Using time causal quantifiers to characterize Sleep stages.

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Abstract

Resent studies found that sleep is essential to helping maintain mood, memory and cognitive performance. Sleep is a dynamic activity, when we sleep we pass throw different state in a cyclic way, wherein key processes for sustaining a healthy condition and overall well-being take place. It is very important that these cycles are maintained for healthy body function in awake state. Because of that, it is paramount to develop tools that can help to detect and classify these states. In this work, we analyzed the EEG signals from 17 subjects. By estimating Shannon's entropy, MPR statistical complexity and the Fisher information measure over the signals we show that it is possible to quantify and classify the sleep stages. Thus, information theory-based measures allow us to characterize the underlying dynamics of EEG time series, identifying the different sleep stages and most importantly define potential electrophysiological biomarkers able to distinguish between pathological and normal conditions.

1 Introduction

We think in sleep as our daily period of rest and recovery from the stresses of everyday life, however, research is revealing that sleep is a dynamic activity during which many processes vital to health and well-being take place. New evidence shows that sleep is essential to helping maintain mood, memory and cognitive performance [1–3]. It also plays a pivotal role in the normal function of the endocrine and immune systems [4]. The incidence of sleep problems in different pathologies is uncontroversial and studies shows a connection between sleep duration and health conditions such as obesity, diabetes, hypertension and depression among many others [5–7].

Recent methodological and technological improvements allow us to examine sleep at a level of detail never before possible. In addition to documenting the more obvious consequences of poor sleep, scientists are increasingly exploring what happens during sleep at the neurological and physiological level. And what they are recognizing is that sleep provides more benefits than previously thought and is absolutely crucial to promoting health and bodily function (REFS: https://www.ncbi.nlm.nih.gov/pubmed/27064792 https://academic.oup.com/sleep/article/37/1/9/2454038).

Although it is common to think of sleep as a time for "shutting down" wakeful processes, sleep is in reality an active physiological process. While metabolism generally slows down during sleep, all mayor organs and regulatory systems continue to function. Roughly speaking, sleep can be categorized into two different functioning modes: rapid eye movement (REM) sleep and non-REM sleep (NREM). NREM sleep is characterized by a reduction in a physiological activity and sleep gets deeper, the brain waves get slower and have greater amplitude, breathing and heart rate slow down and blood pressure drops. The NREM phase consists of four stages: stage 1 (sws1) is characterized by drowsiness or transition from being awake to falling asleep, brain waves and muscle activity begin to slow down during this stage. Stage 2 (sws2) is a period of light sleep during which eye movement stop. Brain waves become slower with occasional bursts of rapid waves called sleep spindles, coupled with spontaneous periods of muscle tone mixed. Stages 3 and 4 (sws3 and sws4), are characterized by the presence of slow brain wave called delta waves interspersed with smaller, faster waves. In these stages sleep is deeper, with no eye movement, decreased muscle activity though muscles retain their ability to function, resembling a coma state.

On the other hand, REM sleep is an active period of sleep marked by intense brain activity. Brain waves are fast and desynchronized similar to those in the waking state, this is also the sleep stage in which most dreams occur. Usually sleepers pass through five stages: sws1, sws2, sws3, sws4 and REM sleep. These stages progress cyclically from sws1 through REM to then go back to sws1 in a loop. A complete sleep cycle takes an average of 90 to 110 minutes, with each stage lasting between 5 to 15 minutes.

It is very important that these cycles are maintained for healthy body function in awake state. Polysomnography studies are performed to investigate problems in the cycles i.e. 12 hours of multi-physiological registers such as electroencephalography (EEG), electrocardiogram (ECG) or electrooculography (EOG) among others. Developing theoretical tools that could provide new insights about how sleep stages mechanism evolve, would crucially change our understanding of sleep cycle processes. In this aim, the use of EEG allow to measures brain electrical activity such as postsynaptic potencials, and it conveys information about the architecture of co-active neural networks on several scales. The analysis of EEG recordings -a non invasive technique- during sleep can be used as a potential biomarker for developmental sleep disorder.

Bandt and Pompe propose the concept of permutation entropy for quantifying the complexity of a system behind a time series [8]. This methodology has been applied for investigating EEG and fMRI signals [9–11] and represents a robust approach to time series analysis on the basis of counting ordinal patterns. The complexity of the brain would represent the amount of "information" contained in the organism, in the sense that it quantifies the dynamical features of the temporal patterns due to functional interactions produced by the underlying structural network. Information theory measures can capture the degree to which the neural system integrates specialized information. Among the most well-known measures we find the Shannon's entropy that calculates the amount of information unknown to the system [12] and the MPR statistical complexity which can distinguish time series generated by stochastic and chaotic systems [13, 14]. Finally, if the goal is to investigate the information in a parameter region of the system, the Fisher information can be used [15].

In this work, we analyzed the EEG signals from 17 subjects with a 12 hours polisomnography recorded from each subject. The signals were preprocessed by experts and cut into subsequences corresponding to different sleep stages. By estimating time causal information quantifiers: Shannon's entropy, MPR statistical complexity and the Fisher information measure over the EEG signal; we show that it is possible to quantify and classify the sleep stages. Thus, information theory-based measures allow us to characterize the underlying dynamics of the EEG time series, identifying the different sleep stages and most importantly define potential electrophysiological biomarkers able to distinguish between pathological and normal conditions.

2 Methods

2.1 Electrophysiological recordings

For our study we used a polysomnography recording belonging to seventeen subjects taken from the Physionet data bank, *The Sleep-EDF Database [Expanded]* [16, 17]. The data are freely available at `www.physionet.org/pn4/sleep-edfx`. The study group was made up with X men and Y women, 25–38 years of age at the time of the recordings. This polysomnograms (PSGs) collection with accompanying hypnograms (expert annotations of sleep stages) comes from two studies (detail in [17, 18]). The recordings are whole-night polysomnographic sleep recordings containing EEG (from Fpz–Cz electrode locations). The EEG signals were each sampled at 100 Hz. The sleep stages were classified in the five stages above-mentioned: *Awake close eyes, REM, sws1, sws2, sws3* and *sws4*.

The EEG recordings were preprocessed with a band-pass filter between 0.5 to 30 Hz and notch filter applied at 60 Hz. The signals were cut into sleep stages subsequences following the annotation made by the expert. Table 1 shows information about the subjects and recordings characteristics used in this work.

2.2 Shannon entropy, Fisher Information and MPR Complexity

For the study of a physical phenomena it is necessary to have a sequence of measurements related to them. These sequences are usually given in the form of time series which allow to extract information on the underlying dynamical systems under study. A time series (i.e. a EEG recording) can be associated to a probability distribution function (PDF) and use information theory quantifiers to characterize its properties. Entropy, regarded as a measure of uncertainty, is the most important example of these quantifiers.

Let us illustrate this point. Given a time series $\mathcal{X}(t) \equiv \{x_t; t = 1, \cdots, N\}$, with N the number of observations, the Shannons logarithmic information measure (*Shannon entropy*) [12] of the associated PDF, $P \equiv \{p_j; j =$

Subject	Gender	Age	N_e of segment for each epoch					
			Awake	REM	sws1	sws2	sws3	sws4
1	F	33	1997	125	58	250	101	119
2	M	34	1885	215	59	373	94	203
3	F	32	3680	346	201	1022	176	25
4	F	31	1824	176	92	660	80	16
5	F	26	1907	163	94	545	73	22
6	M	29	1971	179	184	402	81	38
7	F	25	2008	209	61	485	56	1
8	F	32	1957	199	45	400	54	77
9	F	34	1773	270	137	514	88	6
10	M	34	1780	180	114	616	106	8
11	F	31	2069	102	56	407	35	101
12	F	35	2007	187	90	417	96	33
13	M	30	1958	198	89	403	80	82
14	F	39	1904	168	84	392	59	163
15	F	25	1985	131	68	262	158	192
16	M	26	1739	232	19	561	87	83
17	F	25	1079	265	81	512	103	4

Table 1: Subjects information analyzed in this work. N_e represents the number of segments for the same sleep stage. All segments have the same length, $L = 3000$ data points ($t = 30$ seconds of recording).

$1, \cdots, M\}$ with $\sum_{j=1}^{M} p_j = 1$, and M the number of possible states is defined by:

$$\mathcal{S}[P] \;=\; -\sum_{j=1}^{M} p_j \ln(p_j) \;. \tag{1}$$

When we have total certainty that our system is in the state j the probability $p_j = 1$ and this functional is equal to zero. In contrast, when the probability distribution is uniform, $P_e \equiv \{p_j = 1/M; \forall j = 1, \cdots, M\}$, our knowledge about the system is minimum (all the states have the same probability) and the entropy reach its maximum.

The Shannon entropy $\mathcal{S}$ is a measure of "global character", however in small local regions it lacks sensitivity to strong changes in the PDF. For that case the Fisher information $\mathcal{F}$ is a more effective quantifier [15, 19]:

$$\mathcal{F}[f] \;=\; \int \frac{|\vec{\nabla} f(x)|^2}{f(x)} dx \;, \tag{2}$$

which constitutes a measure of the gradient content of the distribution f (continuous PDF), thus being quite sensitive even to tiny localized perturbations.

The Fisher information can be interpreted as the amount of information that can be extracted from a set of measures, as the ability to estimate a particular parameter and also as a measure of the state of disorder of a system [19, 20], its most important property being the so-called Cramer–Rao bound (REF). In equation (2), the gradient operator, $\vec{\nabla}$, significantly influences the contribution of minute local f -variations to the Fisher information value, so that the quantifier is said to be loca. Local sensitivity is useful in scenarios whose description necessitates an appeal to a notion of "order" [21–23].

For Fisher information measure computation (discrete PDF), we follow the proposal of Dehesa and coworkers in [24] based on amplitude of probability $f(x) = \psi(x)^2$, then:

$$\mathcal{F}[\psi] \;=\; 4 \int \left(\frac{d\psi}{dx} \right) dx \;. \tag{3}$$

and for a discrete distribution:

$$\mathcal{F}[P] \;=\; 4 \sum_{i=1}^{N-1} (\sqrt{p_{i+1}} - \sqrt{p_i})^2 \;. \tag{4}$$

A system in a very ordered state will have a very narrow PDF, the Shannon entropy is $\mathcal{S} \to 0$ and the Fisher information measure $\mathcal{F} \to \mathcal{F}_{max}$. On the other hand, when the system under study lies in a very disorder distribution (flat PDF) $\mathcal{S} \to \mathcal{S}_{max}$, $\mathcal{F} \to 0$. From this simple example we can extrapolate that the Fisher information measure and the Shannon entropy behavior behave reciprocally [25].

