Application of entropies for automated diagnosis of epilepsy using EEG signals: A review

5 authors, including:

U Rajendra Acharya
Ngee Ann Polytechnic, SIM University, SIT-Glas…
481 PUBLICATIONS **8,759** CITATIONS

SEE PROFILE

Vidya K Sudarshan
SIM University
36 PUBLICATIONS **170** CITATIONS

SEE PROFILE

Joel En Wei Koh
Ngee Ann Polytechnic
34 PUBLICATIONS **143** CITATIONS

SEE PROFILE

Some of the authors of this publication are also working on these related projects:

Project   Viusal information for consenus in GDM View project

Project   Segmentation of features in fundus image View project

APPLICATION OF ENTROPIES FOR AUTOMATED DIAGNOSIS OF EPILEPSY USING EEG SIGNALS: A REVIEW

U Rajendra Acharya[1,2,3*], H. Fujita[4], Vidya K Sudarshan[1], Shreya Bhat[5], Joel E.W. Koh[1]

[1]Department of Electronics and Computer Engineering, Ngee Ann Polytechnic, Singapore.

[2]Department of Biomedical Engineering, School of Science and Technology, SIM University, Singapore.

[3]Department of Biomedical Engineering, Faculty of Engineering, University of Malaya, Malaysia

[4]Faculty of Software and Information Science, Iwate Prefectural University (IPU), Iwate, Japan.

[5]Department of Biomedical Engineering, Former M Tech Student, Manipal Institute of Technology, Manipal, Karnataka 576104, India.

*Corresponding author

Postal Address: Department of Electronics and Computer Engineering, Ngee Ann Polytechnic, Singapore 599489

Telephone: (65) 64606135; Email Address: aru@np.edu.sg

ABSTRACT

Epilepsy is the neurological disorder of the brain which is difficult to diagnose visually using Electroencephalogram (EEG) signals. Hence, an automated detection of epilepsy using EEG signals will be a useful tool in medical field. The automation of epilepsy detection using signal processing techniques such as wavelet transform and entropies may optimise the performance of the system. Many algorithms have been developed to diagnose the presence of seizure in the EEG signals. The entropy is a nonlinear parameter that reflects the complexity of the EEG signal. Many entropies have been used to differentiate normal, interictal and ictal EEG signals. This paper discusses various entropies used for an automated diagnosis of epilepsy using EEG signals. We have presented unique ranges for various entropies used to differentiate normal, interictal, and ictal EEG signals and also ranked them depending on the ability to discrimination ability of three classes. These entropies can be used to classify the different stages of epilepsy and can also be used for other biomedical applications.

1

Keywords: Epilepsy, interictal, EEG, entropy, fuzzy, HOS.

1. INTRODUCTION

Epilepsy is a common neurological disorder known to have affected about 3 million people in USA and an estimated 50 million people worldwide (WHO, 2001b from epidemiology, WHO 2012). The incidence and prevalence of epilepsy is about 1-2% of the world's population (Mormann et al., 2007) and increases drastically in elderly population. It is estimated that adults aged 65 years and above are affected by this condition reaching more than 570,000 cases (WHO 2012). Epilepsy is characterised by unexpected repeated and brief disruption of perception or behaviour arising from excessive synchronisation of cortical neural network. Epileptic person encounters constantly recurring abnormal outbreaks of electrical discharges in the brain. The marker of epilepsy is recurrent unprovoked seizures known as epileptic seizures (Blume et al., 2001; Banerjee et al., 2009). According to World Health Organisation (WHO), epilepsy is marked by repeated seizures, which are physical responses to unexpected, usually short, uncontrolled electrical discharges in a group of brain cells (WHO 2011). Based on clinical manifestations or displays, epileptic seizures are grouped into partial or focal, generalised, unilateral and unclassified seizures (James 1997; Tzallas et al., 2007a, 2009). Only a part of cerebral hemisphere is involved in focal epileptic seizures whereas the whole brain is involved for generalized epileptic seizures. Subjects of any age group can be affected by epileptic seizures.

Clinically to predict and diagnose epileptic seizures, the brain activities are to be monitored through EEG signals which contain the markers of epilepsy. EEG signals of epileptic patients exhibit two states of abnormal activities namely interictal or seizure free (in-between epileptic seizures) and ictal (in the course of an epileptic seizure). The interictal EEG signals are transient waveforms and exhibit spikes, sharp or spiky waves.

The ictal EEG signals are continuous waveforms with spikes and sharp wave complexes (McGrogan 2001). Generally, a clinician relies on identifying interictal (seizures free) EEG signals for epilepsy prediction as the ictal segments are obtained rarely. Thus, longer durations of EEG signals are necessary to visually monitor and analyse in order to localize the normal, interictal and ictal episodes for a patient. Epilepsy can be detected by traditional methods by well-trained and experienced neurophysiologists by visual inspection of long durations of EEG signals. This is time –consuming, tedious and subjective. Hence, in order to overcome these limitations, a computer –aided detection of epileptic EEG signals can be used.

Selecting features that best describe the behaviour of EEG signals are important for automated seizure detection performance. Many time-domain (Meier et al., 2008; Minasyan et al., 2010), frequency-domain (Correa et al., 2007; Guler et al., 2005; Subasi 2007; Aarabi et al., 2009; Polat et al., 2007; Chan et al., 2008), time-frequency analysis (Niederhauser et al., 2003), energy distribution in the time-frequency plane (Gabor et al., 1996, 1998; Tzallas et al., 2007), wavelet features (Guler et al., 2005; Abibullaev et al., 2010), and chaotic features such as entropies (Yuan et al., 2011; Minasyan et al., 2010) are used for seizure detection. In many works, combination of two or more features and more than one classifier (Mitra et al., 2009; Ubeyli 2009; Adeli et al., 2010) are used. Various entropy based measures have been used to quantify and better understand EEG complexities which differ in-between and during seizures episodes (Capurro et al., 1999). Literatures show that the entropy has the ability to identify the complexity present in EEG signal using computerised techniques. Acharya et al., 2012a, 2012b, 2013 have used different entropy features (Approximate entropy, Sample entropy, Phase entropy, Shannon entropy, Renyi's entropy and HOS entropies) for the diagnosis of epilepsy using EEG signals. Sharma et al., 2015 have classified the focal and non-focal epilepsy EEG signals using Shannon, Renyi, approximate and sample entropies extracted from intrinsic mode functions extracted from the EEG signals with an

3

accuracy of 87%. However, to best of our knowledge, this is the first paper describing the large set of entropies used for the diagnosis of epilepsy using EEG signals. Therefore, in this review paper, we are proposing unique ranges for various entropies namely Approximate Entropy (ApEn), Fuzzy Entropy (FE), Sample Entropy (SampEn), Renyi's Entropy (RE), Spectral Entropy (SEN), Permutation Entropy (PE), Wavelet Entropy (WE), Tsallis entropy (TE), Higher Order Spectra Entropies (S1, S2, PhEn), Kolmogorov-Sinai entropy (KSE) and Recurrence Quantification Analysis entropy (RQA En) applied on normal, interictal and ictal EEG signals.

