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Methods for Seizure Detection and Prediction: An Overview

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Abstract

Epilepsy is one of the most common neurological diseases and the most common neurological chronic disease in childhood. Electroencephalography (EEG) still remains one of the most useful and effective tools in understanding and treatment of epilepsy. To this end, many computational methods have been developed for both the detection and prediction of epileptic seizures. Techniques derived from linear/nonlinear analysis, chaos, information theory, morphological analysis, model-based analysis, all present different advantages, disadvantages, and limitations. Recently, there is the notion of selecting and combining the most robust features from different methods for revealing various signals' characteristics and making more reliable assumptions. Finally, intelligent classifiers are employed in order to distinguish epileptic state out of normal states. This chapter reviews the most widely adopted algorithms for the detection and prediction of epileptic seizures, emphasizing on information theory based and entropy indices. Each method's accuracy has been evaluated through performance measures, assessing the ability of automatic seizure detection/prediction.

Keywords EEG, Epilepsy, Seizure detection, Seizure prediction, Entropy, Nonlinear analysis, Morphological analysis, Seizure modeling, Classification

1 Introduction

Epilepsy is a chronic neurological disorder characterized by neurological brain dysfunctions resulting in epileptic seizures. An epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal, excessive, and synchronous neuronal activity in the brain [1]. It is estimated that in 2012 between 0.4 and 1 % of the world's population (around 50 million people) have active epilepsy [2]. Among many diagnostic and imaging methods, the electroencephalogram (EEG) is by far the most used and effective technique in the daily clinical treatment. Given that it is noninvasive, is relatively accurate, and has low cost, it has been established as a necessary tool for clinicians and people who deal with epilepsy.

Until recently, seizures were identified only visually by an expert neurologist. However, this procedure constitutes a laborious task especially in the case of long-term EEG recordings.

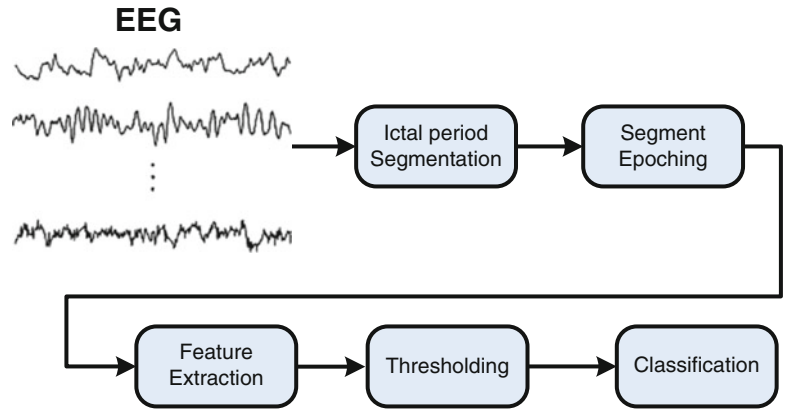

Fig. 1 Schematic representation of seizure detection system

Therefore, automatic computer aided algorithms have evolved in order to shorten and automate this procedure and many seizure detection methods are reported in the international literature [3, 4]. Figure 1 shows a schematic representation of a seizure detection system.

Most studies present their solution to the problem of seizure detection in the context of a decision support system for the neurologist expert. As there are many types of seizures, this is sometimes a difficult task, taking into account the nature, temporal length, and singularities of each seizure type. When a patient experiences seizures of different types one needs to categorize EEG ictal periods into a specific type, although some epileptic syndromes are difficult to be characterized as being of specific category. A more demanding task, which is still considered an open scientific question, is the prediction of a seizure [5], which profoundly will improve the quality of life of people suffering from severe seizures. Besides, the understanding of underlying mechanisms leading in seizures and the origin of a seizure is in each case are still under question.