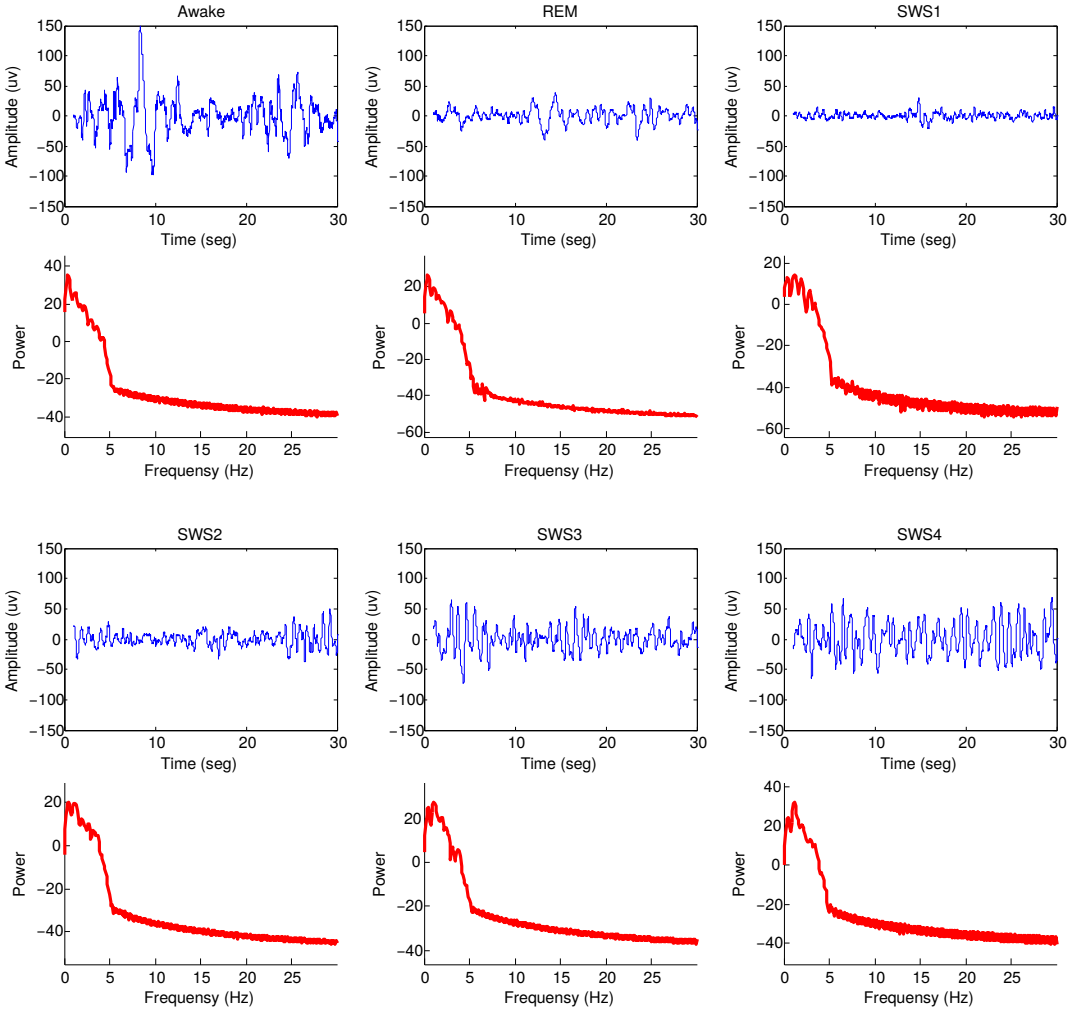

Figure 1: Example of the EEG signals and their respective FFT for each sleep stage: Awake, REM, sws1, sws2, sws3 and sws4.

Nevertheless, the processes present in nature are not, at least directly, quantified by randomness measures, that should make us to look for other types of measures of statistical or structural complexity to understand system dynamics represented by their time series [26]. If we take the two extreme - a perfect order (i.e., a periodic sequence) and a maximal randomness (i.e white noise)- both are very easily described (number of bits [27]) to describe and their complexity should be closed to zero in both cases. At a given distance from these two extremes, it lies a wide range of possible ordinal structures. The statistical complexity measures allows one to quantify this array of behavior [28]. In our work we consider the statistical complexity MPR introduced in [29] because is able to quantify critical details of dynamical processes underlying the data set.

Based in the *Lopez-Ruiz et al.* work [30], this statistical complexity measure is defined through the functional product form

$$\mathcal{C}[P] \;=\; \mathcal{Q}_J[P, P_e] \cdot \mathcal{H}[P] \tag{5}$$

of the normalized Shannon entropy:

$$\mathcal{H}[P] \;=\; \mathcal{S}[P]/\mathcal{S}_{max} \;, \tag{6}$$

with $\mathcal{S}_{max} = \mathcal{S}[P_e] = \ln N$, $(0 \leq \mathcal{H} \leq 1)$ and the disequilibrium $\mathcal{Q}_J$ defined in term of the Jensen–Shannon divergence. That is,

$$\mathcal{Q}_J[P, P_e] \;=\; \mathcal{Q}_0 \; \mathcal{J}[P, P_e] \;, \tag{7}$$

with:

$$\mathcal{J}[P, P_e] \;=\; \mathcal{S}[(P + P_e)/2] - \mathcal{S}[P]/2 - \mathcal{S}[P_e]/2 \;, \tag{8}$$

the above-mentioned Jensen–Shannon divergence and $\mathcal{Q}_0$, a normalization constant ($0 \leq \mathcal{Q}_J \leq 1$), are equal to the inverse of the maximum possible value of $\mathcal{J}[P, P_e]$. This value is obtained when one of the components of the PDF, P, say p_n, is equal to one and the remaining p_j are equal to zero. The statistical complexity depends on two different probability distributions, the one associated with the system under analysis, P, and the uniform distribution, P_e. The distance between this two probability distributions are measured using the Jensen–Shannon divergence [31]. Furthermore, it has been shown that for a given value of $\mathcal{H}$, the range of possible $\mathcal{C}$ values varies between a minimum $\mathcal{C}_{min}$ and a maximum $\mathcal{C}_{max}$, restricting the possible values of the statistical complexity in a given entropy-complexity plane [32]. Because of this, statistical complexity measure, gives important additional information related to the correlational structure between the components of the physical system.

2.3 Time series discretization using Bandt-Pompe approach

The study and characterization of time series $\mathcal{X}(t)$ by recourse to information theory tools assume that the underlying PDF is given a priori. In the literature there are many methods to extract PDF from the time series such as binarization, histograms or wavelet among others. However, an effective method that emerges naturally is the one introduced by Bandt and Pompe called permutation vectors [8].

The permutation vectors method is based on the relative values of the neighbors belonging to the series, and in consequence take in a natural way the time causality in which these values had been generated. To understand the idea let us consider a real-valued discrete-time series $\mathcal{X}(t) = \{x_t \in \mathbb{R}\}$, and let $D \geq 2$ and $\tau \geq 1$ be two integers. They will be called the embedding dimension and the time delay, respectively. From the original time series, we introduce a D-dimensional vector $\mathbf{Y}_t^{(D,\tau)}$:

$$\mathbf{Y}_t^{(D,\tau)} \rightarrow (x_{t-(D-1)\tau}, \ldots, x_{t-\tau}, x_t) \qquad \text{with} \qquad t \geq (D-1)\tau \;. \tag{9}$$

There are conditions on D and τ in order that the vector $\mathbf{Y}_t^{(D,\tau)}$ preserves the dynamical properties of the full dynamical system. The components of the phase space trajectory $\mathbf{Y}_t^{(D,\tau)}$ are sorted in ascending order. Then, we can define a *permutation vector*, $\mathbf{\Pi}_t^{(D,\tau)}$, with components given by the original position of the sorted values in ascending order of the component of $\mathbf{Y}_t^{(D,\tau)}$. Each one of these vectors represents a pattern (or motif). There are $D!$ possible patterns.

To clarify all this technicalities, let us show how all this works with an example. Suppose we have a continuous series such as $\mathcal{X}(t) = \{0.32, 1.8, 5.4, 0.25, 1.7\}$ and take the parameters $D = 3$ and $\tau = 1$. The embedding vectors $\mathbf{Y}_t^{(D,\tau)}$ in this case are defined as $\mathbf{Y}_1^{(3,1)} = (0.32, 1.8, 5.4)$; $\mathbf{Y}_2^{(3,1)} = (1.8, 5.4, 0.25)$; $\mathbf{Y}_3^{(3,1)} = (5.4, 0.35, 1.7)$, and the respective permutation vectors are $\mathbf{\Pi}_1^{(3,1)} = (1, 2, 3)$, $\mathbf{\Pi}_2^{(3,1)} = (3, 1, 2)$ and $\mathbf{\Pi}_3^{(3,1)} = (2, 3, 1)$.

The diversity of the ordering symbols (patterns of length D) derived from a scalar time series can be quantified, by evaluating the so-called permutation entropy (Shannon entropy), the permutation statistical complexity and Fisher permutation information measure. The embedding dimension D plays an important role in the evaluation of the appropriate probability distribution, because D determines the number of accessible states $D!$ and also conditions the minimum acceptable length $M \gg D!$ of the time series that one needs in order to work with reliable statistics [13].

Regarding the selection of the parameters, Bandt and Pompe suggested working with $4 \leq D \leq 6$ and specifically considered an embedding delay $\tau = 1$ in their paper [8]. Nevertheless, it is clear that other values of τ could provide additional information. It has been recently shown that this parameter is strongly related, if it is relevant, to the intrinsic time scales of the system under analysis [33–35]. In this work we used $D = 4$ and $\tau = 1$ for all the analysis, however similar results were obtained for $D = 5$ and $\tau = 1$.

3 Results and Discussion

Seventeen subjects were recorded with a 12 hours polysomnography. The signals were cut in sub-signals correspond to the different periods of sleep stages (*Awake, REM, sws1, sws2, sws3* and *sws4*). The transition between epochs for the subjects enter in each state is described in table 1. Figure 1 is shown as an example of an EEG raw signals and the power spectrum for one typical subject (subject 1) in different sleep stages. All the signals were quantified using the Bandt and Pomp method for the parameters $D = 4$ and $\tau = 1$ this embedding dimension is enough to the capture causality information of the ordinal structure of the time series [8].