The block diagram of proposed automated epilepsy detection is given in Figure 1. The EEG signals are divided into training dataset and testing dataset for building and evaluating the performance of a classifier. An offline training system describes the steps followed in building a classifier for the classification of EEG signals. After EEG signal pre-processing, different entropy algorithms are used for significant feature extraction from the EEG signals. Feature ranking helps to rank the features based on their clinical significance and also enhances the performance of the classifier. Significant features and ground truth of whether the EEG signals are normal, ictal or interictal as concluded by physicians are used to train the classifiers. In an online system, characteristic features are extracted from unclassified test samples and all the classifier parameters are applied to resolve its class label. Classifier performance is evaluated in terms of its accuracy, sensitivity, specificity and positive predictive value (PPV).
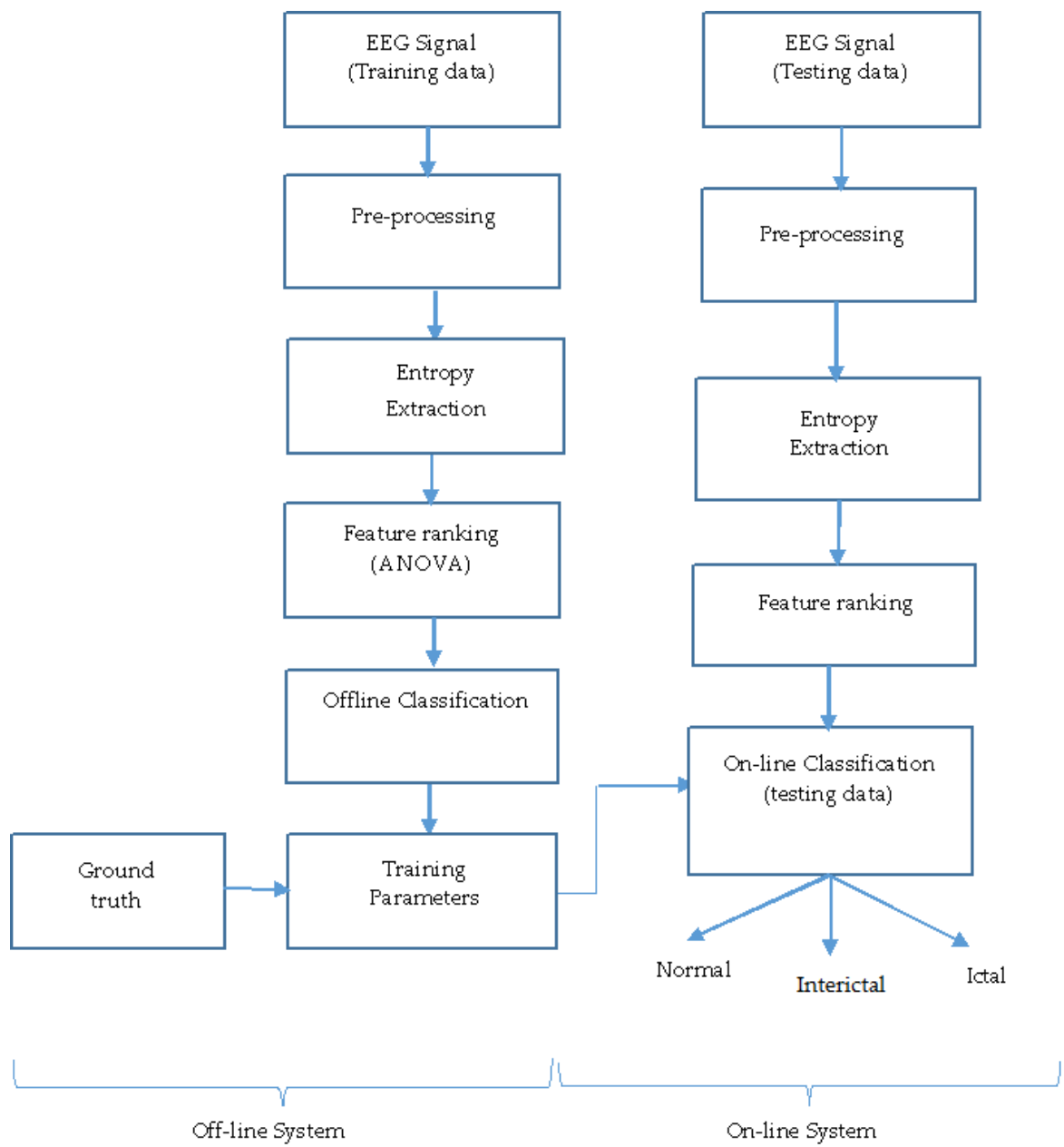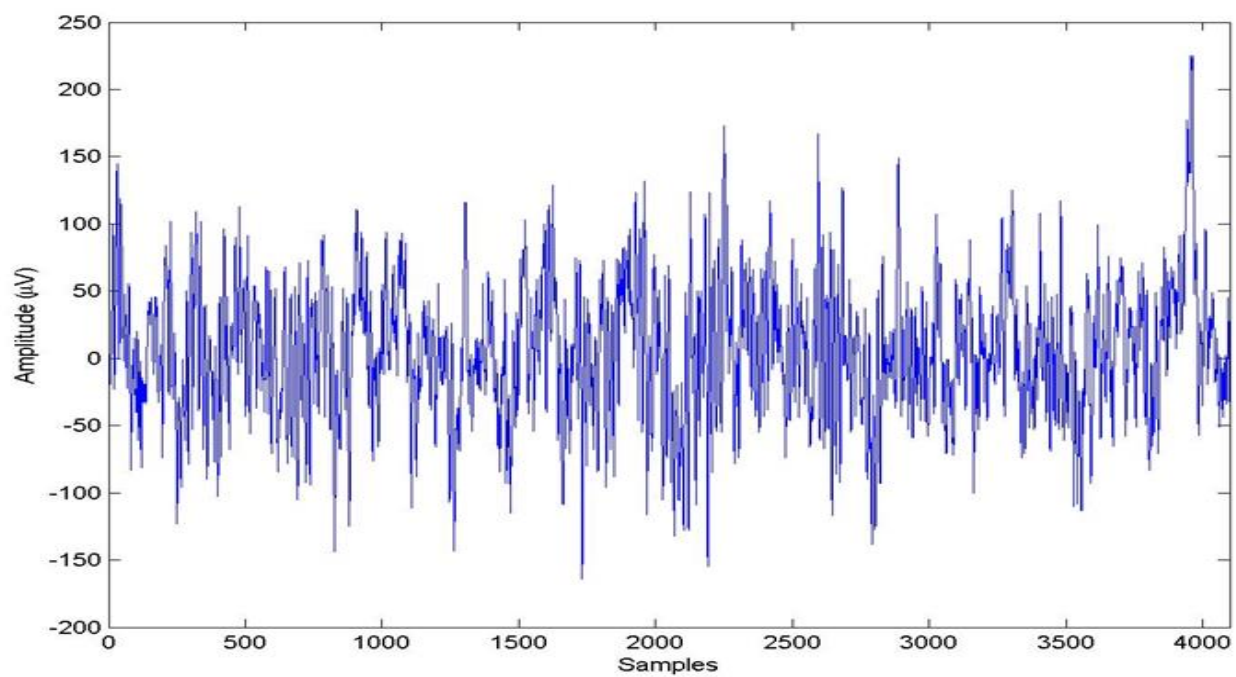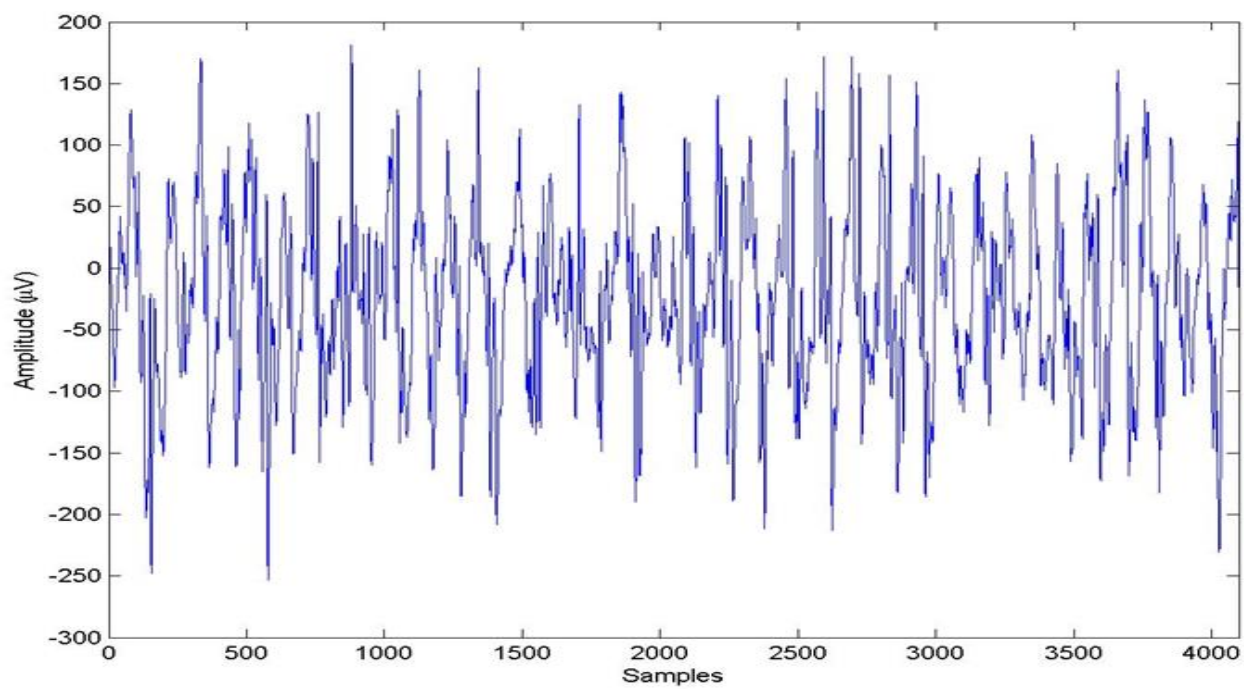
Figure 1 Block diagram of the proposed method.
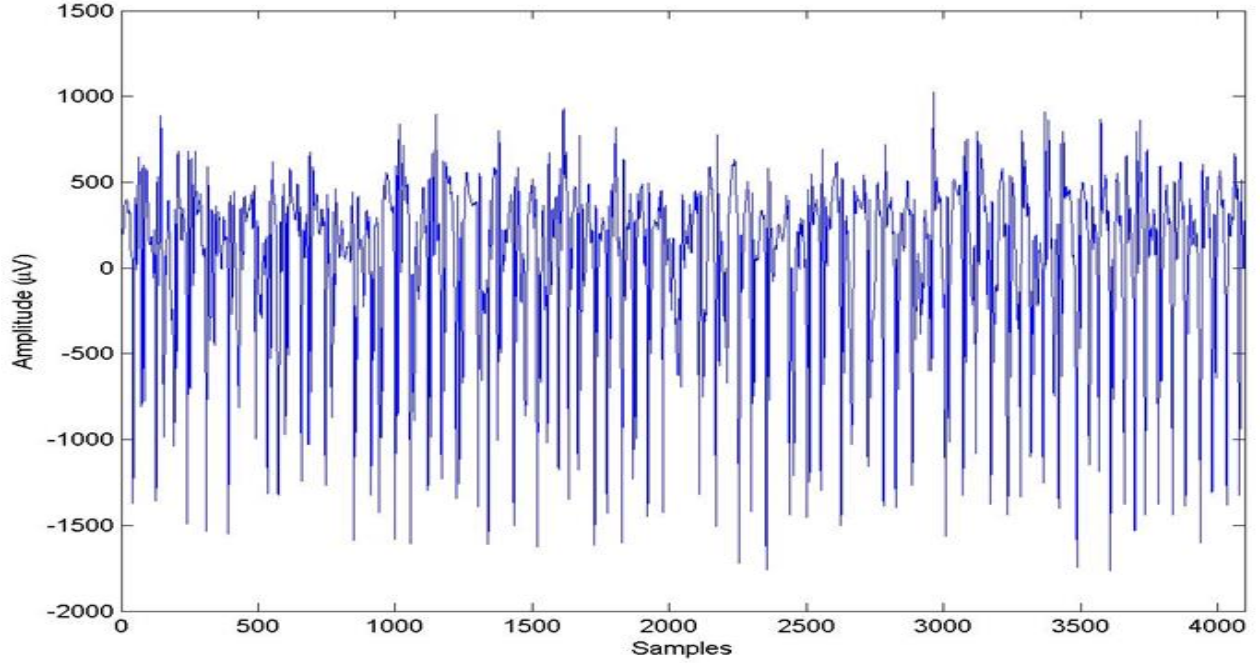
2. MATERIALS AND METHODS

2.1 Data Used

(a)

(b)

(c)

Figure 2 Typical EEG Signals: (a) Normal, (b) Interictal and (c) Ictal.

