ENERGETIC LINK BETWEEN SPIKE FREQUENCIES AND BRAIN FRACTAL DIMENSIONS

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ABSTRACT

Oscillations in brain activity exhibit a power law distribution which appears as a straight line when plotted on logarithmic scales in a log power versus log frequency plot. The line's slope is given by a single constant, the power law exponent. Since a variation in slope may occur during different functional states, the brain waves are said to be multifractal, i.e., characterized by a spectrum of multiple possible exponents. A role for such non-stationary scaling properties has scarcely been taken into account. Here we show that changes in fractal slopes and oscillation frequencies, and in particular in electric spikes, are correlated. Taking into account techniques for parameter distribution estimates, which provide a foundation for the proposed approach, we show that modifications in power law exponents are associated with variations in the Rényi entropy, a generalization of Shannon informational entropy. Changes in Rényi entropy, in turn, are able to modify brain oscillation frequencies. Therefore, results point out that multifractal systems lead to different probability outcomes of brain activity, based solely on increases or decreases of the fractal exponents. Such approach may offer new insights in the characterization of neuroimaging diagnostic techniques and the forces required for transcranial stimulation, where doubts still exist as to the parameters that best characterize waveforms.

SIGNIFICANCE STATEMENT

The generalized informational entropy called "Rényi entropy" does not select the most appropriate probabilistic parameter as Shannon's, rather it builds diversity profiles. By offering a continuum of possible diversity measures at many spatiotemporal levels, it is very useful in the evaluation of the fractal scaling occurring in the brain. Rényi entropy elucidates how power laws behaviours in cortical oscillations are able to modify electric spike frequencies. Through its links with the scale-free behavior of cortical fluctuations, Rényi entropy suggests that the brain changes its fractal exponents in order to control free-energy and scale the entropy of different functional states.

INTRODUCTION

The brain activity observed at many spatiotemporal scales exhibits fluctuations with complex scaling behavior (Newman, 2005), including not only cortical electric oscillations, but also membrane potentials and neurotransmitter release (Linkenkaer-Hansen et al., 2001; Fox and Raichle, 2007; Milstein et al., 2009). In particular, the frequency spectrum of cerebral electric activity displays a scale-invariant behaviour $S(f) = 1/f^{\mu}$, where $S(f)$ is the power spectrum, f is the frequency and μ is an exponent that equals the negative slope of the line in a log power versus log frequency plot (Pritchard, 1992; Van de Ville et al., 2010). The (spatial) fractals and (temporal) power laws can be regarded as intrinsic properties of the brain and characterize a large class of neuronal processes (de Arcangelis and Herrmann, 2010; He et al., 2010); moreover, pink noise distributions contain information about how large-scale physiological and pathological outcomes arise from the interactions of many small-scale processes (Jirsa et al., 2014). The fractal slope is not invariant in the brain, rather is characterized by multiple possible exponents, summarized in a single value, the so called "generalized fractal dimension" γ. It has been demonstrated that different functional states - spontaneous fluctuations, task-evoked, perceptual and motor activity (Buszaki and Watson, 2012), cognitive demands (Buiatti et al., 2007; Fetterhoff et al., 2014), ageing (Suckling et al., 2008) - account for variations in power law exponents across cortical regions (Tinker and Velazquez, 2014; Wink et al., 2008). Accordingly, we may view brain activity as an ensemble of intertwined (mono)fractals, each with its own dimension and scaling slope, each marking dynamical transitions between different response regimes (Papo, 2014). The aim of this review is to evaluate the relationship among scaling exponents, free-energy/spike frequency and generalized informational entropies in the brain. Starting from Rényi entropy, and introducing a link with the power law behavior of cortical fluctuations, we show how the brain might change its fractal exponents, in order to control free-energy and scale the entropy of different functional states.