The first analysis performed was the study of the permutation vectors ($\mathbf{\Pi}^{(D,\tau)}$) distribution. Figure 2 shows the appearance frequency of the permutation patterns correspond to one sub-sequence belong to one subject.

Figure 3 shows the same analysis as before but making an average overall epoch belong to the same subject. Finally Figure 4 is the average overall subjects analyzing in this work. For the three cases, it can be seen that the result is similar. For stages with more brain activity such as Awake and REM, the distribution of permutation patterns tends to have a more uniform PDF. This is given because in these stages the signals are composed for more frequencies which need a greater number of different permutation patterns to be quantified. For the contrary, when subjects enter in deeper sleep stages, begins to appear a predominance of slow waves – in sws3 has 20 to 50 percent delta wave activity, and in sws4, has more than 50 percent delta wave activity EEG [36]. These waves have a high amplitude and low frequency. The signal becomes more periodic and the numbers of patterns required to quantify it decreases. In Figures 2, 3 and 4 it could be observed the predominant patterns are those represent the continuous increase and decrease of the signal.

The following analysis was the application of the three measures introduced in section 2. Figure 5 despite the mean values and the standard deviation for Shannon entropy (Figure 5A), MPR statistical complexity (Figure 5B) and Fisher information (Figure 5B). To expand on this point we present the values for each patients in tables 2, 3, 4 and the average over all patients in table 5.

When the brain is in wakefulness state, it needs to handle internal and external information, this makes it necessary to use the globality of its functions, in particular in the prefrontal cortex. Something similar occurs in REM stage where most of the dreams occurs, and the person continues connected with the external environment, –such as being able to hear noises. Because of this, the EEG signal become more fluctuating and less predictable, causing that entropy of the signal been high 5A. At the same time, the permutation vectors PDF tend to be more uniform both in the Awake and REM states. It is expected that MPR complexity values are lower in these states (see Figure 5B). On the other hand, when the brain enters into sws3 and sws4, slow waves arise and the EEG signal becomes more regular and predictable, leading to a sharp decrease in entropy in these stages. Conversely, the MPR complexity tend to be largest because the permutation patterns move away from the uniform PDF. Finally, Fisher information gives us information of the behavior of the local characteristic of the system. As can be seen in Figure 5C for awake, REM, sws1 and sws2 there are not significant changes, however there is an increase of Fisher information in sws3 and sws4. This conforms out initial assumption that changes in the systems dynamics could be observed more remarkably with global measures.

MPR permutation complexity is a measure derived from nonlinear systems theory that, when is applied to EEG signals, can be indicative of the global dynamical complexity of electrocortical activity. However, to obtain further understanding of our results, we need to plot the localization in the causality entropy–complexity plane of the results obtained in the present work. Figure 3 displays all the results considered here in the $\mathcal{H} \times \mathcal{C}$ location. The continuous lines represent the curves of maximum and minimum statistical complexity, $\mathcal{C}_{max}$ and $\mathcal{C}_{min}$, respectively, as functions of the normalized Shannon entropy [32].

Figure 3 shows the distribution of complexity–entropy mean values for each sleep state. To show that complexity–entropy values are not caused by random behavior of the signal, all the signals belonging to the patients were randomized, the mean value was represented in the plane. As can be seen in Figure 3, the randomized values are found at the extreme maximum entropy and minimum complexity. The signals that have a uniform PDF (as the white noise) lives in this area of plane [13].

The signals belonging to Awake, REM, and sws1 have more complexity and less entropy than random signals but they remind in a location where live noisy activity with low correlation [13] (NO SE ENTEINDE) . When sleep phases transition to sws2, sws3 and sws4, the complexity tend to increase and the entropy to decrease, moving values to the center of the plane. The same behavior can be observed when we analyze correlated noises, as the correlation increases, the entropy–complexity values move from extreme values to the center of the plane [13].

Making use of the idea of the MPR plane to characterize graphically the sleep dynamics, we analyze the signal using the Shannon–Fisher entropy plane, $\mathcal{H} \times \mathcal{F}$. This allows us to quantify the global versus local characteristic of the time series generated by a dynamical processes. In this case the plane can distinguish between regions corresponding to different sleep states from regions corresponding to randomized signals. Here the awake states REM and sws1 are among the high entropy values (between 0.9 and 0.95) and Fisher information values (0.11 and 0.12). As the subjects enter in a deeper state of sleep entropy values are decreasing and Fisher information increasing, combining these two measures it is possible to disentangle states according to their activity level.

4 Conclusion

The study of sleep stages are of vital importance to understand both health and pathological conditions. Dysfunctions in sleep cycles generate problems such as fatigue, muscular pains and attention problem among others. Because of that the detection and proper characterization of sleep stages is of paramount importance. In this work we have been able to identify the different sleep stages using Information Theory tools such as Shannon

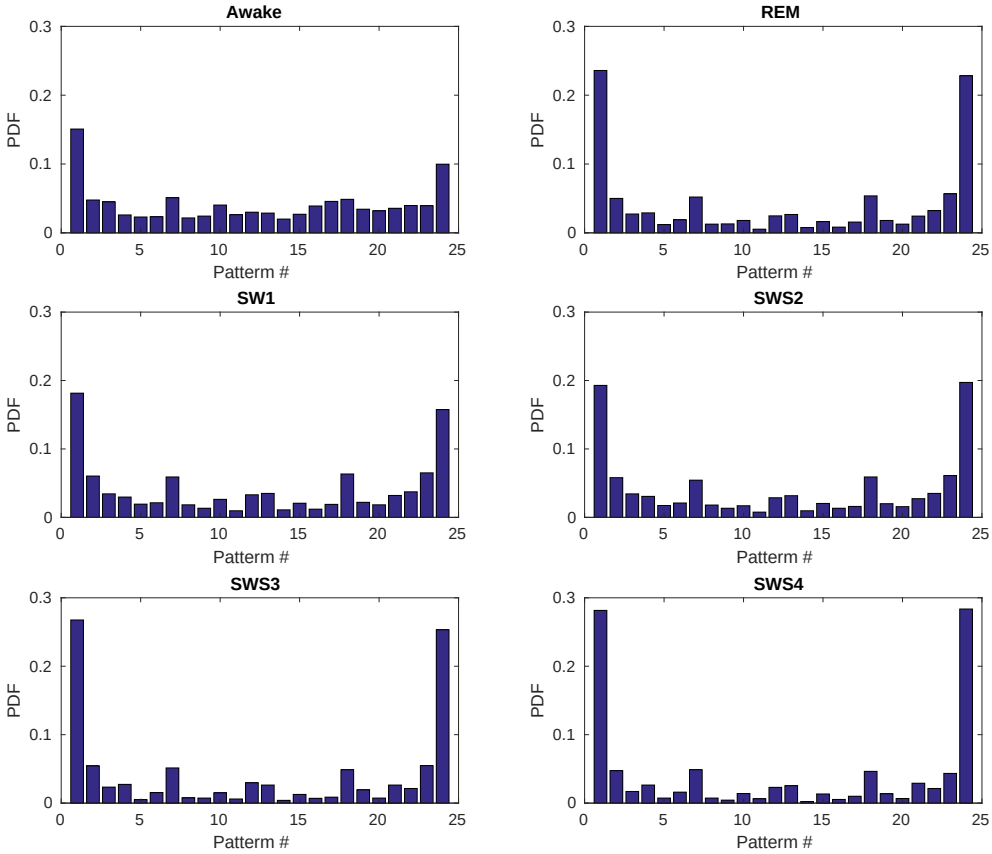

Figure 2: Bandt-Pompe PDF for the different sleep states considerate in detail the present work, for the case $D = 4$ (pattern length) and $\tau = 1$ (time lag). The BP pattern histogram corresponds to one segment for each state belong to subject 1 (table 1). Similar result were found for $D = 5$ and $\tau = 1$

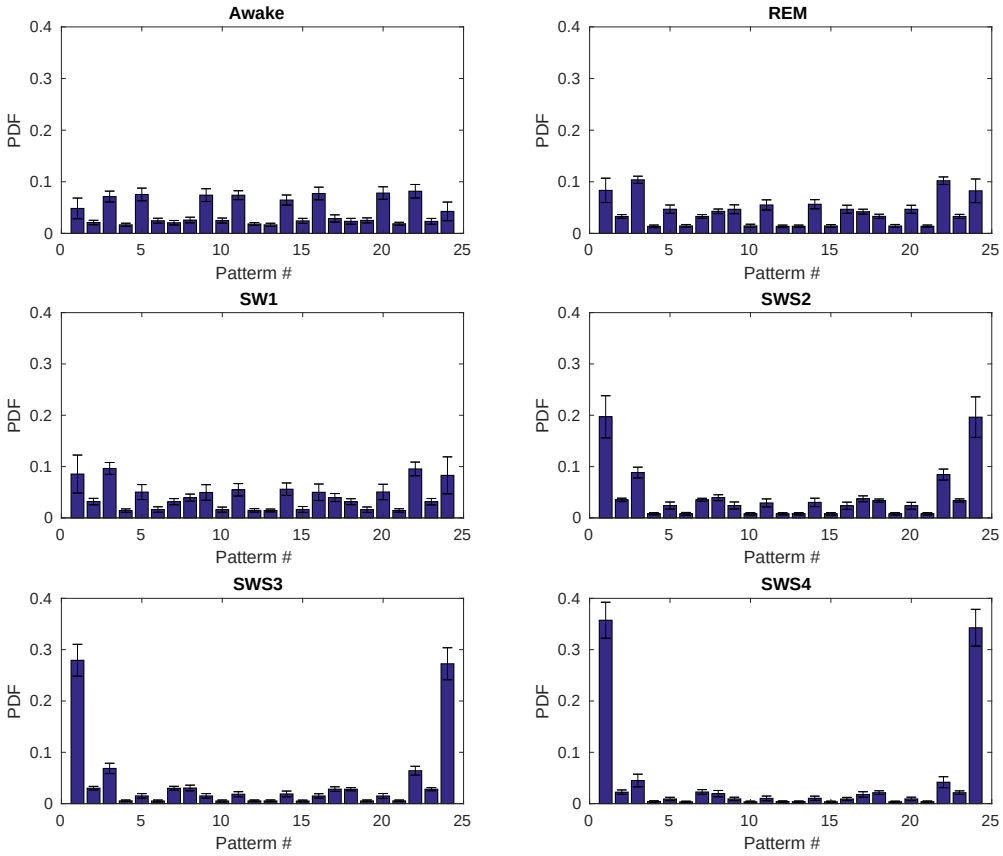

Figure 3: Average Bandt-Pompe PDF for the different sleep states corresponding to subject 1 (table:1), for the case $D = 4$ (pattern length) and $\tau = 1$ (time lag). The pattern histogram are the mean value and standard deviation calculated over all segment. Similar result were found for $D = 5$ and $\tau = 1$.