Towards this direction, many EEG analysis algorithms have been proposed. Linear analysis has been widely used based mainly on synchronization features as a primer and straightforward approach. Although these methods can reveal in some cases the existence of epileptic seizures, they have their limits if someone takes the nature of real human EEG data into account [6, 7]. Under this prism, EEG signals can be interpreted as the result of a system containing highly nonlinear elements. The study of nonlinear EEG dynamics can reveal hidden information and provide a more complete picture about underlying brain processes [8, 9]. Nonlinear analysis has been used with increased accuracy over the last decade in the area of seizure detection and prediction.

2 Methods

In this section, linear methods (highlighting time–frequency methods), nonlinear methods (highlighting measures derived from information theory), methods based on signal's morphological characteristics, and vision-based methods are presented.

2.1 Linear Methods

Linear methods have been widely used in the area of epilepsy detection mainly due to their simplicity and versatility. One of the simplest linear statistic metrics is the variance of the signal. It offers an insight into dynamics underlying the EEG and is usually calculated in consecutive windows. A further linear method is based on the autocorrelation function, exploiting the periodic nature of seizures. Liu et al. [10], using Scored Autocorrelation Moment (SAM) analysis, distinguished EEG epochs containing seizures with an accuracy of 91.4 % although signals did not present differences in their spectral properties.

Furthermore, seizure onset and offset determination may be succeeded using linear prediction filters (LPF) [11]. An LPF estimates the spectral characteristics of a signal, with its accuracy depending on the stationarity of the latter. When there are spikes, sharp waves or rapid changes, the filter's prediction error increases, leading to an identification of a possible seizure.

Discrete wavelet transform (DWT), which is a transformation extracting scale-frequency components from data (each component with resolution matched to its scale) may also be applied in seizure detection. In [12], normal and seizure signals were classified with an accuracy of 99.5 % using DWT and a linear classifier. Another linear feature, the relative fluctuation index [13], can measure the intensity of the fluctuation of EEG signals, which is defined as:

$$F_i = \sum_{j=1}^{M-1} \left| a_i(j+1) - a_i(j) \right|,$$

where a_i denotes the amplitude of the filtered EEG signal at the i^{th} band with length M. During a seizure, there is a larger fluctuation in the EEG signals than during an ictal-free period. Therefore, values of fluctuation index during a seizure are usually larger than during rest EEG. Using this index, along with other features, a study by Yuan et al. [13] achieved 94.90 % mean accuracy in a segment-based aspect and 93.85 % mean accuracy in an event-based aspect.

2.1.1 Time–Frequency Methods

Various studies that employ time–frequency features have also been used in the area of seizure detection [14]. Hassanpour et al. [15] used time–frequency patterns as signatures in order to detect seizures.

Tzallas et al. [16–18] performed an extensive investigation of well-known time–frequency distributions, extracting features from the Power Spectral Density (PSD) time–frequency grid followed by artificial neural network (ANN) classification. With this methodology, an accuracy between 89 and 100 % for three different datasets was achieved using reduced interference time–frequency distribution and ANNs. A time–frequency matched filter was introduced in [19, 20] in order to reveal seizure patterns. Rankine et al. [21] proposed a related methodology analyzing changes in preictal, ictal, and postictal states. Moreover, an improved time–frequency dictionary in terms of reconstruction accuracy and discrimination between seizure and non-seizure states is presented in [22].

2.2 Nonlinear Methods

Epileptic seizures can be seen as manifestations of intermittent spatiotemporal transitions of the human brain from chaos to order [23]. Nonlinear analysis of EEG has attracted increasing interest by many research groups mainly because it incorporates the non-stationary nature of a signal. It perceives brain mechanisms as part of a macroscopic system in a way to understand its spatiotemporal dynamic properties. The revealed underlying information of ongoing EEG leads to promising results not only in the detection but also in the prediction of upcoming seizures [24].