RÉNYI ENTROPY AND ITS THERMODYNAMICAL COUNTERPARTS

Here, we show how a generalization of informational entropies, e.g., the Rényi entropy, may turn out to be a useful tool in the evaluation of multifractal dynamics. The classical informational Shannon entropy is (Shannon, 1948):

$$S(X) = -\sum_{i=1}^{N} p_i \ln p_i. \qquad (1)$$

where X is a random variable with n possible outcomes and $p_i = P$ (for $i = 1,2,3, \dots n$) is the probability distribution P on a finite set. In other words, $S(P)$ is a function of a generic probability distribution p such that, if we modify p, we achieve a different value of entropy on the Shannon's curve. Natural generalizations of the Shannon entropy have been proposed. Among the available ones (e.g., Tsallis, 1988), it is convenient for our purposes to work with the one-parameter class of Rényi entropies with parameter α (Rényi, 1966), a flexible and underestimated information-theory based index. From the standpoint of information theory, Rényi entropy is a measurable quantity with operational definition, as it represents the minimal cost of a message, under the assumption that the cost is an exponential function of the code-length (Cambell, 1965). Rényi entropy can be defined as:

$$H_{\alpha}(X) = \frac{1}{1-\alpha} \ln \sum_{i=1}^{N} p_i^{\alpha}. \qquad (2)$$

where$0 \leq \alpha < \infty$. Rényi entropy approaches Shannon entropy as α tends to 1, so that, for $\alpha \to 1$, we recover the classical Shannon entropy.

Rényi entropy has applications in dynamical systems (Hentschel and Proccacia, 1983), coding (Cambell, 1965), information transfer (Jizba et al., 2012), theories in quantum mechanics (Jizba et al., 2015) and black holes' mutual information (Dong, 2016). Rényi entropy and generalized diversity functions have also been used to quantify ecosystems dynamics: from land cover types (Carranza et al., 2007; De Luca et al., 2011), to coastal dunes environments (Drius et al., 2013), from urban mosaics (Carranza et al., 2007) to species diversity in large areas (Rocchini et al., 2013). Multiscale entropy methods have been found to be suitable for the assessment of human heartbeat fluctuations and coding and noncoding DNA sequences analysis too (Costa et al., 2005).

Unlike the many diversity measures for summarizing landscape structure based on Shannon entropy, Rényi entropy makes it possible to describe the system's status at a specific moment as well as its time-varying trend (Müller et al., 2000; Patil and Taillie, 2001). Diversity cannot be reduced to a single index information, since all its aspects cannot be captured in a single statistics (Gorelick, 2006). A complete characterization of landscape diversity can be achieved if, instead of a single index, a parametric family of indices is used, whose members have varying sensitivities to the presence of rare and abundant elements, as in the case of the Rényi entropy (Jost, 2007). Diversity profiles are flat when the landscape is even, and steeply decrease as the landscape turns uneven (Jost, 2010). Therefore, Rényi's formulation allows a continuum of possible diversity measures which differ in their sensitivity to the rare and abundant elements in a landscape. Because of its build-in predisposition to account for self-similar systems, Rényi entropy is an effective tool to describe multifractal systems (Jizba and Arimitsu, 2001). Although fractal dimension does not encompass the full information of the Rényi entropy for arbitrary distribution, the former is a scaling exponent of the latter. Therefore, the generalized fractal dimension γ and the Rényi exponent α can be thought of as interchangeable. In particular, the Rényi parameter is connected via a Legendre transformation with the multifractal singularity spectrum. This in particular means that, from the maximum entropy point of view, Rényi entropy and power law exponent μ (expressed by the generalized fractal dimension γ) are strictly correlated. See Jizba and Arimitsu (2001) and Jizba and Korbel (2014) for technical details on mathematical proof. Therefore, changes in n and in γ lead to changes in the Rényi parameter α, and vice versa (Słomczynski et al., 2000). Variations in α, in turn, modify the probability distribution on finite sets. Thus, multifractal systems lead to different probability outcomes based solely on increases or decreases of $1/f^{\mu}$ exponents. In sum, the "probabilistic" virtues of Rényi entropy represent a novel physics-based approach to probe neural scale-free dynamics, with the potential to lead to new insights into brain systems at all space-time scales and all levels of complexity.

