \equiv - \int_{-\infty}^{+\infty} p(\Delta x, \Delta t) \ln p(\Delta x, \Delta t) d\Delta x , \quad (\text{A.1})$$

where Δt here denotes a time lag and not the absolute laboratory time. Using the self-similarity condition (1.7), it is easy to prove that

$$S(t) = \delta \ln \Delta t + S_* , \quad (\text{A.2})$$

where $S_* = - \int_{-\infty}^{+\infty} F(x) \ln F(x) dx$. Notice that the scaling is in fact asymptotic, namely it is only exact for $t \rightarrow \infty$, and an effective time

T_* can be introduced as an additional fitting parameter:

$$S(\Delta t) = \delta \ln(\Delta t + T_*) + S_*. \quad (\text{A.3})$$

It is possible to estimate δ by considering the graph $(\Delta t, S(\Delta t))$ in a log-lin plot and then fitting Eq. (A.3) to the data.

The computation of $S(\Delta t)$ requires the evaluation of the PDF $P(x, \Delta t)$. This is done by considering a moving window of length Δt , so that the set of pseudo-trajectories $X_r(k) = X(r+k) - X(r)$, with $0 \leq k \leq \Delta t$, $r = 1, 2, \dots$, is considered. The pseudo-trajectories all start from $X_r(0) = 0$, and, for each Δt , it is possible to evaluate the histogram $P(x, \Delta t)$ of the sequence $X_1(\Delta t), X_2(\Delta t), \dots$ and, then, the DE $S(\Delta t)$.

Detrended Fluctuation Analysis

Given the diffusive variable $X(t)$; $t = 1, 2, \dots$, the DFA essentially estimates the second moment of a proper detrended time series $X(t) - \bar{X}(t)$. The detrending can be done with a n-order polynomial function and the most simple algorithm uses a linear detrending by a least-squares straight line fit [101]. The DFA algorithm works as follows: (i) for each discrete time L , the time series $X(t)$ is split into not-overlapping time windows of length L : $[kL + 1, kL + L]$, $k = 0, 1, \dots$; (ii) for each time window $[kL + 1, kL + L]$ the local trend is evaluated with a least-squares straight line fit: $\bar{X}_{k,L}(t) = a_{k,L}t + b_{k,L}$; $kL < t \leq (k+1)L$; (iii) the fluctuation is derived in the usual way: $\tilde{X}_{k,L}(t) = X(t) - \bar{X}_{k,L}(t) = X(t) - a_{k,L}t - b_{k,L}$; $kL < t \leq (k+1)L$; (iv) the mean-square deviation of the fluctuation is calculated over every window:

$$F^2(k, L) = \frac{1}{L} \sum_{t=kL+1}^{(k+1)L} \tilde{X}_{k,L}^2(t) = \frac{1}{L} \sum_{t=kL+1}^{(k+1)L} (X(t) - \bar{X}_{k,L}(t))^2 ; \quad (\text{A.4})$$

and, finally, averaged over all the time windows, thus getting $F^2(L)$. In the case of a self-similar process, it results: $F(L) \sim L^H$. The parameter H can be derived by a linear fitting applied to the function $z = Hy + C$, with $z = \log(F(L))$ and $y = \log(L)$. The DFA output is $H = 0.5$ for the case of uncorrelated (white) noise (e.g., Brownian motion), where the integrated process $X(t)$ display the typical

Gaussian PDF $G(x, t)$ with so-called *normal* scaling of the variance: $\langle X^2 \rangle(t) \sim t$. $H \neq 0.5$ is denoted as anomalous scaling, is a signature of long-range (power-law) correlations and, thus, cooperation and complexity. In particular, $H < 0.5$, also denoted as *subdiffusion*, corresponds to a anti-correlated (anti-persistent) signal, while $H > 0.5$, also denoted as *superdiffusion*, corresponds to a positively correlated (persistent) signal.