The EEG recordings used to test the efficiency of different entropies in epileptic seizure detection were collected from open database available at the University of Bonn (Andrzejak et al., 2011). All the EEG data taken were free of any artefacts. EEG data can be divided into five sub-groups. The first two sub-groups contain EEG signals obtained from normal subjects with eyes-closed and eyes-open respectively. The next two sub-groups define interictal states and the fifth sub-group contains seizure patients. Thus, two class problem deals with (i) normal and seizure patients and (ii) interictal and ictal patients. Three class problem is normal, interictal and seizure patients. Five class problem deals with normal with eyes-closed, normal with eyes-open, interictal (two classes) and seizure patients.

The data includes five sets of EEG segments (Z, O, N, F, and S) from five healthy subjects recorded during the awake condition with eyes closed (Set Z) and eyes open (Set O) and epileptic subjects undergoing pre-surgical evaluations (having both

7

segments interictal and ictal) each having length of 23.6 seconds. The depth electrodes implanted were used to record the interictal segments during seizure free intervals or in-between seizures (i) from the hippocampal formation of the opposite hemisphere (Set N), and (ii) from the epileptogenic zone (Set F). Both the depth electrode and strip electrode implanted into the neocortex were used to record ictal segments (Set E). Total of 100 files were selected from each normal and epileptic (interictal = 100, ictal = 100 files) subjects. Each EEG file of 4096 samples was considered as a separate EEG signal resulting in a total of 300 EEGs. In this study, datasets O, F and S are used for further analysis. Figure 2 shows the three typical EEG signals.

2.2 Entropy Selection and Extraction

In developing an automated epilepsy detection, various features which better describe the behaviour (either static or dynamical) of seizures (Tong et al., 2009) are to be extracted. In this review paper, entropy features based on various methods are evaluated to differentiate EEG signals into normal, interictal and ictal classes. Brief descriptions of entropies used in EEG signal classification are provided in this section.

Entropy is a measure of rate of information generation which can be used in the signal processing to separate the useful signal from an intrusive noise (Lemons, 2013). Usually a high entropy value corresponds to increased irregularity or unpredictability while a low value corresponds to high regularity. Entropy is a nonlinear index that reflects the degree of chaos within a system (Lemons et al., 2013). It is often used to analyse epileptic EEG signals to detect whether there is an epileptic attack or to inspect the state of epileptic seizures. The entropy parameter is broadly categorised into spectral and embedding entropies. The entropies computed from amplitude components of the power spectrum of the signal are referred as spectral entropies whereas entropies calculated using the time series directly are defined as the embedding entropies (Kannathal et al., 2005).

8

(i) Kolmogorov-Sinai Entropy (KSE): It evaluates the uncertainty of the signal with respect to time (Farmer et al., 1982) and is computed from the embedded time series signal (Kantz et al., 1997). It is also defined as metric entropy which is zero for non-chaotic signals and is greater than zero for chaotic signals. Entropy is calculated by finding points that are closer to each other on the trajectory in a phase space and are uncorrelated with time. Rate of divergence of these point pairs produces the KSE value. Let t_{div} be the average time taken for the point pairs to move apart. Thus, KSE can be calculated from the following equation

$$< t_{div} > = 2^{-KSt} \qquad (1)$$

where KSE is expressed in bits per second. The reconstruction of a system's trajectory from an embedding space leads to the computation of KSE as depicted in Eq. (2).

$$KSE = \lim_{r \to 0} \lim_{m \to \infty} \frac{1}{\tau} \frac{C_m(r, N_m)}{C_{m+1}(r, N_{m+1})} \qquad (2)$$

Where $C_m(r, N_m)$ is called as a correlation function that gives the probability of two points being closer to each other than r. Higher KSE value indicates higher unpredictability. Thus, KSE does not provide accurate results for the signals with slightest noise.

The main advantage of this entropy is that it is useful in differentiating the regular and chaotic systems (Misiurewicz 1976; Falniowski 2014). It underestimates and decays towards zero as the length of a given time series becomes large, which is the main limitation of this entropy (Cover et al., 1991).

(ii)Approximate Entropy (ApEn): It is used to evaluate the instability of variation in the signal (Pincus et al., 1991; 1992). It detects changes in the underlying episodic behavior and compares the similarity of the samples by pattern length (m) and similarity

coefficient (r). ApEn is a scale invariant measure because the similarity criterion is equivalent to the standard deviation of the data. Highly irregular time series gives a high ApEn value and a time series with more number of similar patterns gives a low ApEn value. Mathematically, ApEn is calculated by

$$ApEn = \ln\left(\frac{C_m(r)}{C_{m+1}(r)}\right) \qquad (3)$$

Where $C_m(r)$ is the pattern mean of length m and $C_{m+1}(r)$ is the pattern mean of length $m+1$. The pattern mean is calculated by computing the count of similar patterns of length, m and length, $m+1$. In this work we have chosen m = 2 and r=0.2 times the standard deviation of the EEG signal (Thakor et al., 2004; Pincus 1991). Let $C_{im}(r)$ indicate the count of patterns of length m and is defined by the following equation.

$$C_{im}(r) = \frac{n_{im}(r)}{N - m + 1} \qquad (4)$$

ApEn depends on pattern length, which is inconsistent and counts the sequence that matches itself to avoid the condition $\ln(0)$. The advantages of this entropy are: (i) it can be calculated for a relatively short series of noisy data (Seely et al., 2004), (ii) it can potentially differentiate a variety of systems such as periodic and multiple periodic systems, chaotic systems, and stochastic systems (Pincus 1991), and (iii) it can give statistically accurate results compared to the KS entropy (Pincus 1991).

The drawbacks of approximate entropy are: (i) it is heavily dependent on the input signal length. Especially short signals lead to a lower value than expected (Richman et al., 2000), (ii) significant noise compromises meaningful interpretation of this entropy (Seely et al., 2004), (iii) this entropy is a biased statistic as it depends on length of the time series, and counts self-matches (Goldberger et al., 1991; Pincus 1995), and (iv) consistency is absent and is largely dependent on length of the data.

(iii)Sample Entropy (SampEn): It measures the regularity of a physiological signal and is independent of the pattern length. If SampEn value of one dataset is higher than the other for a given pattern length (m) and similarity criterion (r) then it remains higher for all the different values of m and r. Thus, SampEn is relatively consistent and reduces the bias of approximate entropy (Richman et al., 2000). High value of SampEn implies that the signal is highly unpredictable and a low SampEn value implies the signal is predictable. SampEn can be computed by

$$SampEn = -\log\left(\frac{A}{B}\right) \tag{5}$$

where A contains the total number of vector pairs of length $m+1$ and B contains total number of vector pairs of length m. The value of m is taken as 2 in this work (Song et al., 2010). The advantages of this entropy are: (i) it can be used for shorter series of noisy data, (ii) it is able to differentiate large variety of systems, (iii) it performs much better than the approximate entropy with theory for random numbers (Richman et al., 2000), (iv) it maintains relative consistency (Richman et al., 2000), (v) self-matches are not counted, which reduces the bias, and (vi) the entropy values are more consistent across different pattern lengths. However, the main drawback of this entropy is its inconsistency for the sparse data (Richman et al., 2000).

(iv) **Spectral Entropy (SEN):** Spectral Entropy, a normalized form of Shannon's entropy, which uses the power spectrum amplitude components of the time series for entropy evaluation (Shannon, 1948, Fell et al, 1996). It quantifies the spectral complexity of the EEG signal. SEN is obtained by multiplying the power in each frequency p_f by the logarithm of the same power, and the product is multiplied by −1. The *SEN* is given by

$$SEN = \sum_f p_f \log\left(\frac{1}{p_f}\right) \tag{4}$$

11

Shannon's Entropy (ShEn) is the measure of set of relational parameters that vary linearly with the logarithm of the number of possibilities (Lemons DS, 2013). It is also a measure of data spread and is most commonly used to assess the dynamical order of a system (Shanon 1948).

The main advantage of ShEN is that, it is better adapted to normal distributions (Tellenbach et al., 2009). However, few drawbacks of this entropy are: (i) the possibility of losing more information due to aggregation, (ii) the possibility of over-estimation of entropy level if too many zones are used (Hekkila et al., 2006), and (iii) this method fails to explain temporal relationships between different values extracted from a time series signal (Feldman et al., 1998).

(v)<mark>*Renyi's Entropy (REN):*</mark> It is a generalised form of ShEn and is used for estimating the spectral complexity of a time series signal (Renyi 1961; Grassberger et al., 1991). Mathematically, REN can be calculated by

$$REN \ (\alpha) = -\frac{\alpha}{1-\alpha}\sum \log p_i^{\alpha} \tag{7}$$

Where the order, $\alpha \neq 1$, p_i defines the total spectral power. REN with order, $\alpha \geq 2$ provides a lower bound for its smooth entropy as REN with order $\alpha = 1$ is analogous to ShEN and it produces superficial amount of smooth entropy (Cachin, 2001). In this work, we have chosen $\alpha = 2$ for REN.