On the other hand, informational entropies are closely related to thermodynamic entropy. Because thermodynamic variables and Rényi parameter are in straight relation (Baez, 2011), changes in thermodynamic parameters lead to different probability outcomes. The connection between informational entropies and their thermodynamical counterparts, e.g., the Boltzmann-Gibbs entropy, is given by a standard procedure of maximum entropy (MaxEnt) distribution and thermodynamical limit ($N \to \infty$). The significance of entropy in statistical physics lies in the fact that the distribution which maximizes entropy under given constraints is the preferred one. The so-called MaxEnt principle, introduced by Jaynes (1957), leads to the classical distribution $p(E) = 1/Z\, e^{-\beta E}$, where $\beta = 1/k_B T$ is the inverse temperature.

A "TOP-DOWN" APPROACH TO RÉNYI ENTROPY

Here, we introduce a different approach to Rényi entropy and show how to use it for the assessment of thermodynamical parameters. Shannon entropy elucidates how changing the probabilities usually occurs when we have prior information. But suppose we address the issue from the reverse perspective: when the entropy changes, how does its variation influence the distributions? Given a distribution P, what information content is measured by a given entropy? Which factors are able to modify the entropy and to lead to different probability distributions? In the case of information entropy, we have a function $y = f(x)$, in which x is the input (the probability) and y is the output (the entropy). However, if we change y with y', can we find an y' such that $y' = f(x')$? We know that when p changes, S changes, but is the reverse true? is it possible the opposite, such that if S changes, p changes? Further, if we are hypothetically able to change S, is it possible to achieve the corresponding values of probability distribution p? Are there cases in which changes in S are known *a priori*, without a previous knowledge of p?

The "reversal" of Rényi entropy is easily explainable in topological terms, as a straightforward extension of the point-based Rényi Friendship Theorem (Huneke, 2002). Indeed, the above mentioned correlation between Rényi entropy and thermodynamic free-energy can be elucidated via the Friendship Theorem, in terms of the vertices of a particular graph

(Havrda and Charvat, 1967, Rényi, 1966), illustrated in **Figure 1A**. It is Huneke's simplified version of the Friendship Theorem (Huneke, 2002) that we give next.

Friendship Theorem. *If G is a graph in which any two vertices have exactly one common neighbour, then G has a vertex joined to all other vertices in the graph.*

This theorem can be reformulated in terms of points and regions. In this reformulation, points x, y are connected, provided there is a straight edge whose endpoints are x, y.

Point-based Friendship Theorem. *If X is a nonempty set of points in which any two points are connected to a common point, then X has a point p that is connected to every other point in the set.*

This situation is illustrated in **Figure 1A**.

It is now a straightforward step to obtain a Rényi entropy-based Friendship Theorem.

Rényi Entropy-based Friendship Theorem. *If X maps to is a nonempty set of points in which any two points are connected to a common point, then X has a point p that is connected to every other point in the set.*

The situation described by the Rényi Entropy-Based Friendship Theorem is illustrated in **Figure 1B**. If X is a region on an n-sphere, $H_{\alpha_1}(X), H_{\alpha_2}(X)$ are Rényi entropies of region X with respect to parameters α_1 and α_2. In addition, it is assumed that X is a smooth manifold and $f : H_\alpha(X) \to X \in 2^{Rn}$ is a homeomorphism that maps $H_{\alpha_1}(X), H_{\alpha_2}(X)$ to a region X in Euclidean space R^n. The vectors in X represent observations such as thermodynamical parameters (in our case, free-energy) that give rise to the n-sphere entropies shown in **Figure 1B**. We know from the Borsuk-Ulam Theorem (Borsuk, 1933; Tozzi and Peters, 2016a and 2016b) that, whenever there is a continuous function f on n-sphere, a pair of antipodal points is mapped by f to a value in R^n, which has a region-based extension (Peters, 2016). In particular, given the homeomophism f which is a continuous function on an n-sphere S^n whose surface values are Rényi entropies, then we know there is a pair of Rényi entropies that are mapped by f to $X \in 2^n$. In fact, we arrive at a reversal of Rényi entropies, in the sense that, starting from known values of entropy, we are able to achieve single probability values in lower dimensions.