Bibliography

Miscellaneous

- [1] R. Segev, J. Goodhouse, J. Puchalla, and M. J. Berry, “Recording spikes from a large fraction of the ganglion cells in a retinal patch,” *Nat. Neurosci.*, vol. 7, no. 10, p. 1154–1161, 2004.
- [2] O. Stetter, D. Battaglia, J. Soriano, and T. Geisel, “Model-free reconstruction of excitatory neuronal connectivity from calcium imaging signals,” *PLoS Comput. Biol.*, vol. 8, no. 8, p. e1002653, 2012.
- [3] J. G. Orlandi, J. Soriano, E. Alvarez-Lacalle, S. Teller, and J. Casademunt, “Noise focusing and the emergence of coherent activity in neuronal cultures,” *Nature Physics*, vol. 9, no. 9, pp. 582–590, 2013.
- [4] R. Albert and A.-L. Barabási, “Statistical mechanics of complex networks,” *Rev. Mod. Phys.*, vol. 74, pp. 47–97, 2002.
- [5] S. Boccaletti, V. Latora, Y. Moreno, M. Chavez, and D.-U. Hwang, “Complex networks: Structure and dynamics,” *Phys.*

- Rep.*, vol. 424, no. 4-5, pp. 175–308, 2006.
- [6] M. E. J. Newman, “The structure and function of complex networks,” *SIAM Review*, vol. 45, p. 167â256, 2003.
- [7] A. Barrat, M. Barthélemy, and A. Vespignani, *Dynamical Processes on Complex Networks*. Cambridge: Cambridge University Press, 2008.
- [8] T. Mora and W. Bialek, “Are biological systems poised at criticality ?” *J Stat Phys*, vol. 144, pp. 268–302, 2011.
- [9] S. Boccaletti, G. Bianconi, R. Criado, C. I. D. Genio, J. Gómez-Gardenes, M. Romance, I. Sendina-Nadal, Z. Wang, and M. Zanin, “The structure and dynamics of multilayer networks,” *Phys. Rep.*, vol. 544, no. 1, pp. 1–122, 2014.
- [10] D. Y. Kenett, M. Perc, and S. Boccaletti, “Networks of networks - an introduction,” *Chaos Soliton Fract*, vol. 80, pp. 1–6, 2015.
- [11] P. Paradisi, G. Kaniadakis, and A. M. Scarfone, Eds., *The emergence of self-organization in complex systems*. Amsterdam: Elsevier, 2015, special Issue - Chaos, Solitons & Fractals, Vol. 81(B), Pages 407-588.
- [12] P. Paradisi, G. Kaniadakis, and A. M. Scarfone, “The emergence of self-organization in complex systems - preface,” *Chaos Soliton Fract*, vol. 81, no. Part B, pp. 407–11, 2015.
- [13] P. Paradisi and P. Allegrini, “Scaling law of diffusivity generated by a noisy telegraph signal with fractal intermittency,” *Chaos Soliton Fract*, vol. 81, no. Part B, pp. 451–62, 2015.
- [14] M. Zanin, D. Papo, P. A. Sousa, E. Menasalvas, A. Nicchi, E. Kubik, and S. Boccaletti, “Combining complex networks and data mining: why and how,” *Phys Rep*, vol. 635, pp. 1–44, 2016.

-
- [15] E. Ott, *Chaos in Dynamical Systems*, 2nd ed. Cambridge: Cambridge University Press, 2002.
- [16] D. Sornette, *Critical Phenomena in Natural Sciences*, 2nd ed., ser. Springer Series in Synergetics. Berlin: Springer-Verlag, 2006.
- [17] R. Metzler and J. Klafter, “The random walk’s guide to anomalous diffusion: a fractional dynamics approach,” *Phys Rep*, vol. 339, pp. 1–77, 2000.
- [18] P. Paradisi, D. Chiarugi, and P. Allegrini, “A renewal model for the emergence of anomalous solute crowding in liposomes,” *BMC Syst Biol*, vol. 9, no. suppl 3, p. s7, 2015.
- [19] P. Paradisi, R. Cesari, A. Donateo, D. Contini, and P. Allegrini, “Scaling laws of diffusion and time intermittency generated by coherent structures in atmospheric turbulence,” *Nonlin. Processes Geophys.*, vol. 19, pp. 113–126, 2012, [Corrigendum, *Nonlin. Processes Geophys.*, 19:685, 2012].
- [20] P. Paradisi, R. Cesari, A. Donateo, D. Contini, and P. Allegrini, “Diffusion scaling in event-driven random walks: an application to turbulence,” *Rep Math Phys*, vol. 70, pp. 205–220, 2012.
- [21] F. Mainardi, *Fractional calculus and waves in linear viscoelasticity: an introduction to mathematical models*. World Scientific, 2010.
- [22] P. Paradisi, R. Cesari, F. Mainardi, A. Maurizi, and F. Tampieri, “A generalized Fick’s law to describe non-local transport effects,” *Phys. Chem. Earth*, vol. 26, no. 4, pp. 275–279, 2001.
- [23] P. Pramukul, A. Svenkeson, P. Grigolini, M. Bologna, and B. West, “Complexity and the fractional calculus,” *Adv Math Phys*, vol. 2013, p. 498789, 2013.