The significant advantages of REN are: (i) at the rescaling of the variables, this entropy changes by an additive constant, and (ii) it remains unchanged for the different density functions. In other words, it do not vary irrespective of the density functions used (Sonnino et al., 2013). The main drawback is that it is not a sub-additive, recursive, nor it possess the branching and sum properties (Aczel et al., 1975).

(vi)<mark>*Permutation Entropy*</mark> *(PE):* It is the complexity estimation of time series by identifying the couplings between the time series signal (Bandt et al., 2002). The dynamics associated with the EEG signal can be derived by assessing the presence and

absence of permutation patterns of varying elements in the given time series signal. At high frequencies, permutation entropy elevates with asymmetry of the time series while at low frequencies, the permutations corresponding to peaks and troughs observed are seldom. PE is given by

$$PE = -\sum_{j=1}^{n} p_j \log_2 p_j \qquad (8)$$

Where p_j represents relative frequencies of the possible sequence patterns, n implies permutation order of $n \geq 2$. In this work, we have chosen the embedding dimension of 3 and delay of 1(Nicolaou et al., 2012; Band et al., 2002; Riedl et al., 2013).

Permutation entropy is a measure of chaotic and non-stationary time series signal in the presence of dynamical noise. This method is robust, efficient and produces fast results irrespective of noisy data. Thus, it can be used for processing of huge data sets without pre-processing of data and fine-tuning of complexity parameters (Bandt et al., 2002).

The advantages of this entropy are: (i) it is simple, robust and less prone to computational complexity (Li et al., 2007), (ii) it is applicable to real and noisy data, (iii) it does not require any model assumption and is suitable for the analysis of nonlinear processes (Zanin et al., 2012), and (iv) it is useful to analyze huge data sets and requires less pre-processing time and fine-tuning of parameters (Zanin et al., 2012). The main limitation is its inability to distinguish well defined patterns of a particular design (Fadlallah et al., 2013).

(vii) Tsalli's Entropy (TE): It helps in characterizing the physical behavior of a system. It describes systems with long-term memory effects, long-range interactions and multifractal space-time constraints (Bezerianos et al., 2003). Tsalli's coefficients help in differentiating EEG spikes, bursts and continuous rhythms. Mathematically, TE is defined as

$$TE = \frac{1 - \sum_{i=1}^{W} p_i^q}{q - 1} \qquad (9)$$

Where q is a measure of nonextensivity, p_i describes the discrete set of probabilities with W microscopic configurations (Tong et al., 2003). In this work, we have taken $q = 2$. TE can be used to measure the abrupt changes and long-term memory effects in a time series signal unlike the ShEn. It is a constructive tool in characterizing fractal stochastic processes.

The advantages of this entropy are: (i) this method helps in measuring the uncertainity of generalized systems (ii) it is better suited to deal with non-Gaussian measures (Tellenbach et al., 2009), and (iii) it can provide more detailed information than the conventional Shannon, especially when used to evaluate different rhythms and burst EEG analysis (Capurro et al., 1999).

The main drawback is the selection of q-index, which is done randomly without any automated method or theory for its computation (Rodrigues et al., 2009).

(viii) Fuzzy Entropy (FE): It represents the information of randomness and is defined as the entropy of fuzzy set whose elements have different degrees of membership. Membership functions vary in the unit interval of 0 and 1. Fuzzy entropy is defined as

$$H[A] = \int_{-\infty}^{\infty} S(C_r\{A \ge t\}) \, dt \qquad (10)$$

where A is the fuzzy variable, C_r is the credibility measure (Kosko, 1986). Fuzzy entropy measures ambiguous uncertainties from the highly irregular signals whereas ShEn deals with the measure of probabilistic uncertainties. The advantage of this entropy is that, it is insensitive to noise; and is highly sensitive to changes in the information content (Pal et al., 1980).

(ix)Wavelet Entropy (WE): The Orthogonal Discrete Wavelet Transform (ODWT) is a quantitative measure in the study of dynamical brain signals. The ODWT defines the

relative wavelet entropy as the measure of relative energies in the different frequency bands of the EEG signals. It computes the degree of similarity between different fractions of signal whereas WE is a measure of the degree of disorder associated with the multi-frequency signal response (Rosso et al., 2001). Wavelet entropy is computed by

$$WE = -\sum_{i<0} p_i \ln p_i \qquad (11)$$

Where p_i defines the probability distribution of a time series signal and i defines different resolution levels. Wavelet entropy can be used in identifying the underlying episodic behavior of a signal and it can provide efficient result for a periodic mono-frequency signal (Rosso et al., 2001).

The advantages of this entropy are it can detect the fine changes in a non-stationary signal (Rosso et al., 2001), requires less computational time, noise contributions can be easily eliminated, and performance does not depend on any parameter.

(x)Normalized Bispectrum Entropy(S1,S2) and Phase Entropy(PhEn): Second order measures such as autocorrelation function or power spectrum provides a partial explanation of a random process. The principles of power spectrum are extended to higher orders called HOS to determine the subtle changes and the shape of a waveform. HOS does not contain additional information of a Gaussian process as it is completely defined by second order statistics. Hence, HOS of a Gaussian process is identically zero (Nikias et al., 1993; Nikias et al., 1987).

HOS are the spectral representations of higher order moments of an irregular signal. It detects the nonlinearity, deviations from Gaussianity and preserves the phase characteristics of a signal (Nikias et al., 1993). Two approaches can be employed in the estimation of HOS. They are (a) Indirect method where the estimate of cumulant function is followed by its Fourier transform and (b) Direct method that deals with segment averaging.

In the direct approach, data is divided into segments with equal number of overlapping blocks. The Fast Fourier transform (FFT) is computed for each block and the product of spectral coefficients results in 'raw' HOS. The weighted average of raw HOS gives rise to the third order moment called the bispectrum. It contains two frequencies (f_1 and f_2) and is given by

$$B(f_1, f_2) = E\left[X(f_1)X(f_2)X(f_1 + f_2)\right] \qquad (12)$$

Where $X(f)$ is the Fourier transform of a signal $x(nT)$. It is a complex quantity as it analyzes the interactions between three frequency components $(f_1, f_2, f_1 + f_2)$. The frequency f can be normalized to lie between 0 and 1 by the Nyquist frequency.

Bispectral entropy have proposed (Chua et al., 2008) normalized bispectral entropies similar to spectral entropies (Inouye et al., 1991),

$$S1 = -\sum_{n=0}^{N-1} p_n \log p_n \qquad (13)$$

where $p_n = \dfrac{|B(f_1, f_2)|}{\sum\limits_{f_1, f_2 \in \Omega} |B(f_1, f_2)|}$, N is an integer.

Bispectral squared entropy,

$$S2 = -\sum_{n=0}^{N-1} q_n \log q_n \qquad (14)$$

where $q_n = \dfrac{|B(f_1, f_2)|^2}{\sum\limits_{f_1, f_2 \in \Omega} |B(f_1, f_2)|^2}$, N is an integer.

Phase entropy (PhEn),

$$PhEn = \sum_{n=0}^{N-1} p(y_n) \log p(y_n) \qquad (15)$$

$$\text{where} \quad p(y_n) = \frac{1}{L} \sum_{f_1, f_2 \in \Omega} l(\phi(B(f_1, f_2)) \in y_n),$$

$$y_n = \left\{ \phi \Big| -\pi + \frac{2\pi n}{N} \leq \phi < -\pi + \frac{2\pi(n+1)}{N} \right\}, n = 0,1,\ldots N-1$$

where N = an integer, L = number of points within Ω, ϕ = the phase angle of the bispectrum, l = indicator function ($l = 1$ when phase angle is within the y_n range).

Some of the advantages of HOS entropies are (i) it is a third order statistical analysis and a nonlinear method with high signal to noise ratio (SNR) (Nikias et al., 1993; Nikias et al., 1987), (ii) it can capture interaction among its frequency components and phase coupling (Nikias et al., 1993b), and (iii) it accurately captures the subtle variation in the bio-signals (Chua et al., 2009; 2011).

(xi)Recurrence Quantification Analysis Entropy (RQAEn): It is a measure of the average information contained in the line-segment distribution. It is one of the Recurrence Quantification Analysis (RQA) method based on state-space trajectories. It helps in the quantification of number and duration of recurrences of a dynamical system (Zbilut et al., 1992). RQA measures the hidden periodicities of a time series signal and is calculated to represent a non-stationary input signal in terms of its complexity and nonlinearity (Zbilut et al., 1992).

Recurrence entropy helps in the detection of chaos-chaos transitions, unstable periodic orbits, time delays and extracts useful information from short and non-stationary input data (Marwan et al., 2002).

3. STATISICAL STUDY OF ENTROPY FEATURES

In this review paper, all the entropy features extracted are subjected to statistical analysis to identify the clinical significance between three classes (normal, interictal and

ictal). Features are tested using Analysis Of Variance (ANOVA) statistical test (Kobayashi et al., 2011). The test determines F-value and p-value (probability-value) for three groups of features. F-value and p-value are inversely related. Thus, features with high F-value have p-value near to zero and vice versa. Other ranking methods such as Bhattacharyya distance (Derpanis, 2008; EoM, 2015), Wilcoxon signed rank test (Hwang et al., 2010; Yuan et al., 2014), Receiver Operating Characteristic Curve (ROC) (ROC, 2015), and fuzzy max-relevance and min redundancy (*mRMR) (Ann et al., 2008)* can also be used to rank the features.