Summarizing, our aim was to describe a case of "reverse" Rényi entropy: instead of the customary "bottom-up approach" (given known values of p, we obtain S), we can start from a "top-down" approach (given known changes in S, we obtain the unknown values of p). In technical terms, we consider entropy as a functional for an arbitrary distribution p and investigate its modifications, when a change in parameter α occurs, but the entropy S_α as a number remains the same. Let us have a distribution $P = (p_1, \ldots, p_n)$ and entropy $H_\alpha(P)$. We would like to find a distribution Q s.t. $H_\alpha(P) = H_{\alpha'}(Q)$ for given α'. There are many possible distributions Q, but there is one special class Q_t, for which is $q_i = \frac{1}{n} + \left(p_i - \frac{1}{n}\right) t$. It is easy to show that $\sum_{i=1}^{n} q_i = 1$. The main advantage is that such class of distribution is partially ordered by the operation of majorization. Finally, parameter t can be obtained from the equation: $H_\alpha(P) = H_{\alpha'}(Q_t)$.

Is this a counterintuitive operation useful? Under which circumstances prior information on the level of entropy S is able to influence the probabilities? In the next chapter, we will point up that a clear correlation does exist between free-energy, multifractal spectrum and brain functions, when evaluated in terms of the probability states of spike frequencies dictated by "top-down" Rényi entropy.

THE "TOP-DOWN" APPROACH TO RÉNYI ENTROPY AND CORRELATIONS BETWEEN THERMODYNAMIC PARAMETERS AND POWER LAWS IN THE BRAIN

Here we correlate the "top-down" formulation of Rényi entropy with brain dynamics. In particular, we show how such Rényi entropy allows us to establish a connection between cortical power laws and spike frequencies.

Scale-free behavior is related to the frequency of brain oscillations, in particular to the frequency of electric spikes. Recent papers, starting to uncover connections between the exponent of a fractal scaling in escape paths from energy basins and the activation free-energy (Perkins et al., 2014), point towards cortical fluctuations in power law exponents that are able to modify the brain energy. Furthermore, exponential power law distribution can be described in terms of a skewness parameter controlling frequencies peakedness (Çankaya et al., 2015). It means that spike frequency's intrinsic asymmetry can be efficiently modelled too. Throughout the increases in free-energy, the $1/f^\mu$ exponent varies across brain regions. The ongoing fluctuations with complex scale-free properties can thus be absorbed into a free-energy framework: the critical slowing implicit in power law scaling of dynamics is mandated by any system that minimizes its energetic expenditure (Friston, 2015). In turn, brain free-energy is correlated with the frequency of electric spikes. Indeed, each spike has a specific metabolic cost of 6.5 μmol/ATP/gr/min (Attwell and Laughlin, 2001; Sengupta et al., 2013). A recent study suggests that, because of the Ohm's law, energy consumption due to the "amplitude" of the oscillation is negligible, as compared with energy consumption due to the "frequency" of the oscillation (Tozzi et al., 2016). It means that electric spike frequency is correlated with brain fractal dimensions.

When generating a synthetic multifractal system in a log amplitude versus log frequency scatter plot, different series of free-scale oscillations with diverse power law exponents are achieved (**Figure 2A**). For sake of clarity, **Figure 2A** displays just the slope $\gamma = 2.1$. In order to correlate the probability p with log frequency, the values of log frequency can be projected to the x-axis of the Shannon's plot. The procedure is displayed in **Figure 2B**, where the two possibilities with probabilities $p = 0$ and $p = 1$ stand for $p = 0.2$ Hz and 16 Hz, respectively, and the intermediate values for the in-between frequencies, each one characterized by its probability p. **Figure 2B** displays the values of Rényi entropy (where $\alpha = 1$ corresponds to the slope $\gamma = 1$) on the y-axis, plotted as a function of p (and thus of log frequency) on the x-axis.