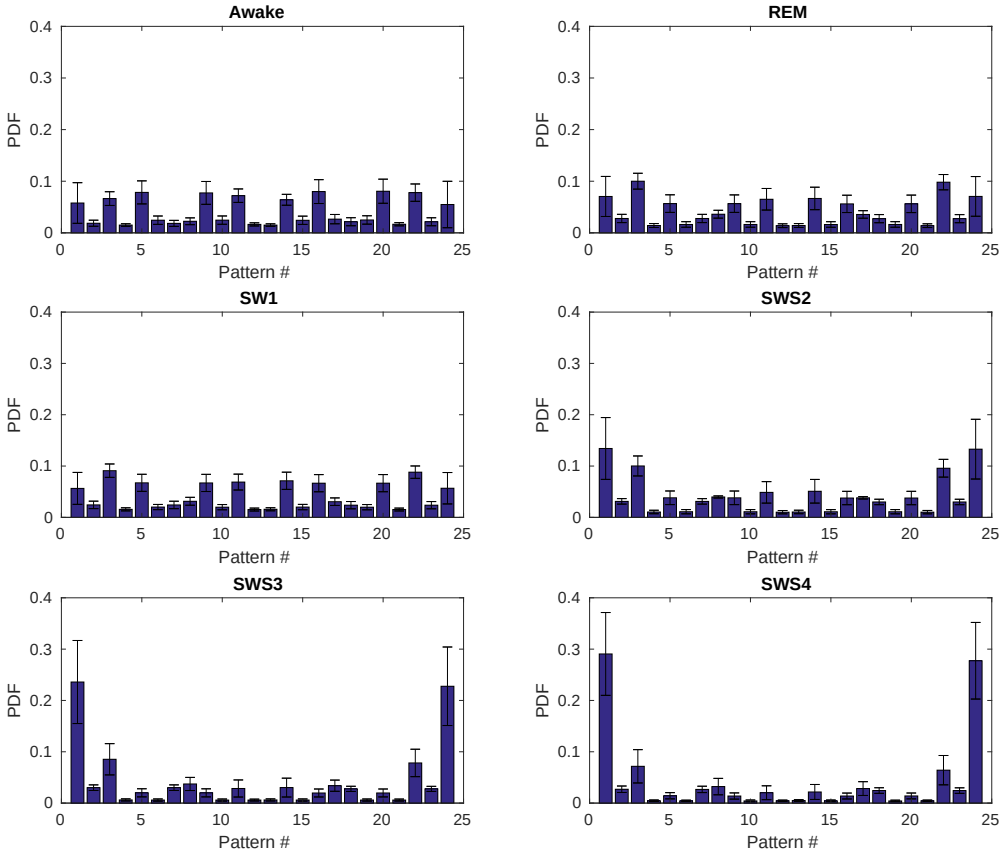

Figure 4: Average Bandt-Pompe PDF for the different sleep states considerate in detail the present work, for the case $D = 4$ (pattern length) and $\tau = 1$ (time lag). The BP pattern histogram is the mean value and standard deviation calculated over all subject and all segment see (table 1). Similar result were found for $D = 5$ and $\tau = 1$.

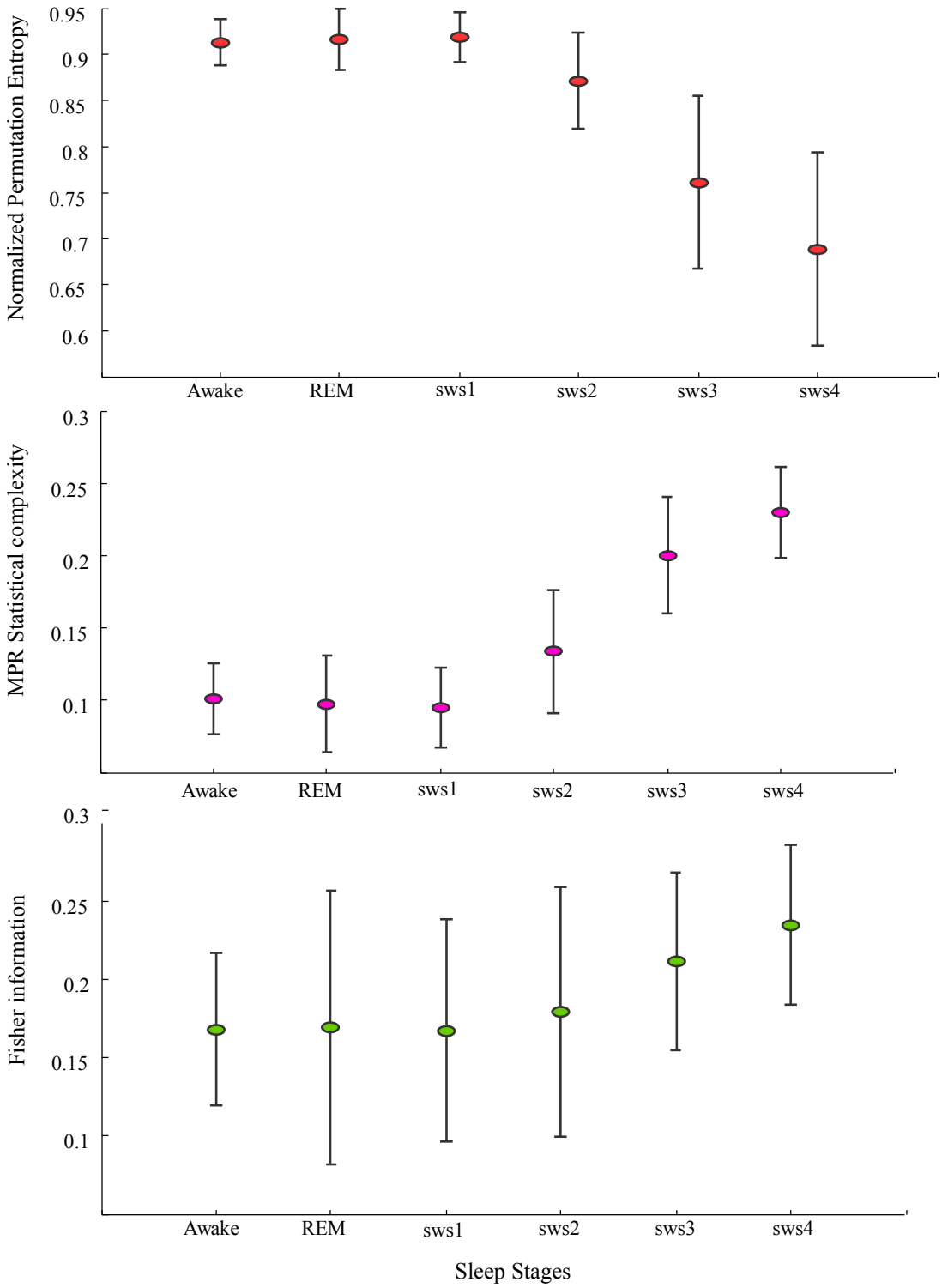

Figure 5: A) Normalized Shannon entropy ($\mathcal{H}$) vs Sleep stages. B) MPR statistical complexity ($\mathcal{C}$) vs Sleep Stages. C) Fisher information ($\mathcal{F}$) vs Sleep stages. For all time causal quantifiers ($D = 4$ and $\tau = 1$) the average values and standard deviation estimated considering 17 patient with all their epoch see (table 1).

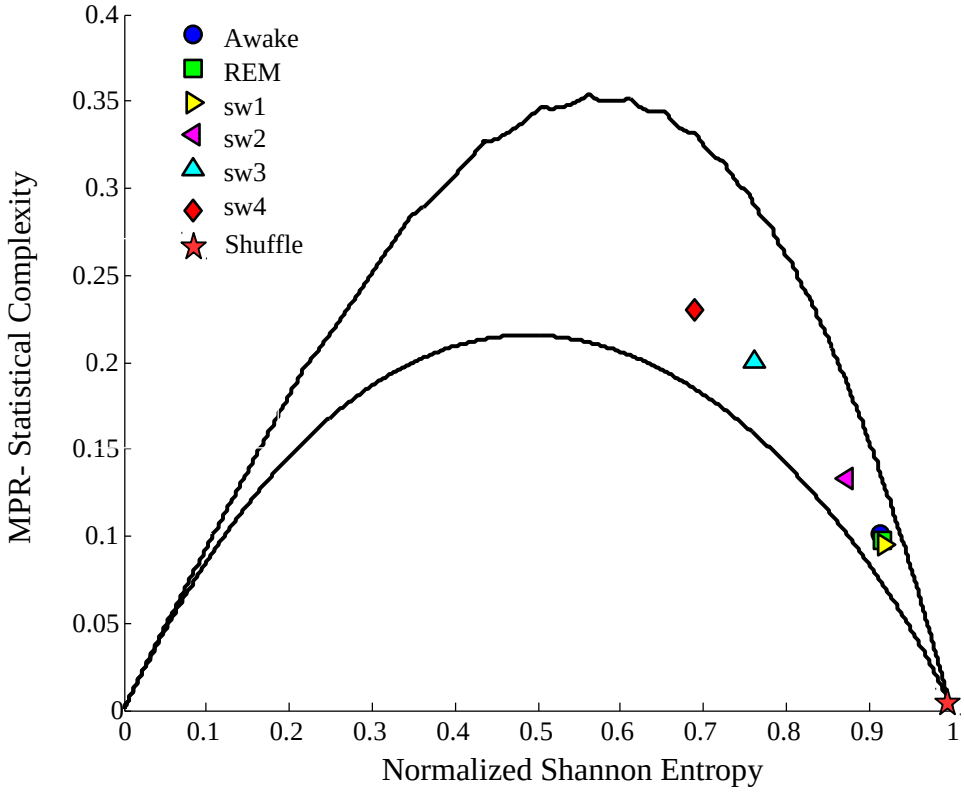

Figure 6: Entropy–Complexity plane ($\mathcal{H} \times \mathcal{C}$) for the 6 different sleep state. Each dot represent the mean value over 17 subject take in the study using the permutation parameter $D = 4$ and $\tau = 1$. The awake, REM and sws1 states are located in a region with greater entropy and less complexity. As the subjects are introduced in deeper sleep stages their complexity increases and their entropy decreases. All states are clearly discriminated from the randomized signals (star) which are at the end of the plane. The similar result were obtained for the parameter $D = 5$ and $\tau = 1$.