- [24] P. Paradisi, “Fractional calculus in statistical physics: The case of time fractional diffusion equation,” *Communications in Applied and Industrial Mathematics*, 2015, doi: 10.1685/journal.caim.530.
- [25] G. Pagnini and P. Paradisi, “A stochastic solution with gaussian stationary increments of the symmetric space-time fractional diffusion equation,” *Fractional Calculus and Applied Analysis*, vol. 19, no. 2, pp. 408–440, 2016.
- [26] P. Allegrini, D. Menicucci, R. Bedini, L. Fronzoni, A. Gemignani, P. Grigolini, B. J. West, and P. Paradisi, “Spontaneous brain activity as a source of ideal $1/f$ noise,” *Phys Rev E*, vol. 80, no. 6 Pt 1, p. 061914, 2009.
- [27] P. Allegrini, D. Menicucci, R. Bedini, A. Gemignani, and P. Paradisi, “Complex intermittency blurred by noise: theory and application to neural dynamics,” *Phys Rev E*, vol. 82, no. 1 Pt 2, p. 015103, 2010.
- [28] P. Allegrini, P. Paradisi, D. Menicucci, and A. Gemignani, “Fractal complexity in spontaneous eeg metastable-state transitions: new vistas on integrated neural dynamics,” *Front Physiol.*, vol. 1, p. 128, 2010, doi: 10.3389/fphys.2010.00128.
- [29] P. Allegrini, P. Paradisi, D. Menicucci, R. Bedini, A. Gemignani, and L. Fronzoni, “Noisy cooperative intermittent processes: from blinking quantum dots to human consciousness,” *J Phys Conf Ser*, vol. 306, no. 1, p. 012027, 2011.
- [30] P. Paradisi, P. Allegrini, A. Gemignani, M. Laurino, D. Menicucci, and A. Piarulli, “Scaling and intermittency of brain events as a manifestation of consciousness,” *AIP Conf. Proc.*, vol. 1510, pp. 151–161, 2013.
- [31] P. Allegrini, P. Paradisi, D. Menicucci, M. Laurino, R. Bedini, A. Piarulli, and A. Gemignani, “Sleep unconsciousness and

-
- breakdown of serial critical intermittency: New vistas on the global workspace,” *Chaos Soliton Fract*, vol. 55, pp. 32–43, 2013.
- [32] P. Allegrini, P. Paradisi, D. Menicucci, M. Laurino, , A. Piarulli, and A. Gemignani, “Self-organized dynamical complexity in human wakefulness and sleep: different critical brain-activity feedback for conscious and unconscious states,” *Phys Rev E*, vol. 92, no. 3, p. 032808, 2015.
- [33] D. R. Cox, *Renewal Theory*. London: Methuen & Co. Ltd., 1962.
- [34] O. C. Akin, P. Paradisi, and P. Grigolini, “Periodic trend and fluctuations: The case of strong correlation,” *Physica A*, vol. 371, pp. 157–170, 2006.
- [35] P. Paradisi, P. Grigolini, S. Bianco, and O. C. Akin, “Renewal aging in non-homogeneous poisson processes with periodic rate modulation,” *Int. J. Bif. Chaos*, vol. 18, no. 9, pp. 2681â–2691, 2008.
- [36] P. Paradisi, R. Cesari, and P. Grigolini, “Superstatistics and renewal critical events,” *Cent Eur J Phys*, vol. 7, pp. 421–431, 2009.
- [37] O. C. Akin, P. Paradisi, and P. Grigolini, “Perturbation-induced emergence of poisson-like behavior in non-poisson systems,” *J. Stat. Mech.: Theory Exp.*, p. P01013, 2009.
- [38] S. Bianco, P. Grigolini, and P. Paradisi, “A fluctuating environment as a source of periodic modulation,” *Chem. Phys. Lett.*, vol. 438, no. 4-6, pp. 336–340, 2007.
- [39] P. Paradisi, R. Cesari, D. Contini, A. Donateo, and L. Palatella, “Characterizing memory in atmospheric time series: an alternative approach based on renewal theory,” *Eur Phys J Special Topics*, vol. 174, pp. 207–218, 2009.