Once plotted the log frequency on the x-axis of the probabilities, modifications of the α exponent lead to different values of brain oscillations. The curves in **Figure 3** illustrate, as an example, the case of the "classical" Rényi entropy. At a given fixed value of p on the x-axis, changing the exponent α leads to an increase in Rényi entropy, and vice versa. In the "reverse" example depicted in **Figure 3B**, at a given fixed value of Rényi entropy on the y-axis, a variation in Rényi exponent modifies the probabilities, leading to a different probability distribution (and thus a different oscillation frequency). In other words, at each given value of Rényi entropy, a simple variation in power law exponent n modifies the value of p. Therefore, changes in α exponent are correlated with the occurrence of different spike frequencies.

CONCLUSIONS

We showed how increases or decreases in the $\frac{1}{f^{\mu}}$ power slope in the brain multifractal system might play a role in oscillations frequency. In other words, are we allowed to link probability outcomes with cortical electric spikes. Primitive changes in a sole parameter (the power law slope) lead to different probability distributions in cortical spike frequencies, through modifications in Rényi entropy. The "inverse" top-down approach to Rényi entropy (e.g., starting from known entropy changes, we achieve the unknown probability distributions) allows us to evaluate nervous system's macro-states based on a sole order parameter, although lacking knowledge of micro-states. The rationale for using the Rényi entropy does not lie in selecting the most appropriate parameter, rather in constructing "diversity profiles" (Patil and Taillie, 2001). Rényi entropy offers a "continuum of possible diversity measures" (Ricotta and Avena, 2003) at diverse spatiotemporal scales, which differ in their sensitivity to rare and abundant picture indexes, becoming increasingly regulated by the commonest when α gets higher. The change in α exponent can be regarded as a scaling operation that takes place not in the real, but in the data space (Podani, 1992). In sum, the Rényi α parameter is not redundant and allows us to consider several measures at a time. We can thus evaluate how changes in the Rényi parameter influence the structure of information measures in the probability space of brain activity. Rényi parameter's interpretation becomes clearer if we think that, in touch with thermodynamics, for values of α closer to the central spike frequencies: a) the entropy is sharply peaked around the maximal state, b) the entropy of non-maximal states rapidly decreases, and c) the most probable state is just one, whereas the other ones are suppressed. On the contrary, for values of α closer to the lowest and the highest spike frequencies, the distribution of near-optimal states is much broader and the entropy is flatter around the maximal value. Therefore, many energy states are occupied with high probability.

We hypothesize that, in order to optimize its activity, the brain displays an intrinsic mechanism of fluctuations equipped with complex temporal and spatial scaling properties. In this framework, changes in power law exponents play a crucial role in information processing, leading to variations not only in entropy and probability, but also in spike frequency. Complex scale-free statistics are thus fixed points of renormalization flows and can be understood as asymptotic behaviors emerging as the system is rescaled (Fraiman and Chialvo, 2012). Cognitive tasks are modulated by the $1/f^{\mu}$ exponents of the brain fluctuation probability function, leading either to a shrinking of multifractal spectrum, or transitions from mono- to multi-fractal distributions (Popivanov et al., 2006). The values corresponding to different distributions of oscillation frequencies and brain multifractal spectrum can be calculated in real neuroimaging data. Pairwise entropy methods in neuroimaging techniques (Watanabe et al., 2014) might benefit of such a reverse Rényi entropy-based approach. Indeed, the changes in Rényi α exponent (caused by variations in multifractal exponents), might lead to modification not just in electric spikes' frequency, but also in the frequency of other types of brain oscillations, such as neurotransmitter release, and so on.

Because scale-free behaviour is able to modify spike frequencies, we suggest that brain electric streams could be modulated through the superimposition of external electric currents characterized by carefully chosen power law exponents. Therefore, we suggest that transcranial electrical stimulation's techniques might take into account not just amplitudes and frequencies of the applied waveforms (Reato et al., 2013), but also their scaling slopes. A possible field of application are diseases such as Alzheimer’s disease, depression, attention deficit hyperactivity disorder, autism (Fox and Raichle, 2007; Sunderam et al., 2009). They could be ameliorated, or even removed, by artificial fields of appropriate power law exponents, that could be able to “recovery” and restore physiological brain functions .