Ten-fold cross validation approach can be used to develop the automated system. Around 90% of the entropy features are used for training and around 10% are used for testing the dataset. This is the standard approach that helps to develop robust classifiers and efficient diagnostic system (Bishop, 2006).

A total of 13 entropy features such as - Approximate entropy (ApEn), Fuzzy entropy (FE), Sample entropy (SampEn), Renyi's entropy (REN), Spectral entropy (SEN), Permutation entropy (PE), Wavelet entropy (WE), Tsallis entropy (TE), Phase entropy (PhEn), Bispectral entropy (S1), Bispectral squared entropy (S2), Kolmogorov-Sinai entropy (KSE) and Recurrence Quantification Analysis entropy (RQA En) are extracted from 300 EEGs (100 from each datasets O, F and S). Table 1 presents the mean and standard deviation (SD) values of these entropies for three different classes; normal, interictal and ictal.

Various features extracted from normal, interictal and ictal EEG signals provided sufficient discrimination between the three classes ($p<0.0001$). The good discrimination capability of these features is evaluated by p-value and the ANOVA F value is used to rank all the entropic features. It is reported that the brain activity is more predictable during seizures than non-seizure phase and is reflected by a sudden drop in the entropy values (Greene et al., 2008; Aarabi et al., 2009; Kelly et al., 2010; Iasemidis et al., 2003). From the results listed in Table 1, it can be observed that most of the entropy features

are best suitable for the classification of epileptic EEG signals. Among these entropies, Renyi's entropy, SampEn, SEN and PE bags top position with significantly higher discrimination F-values.

The F-values help in characterizing the entropy performance and the features with highest F-values are ranked the highest as they provide significant differentiation between the normal, interictal and ictal classes. Thus, it is presumed that summation of various entropies can help in improving the rate of classification.

Table 1 Results (Mean, SD) of normal, interictal and ictal classes using entropies and *p*<0.0001.

Features	Normal		Interictal		Ictal		F-Value
	Mean	SD	Mean	SD	Mean	SD	
REN	-1.90E+01	5.23E-01	-1.89E+01	1.12E+00	-2.18E+01	1.12E+00	290.8153
SampEn	1.45E+00	9.71E-02	1.13E+00	1.90E-01	1.09E+00	1.44E-01	177.2937
SEN	-4.74E+06	1.52E+06	-5.27E+06	4.48E+06	-2.73E+07	1.68E+07	163.5236
PE	1.39E+00	1.00E-01	1.44E+00	8.42E-02	1.24E+00	8.85E-02	132.8653
FE	2.34E+00	2.04E-01	1.56E+00	3.13E-01	1.82E+00	4.86E-01	126.7034
TE	-2.12E+07	1.18E+07	-3.36E+07	9.09E+07	-4.77E+08	4.13E+08	112.9842
ApEn	2.27E+00	3.32E-02	1.86E+00	3.31E-01	1.93E+00	2.15E-01	91.7992
WE	-7.03E+07	5.97E+07	-2.32E+08	9.92E+08	-2.75E+09	2.54E+09	91.3993
RQAEn	2.93E-02	5.91E-03	5.75E-02	4.81E-02	9.14E-02	3.91E-02	74.7212
S1	5.86E-01	7.26E-02	4.51E-01	9.15E-02	5.01E-01	9.21E-02	62.9000
S2	3.49E-01	1.06E-01	1.83E-01	9.62E-02	2.75E-01	1.30E-01	55.1414
PhEn	3.38E+00	1.14E-01	3.05E+00	4.58E-01	3.10E+00	2.32E-01	35.4182
KSE	7.05E-03	1.35E-02	2.45E-02	5.26E-02	3.36E-02	7.55E-02	6.3297

4. DISCUSSION

Various studies are reported for automated classification of EEG signals into two, three, and five epileptic classes. They are briefly described below.

Two Class: normal and ictal (epileptic) signals

Kannathal et al., 2005 used various entropy features namely, Kolmogorov-Sinai entropy, approximate entropy, Renyi's entropy and Shannon's entropy to differentiate the epilepsy from normal EEG signals. Among four entropy features extracted, Kolmogorov-Sinai entropy outperformed the rest in differentiating the normal and epilepsy EEG signals (p-value < 0.05). The study reported a classification accuracy of around 90% using Adaptive Neuro-Fuzzy Inference System (ANFIS) classifier. Polat et al., 2007 developed epilepsy detection algorithm by combining Fast Fourier Transform (FFT) feature extraction technique and Decision Tree (DT) classifier. The study algorithm extracted power spectral density features using FFT based Welch method from EEG recordings. Classification accuracy of 98.72% is reported using DT classifier. Srinivasan et al., 2007 applied approximate entropy to develop an automated EEG classification tool for epilepsy detection based on neural network. The algorithm extracted ApEn from the EEG signal and used as input to the Probabilistic Neural Network (PNN) classifier. The experimental results reported an accuracy of 100% in classification of epileptic EEG signals from normal.

Ocak et al., 2009 separated normal and epileptic EEG signals using Discrete Wavelet Transform (DWT). Approximate entropy is applied on the DWT coefficients and a classification accuracy of 96% is obtained. Kumar et al., 2012 applied DWT to the normal and epileptic EEG signals and used ApEn algorithm for feature extraction. They obtained an accuracy of 100% using feed-forward back propagation neural network classifier. In another twin study by Kumar et al., 2014, 100% classification accuracy is reported using DWT, ApEn with Support Vector Machine (SVM) classifier. Liang et al., 2010 computed approximate entropy on the spectral coefficients extracted from normal and epileptic EEG signals. SVM with radial basis kernel (RBF) is used to obtain an accuracy of 98.3% using 21 features. Shen et al., 2013 used sample entropy with SVM

classifier to classify EEG signals of normal and epileptic and marked an accuracy of 99.2%.

Few studies explored permutation entropy features [Nicolaou et al., 2012], wavelet entropy features [Kumar et al., 2010; Wang et al., 2011] and multi-discrete wavelet transforms [Akareddy et al., 2013] to obtain a substantial classification accuracy of more than 92%. Liang et al., 2010 computed approximate entropy on the spectral coefficients extracted from normal and epileptic EEG signals. SVM coupled with RBF is used and an accuracy of 98.3% is obtained using 21 features. Shen et al., 2013 used sample entropy with SVM classifier to classify EEG signals of normal and epileptic and marked an accuracy of 99.2%. Ahammad et al., 2014 applied energy, spectral entropy, standard deviation, maximum, minimum and mean-DWT-linear classifier to achieve an accuracy of 98.5% using data from CHB-MIT repository. Gandhi et al., 2012 reported 100% accuracy in two-class (normal and epileptic) classification problem using DWT, spectra entropy and energy features coupled with PNN classifier.

Two Classes: interictal (either of one class - N or F) and ictal (epileptic – S) signals

Few studies have evaluated the entropy features from EEG signals to characterize two classes namely interictal and ictal EEGs. Yuan et al., 2011 presented a new approach to differentiate interictal and ictal EEG signals using nonlinear dynamical features such as scaling exponent computed from Detrended Fluctuation Analysis (DFA), Hurst exponent and ApEn. They used two data sets containing EEG recordings of interictal and ictal. The study trained single hidden layer feedforward neural network using Extreme Learning Machine (ELM) algorithm for the classification of EEG signal features. They reported a classification accuracy of 96.5%. Song et al.,2012 also used optimised sample entropy algorithm combined with ELM for differentiation of interictal and ictal EEG signals and reported an accuracy of 99%. Recently Zhang et al.,

2013 proposed automatic identification of interictal and ictal EEG signals using ApEn. The study collected EEG recordings (interictal and ictal stage) of four patients having partial epileptic seizures. The ApEn features evaluated from these four patients signals are subjected to SVM for automated differentiation. Their study reported an accuracy of 93.33% in identifying interictal and ictal states. Xiang et al., 2015 proposed an algorithm using fuzzy entropy (FE) to inspect the seizures free and seizures states from EEG signals. The study used two datasets to carry out two classification experiments (i) interictal and ictal based on the N and S datasets (EEG signals recorded from the hippocampal formation of the opposite hemisphere and seizure activity), and (ii) interictal and ictal based on the F and S datasets (EEG signals recorded from the epileptogenic zone and seizure activity). The algorithm computed FE features at different epileptic states of EEG signals which are further subjected to SVM classifier. Their study demonstrated an accuracy of 100% accuracy, sensitivity of 100%, and specificity of 100% in classifying interictal and ictal EEG signals (N and S datasets). Also obtained an accuracy of 88.5%, sensitivity of 90.36%, and specificity of 87.63% in classifying interictal and ictal EEG signals (F and S datasets). Bruzzo et al., 2008 used permutation entropy (PE) to extract significant features from interictal and epileptic EEG signals. They observed Area Under Curve (AUC) to be 0.85 using Receiver Operating Curve (ROC) plot. Aarabi et al., 2009 studied entropy features using interictal and epileptic data collected from Freiburg Seizure Prediction EEG database. They marked a classification accuracy of 98.7% using frequency and time analysis-fuzzy rule based classification. Li et al., 2014 used PE features for the classification of interictal and epileptic data and observed that entropy value gradually decreased from seizure-free to seizure-phase.