- [40] P. Paradisi, P. Allegrini, F. Barbi, S. Bianco, and P. Grigolini, “Renewal, modulation and blinking quantum dots,” *AIP Conf. Proc.*, vol. 800, no. 1, pp. 92–97, 2005.
- [41] S. Bianco, P. Grigolini, and P. Paradisi, “Fluorescence intermittency in blinking quantum dots: renewal or slow modulation ?” *J. Chem. Phys.*, vol. 123, no. 17, p. 174704, 2005.
- [42] P. Allegrini, F. Barbi, P. Grigolini, and P. Paradisi, “Renewal, modulation, and superstatistics in times series,” *Phys. Rev. E*, vol. 73, no. 4, p. 046136, 2006.
- [43] P. Grigolini, “Emergence of biological complexity: Criticality, renewal and memory,” *Chaos Soliton Fract.*, vol. 81, no. Part B, pp. 575–88, 2015.
- [44] M. T. Beig, A. Svenkeson, M. Bologna, B. J. West, and P. Grigolini, “Critical slowing down in networks generating temporal complexity,” *Physical Review E*, vol. 91, p. 012907, 2015.
- [45] M. Turalska, B. J. West, and P. Grigolini, “Temporal complexity of the order parameter at the phase transition,” *Physical Review E*, vol. 83, p. 061142, 2011.
- [46] P. Grigolini and D. R. Chialvo, “Emergent critical brain dynamics - editorial,” *Chaos Solit Fract.*, vol. 55, no. 1-2, 2013.
- [47] P. Grigolini and D. R. C. (Eds.), Eds., *Emergent Critical Brain Dynamics*. Amsterdam: Elsevier, 2013, special Issue - Chaos, Solitons & Fractals, Vol. 55, Pages 1-120.
- [48] J. M. Beggs and D. Plenz, “Neuronal avalanches in neocortical circuits,” *J Neurosci*, vol. 23, pp. 11 167–11 177, 2003.
- [49] D. Plenz and T. C. Thiagarjan, “The organizing principles of neuronal avalanches: cell assemblies in the cortex ?” *Trends Neurosci.*, vol. 30, p. 101â110, 2007.

-
- [50] D. Fraiman, P. Balenzuela, J. Foss, and D. R. Chialvo, “Ising-like dynamics in large-scale functional brain networks,” *Physical Review E*, vol. 79, p. 061922, 2009.
- [51] R. V. Solé and J. Bascompte, *Self-organization in Complex Ecosystems*. Princeton: Princeton University Press, 2006.
- [52] W. Gerstner and W. M. Kistler, *Spiking Neuron Models*. Cambridge: Cambridge University Press, 2002.
- [53] F. D. Stefani, J. P. Hoogenboom, and E. Barkai, “Beyond quantum jumps: Blinking nanoscale light emitters,” *Phys Today*, vol. 62, pp. 34–39, 2009.
- [54] T. Maillart, D. Sornette, S. Frei, T. Duebendorfer, and A. Saichev, “Quantification of deviations from rationality with heavy tails in human dynamics,” *Phys Rev E*, vol. 83, p. 056101, 2011.
- [55] S. Laureys and G. Tononi, Eds., *The neurology of consciousness*. Amsterdam: Elsevier, 2009.
- [56] P. Allegrini, P. Paradisi, D. Menicucci, and A. Gemignani, “Is temporal scaling at the basis of allometry? comment on ‘physiologic time: A hypothesis’ by west and west,” *Phys Life Rev*, vol. 10, pp. 233–234, 2013.
- [57] A. A. Fingelkurts, A. A. Fingelkurts, and C. F. H. Neves, “Brain-mind operational architectonics imaging: Technical and methodological aspects,” *The Open Neuroimaging Journal*, vol. 2, pp. 73–93, 2008.
- [58] —, “Natural world physical, brain operational, and mind phenomenal space-time,” *Physics of Life Reviews*, vol. 7, pp. 195–249, 2010.
- [59] —, “Consciousness as a phenomenon in the operational architectonics of brain organization: criticality and self-organization
-