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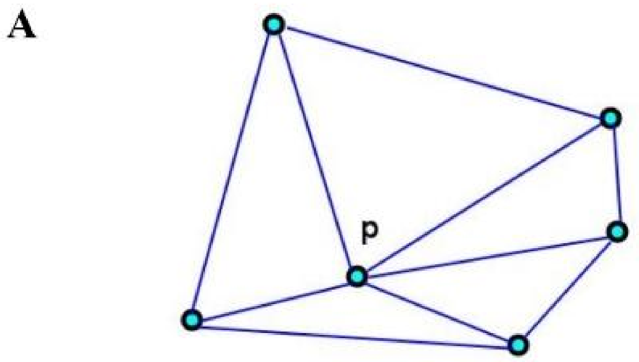

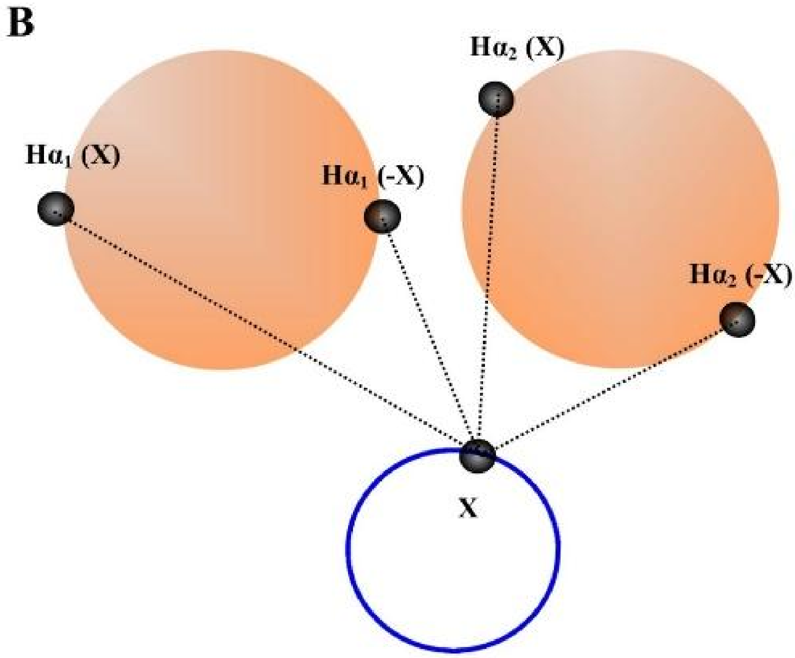

Figure 1A. Point-Based Friendship Theorem. See the main text for further details. **Figure 1B**. Rényi entropy-Based Friendship Theorem. It is grounded on the original Borsuk-Ulam theorem, which states that every continuous map $f : S^n \rightarrow R^n$ must identify a pair of antipodal points (on S^n). Another less technical definition of the Borsuk-Ulam theorem is: if a sphere is mapped continuously into a plane set, there is at least one pair of antipodal points having the same image; that is, they are mapped in the same point of the plane (Borsuk, 1933; Tozzi and Peters, 2016a).