Three Classes: normal, interictal (N or F) and ictal

Few researchers developed the state-of-the-art methods to characterise the EEG signals into normal, interictal and ictal classes for better diagnosis, prediction and treatment. Recently Acharya et al., 2013 applied Continuous Wavelet Transforms (CWT) to the EEG signals. Higher Order Spectra (HOS) and texture features are extracted from the CWT plot and characteristic features are fed to four different classifiers; DT, PNN, SVM and k-nearest neighbour (kNN) classifier. They observed that SVM classifier coupled with RBF yielded the highest classification accuracy of 96%, sensitivity of 96.9% and specificity of 97%. They concluded that their technique could be used as an automatic seizure monitoring software. Martis et al., 2013 explored a novel nonlinear method with time-frequency representation called Intrinsic Time-scale Decomposition (ITD). ITD representation is used to identify the subtle variations in the EEG signals and significant energy, Fractal Dimension (FD), SampEn features are calculated from ITD. These features are fed to DT classifier and a classification accuracy, specificity, sensitivity of 95.6%, 99%, 99.5% is obtained respectively. Kumar et al., 2014 used fuzzy approximate entropy to evaluate the complexity of EEG signals recorded from five healthy (both with eyes open and closed) and epileptic subjects. In their study the EEG are decomposed into different frequency sub-bands signals using DWT and computed fuzzy approximate entropy from these sub-bands. The study reported that the fuzzy approximate entropy features are significant in the classification of two classes (interictal and ictal EEG signals) and also three classes (normal, interictal and ictal EEG signals). Using SVM classifier, they reported an accuracy of 100% for normal versus ictal signals; 99.3% for normal (eyes open) data, and 99.65% for normal (eyes closed) data versus ictal signals. In addition accuracies of 99.6% (SVM -RBF) and 99.85% (SVM-linear) are reported for classification of interictal and ictal EEG signals.

Chua et al., 2009 obtained an accuracy of 93% in classifying normal, interictal and ictal EEG signals using bispectrum entropies and phase entropies with Gaussian Mixture Model (GMM) classifier. In another consecutive study by Chua et al., 2011,

features from HOS and power spectrum were extracted to differentiate between normal, interictal and ictal EEG signals. Classification accuracy obtained using HOS features and power spectrum features are compared. It is observed that HOS features yielded higher accuracy of 93.1% than spectrum features yielding an accuracy of 88.7% using GMM classifier. Acharya et al., 2012a reported an accuracy of 98.1% in the classification of normal, interictal and ictal EEG signals using ApEn, SampEn, phase entropies (S1 and S2) coupled with fuzzy classifier. In another study by the same group obtained a classification accuracy of 99.7% using entropies, HOS, FD and Hurst exponent features with fuzzy classifier (Acharya et al., 2012b). Quiroga et al., 2000 classified normal and epileptic EEG signals into three-classes using Kulback-Leibler and renormalized entropies. They concluded that Kulback-Leibler provided better classification results than renormalized entropies. Recurrence Plots (RP) and Recurrence Quantification Analysis (RQA) parameters are also explored in the classification of normal, ictal and interictal EEG signals. Acharya et al., 2011 used ten RQA features in the classification of three types of EEG segments. They employed seven different classifiers such as DT, SVM, GMM, KNN, PNN, fuzzy Sugeno classifier (FSC) and naive Bayes classifer (NBC) classifier and evaluated their performance. They observed that SVM classifier yielded the highest accuracy of 95.6% with sensitivity and specificity of 98.9% and 97.8% respectively. Song et al., 2010 applied SampEn to the normal, interictal and ictal EEG segments combined with ELM and achieved an accuracy of 95.7%. Martis et al., 2012 explored spectral entropy features with Empirical Mode Decomposition (EMD) and decision tree (C4.5) classifier. EEG signals are decomposed using EMD to obtain Intrinsic Mode Functions (IMF) represented as amplitude and frequency modulated waves. Spectral features such as spectral peaks, spectral entropy and energy are extracted from each IMF segments. These features are fed to C4.5 decision tree classifier and obtained an accuracy of 95.3%.

Five classes: normal (two classes), interictal (two classes) and ictal signals

Researchers have even studied five sets of EEG signals normal (two classes – signals recorded with eyes open and closed or signals from data sets Z and O), interictal (two classes – signals from data sets N and F), and ictal segments using wavelet-based technique (Guler et al., 2005).

Guo et al., 2010 applied multi-wavelet transform and ApEn to the EEG signals of normal and epilepsy coupled with Multi-Level Probabilistic Neural Network (MLPNN) classifier. They reported a classification accuracy of 98.2% for the classification of normal (signals of two data sets), interictal (two classes), and ictal classes.

Table 2 shows that the various researchers have experimented different entropies in EEG signal analysis and classification. Many researchers (Yuan et al., 2011; Song et al., 2012; Zhang et al., 2013; Xiang et al., 2015) have used one entropy feature for EEG signal analysis and reported an accuracy of more than 92% in classification of normal, interictal, ictal signals. Few other researchers (Kannathal et al., 2005; Acharya et al., 2012a, 2012b, 2013; Chua et al., 2009, 2011) have used combination of entropies features for the detection of normal, interictal and ictal EEG signals. The combination of different entropies has been reported an accuracy of more than 92% in EEG signal classification. However, the combination of entropies has improved the classification efficiency. In other words, the combination of entropies should be such that the (main advantage of combining the entropies would be that the) limitation of one entropy will be overcome by the adding more entropies.

In this review paper, different entropies are used to classify in to normal, interictal, and ictal EEG signals. The results demonstrate that the entropies can be used as one of the state-of-the-art-methods for the classification of EEG signals into different epileptic states.
The application of entropies for feature extraction from EEG signals is found to have the following advantages:

(i) It can be used in the signal processing to separate the useful signal from redundant information.

(ii) It usually has high value for highly irregular or unpredictable signal and low value for highly regular signal. Thus, it is easier to identify the abnormal activities in the signal.

(iii) It can be used to automatically identify ictal segments that are difficult to localize visually. Also, it can be used to differentiate focal and non-focal EEG signals.

(iv) The results shown in Table 1 shows unique ranges for various entropies and also their ranking using F-value.

(v) These entropy features can be used for other biomedical application like cardiac abnormalities, eye diseases, early stage of diabetes, Alzheimer's disease, autism, fatty liver disease, and stroke detection and treatment.

Table 2 Summary of studies conducted for automated epilepsy detection using entropy features.

Authors	Method	Accuracy (%)	Database
Studies that dealt with a two-class (normal vs. epileptic) problem			
Kannathal et al, 2005b	Entropy Measures – ANFIS	92.2	The Bonn University - Germany
Srinivasan et al, 2007	ApEn-Elman Network	100	The Bonn University- Germany
Ocak et al, 2009	ApEn on DWT coefficients and classifier	96	The Bonn University- Germany
Kumar et al,2012	DWT+ApEn-feed-forward back-propagation neural network	100	The Bonn University- Germany
Kumar et al, 2014	DWT+fApEn-SVM	100	The Bonn University- Germany
Nicolaou et al, 2012	PE-SVM	93.5	The Bonn University - Germany
Wang et al,2011	Wavelet packet entropy- hierarchical	99.4	The Bonn University - Germany

Akareddy et al,2013	Multi-DWT+ Improved ApEn-ANN	90	CHB-MIT
Liang et al, 2010	Weights of the AR model and ApEn (a total of 21 features) - SVM (RBF)	98.3	The Bonn University - Germany
Shen et al, 2013	SampEn-SVM-GA	99.2	Private
Kumar et al, 2010	Wavelet entropy-Elman network	99.2	The Bonn University - Germany
Ahammad et al, 2014	Energy, spectral entropy, standard deviation, maximum, minimum, and mean-DWT-linear classifier	98.5	CHB-MIT/ The Bonn University - Germany
Gandhi et al,2012	DWT-Spectral entropy +Energy-PNN	100	Private/The Bonn University -Germany
Studies that dealt with a two-class (interictal vs. epileptic) problem			
Song et al, 2012	Optimised-SampEn-ELM	99	The Bonn University - Germany
Yuan et al, 2011	ApEn/ Hurst exponent/ DFA-SVM/ANN	96.5	The Bonn University - Germany
Aarabi et al,2009	Entropy/Frequency and Time Analysis-fuzzy rule-based	98.7	Freiburg Seizure Prediction EEG (FSPEEG) database (Maiwald et al., 2004)
Zhang et al, 2013	ApEn-SVM	93.3	Private
Bruzzo et al, 2008	PE-ROC	AUC=0.85	Private
Li et al, 2014	PE	PE gradually decreases from the seizure-free to the seizure phase	Private
Xiang et al, 2015	FE-SVM	98.3-CHB-MIT 100-Bonn	CHB-MIT/Bonn
Studies that dealt with three-class (normal vs. inter-ictal vs. epileptic) problem			
Chua et al, 2009	S1,S2 and bispectrum magnitude - Gaussian mixture model	93.1	The Bonn University - Germany
Chua et al, 2011	Magnitude + PhEn, S1, and S2-GMM	93.1	The Bonn University - Germany
	Power spectrum + GMM	88.7	

Acharya et al, 2009	Non-linear parameters –ApEn, Gaussian mixture model	95	The Bonn University - Germany
Acharya et al, 2012a	ApEn, SampEn, PhEn, S1, and S2 – Fuzzy	98.1	The Bonn University - Germany
Acharya et al, 2012b	Entropies + HOS +Higuchi FD + Hurst-Fuzzy	99.7	The Bonn University - Germany
Acharya et al,2013	CWT+S1+S2+PhEn +Texture-SVM	96	The Bonn University - Germany
Martis et al, 2012	SEN-EMD- C4.5	95.3	The Bonn University - Germany
Martis et al, 2013	SampEn-DT	95.7	The Bonn University - Germany
Song et al,2010	SampEn-ELM	95.7	The Bonn University - Germany
Acharya et al, 2011	RE+RQA-SVM	95.6	The Bonn University - Germany
Quiroga et al, 2000	Kulback-Leibler and renormalized entropies	KL entropy better distinguishes seizure and background EEGs than renormalized entropy	The Bonn University - Germany
Studies that dealt with five-class (normal – two class vs. inter-ictal – two class vs. ictal) problem			
Guo et al, 2010	Multi wavelet transform +ApEn—MLPNN	98.2	The Bonn University – Germany

5. CONCLUSION

Epilepsy is a neurological disorder caused by recurring seizures and can be assessed by EEG signals. The EEG signal is nonlinear nature and has higher inter and intraobserver variability. Thus, automated detection of epileptic EEG signals may prove to be useful in the monitoring and treatment of epilepsy patients. The nonlinear and chaotic nature of the EEG signals can be evaluated efficiently using entropy features. It exhibits the degree of variability and complexity present in the EEG signals. This comprehensive review presents the application of various entropies to discriminate normal, interictal and ictal EEG signals. Table 1 summarizes the performance of all the

entropies and it can be concluded that RE, SampEn, SEN and PE are highly discriminative features to classify normal, interictal and ictal EEG signals.