- considerations,” *Chaos, Solitons & Fractals*, vol. 55, pp. 13–31, 2013.
- [60] A. Saichev and D. Sornette, “Distribution of inter-earthquake times explained,” *Phys Rev Lett*, vol. 97, p. 078501, 2006.
- [61] I. Y. Wong, M. L. Gardel, D. R. Reichman, E. R. Weeks, M. T. Valentine, A. R. Bausch, and D. A. Weitz, “Anomalous diffusion probes microstructure dynamics of entangled f-actin networks,” *Phys Rev Lett*, vol. 92, p. 178101, 2004.
- [62] A. V. Weigel, B. Simon, M. M. Tamkun, and D. Krapf, “Ergodic and nonergodic processes coexist in the plasma membrane as observed by single-molecule tracking,” *Proc. Nat. Acad. Sci. USA*, vol. 108, pp. 6438–6443, 2011.
- [63] J. H. Jeon, V. Tejedor, S. Burov, E. Barkai, C. Selhuber-Unkel, K. Berg-SÅžrensen, L. Oddershede, and R. Metzler, “In vivo anomalous diffusion and weak ergodicity breaking of lipid granules,” *Phys. Rev. Lett.*, vol. 106, p. 048103, 2011.
- [64] R. Metzler, J. H. Jeon, A. G. Cherstvy, and E. Barkai, “Anomalous diffusion models and their properties: non-stationarity, non-ergodicity, and ageing at the centenary of single particle tracking,” *Phys. Chem. Chem. Phys.*, vol. 16, no. 4, pp. 24 128–24 164, 2014.
- [65] M. I. Rabinovich, R. Huerta, and V. S. Afraimovich, “Dynamics of sequential decision making,” *Phys Rev Lett*, vol. 97, p. 188103, 2006.
- [66] M. I. Rabinovich, R. Huerta, P. Varona, and V. S. Afraimovich, “Transient cognitive dynamics, metastability, and decision making,” *PLoS Comput Biol*, vol. 4, no. 5, p. e1000072, 2008.
- [67] M. I. Rabinovich, V. S. Afraimovich, C. Bick, and P. Varona, “Information flow dynamics in the brain,” *Phys. Life Rev.*, vol. 9, pp. 51–73, 2012.

-
- [68] P. Bhadola and N. Deo, “Study of rna structures with a connection to random matrix theory,” *Chaos Soliton Fract*, vol. 81, no. Part B, pp. 542–50, 2015.
- [69] F. Furstenberg, M. Dolgushev, and A. Blumen, “Exploring the applications of fractional calculus: Hierarchically built semi-flexible polymers,” *Chaos Soliton Fract*, vol. 81, no. Part B, pp. 527–33, 2015.
- [70] U. K. Basak and A. Datta, “Fractal dimension and complexity in the long-term dynamics of a monomolecular layer,” *Chaos Soliton Fract*, vol. 81, no. Part B, pp. 534–41, 2015.
- [71] D. Gatherer, “So what do we really mean when we say that systems biology is holistic?” *BMC Syst Biol*, vol. 4, p. 22, 2010.
- [72] E. Geneston, R. Tuladhar, M. T. Beig, M. Bologna, and P. Grigolini, “Ergodicity breaking and localization,” *Phys Rev E*, vol. 94, p. 012136, 2016.
- [73] J. B. Bassingthwaite, L. S. Liebovitch, and B. J. West, *Fractal physiology*. Springer, 1994.
- [74] A. Goldberger, L. A. N. Amaral, J. M. Hausdorff, P. C. Ivanov, C.-K. Peng, and H. E. Stanley, “Fractal dynamics in physiology: Alterations with disease and aging,” *Proc. Nat. Acad. Sci. USA*, vol. 99, no. Suppl. 1, pp. 2466–2472, 2002.
- [75] B. Kolb and I. Q. Whishaw, *Fundamentals of Human Neuropsychology*, 6th ed. Worth Publishers, 2008.
- [76] T. Cakir, S. Alsan, S. Selma, A. Hale, U. Ata, and O. Kutlu, “Reconstruction and flux analysis of coupling between metabolic pathways of astrocytes and neurons: application to cerebral hypoxia,” *Theor Biol Med Model*, vol. 4, no. 1, p. 48, 2007.
- [77] M. V. Sofroniew and H. V. Vinters, “Astrocytes: Biology and pathology,” *Acta Neuropathol*, vol. 119, no. 1, pp. 7–35, 2010.
-