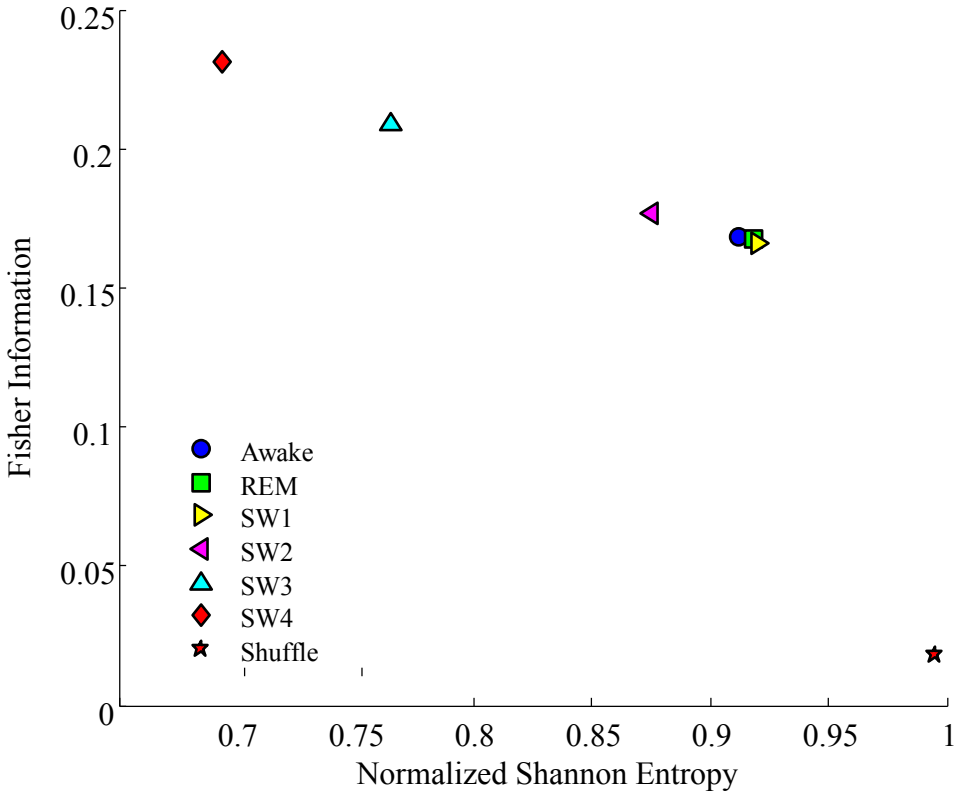

Figure 7: Shannon–Fisher information plane ($\mathcal{H} \times \mathcal{F}$) for the 6 different sleep state. Each dot represent the mean value over 17 subject take in the study using the permutation parameter $D = 4$ and $\tau = 1$. The awake, REM and sws1 states are located in a region with greater entropy and meddle Fisher values. As the subjects remain in deeper sleep stages the Fisher values start to increases and their entropy decreases. All states are clearly discriminated from the randomized signals (star) which are at the bottom of the plane. Similar result were obtained for the parameter $D = 5$ and $\tau = 1$.

Subject	AWAKE		REM		SWS1		SWS2		SWS3		SWS4	
	mean	std	mean	std	mean	std	mean	std	mean	std	mean	std
1	0,94	0,01	0,93	0,01	0,93	0,02	0,83	0,05	0,72	0,05	0,60	0,06
2	0,94	0,01	0,92	0,02	0,94	0,01	0,92	0,02	0,86	0,03	0,78	0,05
3	0,88	0,05	0,90	0,02	0,92	0,03	0,80	0,07	0,60	0,05	0,56	0,03
4	0,88	0,05	0,91	0,02	0,92	0,03	0,82	0,06	0,63	0,04	0,57	0,02
5	0,93	0,02	0,91	0,02	0,92	0,02	0,82	0,07	0,66	0,06	0,60	0,04
6	0,92	0,03	0,92	0,02	0,91	0,04	0,84	0,05	0,70	0,05	0,63	0,04
7	0,92	0,04	0,94	0,01	0,95	0,01	0,90	0,04	0,79	0,04	0,70	0,00
8	0,85	0,07	0,89	0,07	0,88	0,05	0,88	0,06	0,82	0,04	0,80	0,02
9	0,94	0,02	0,92	0,04	0,90	0,04	0,90	0,04	0,83	0,03	0,80	0,02
10	0,92	0,04	0,94	0,01	0,94	0,01	0,93	0,02	0,85	0,03	0,82	0,02
11	0,91	0,02	0,95	0,01	0,93	0,02	0,93	0,02	0,84	0,03	0,72	0,05
12	0,93	0,03	0,91	0,02	0,93	0,03	0,85	0,06	0,61	0,06	0,51	0,02
13	0,93	0,02	0,81	0,04	0,84	0,06	0,80	0,05	0,80	0,04	0,75	0,02
14	0,91	0,02	0,93	0,01	0,91	0,03	0,93	0,01	0,89	0,03	0,82	0,03
15	0,93	0,04	0,90	0,04	0,93	0,04	0,80	0,05	0,73	0,05	0,57	0,07
16	0,93	0,03	0,93	0,04	0,94	0,01	0,90	0,04	0,79	0,05	0,69	0,05
17	0,89	0,03	0,95	0,01	0,93	0,02	0,94	0,02	0,84	0,04	0,79	0,03

Table 2: Shannon entropy values ($\mathcal{H}$) for each subject analyzed in this work. The table shows the average value and standard deviation over all segments belonging to the same sleep stage. The parameter used were $D = 4$ and $\tau = 1$.

entropy, Fisher information and MPR complexity.

In the awake state, the human brain needs to handle both external and internal information and the informational content is overall greater than in other deeper stages. Because of this, the electrical activity becomes more complex with greater variability as detected in the brain waves. Thus, a large numbers of different patterns show up in more active in wakefulness in comparison with the others states. This behavior is also reflected in its high permutation entropy values as in the low values of MPR conmplexity and Fisher information. Similar results are found in the REM phase which is characterized by strong brain activity since it is the phase where most of the dreaming occur.

In deeper dream stages - sws3 and sws4 - it is observed a decrease in most of the vital signals (respiration, blood pressure, etc). Brain signals become slower and more repetitive with a marked predominance of delta waves. The number of patterns required to mapping the signal diminish. For this the signal becomes more predictable giving a decrease in the permutation entropy values and and show an increase in the MPR complexity and Fisher information values.

The MPR complexity and permutation entropy measures have shown that they can be useful tools to distinguish and characterize different sleep states. The Fisher information has distinguished between the sws4 and the others stages, but can not detect the difference between each (WHICH SPECIFICALLY) stages. This can be explained because Fisher information models the local dynamics while and may result inadequate to model stages that mediate in global brain activity, for those states global analysis tools such as entropy o MPR complexity are required.

The complexity–entropy plane allows to analyze the values distribution for each sleep stage in a bidimensional plane. This method enables a better visual distinction between stages in a fast and easy way. This work makes a substantiated case for the use of information-theoretic tools for analysis of the EEG signals, complementing the visual inspection used by electrophysiologists. Given the importance that sleep cycles have in people's health, in future work we will focus on applying these analytical method for the study of pathological EEGs. To that end, data from patients with insomnia, circadian rhythmic sleep-awake and parasomnia among others, will be explored using these techniques in order to validate them as biomarkers.

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Subject	AWAKE		REM		SWS1		SWS2		SWS3		SWS4	
	mean	std	mean	std	mean	std	mean	std	mean	std	mean	std
1	0,07	0,01	0,08	0,01	0,08	0,02	0,17	0,03	0,22	0,02	0,25	0,01
2	0,10	0,02	0,08	0,01	0,07	0,01	0,10	0,02	0,15	0,03	0,20	0,03
3	0,12	0,04	0,11	0,02	0,10	0,03	0,18	0,04	0,26	0,01	0,26	0,00
4	0,13	0,04	0,10	0,02	0,09	0,03	0,17	0,04	0,25	0,01	0,26	0,00
5	0,08	0,03	0,11	0,02	0,09	0,02	0,17	0,04	0,25	0,02	0,26	0,01
6	0,09	0,02	0,09	0,02	0,10	0,04	0,15	0,03	0,23	0,02	0,25	0,01
7	0,10	0,04	0,07	0,01	0,07	0,01	0,11	0,04	0,19	0,02	0,23	0,00
8	0,17	0,07	0,13	0,07	0,14	0,05	0,13	0,05	0,19	0,04	0,21	0,02
9	0,07	0,02	0,10	0,04	0,11	0,04	0,12	0,04	0,18	0,02	0,20	0,01
10	0,10	0,04	0,07	0,01	0,18	0,01	0,16	0,02	0,08	0,02	0,08	0,01
11	0,11	0,03	0,06	0,01	0,08	0,02	0,08	0,02	0,16	0,02	0,23	0,03
12	0,08	0,03	0,10	0,02	0,08	0,03	0,15	0,04	0,25	0,02	0,27	0,00
13	0,08	0,02	0,21	0,03	0,18	0,06	0,21	0,04	0,21	0,03	0,25	0,01
14	0,11	0,02	0,08	0,01	0,10	0,03	0,08	0,01	0,13	0,03	0,18	0,02
15	0,09	0,04	0,11	0,03	0,08	0,03	0,18	0,03	0,22	0,03	0,26	0,01
16	0,09	0,03	0,09	0,04	0,07	0,01	0,11	0,03	0,19	0,03	0,23	0,02
17	0,12	0,04	0,07	0,01	0,08	0,02	0,08	0,02	0,16	0,02	0,19	0,02

Table 3: MPR Complexity values ($\mathcal{C}$) for each subject analyzed in this work. The table shows the average value and standard deviation calculated over all segments belonging to the same sleep stage. The parameter used were $D = 4$ and $\tau = 1$.