6. REFERENCES

Aarabi A, Fazel-Rezai R, Aghakhani Y. A fuzzy rule-based system for epileptic seizure detection in intracranial EEG. Clinical Neurophysiology, 2009; 120: 1648-1657.

Acharya UR, Chua KC, Lim TC, Dorithy, Suri JS. Automatic identification of epileptic EEG signals using nonlinear parameters. J Mech Med Biol, 2009; 9(4): 539–553.

Acharya UR, VinithaSree S, Chattopadhyay S, Yu W, Alvin APC. Application of recurrence quantification analysis for the automated identification of epileptic EEG signals, International Journal of Neural Systems, 2011; 21 (3): 199-211.

Acharya UR, Molinari F, VinithaSree S, Chattopadhyay S, Kwan-Hoong Ng, Suri JS. Automated diagnosis of epileptic EEG using entropies. Biomed. Signal Process. Control, 2012a; 7(4): 401–408.

Acharya UR, VinithaSree S, Alvin APC, Suri JS. Application of non-linear and wavelet based features for the automated identification of epileptic EEG Signals. Intl J Neural Syst, 2012b; 22(2): 1250002-1 -14.

Acharya UR, Yanti R, Zheng JW, Krishnan MM., Tan JH, Martis RJ, Lim CM. Automated diagnosis of epilepsy using CWT, HOS and texture parameters. Int. J. Neural Syst, 2013; 23: 1350009.

Aczel J, Daroczy Z. On the measures of information and their characterization. Academic press, New York, 1975.

Ahammad N, Fathima T, Jospeh P, Detection of Epileptic Seizure Event and Onset Using EEG. BioMed Research International, 2014; Article ID 450573: 7 pages.

Akareddy S, Kulkarni PK. EEG signal classification for Epilepsy Seizure Detection using Improved Approximate Entropy. International Journal of Public Health Science (IJPHS), 2013; 2(1): 23-32.

Andrzejak RG, Lehnertz K, Rieke C, Mormann F, David P, Elger CE. Indications of nonlinear deterministic and finite dimensional structures in time series of brain electrical activity: Dependence on recording region and brain state. Phys. Rev. E,2001; 64: 061907

Ann S, Hu Q, Yu D. Fuzzy entropy based Max-Relevancy and Min-Redundancy feature selection. IEEE Conference on Granular Computing, Hangzhou, 26-28th August 2008, IEEE, China, pp.101-106.

Bandt C, Pompe B. Permutation entropy: A natural complexity measure for time series. Rev. Lett. 2002; 88: 174102.

Bishop CM. Pattern Recognition and Machine Learning (Information Science and Statistics). Springer-Verlag New York Inc, Secaucus, New Jersey, United States 2006.

Bonn database (http://www.meb.uni-bonn.de/epileptologie/science/physik/eegdataold.html)

Bruzzo AA, Gesierich B, Santi M, Tassinari CA, Birbaumer N, Rubboli G. Permutation entropy to detect vigilance changes and pre-ictal states from scalp EEG in epileptic patients. A preliminary study. Neurol Sci. 2008; 29(1):3-9.

Cachin C. (2001). Smooth Entropy and Renyi Entropy, Advances in Cryptology-EUROCRYPT '97, Vol. 1233, Springer Berlin Heidelberg, pp.193-208.

Cao Y, Tung W, Gao JB, Protopopescu VA, Hively LM. Detecting dynamical changes in time series using the permutation entropy. Phys. Rev. E, 2004; 70: 046217.

Capurro A, Diambra L, Lorenzo D, Macadar O, Martin M, Mostaccio C, Plastino A, Perez J, Rofman E, Torres M, Velluti J. Human brain dynamics: the analysis of EEG signals with Tsallis information measure. Phys A, 1999; 265: 235-254.

Chan AM, Sun FT, Boto EH, Wingeier BM. Automated seizure onset detection for accurate onset time determination in intracranial EEG. Clinical Neurophysiology, 2008; 119: 2687-2696.

CHB-MIT database (http://physionet.org/cgi-bin/atm/ATM).

Chua KC, Chandran V, Acharya UR, Lim CM. Cardiac state diagnosis using higher order spectra of heart rate variability. Journal of Medical Engineering & Technology, 2008; 3232 (2) :145–155.

Chua KC, Chandran V, Acharya UR, Lim CM. Automatic Identification Of Epileptic EEG signals Using Higher Order Spectra. Journal of Engineering in Medicine,2009; 223 (4): 485-495.

Chua KC, Chandran V, Acharya UR, Lim CM. Application of higher order spectra to identify epileptic EEG. J Med Syst, 2011; 35(6):1563-1571.

Correa AG, Laciar E, Patino HD, Valentinuzzi ME. Artifact removal from EEG signals using adaptive filters in cascade. Journal of Physics: Conference Series, 2007; 90: 012081.

Cover TM, Thomas JA. Elements of information theory. Wiley 1991.

Derpanis, K. G. (2008). The Bhattacharyya Measure. Information available at: http://www.cse.yorku.ca/~kosta/CompVis_Notes/bhattacharyya.pdf (date accessed on 04/27/2015).

EoM- Encyclopaedia of Mathematics, Bhattacharyya distance, Information available at: http://www.encyclopediaofmath.org/index.php/Bhattacharyya_distance (date accessed on 04/27/2015).

Fadlallah B, Chen B, Keil A, Principe J. Weighted-permutation entropy: a complexity measure for time series incorporating amplitude information. Phys Rev E Stat Nonlin Soft Matter Phys, 2013: 87)2): 022911.

Falniowski F. On the connections of generalized entropies with Shannon and Kolmogorov-Sinai entropies. Entropy, 2014; 16: 3732-3753.

Feldman DP, Crutchfield JP. Measures of statistical complexity: Why? Phys. Lett. A, 1998; 238: 244-252.

Gabor AJ. Seizure detection using a self-organizing neural network: validation and comparison with other detection strategies. Electroencephalogr Clin Neurophysiol, 1998; 107(1): 27-32.

Gandhi T, Panigrahi BK, Bhatia M, Anand S. Discrete harmony search based expert model for epileptic seizure detection in electroencephalography. Expert Systems with Applications, 2012, 39(4): 4055–4062.

Guler I, Ulbeyi ED. Adaptive neuro-fuzzy inference system for classification of EEG signals using wavelet coefficients. J Neurosci Methods, 2005; 148: 113-121.

Guo L, Rivero D, Pazos A. Epileptic seizure detection using multiwavelet transform based approximate entropy and artificial neural networks. Journal of Neuroscience Methods, 2010; 193(1): 156-163.

Hwang T, Sun C H, Yun T, Yi G S (2010), FiGS: a filter-based gene selection workbench for microarray data. BMC Bioinformatics, 11, Information available at: http://www.biomedcentral.com/1471-2105/11/50 (date accessed on 04/10/2015).

Hekkila EJ, Hu L. Adjusting spatial-entropy measures for scale and resolution effects. Environment and planning B: Planning and Design, 2006; 33: 845-861.

Inouye T, Shinosaki K, Sakamoto H, Toi S, Ukai S, Iyama A, Katsuda Y, Hirano M, Quantification of EEG irregularity by use of the entropy of the power spectrum. Electroencephalography and Clinical Neurophysiology, 1991; 79: 204–210.

James, C. J. Detection of epileptiform activity in the electroencephalogram using the electroencephalogram using artificial neural networks. University of Canterbury, Christchurch New Zealand, 1997.

Kannathal N, Acharya UR, Lim CM, Sadasivan PK. Characterization of EEG – A comparative study. Computer Methods and Programs in Biomedicine, 2005a; 80 (1): 17-23.

Kannathal N, Lim CM, Acharya UR, Sadasivan PK. Entropies for detection of epilepsy in EEG. Computer Methods and Programs in Biomedicine, 2005b; 80 (3): 187-194.

Kobayashi H, Mark BL, Turin W. Probabaility, Random Processes and Statistical Analysis: Applications to Communications, Signal Processing, Queueing Theory and Mathematical Finance. Cambridge University Press, 2011.

Kosko, B. Fuzzy entropy and conditioning. Information Sciences, 1986; 40: 165-174.

Kumar Y, Dewal ML, Anand RS.   Epileptic seizures detection in EEG using DWT-based ApEn and artificial neural network. Signal, Image and Video Processing, 2012; 8(7): 1323-1334.

Kumar Y, Dewal ML, Anand RS. Epileptic seizure detection using DWT based fuzzy approximate entropy and support vector machine. Neurocomputing, 2014; 133: 271-279.

Kumar SP, Sriraam N, Benakop PG, Jinaga BC. Entropies based detection of epileptic seizures with artificial neural network classifiers. Expert Systems with Applications, 2010; 37(4): 3284-3291.