- [78] A. A. Fingelkurts and A. A. Fingelkurts, “Operational architectonics of the human brain biopotential field: towards solving the mind-brain problem,” *Brain Mind*, vol. 2, pp. 261–296, 2001.
- [79] A. Y. Kaplan, A. A. Fingelkurts, A. A. Fingelkurts, B. S. Borisov, and B. S. Darkhovsky, “Nonstationary nature of the brain activity as revealed by eeg/emg: methodological, practical and conceptual challenges,” *Signal Processing*, vol. 85, pp. 2190–2212, 2005.
- [80] D. Zipes and J. Jalife, *Cardiac Electrophysiology: From Cell to Bedside*, 6th ed. Philadelphia: Saunders Elsevier, 2014.
- [81] G. Billman, “Heart rate variability - a historical perspective,” *Front. Physio.*, vol. 2, p. 86, 2011, doi: 10.3389/fphys.2011.00086.
- [82] P. Allegrini, P. Grigolini, P. Hamilton, L. Palatella, and G. Raffaelli, “Memory beyond memory in heart beating, a sign of a healthy physiological condition,” *Phys Rev E*, vol. 65, no. 4, p. 041926, 2002.
- [83] L. Tang, H. Lv, F. Yang, and L. Yu, “Complexity testing techniques for time series data: a comprehensive literature review,” *Chaos Soliton Fract*, vol. 81, p. 117â135, 2015.
- [84] P. Allegrini, P. Grigolini, and L. Palatella, “Intermittency and scale-free networks: a dynamical model for human language complexity,” *Chaos Solit Fract*, vol. 20, pp. 95–105, 2004.
- [85] P. Allegrini, R. Balocchi, S. Chillemi, and et al., “Long- and short-time analysis of heartbeat sequences: Correlation with mortality risk in congestive heart failure patients,” *Phys Rev E*, vol. 67, no. 6, p. 062901, 2003.
- [86] R. Maestri, G. D. Pinna, P. Allegrini, and et al., “Linear and non-linear indices of heart rate variability in chronic heart failure: mutual interrelationships and prognostic value,” *Comput Cardiol*, vol. 32, pp. 981–984, 2005.