Subject	AWAKE		REM		SWS1		SWS2		SWS3		SWS4	
	mean	std	mean	std	mean	std	mean	std	mean	std	mean	std
1	0,14	0,02	0,14	0,01	0,13	0,01	0,16	0,02	0,20	0,02	0,24	0,02
2	0,16	0,02	0,15	0,01	0,15	0,01	0,15	0,01	0,17	0,01	0,19	0,02
3	0,15	0,03	0,14	0,02	0,14	0,02	0,17	0,03	0,24	0,02	0,26	0,01
4	0,15	0,03	0,15	0,03	0,14	0,03	0,18	0,04	0,23	0,02	0,25	0,01
5	0,15	0,06	0,16	0,02	0,16	0,02	0,19	0,02	0,24	0,02	0,26	0,01
6	0,13	0,02	0,10	0,02	0,12	0,02	0,13	0,02	0,19	0,02	0,22	0,02
7	0,18	0,08	0,14	0,03	0,13	0,02	0,14	0,03	0,17	0,02	0,21	0,00
8	0,35	0,18	0,28	0,17	0,28	0,12	0,24	0,15	0,33	0,16	0,31	0,12
9	0,13	0,03	0,20	0,09	0,21	0,08	0,21	0,09	0,23	0,05	0,22	0,03
10	0,19	0,09	0,15	0,01	0,15	0,02	0,14	0,01	0,17	0,01	0,18	0,01
11	0,17	0,02	0,13	0,01	0,14	0,02	0,13	0,01	0,16	0,02	0,20	0,02
12	0,15	0,05	0,13	0,01	0,12	0,01	0,15	0,02	0,24	0,02	0,28	0,01
13	0,15	0,04	0,47	0,09	0,39	0,16	0,47	0,13	0,35	0,10	0,37	0,05
14	0,17	0,02	0,16	0,02	0,18	0,03	0,15	0,02	0,16	0,02	0,18	0,01
15	0,17	0,10	0,14	0,02	0,13	0,02	0,17	0,02	0,19	0,02	0,25	0,03
16	0,15	0,03	0,13	0,02	0,13	0,01	0,14	0,02	0,17	0,02	0,21	0,02
17	0,15	0,03	0,13	0,02	0,13	0,01	0,14	0,02	0,17	0,02	0,21	0,02

Table 4: Fisher Information values ($\mathcal{F}$) for each subject analyzed in this work. The table shows the average value and standard deviation of the calculated over all segments belonging to the same sleep stage. The parameter used were $D = 4$ and $\tau = 1$.

	AWAKE		REM		SWS1		SWS2		SWS3		SWS4	
	mean	std	mean	std	mean	std	mean	std	mean	std	mean	std
$< \mathcal{H} >$	0,91	0,02	0,92	0,03	0,92	0,03	0,88	0,05	0,77	0,09	0,69	0,10
$< \mathcal{C}_J >$	0,10	0,02	0,10	0,03	0,09	0,03	0,13	0,04	0,20	0,04	0,23	0,03
$< \mathcal{F} >$	0,17	0,05	0,17	0,09	0,17	0,07	0,18	0,08	0,21	0,06	0,23	0,05

Table 5: Mean and standard deviation of the values for the quantifiers $\mathcal{H}$, $\mathcal{C}$, $\mathcal{F}$ belong to each sleep state. They were calculated over all the segments and all the patients analyzed in this work. The parameter used were $D = 4$ and $\tau = 1$.

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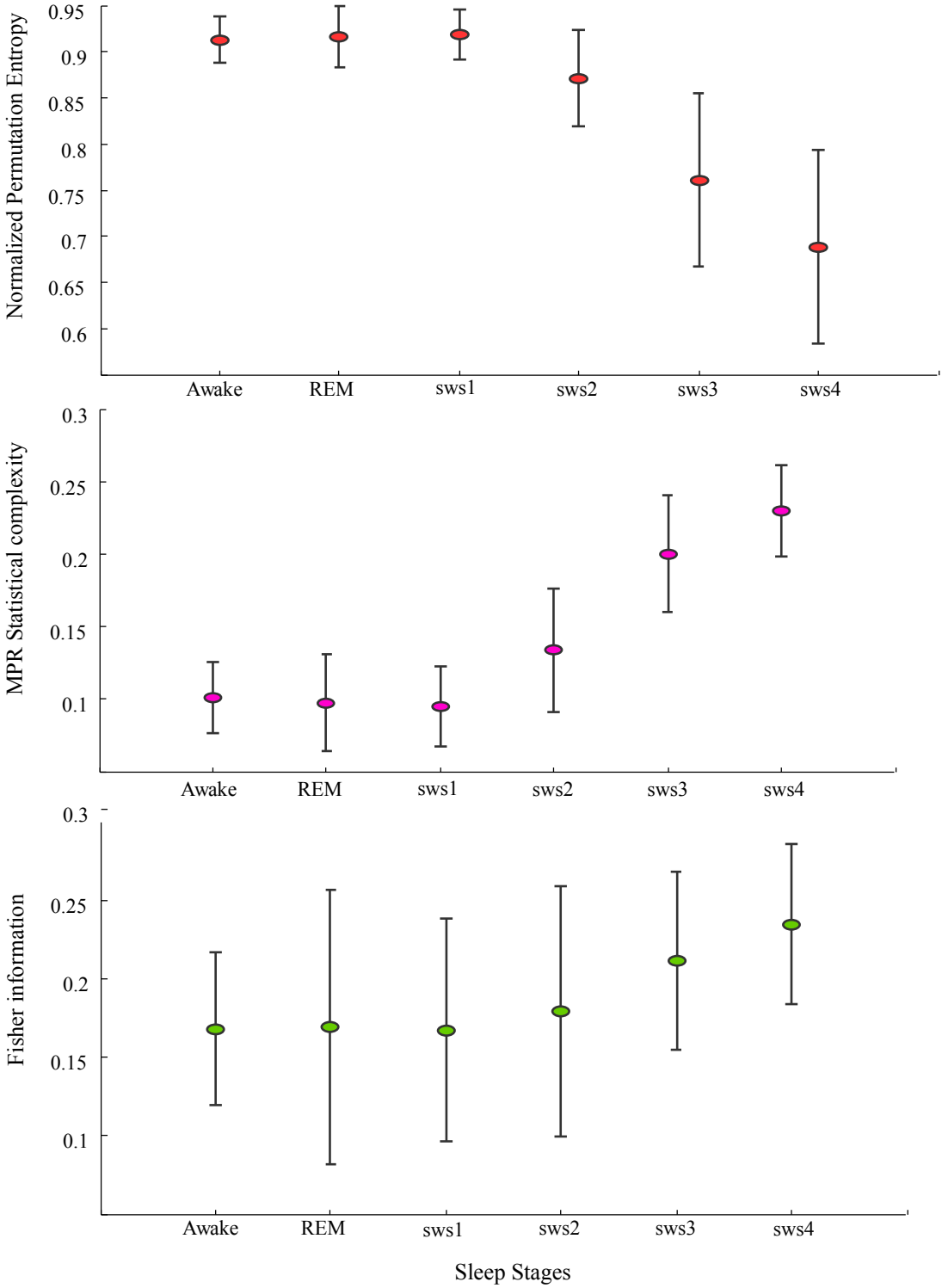
Normalized Permutation Entropy
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0.9
0.85
0.8
0.75
0.7
0.65
0.6
Awake
REM
sws1
sws2
sws3
sws4
MPR Statistical complexity
0.3
0.25
0.2
0.15
0.1
Awake
REM
sws1
sws2
sws3
sws4
Fisher information
0.3
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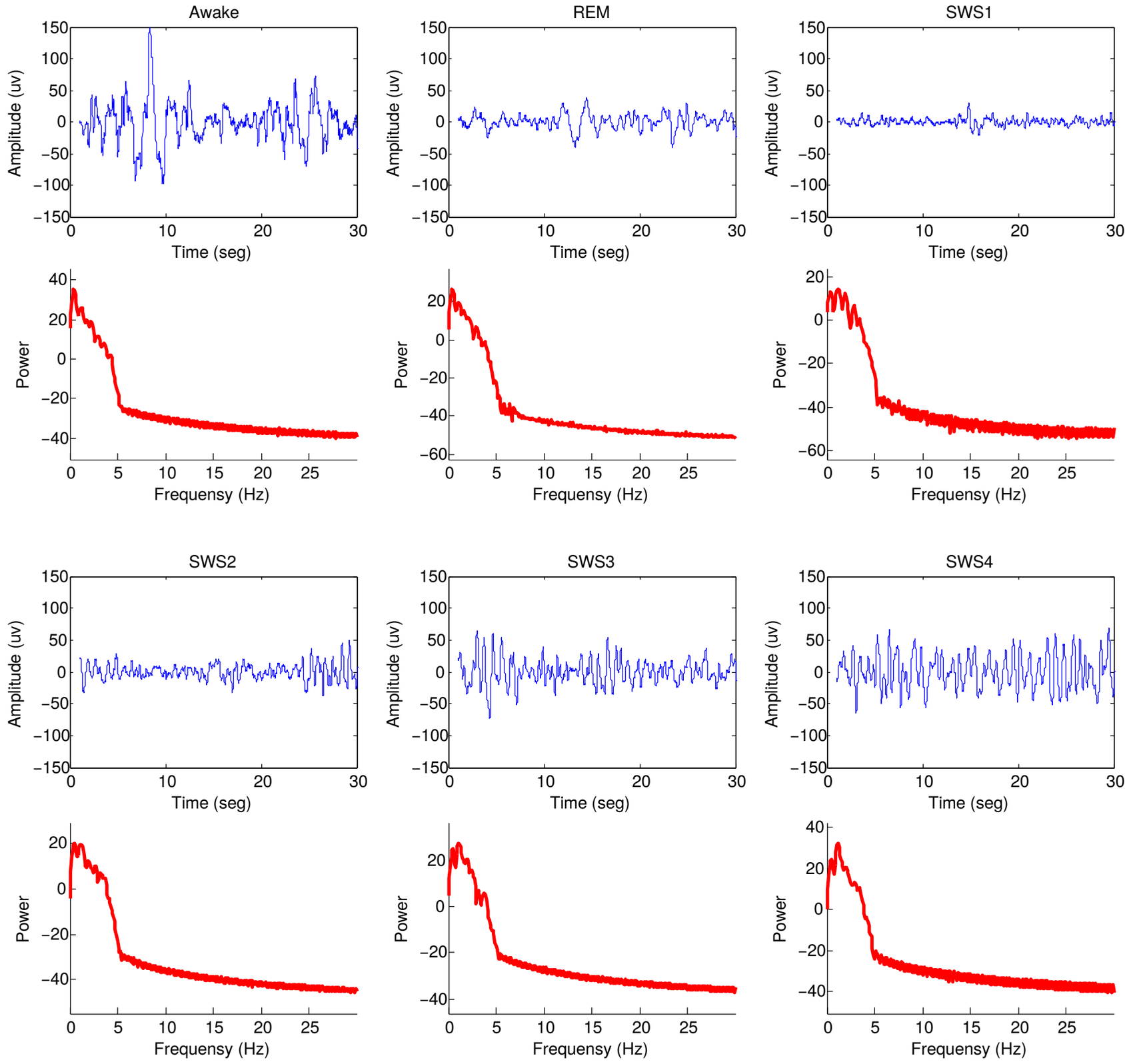
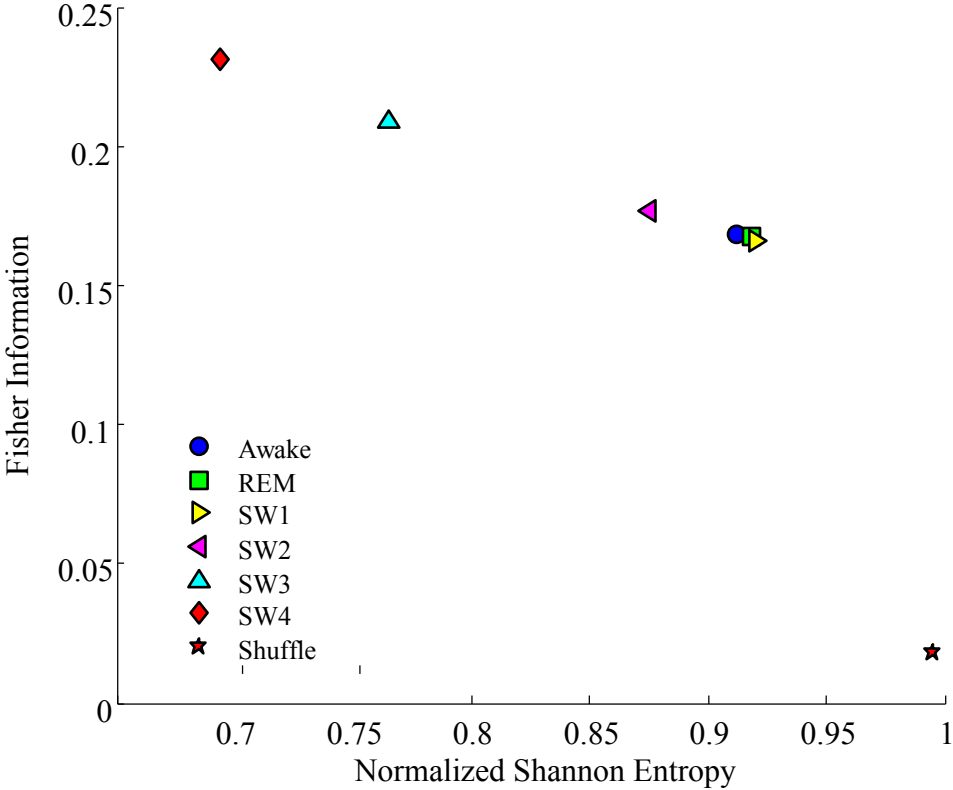
Awake
REM
sws1
sws2
sws3
sws4
Sleep Stages