2.2.1 Fractal Dimension

Fractal dimension is a nonlinear time domain measure characterizing the complexity of a time series. The degree of complexity increases if the fractal dimension increases. Various algorithms have been developed [25] in order to calculate the fractal dimension such as box counting [26], Katz's algorithm [27], Petrosian's algorithm [28], and Higuchi's algorithm [29]. According to the last, the time series $x(i), i = 1, 2, \ldots, N$ formulates the vector

$$X_m^k = \left\{ x(m), x(m+k), \ldots, x\left(m + \left\lfloor \frac{N-m}{k} \right\rfloor \cdot k \right) \right\},$$

where k is the time lag, $m = 1,2, \ldots, k$ and $\lfloor y \rfloor$ the round down integer of argument y. For each $X_m{}^k$, the average is formed:

$$L_m(k) = \frac{\sum_{i=1}^{\left\lfloor \frac{(N-m)}{k} \right\rfloor} \left| x(m+ik) - x\left(m + (i-1)k \right| (n-1)}{\left\lfloor \frac{N-m}{k} \right\rfloor \cdot k}$$

AU1

Finally, the sum of averages is calculated as

$$L(k) = \sum_{m=1}^{k} L_m(k)$$

The linear estimation of the slope of the curve $\ln(L(k))$ versus $\ln(1/k)$ is an estimate of the fractal dimension.

2.2.2 Lyapunov Exponent

Lyapunov exponent (λ) is a nonlinear metric measuring the exponential divergence of two time series trajectories in phase space. Considering the m-dimensional time vector of a time series $X = \{x(t), x(t+1), \ldots, x(t+m-1)\}$ and two neighboring points X_{t_0} and X_t in phase space at time t_0 and t respectively, the distances of the points in the ith direction are $dX_i|_{t_0}$ and $dX_i|_t$ respectively. Given the following equation,

$$dX_i|_t \approx e^{\lambda_i t} dX_i|_{t_0}$$

the Lyapunov exponents are λ_i.

Finally, the maximal Lyapunov exponent can be defined as

$$\lambda_{\max} = \lim_{t\to\infty} \lim_{dX_i|_{t_0}\to 0} \lim \frac{1}{t} \ln \frac{dX_i|_t}{dX_i|_{t_0}}$$

and measures the biggest increase rate of the error in the initial conditions. Lyapunov exponents characterize the chaotic nature of a time series, i.e., a slight shift in initial conditions can lead to a non-deterministic difference in the phase space trajectory. Using Lyapunov exponents and recurrent neural networks, Guler et al. [30] achieved 96.79 % accuracy rate in the detection of epileptic seizures.

On the other hand, Kannathal et al. [31] tested nonlinear measures including the correlation dimension (CD), maximal Lyapunov exponent, Hurst exponent (H), and Kolmogorov–Sinai entropy (K–S entropy) in order to distinguish epileptic from normal EEG activity. All measures showed high discriminating ability, with slightly better results being reported for the CD (p-value: 0.0001) and K–S entropy (p-value: 0.0001).

2.3 Information Theory Based Analysis and Entropy

Entropy is a physical measure derived from thermodynamics, describing the order or disorder of a physical system. High entropy values equal to high levels of disorder of a system, whereas low values describe a more ordered system, capable of producing more work. Signal processing and analysis research disciplines borrowed entropy from information theory in order to address and describe the irregularity, complexity, or unpredictability characteristics of a signal. Given these properties, entropy has been widely used towards automatic seizure detection [3, 32, 33].

2.3.1 Shannon Entropy

After some initial approaches by H. Nyquist and R. Hartley, research leaders at Bell Labs, Shannon established in 1948 quantitatively the foundations of information theory [34]. According to these, a signal is divided into J non-overlapping value bins and the ratios of samples falling into j^{th} bin to the total samples N are calculated

$$H = -\sum_{j=1}^{J} p_j \log_2\left(p_j\right) \quad \text{where} \quad p_j = \frac{N\left(x_j\right)}{N},$$

where $N(x_j)$ is the amount of samples that fall into bin j of total J bins to the total samples N. EEG Shannon entropy has been correlated with desflurane effect compartment concentrations [35]. It has also been used in order analyze long term EEG coming from patients with frontal lobe epilepsy [36].