-
- [87] R. Maestri, G. D. Pinna, A. Accardo, and et al., “Nonlinear indices of heart rate variability in chronic heart failure patients: redundancy and comparative clinical value,” *J Cardiovasc Electr*, vol. 18, no. 4, pp. 425–433, 2007.
- [88] Y. Ashkenazy, P. Ivanov, S. Havlin, C. Peng, A. Goldberger, and H. Stanley, “Magnitude and sign correlations in heartbeat fluctuations,” *Phys. Rev. Lett.*, vol. 86, no. 9, pp. 1900–3, 2001.
- [89] P. Ivanov, L. N. Amaral, A. Goldberger, S. H. S, M. Rosenblum, H. Stanley, and Z. Struzik, “From 1/f noise to multifractal cascades in heartbeat dynamics,” *Chaos*, vol. 11, no. 3, pp. 641–652, 2001.
- [90] M. Chang, C. Peng, and H. Stanley, “Emergence of dynamical complexity related to human heart rate variability,” *Phys. Rev. E*, vol. 90, no. 6, p. 062806, 2014.
- [91] G. Valenza, P. Allegrini, A. Lanatá, and E. P. Scilingo, “Dominant lyapunov exponent and approximate entropy in heart rate variability during emotional visual elicitation,” *Front Neuroeng*, vol. 5, p. 3, 2012.
- [92] O. Pahlm and L. Sornmo, “Software qrs detection in ambulatory monitoring - a review,” *Med. Biol. Eng. Comput.*, vol. 22, p. 289–297, 1984.
- [93] H. E. Stanley, *Introduction to Phase Transitions and Critical Phenomena*. Oxford: Oxford University Press, 1987.
- [94] E. Tagliazucchi, P. Balenzuela, D. Fraiman, and D. R. Chialvo, “Criticality in large-scale brain fmri dynamics unveiled by a novel point process analysis,” *Frontiers in Physiology*, vol. 3, no. 15, 2012.
- [95] P. Allegrini, J. Bellazzini, G. Bramanti, M. Ignaccolo, P. Grigolini, and J. Yang, “Scaling breakdown: A signature of aging,” *Phys Rev E*, vol. 66, p. 015101, 2002.
-

- [96] P. Allegrini, F. Barbi, P. Grigolini, and P. Paradisi, “Aging and renewal events in sporadically modulated systems,” *Chaos Soliton Fract*, vol. 34, pp. 11–18, 2007.
- [97] E. W. Montroll, “Random walks on lattices,” *Proc. Symp. Appl. Math. Am. Math. Soc.*, vol. 16, pp. 193–220, 1964.
- [98] E. W. Montroll and G. H. Weiss, “Random walks on lattices. II,” *J Math Phys*, vol. 6, pp. 167–181, 1965.
- [99] G. H. Weiss and R. J. Rubin, “Random walks: Theory and selected applications,” *Adv. Chem. Phys.*, vol. 52, pp. 363–505, 1983.
- [100] N. Scafetta and P. Grigolini, “Scaling detection in time series: diffusion entropy analysis,” *Phys Rev E*, vol. 66, p. 036130, 2002.
- [101] C.-K. Peng, S. V. Buldyrev, S. Havlin, M. Simons, H. E. Stanley, and A. L. Goldberger, “Mosaic organization of dna nucleotides,” *Phys Rev E*, vol. 49, pp. 1685–1689, 1994.
- [102] P. Gong, A. R. Nikolaev, and C. van Leeuwen, “Intermittent dynamics underlying the intrinsic fluctuations of the collective synchronization patterns in electrocortical activity,” *Phys Rev E*, vol. 76, no. 1, p. 011904, 2007.
- [103] M. E. Raichle, A. M. M. Leod, A. Z. Snyder, W. J. Powers, D. A. Gusnard, and G. L. Shulman, “A default mode of brain function,” *Proc. Natl. Acad. Sci. U.S.A.*, vol. 98, pp. 676–682, 2001.
- [104] C. F. Beckmann, M. D. Luca, J. T. Devlin, and S. N. Smith, “Investigation into resting-state connectivity using independent component analysis,” *Philos. Trans. R. Soc. Lond., B, Biol. Sci.*, vol. 360, p. 1001â1013, 2005.