Lemons DS, A Student's Guide to Entropy, Cambridge University Press, 2013.

Li X, Ouyang G, Richards DA. Predictability analysis of absence seizures with permutation entropy. Epilepsy Res. 2007; 77: 70.

Li J, Yan J, Liu X, Ouyang G. Using Permutation Entropy to Measure the Changes in EEG Signals During Absence Seizures. Entropy, 2014; 16: 3049-3061.

Li NI, Ting CJ, Rubin W. Dynamic multivariate multiscale entropy based analysis on brain death diagnosis. Technological Sciences, 2015; 58(3): 425-433.

Liang SF, Wang HC, Chang WL.Combination of EEG Complexity and Spectral Analysis for Epilepsy Diagnosis and Seizure Detection. EURASIP Journal on Advances in Signal Processing, 2010;2010: 853434.

Maiwald T, Winterhalder M, Aschenbrenner-Scheibe R, Voss HU, Schulze-Bonhage A, Timmer J. Comparison of three nonlinear seizure prediction methods by means of the seizure prediction characteristic. Physica D, 2004; 194: 357-368.

Martis RJ, Acharya UR, Tan JH, Petznick A, Yanti R, Chua KC, Ng EYK, Tong L.Application of empirical mode decomposition (EMD) for automated detection of epilepsy using EEG signals.International Journal of Neural Systems, 2012; 22(6): 1250027-1 - 16.

Martis RJ, Acharya UR, Tan JH, Petznick A, Tong L, Chua CK, Ng EY. Application of intrinsic time-scale decomposition (ITD) to EEG signals for automated seizure prediction. Int. J. Neural Syst. 2013; 23: 1350023.

Marwan N, Wessel N, Meyerfeldt U, Schirdewan A, Kurths J. Recurrence plot based measures of complexity and its application to heart rate variability data. Physical Review E, 2002; 66 (2): 026702.

McGrogan, N. Neural Network Detection of Epileptic Seizures in the Electroencephalogram. Oxford University, Oxford, 2001.

Meier R, Dittrich H, Schulze-Bonhage A, Aertsen A. Detecting epileptic seizures in long-term human EEG: A new approach to automatic online and real-time detection and classification of polymorphic seizure patterns. Journal Clin Neurophysiol, 2008; 25: 119-131.

Minasyan G R, Chatten JB, Harner RN. Patient specific early seizure detection from scalp EEG.J clin. Neurophysiology, 2010; 27: 163-178.

Misiurewicz M. A short proof of the variational principle for Z_+^n action on a compact space. Asterisque, 1976; 40: 147-157.

Mormann, F., Andrzejak, R. G., Elger, C. E., Lehnertz, K. Seizure prediction: thelong and winding road. Brain, 2007; 130(Pt 2): 314-333.

Nicolaou N and Georgiou J. Detection of epileptic electroencephalogram based on permutation entropy and support vector machine. Expert Systems with Applications, 2012; 39: 202–209.

Niederhauser JJ, Esteller R, Echauz J, Vachtsevanos G, Litt B. Detection of seizure precursors from depth-EEG using a sign periodogram transform. IEEE trans Biomed Eng, 2003; 50: 449-458.

Nikias CL, Raghuveer MR. Bispectrum estimation—a digital signal processing framework. Proceedings of the IEEE, 1987; 75: 869–891.

Nikias CL, Mendel JM. Signal Processing with Higher Order Spectra. IEEE Signal Processing Magazine, 1993; 10(3): 10-37.

Nikias CL, Petropulu AP. Higher-order spectra analysis: a nonlinear signal processing framework. PTR Prentice Hall, Englewood Cliffs, NJ, 1993b.

Ocak H. Automatic detection of epileptic seizures in EEG using discrete wavelet transform and approximate entropy. Expert Systems with Applications, 2009; 36 (2) : 2027-2036.

Pal SK, Petrosino A, Maddalena L. Handbook on soft computing for video surveillance: Chapter 9: Chakraborty B, Bhattacharyya S, and Dutta P. An unsupervised video shot boundary detection technique using fuzzy entropy estimation of video content. Chapman and Hall, 2012: 237.

Pincus SM. Appoximate entropy as a measure of system complexity. Proc Natl Acad Sci, 1991; 88: 2297-2301.

Pincus SM. Approximate entropy (ApEn) as a complexity measure. Chaos, 1995; 5(1): 110-117.

Quiroga RQ, Arnhold J, Lehnertz K, Grassberger P.Kulback-Leibler and renormalized entropies: Applications to electroencephalograms of epilepsy patients. Physical Review E, 2000; 42(6): 8380-86.

Richman JS and Moorman JR. Physiological time-series analysis using approximate entropy and sample entropy. American Journal of Physiology- Heart and Circulatory Physiology, 2000; 278: 2039-2049.

Riedl M, Müller A. Wessel N. Practical considerations of permutation entropy. Eur. Phys. J. Spec. Top. 2013; 222: 249–262.

Rodrigues PS, Giraldi GA. Computing the q-index for Tsallis Nonextensive Image Segmentation. 2009 XXII Brazilian Symposium on Computer Graphics and Image Processing, 11-15th October 2009, Rio de Janiero, 232-237.

Rosso OA, Blanco S, Yordanova J, Kolev V, Figliola A, Schurmann M, Basar E. Wavelet entropy: A new tool for analysis of short duration electrical signals. Journal of Neuroscience Methods, 2001; 105: 65-75.

ROC- The Area Under an ROC curve; Information available at: http://gim.unmc.edu/dxtests/roc3.htm (date accessed on 04/27/2015).

Seely AJE, Macklem PT. Complex systems and the technology of variability analysis. Crit care, 2004; 8(6): R367-R384.

Sharma R, Pachori RB, Acharya UR. Application of Entropy Measures on Intrinsic Mode Functions for the Automated Identification of Focal Electroencephalogram Signals. Entropy, 2015; 17:669-691.

Shen PC, Liu ST, Zhou WZ, Lin FS, Lam AYY, Sung HY, Chen W, Lin JW, Chiu MJ, Pan MK, Kao JH, Lai F.A Physiology-Based Seizure Detection System for Multichannel EEG. PLOS One, 2013; 8: e65862.

Song Y, Lio P. A new approach for epileptic seizure detection: sample entropy based feature extraction and extreme learning machine. J. Biomedical Science and Engineering, 2010; 3: 556-567.

Song Y, Crowcroft J, Zhang J. Automatic epileptic seizure detection in EEGs based on optimized sample entropy and extreme learning machine. Journal of Neuroscience Methods, 2012; 210 (2): 132-146.

Sonnino G, Steinbrecher G, Sonnino A. The Renyi entropy of Levy distribution. Physics AUC, 2013; 23: 10-17.

Srinivasan V, Eswaran C, Sriraam N. Approximate Entropy-Based Epileptic EEG Detection Using Artificial Neural Networks. IEEE transaction on Information Technology in Biomedicine, 2007; 11 (3): 288-295.

Subasi A. Signal Classification using wavelet feature extraction and a mixture of expert model. Expert Systems with Applications, 2007; 32(4): 1084-1093.

Tellenbach B, Burkhart M, Sornette D, Maillart T. Beyond Shannon: characterizing internet traffic with generalized entropy metrics. Moon SB et al., Eds: PAM 2009, Springer-Verlag Berlin Heidelberg LNCS 5448: 239-248.

Thakor NV, Tong S. Advances in quantitative electroencephalogram analysis methods. Annual reviews, 2004; 6: 453-495.

Tzallas AT, Tsipouras MG, Fotiadis DI. Automatic seizure detection based on time-frequency analysis and artificial neural networks. ComputIntellNeurosci, 2007a; 2007: 80510.

Tzallas AT, Tsipouras MG, Fotiadis DI.Epileptic seizure detection in EEGs using time-frequency analysis. IEEE Trans InfTechnol Biomed, 2009; 13(5): 703-710.

Veisi I,Pariz N,Karimpour A. Fast and Robust Detection of Epilepsy in Noisy EEGSignals Using Permutation Entropy. In Proceedings of the 7th IEEE International Conferenceon Bioinformatics and Bioengineering, Boston, MA, USA, 14–17 October 2007;200–203.

Wang D, Miao D, Xie C. Best basis-based wavelet packet entropy feature extraction and hierarchical EEG classification for epileptic detection. Expert Systems With Applications, 2011; 38: 14314–14320

WHO. World health organization: epilepsy: epidemiology, aetiology and prognosis. WHO factsheet. 2001.

Xiang J, Li C, Li H, Rui C, Wang B, Han X, Chen J. The detection of epileptic seizure signals based on fuzzy entropy. J Neurosci Methods, 2015 (doi: 10.1016/j.jneumeth.2015.01.015.).

Yuan Q, Zhou W, Li S, Cai D. Epileptic EEG classification based on extreme learning machine and nonlinear features. Epilepsy Research, 2011; 96: 29-38.

Yuan Y, van Allen E M, Omberg L, Wagle N, Amin-Mansour A, et al. Assessing the clinical utility of cancer genomic and proteomic data across tumor types. Nature Biotechnology, 2014; 32: 644-652.

Zanin M, Zunino L, Rosso OA, Papo D. Permutation entropy and its main biomedical and econophysics application: A review. Entropy, 2012; 14: 1553-1577.

Zbilut JP, Webber CL Jr. Embeddings and delays as derived from quantification of recurrence plots. Physical Letters A, 1992; 171 (3–4): 199–203.

Zhang Z, Zhou Y, Chen Z, Du S, Huang R. Approximate entropy and support vector machines for electroencephalogram signal classification. Neural Regen Res. 2013; 8(20): 1844–1852.