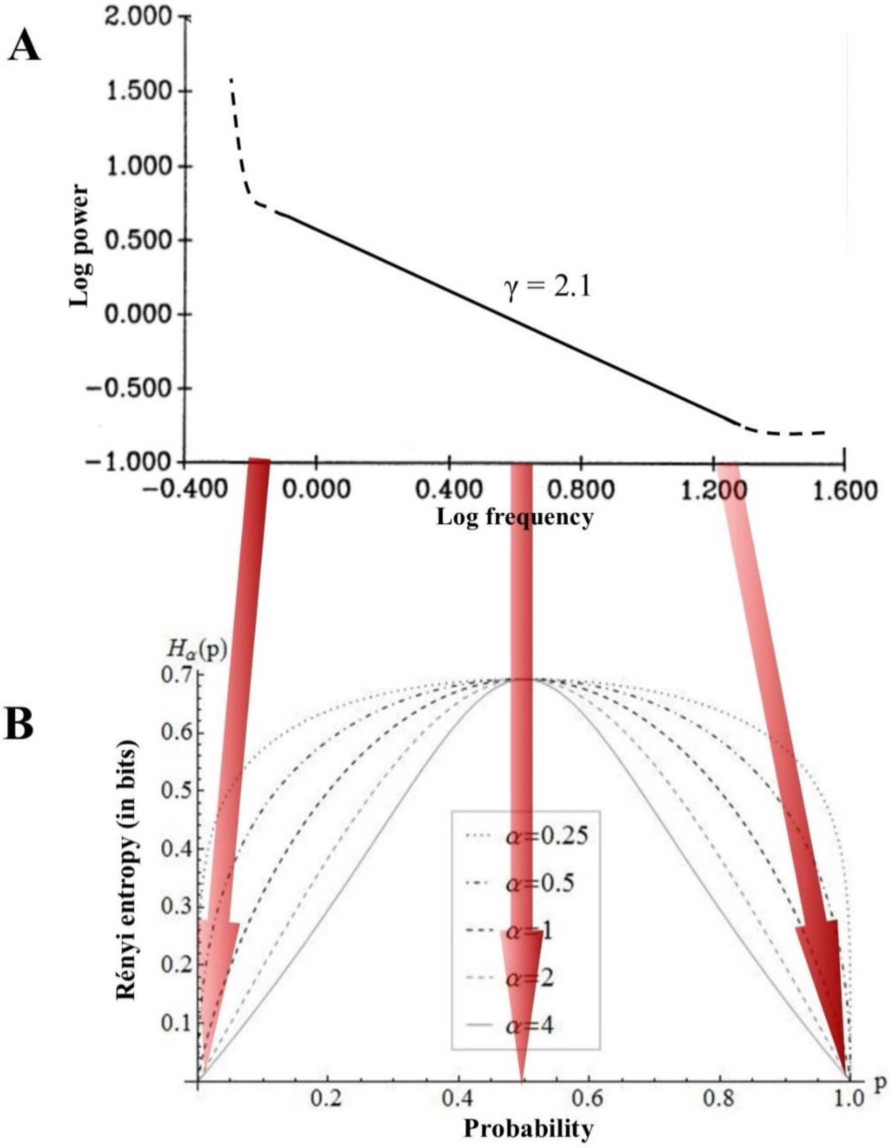

Figure 2A. Log amplitude versus log frequency scatter plot of brain spikes detected by EEG techniques (modified from Pritchard, 1992). The Figure displays on the x-axis the frequency (in Hz) and on the y-axis the power (in μV^2) of the electric spikes. Note that the scale is logarithmic: this means that on the x axis -0.400 = 0,39 Hz, 0 =1 Hz, 0.4 = 2.52 Hz, 1.2 = 16 Hz, and so on. In turn, on the y axis, -1.000 = 0,1 μV^2, -0.5 = 0,32 μV^2, 0.000 = 1 μV^2, 1.000 = 10 μV^2, and so on. The figure also depicts a possible fractal dimension, equipped with slope γ = 2.1. Note that the γ exponents, together with scale-free behavior, are lost at the slope's tails (dotted lines on the right and left of the main slope). **Figure 2B.** The Rényi entropy is plotted as probability distribution $P = (p, 1 - p)$ for different values of the Rényi parameter α. The solid curves show five cases of Rényi entropy, with exponents α=0.25, α=0.5, α=1 α=2 and α=4. The curve α=1 stands for the Shannon entropy (under ergodic conditions). The three arrows depict how the frequency parameter of **Figure 2A** can be embedded into the Rényi's plot of **Figure 2B**, via affine connections.