-
- [105] M. Wolf, G. Varigos, D. Hunt, and J. Sloman, "Sinus arrhythmia in acute myocardial infarction," *Med. J. Aust.*, vol. 2, p. 52â53, 1978.
- [106] T. F. of the European Society of Cardiology, the North American Society of Pacing, and Electrophysiology, "Heart rate variability: standards of measurement, physiological interpretation, and clinical use," *Circulation*, vol. 93, p. 1043â1065, 1996.
- [107] R. Kleiger, J. Miller, J. Bigger, and A. Moss, "Decreased heart rate variability and its association with increased mortality after acute myocardial infarction," *Am. J. Cardiol.*, vol. 59, p. 256â262, 1987.
- [108] C. Peng, S. Havlin, H. Stanley, and A. Goldberger, "Quantification of scaling exponents and crossover phenomena in nonstationary heartbeat time series," *Chaos*, vol. 5, p. 82â87, 1995.
- [109] M. Tulppo, A. Kiviniemi, A. Hautala, M. Kallio, T. Seppanen, T. Makikallio, and H. Huikuri, "Physiological background of the loss of fractal heart rate dynamics," *Circulation*, vol. 112, p. 314â319, 2005.
- [110] N. Iyengar, C. Peng, R. Morin, A. Goldberger, and L. Lipsitz, "Age-related alterations in the fractal scaling of cardiac interbeat interval dynamics," *Am. J. Physiol.*, vol. 271, p. R1078âR1084, 1996.
- [111] S. Vikman, T. Makikallio, S. Yli-Mayry, S. Pikkujamsa, A. Koivisto, P. Reinikainen, K. Airaksinen, and H. Huikuri, "Altered complexity and correlation properties of r-r interval dynamics before the spontaneous onset of paroxysmal atrial fibrillation," *Circulation*, vol. 100, p. 2079â2084, 1999.
- [112] H. Huikuri, A. Poutiainen, T. Makikallio, M. Koistinen, K. Airaksinen, R. Mitrani, R. Myerburg, and A. Castellanos, "Dynamic

- behaviour and autonomic regulation of ectopic atrial pacemakers,” *Circulation*, vol. 100, p. 1416–1422, 1999.
- [113] T. Makikallio, S. Hoiber, L. Kober, C. Torp-Pedersen, C. Peng, A. Goldberger, and H. Huikuri, “Fractal analysis of heart rate dynamics as a predictor of mortality in patients with depressed left ventricular function after acute myocardial infarction,” *Am. J. Cardiol.*, vol. 83, pp. 836–839, 1999.
- [114] V. Jokinen, J. Tapanainen, T. Seppanen, and H. Huikuri, “Temporal changes and prognostic significance of measures of heart rate dynamics after acute myocardial infarction in the beta-blocking era,” *Am. J. Cardiol.*, vol. 92, pp. 907–912, 2003.
- [115] J. Perkiomaki, W. Zareba, J. Ruta, S. Dubner, C. Madoery, P. Deedwania, M. Karcz, A. de Luna Bayes, and I. Investigators, “Fractal and complexity measures of heart rate dynamics after acute myocardial infarction,” *Am. J. Cardiol.*, vol. 88, pp. 777–781, 2001.
- [116] R. Maestri, G. Pinna, A. Porta, R. Balocchi, R. Sassi, M. Signorini, M. Dudziak, and G. Raczak, “Assessing nonlinear properties of heart rate variability from short-term recordings: are these measurements reliable ?” *Physiol. Meas.*, vol. 28, p. 1067–1077, 2007.
- [117] J. Perkiomaki, “Heart rate variability and non-linear dynamics in risk stratification,” *Front. Physio.*, vol. 2, p. 81, 2011, doi: 10.3389/fphys.2011.00081.
- [118] H. J. Federoff and L. O. Gostin, “Evolving from reductionism to holism: Is there a future for systems medicine ?” *JAMA - J Am Med Assoc*, vol. 302, no. 9, pp. 994–996, 2009.
- [119] G. Valenza, N. Toschi, and R. Barbieri, Eds., *Uncovering brain–heart information through advanced signal and image processing*.

London: The Royal Society Publ., 2016, theme Issue - *Philos Trans R Soc A*, Vol. 374, Issue 2067.

- [120] G. Valenza, N. Toschi, and R. Barbieri, "Introduction: Uncovering brainâheart information through advanced signal and image processing," *Philos Trans R Soc A*, vol. 374, no. 2067, p. 20160020, 2016.
- [121] G. Valenza, A. Greco, C. Gentili, A. Lanata, L. Sebastiani, D. Menicucci, A. Gemignani, and E. P. Scilingo, "Combining electroencephalographic activity and instantaneous heart rate for assessing brainâheart dynamics during visual emotional elicitation in healthy subjects," *Philos Trans R Soc A*, vol. 374, no. 2067, p. 20150176, 2016.
- [122] S. Schulz, M. Bolz, K.-J. Bar, and A. Voss, "Central and autonomic nervous system coupling in schizophrenia," *Philos Trans R Soc A*, vol. 374, no. 2067, p. 20150178, 2016.