Awake
REM
SWS1
SWS2
SWS3
SWS4
Amplitude (uv)
Time (seg)
Power
Frequensy (Hz)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0.2
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Fisher Information
Awake
REM
SW1
SW2
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SW4
Shuffle
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0.8
0.85
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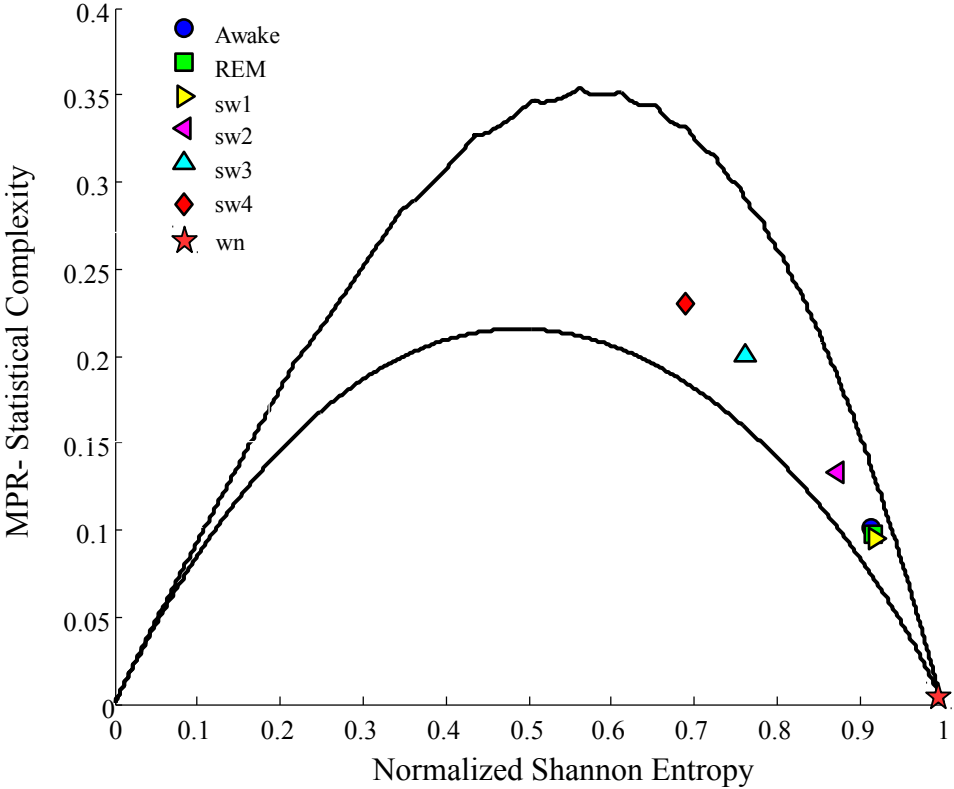
0.95
1
Normalized Shannon Entropy