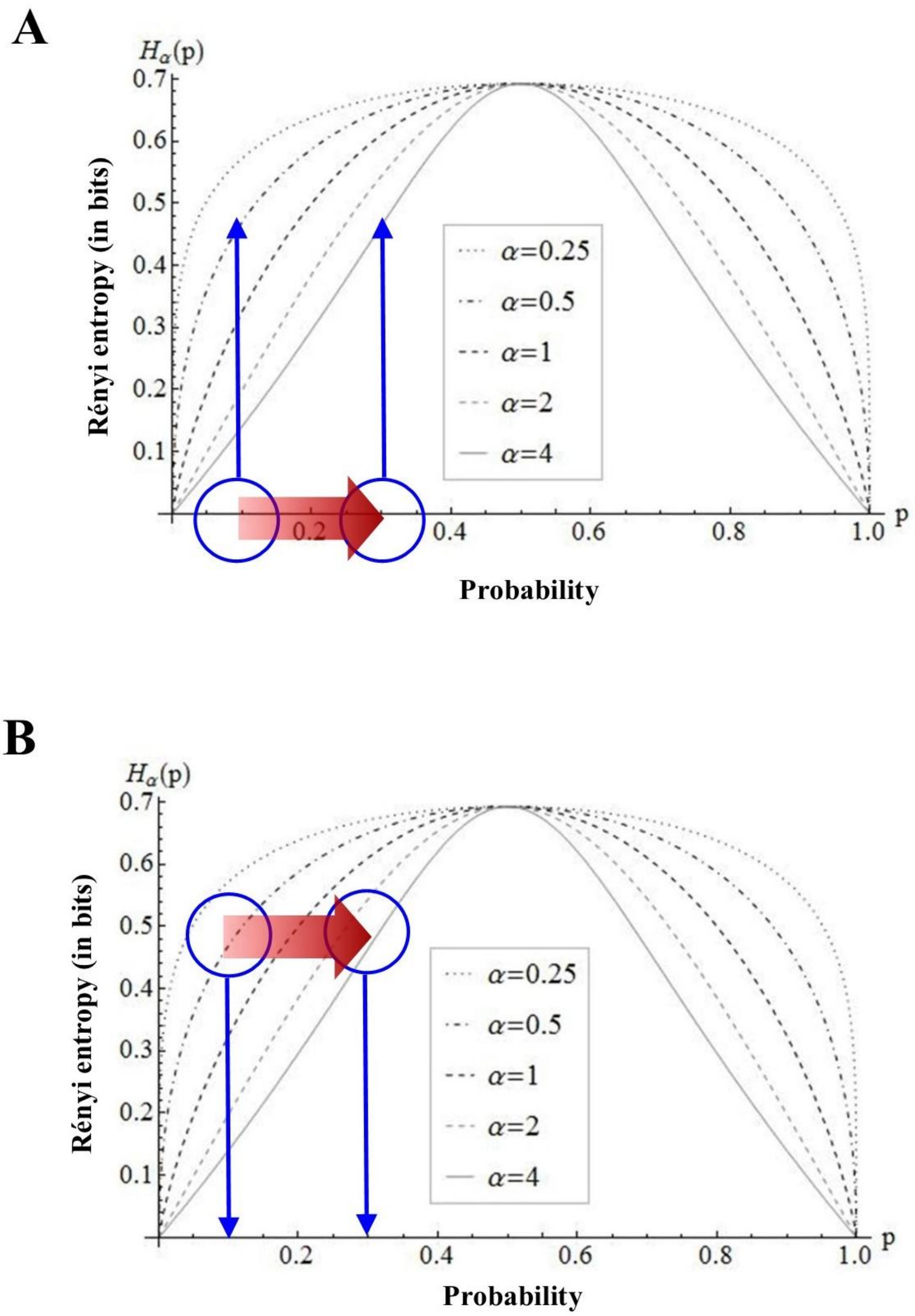

Figure 3A. Schematic representation of the “classical” Rényi entropy. The large arrow depicts how, at a fixed value of entropy (in this example, 0.45) on the y-axis, when p changes (from 0.1 to 0.3) on the x-axis, also the corresponding values of α change (from 0.5 to 4). **Figure 3B.** Schematic representation of the “reverse” Rényi entropy, illustrating the virtues of “top-down” entropy in the evaluation of probability distributions: at the fixed value of Rényi entropy=0.45 on the y-axis, when α changes from 0.5 to 4, we achieve a different value of p (from 0.1 to 0.3) on the x-axis.