Awake
REM
sw1
sw2
sw3
sw4
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MPR- Statistical Complexity
Normalized Shannon Entropy
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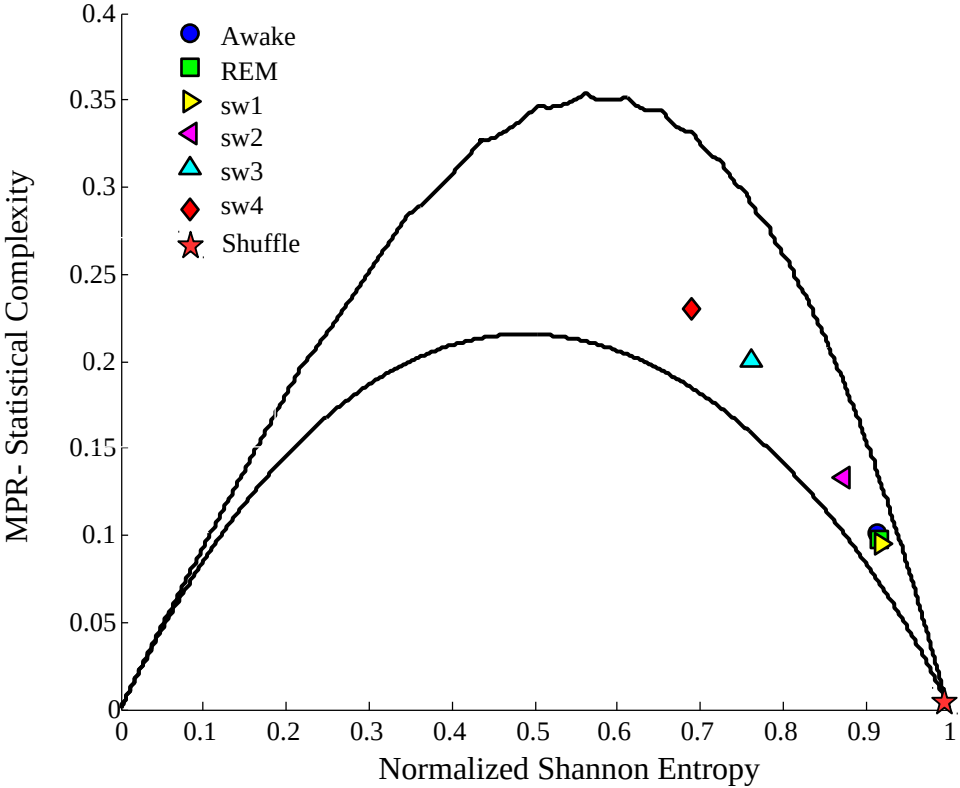
Awake
REM
sw1
sw2
sw3
sw4
Shuffle
MPR- Statistical Complexity
Normalized Shannon Entropy
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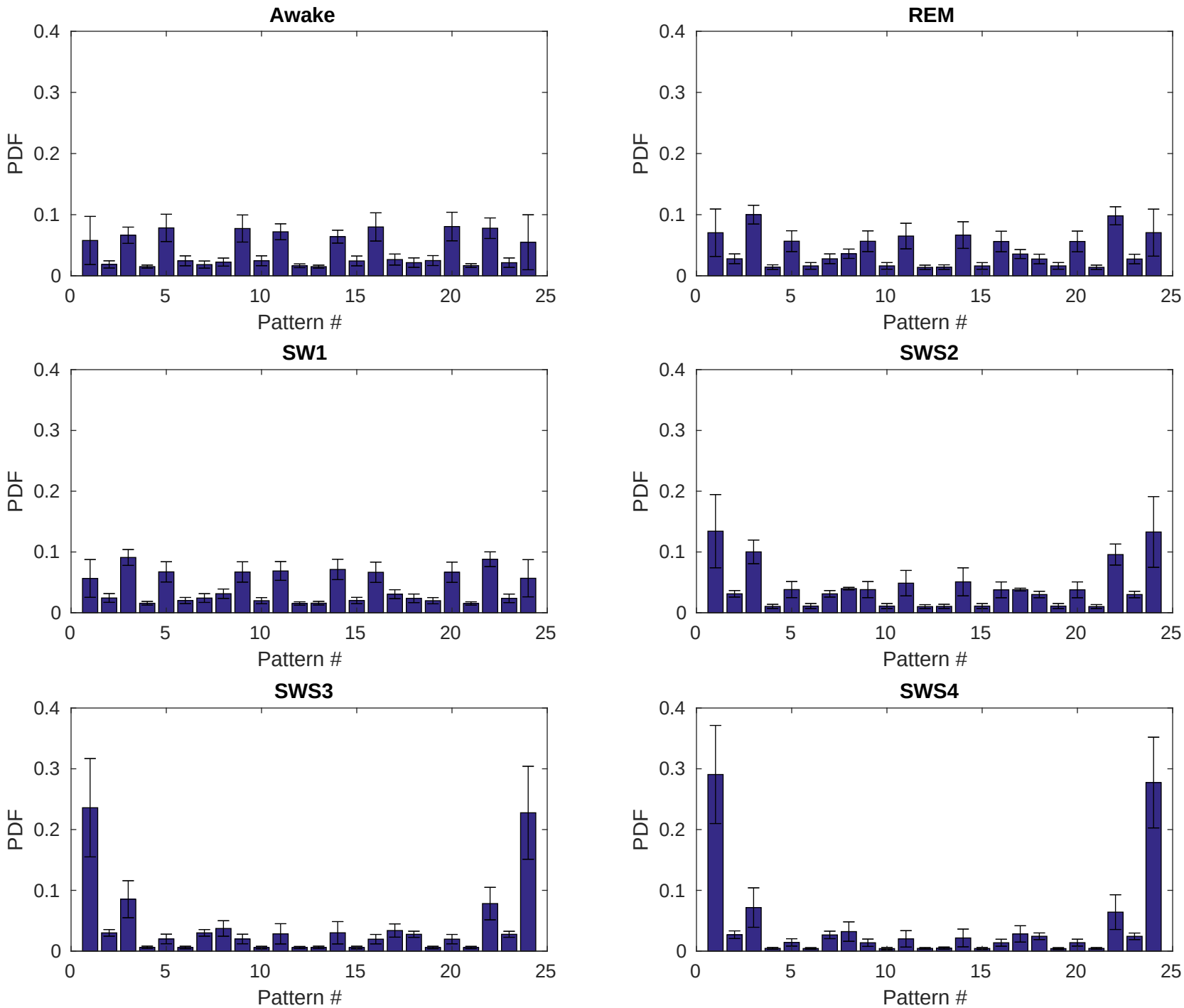
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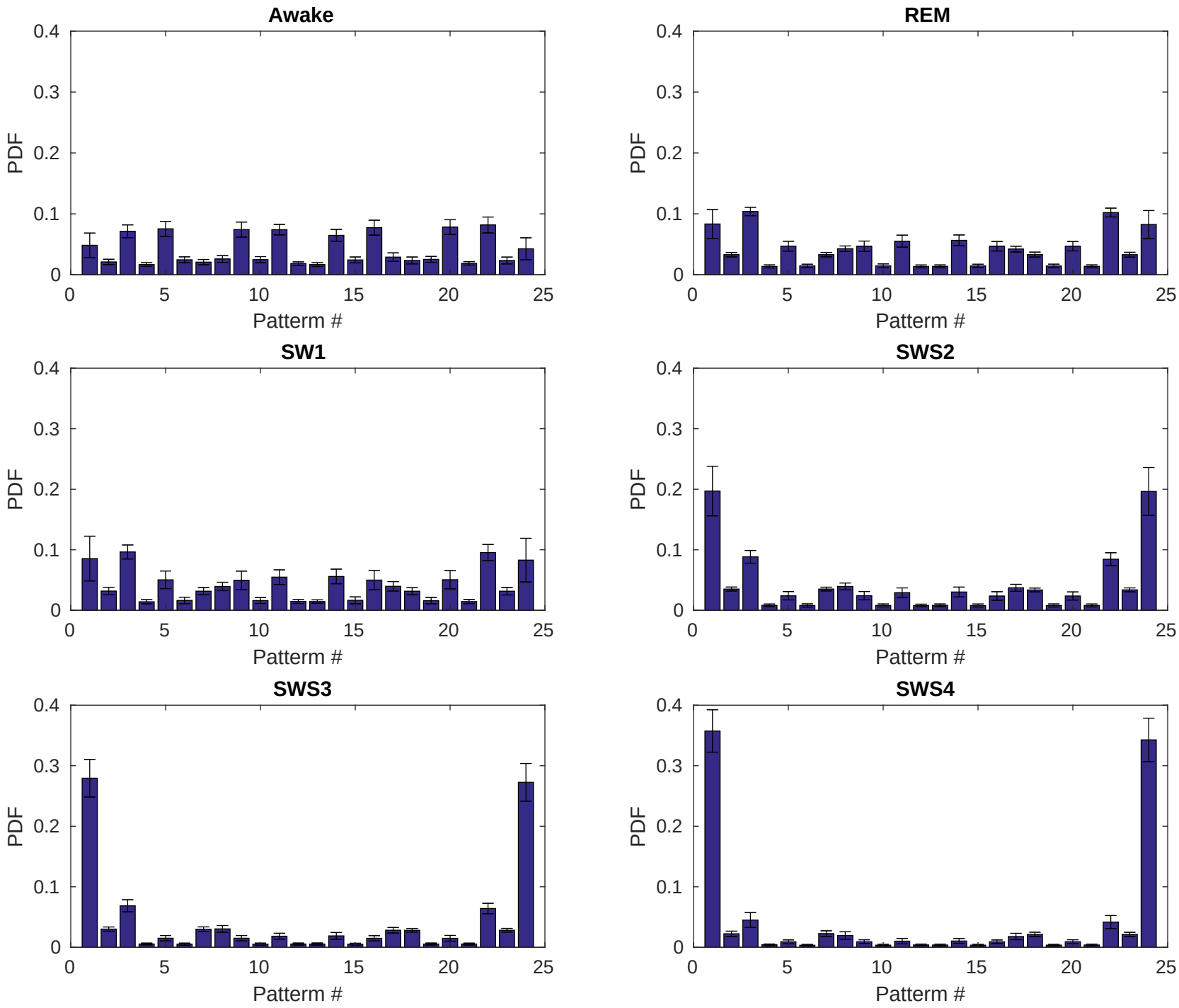
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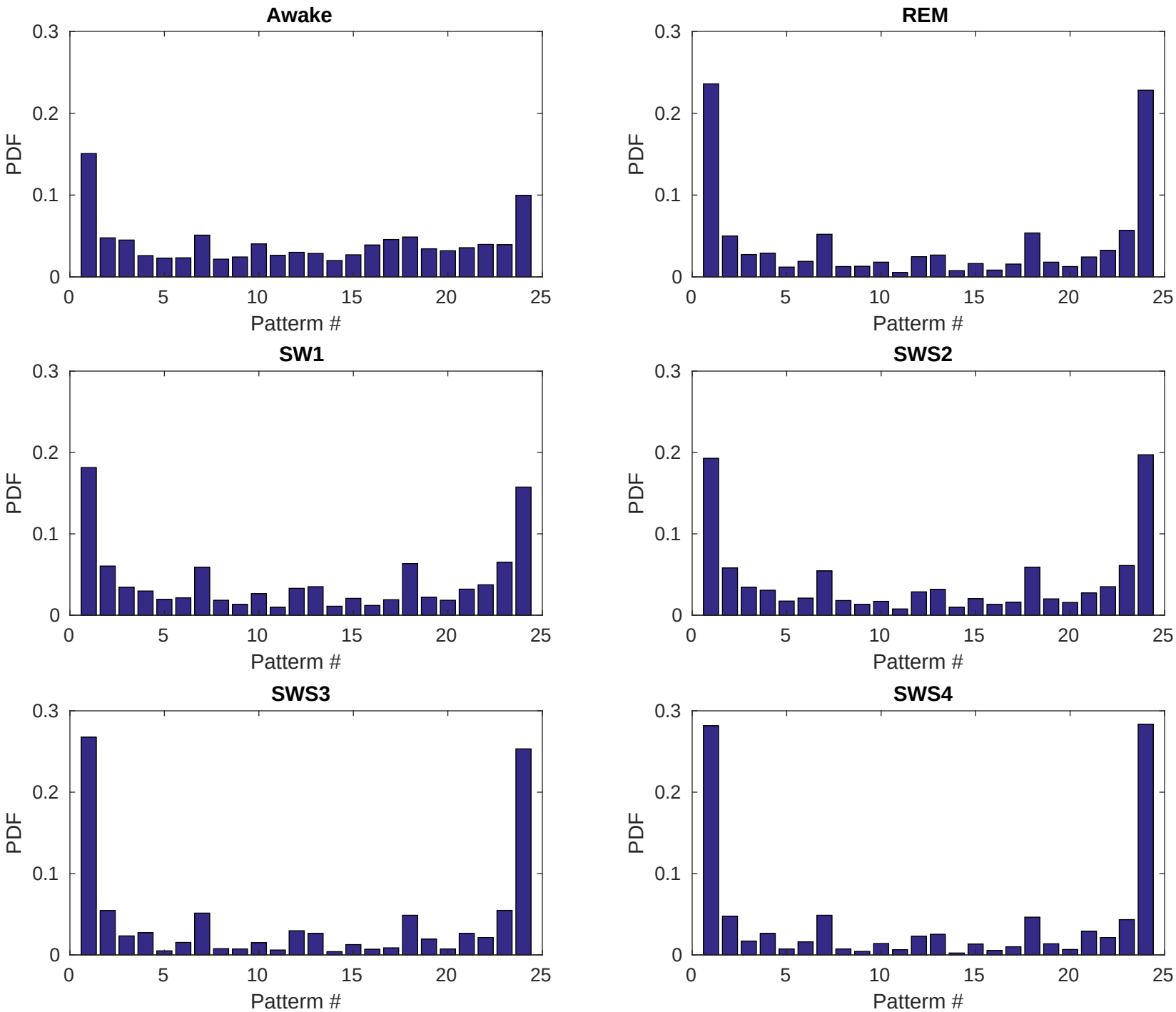
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