2.3.2 Spectral Entropy

Spectral Entropy was introduced by Inouye [37, 38] measuring the proportional contribution of each spectral component to the total spectral distribution [39].

$$H = -\sum_{j=1}^{J} p_j \log_2\left(p_j\right) \quad \text{where} \quad p_j = \frac{S_j}{S},$$

where S is the total spectrum and S_j is the spectrum at frequency bin j of total J bins.

A traditional approach to estimate spectral entropy is through Fourier power spectrum [40, 41], which is applicable mainly where a signal's stationarity conditions are satisfied, e.g., the resting EEG. However, many clinical applications are highly non-stationary with transient and rapid changes in their spectra distributions. In addition to that, a time-varying entropy index is necessary in some cases [42]. This can be partially dealt with the short time Fourier transform (STFT) revealing spectral distributions over successive windows [40]. However, this approach faces the intrinsic problem of window size selection that arises from the Heisenberg Fourier Uncertainty Principle [43].

$$\Delta t \Delta f \geq \frac{1}{4 \cdot \pi}$$

Due to this, a small window size increases temporal resolution but makes spectral resolution poor whereas a wide window size achieves the opposite effect. It is considered that the optimal distribution is a Gaussian that minimizes the product of time–frequency variances [44].

To overcome these limitations, Quiroga et al. [45] introduced wavelet entropy (WE) which is based on multi-resolution decomposition by means of the wavelet transform (WT). This technique has already been applied in EEG/ERP signal analysis [46–48]. The problem with this approach is that the results are strongly dependent on the selection of the mother wavelet function. WE was efficiently applied in order to discriminate between EEG signals of controls and epileptic patients [49–51]. Rosso et al. [52] compares the Gabor transform and the wavelet transform claiming the superiority of the second because a variable window is used for the analysis. Subsequently, the time evolution of wavelet entropy and

relative wavelet entropy was investigated, showing significant decrease during ictal periods. However, different wavelet basis functions can produce different results, making their interpretation sometimes ambiguous.

In order to yield an optimal time–frequency distribution and subsequently time–frequency spectral entropy, adaptive algorithms are used. Adaptive Optimal Kernel (AOK) time–frequency representation [53] is an effective method in representing signals in the time frequency plane. The main advantage of having an adaptive signal-dependent method is that in each case the kernel is selected according to how well it is suited to signal's characteristics. The method is adjusted by the choice of the kernel which involves a compromise between cross term reduction, loss of time–frequency resolution, and maintenance of certain properties of distribution [44, 54]. Spectral entropy by using this method was presented in [55].

2.3.3 Approximate Entropy

Approximate entropy (ApEn) was introduced by Pincus [56] to quantify the regularity and predictability of a time series data of physiological signals. Being a modification of the Kolmogorov–Sinai entropy [57], it was especially developed for determination of the regularity of biologic signals in the presence of white noise [58].

Given a time series $X(n) = \{x(n)\} = \{x(1), x(2), \ldots, x(N)\}$ of N samples, the ApEn value is calculated through the following steps:

1. The vector sequences $X_m(i) = \{x(i), x(i+1), \ldots, x(i+m-1)\}$ which represent m consecutive values commencing with the i^{th} point are formed.
2. The distance between $x_m(i)$ and $x_m(j)$ is calculated, defined by

$$d[X_m(i), X_m(j)] = \max_{1 \le k \le m} \{|x(i+k-1) - x(j+k-1)|\}$$

3. For each $x_m(i)$ the number $N_i^m(r)$ of vectors is calculated

$$d[X_m(i), X_m(j)] \le r$$

with r representing the noise filter level.
Then, the parameters $C_i^m(r)$ are estimated as,

$$C_i^m(r) = \frac{N_i^m(r)}{N - m + 1}$$

4. $\phi^m(r)$ is defined as the mean value of the parameters C_i^m:

$$\phi^m(r) = \frac{\sum_{i=1}^{N=m+1} \ln C_i^m(r)}{N - m + 1}$$

5. ApEn(m, r, N) is calculated using $\phi^m(r)$ and $\phi^{m+1}(r)$ as

$$\mathrm{ApEn}(m, r, N) = \phi^m(r) - \phi^{m+1}(r)$$

ApEn has already been used in many applications such as analysis of heart rate variability [59–62], analysis of the endocrine hormone release pulsatility [63], and detection of epilepsy [64, 65]. The majority of studies indicate that during ictal periods ApEn presents a significant decrease in comparison with EEG during normal periods [3, 65, 66]. ApEn was also used in order to classify EEG signals among five different states (including an ictal state) with an increased accuracy [67].

The calculation of ApEn depends on the parameters embedding dimension (m), noise filter level (r), and data length (N). Besides, it is arguable whether the standard deviation used at the noise filter level would be calculated from the original data series or from the individual selected EEG segments. However, there is no specific guideline for their optimal determination even though most research studies use the parameters described in [56, 61] as a rule of thumb. But ApEn statistics do not present relative consistency [61] leading to problems in hypothesis formulation and testing. As signals of different source and pathologies can have quite different properties, these parameters should be determined, based on the specific use. The need for a consistent determination of parameters was studied in a recent work [68] where a preliminary analysis of these parameters was established.

2.3.4 Sample Entropy

Sample entropy (SampEn), which is presented in [61], also estimates complexity in time series providing an unbiased measure regarding the length of time series.

$$H = \ln\left(\frac{A^m(r)}{B^m(r)}\right)$$

The calculation of sample entropy starts with the steps 1 and 2 already described for the ApEn calculation. The following steps are given below:

3. For each $X_m(i)$ the number $N_i^m(r)$ of vectors is calculated

$$d[X_m(i), X_m(j)] \leq r$$

with r representing the noise filter level.
Then, the parameters $B_i^m(r)$ and $B^m(r)$ are defined as,

$$B_i^m(r) = \frac{N_i^m(r)}{N - m - 1}$$

$$B^m(r) = \frac{1}{N - m} \sum_{i=1}^{N-m} B_i^m(r)$$

4. The dimension is incremented to $m = m + 1$ and the number $N_i^{m+1}(r)$ is calculated so that

$$d[X_{m+1}(i), X_{m+1}(j)] \leq r$$

Then, the parameters $A_i^m(r)$ and $A^m(r)$ are defined as

$$A_i^m(r) = \frac{N_i^{m+1}(r)}{N - m - 1}$$

$$A^m(r) = \frac{1}{N - m} \sum_{i=1}^{N-m} A_i^m(r)$$

5. Finally, sample entropy is defined as

$$\text{SampEn}(m, r) = \ln\left[\frac{B^m(r)}{A^m(r)}\right]$$

The advantage of SampEn is that its calculation is independent of time series size as it restricts self-matches and uses a simpler calculation algorithm, reducing execution time [61]. However, despite its advantages, SampEn is not widely used [69]. Sample entropy was used as feature for automatic seizure detection in [70]. It was also applied in [71] combined with Lempel–Ziv as indicators to discriminate focal myoclonic events and localize myoclonic focus.

2.3.5 Kullback–Leibler Entropy

Kullback–Leibler entropy (K–L entropy) measures the degree of similarity between two probability distributions and can be interpreted as a method quantifying differences in information content [72]. K–L entropy was applied to intracranial multichannel EEG recordings and indicates its ability to detect seizure onset based on spectral distribution properties [73].

2.3.6 Lempel–Ziv Complexity

The Lempel–Ziv measure estimates the rate of recurrence of patterns along a time series, reflecting a signal's complexity. Lempel–Ziv has been applied to epileptic EEG signal showing increased values during ictal periods [74]. Another work has applied LZ complexity on E-ICA and ST-ICA transformed signals in an attempt to isolate seizure activity [75]. Both of these studies have been applied to limited datasets, pointing out the need of a more thorough evaluation.

2.3.7 Permutation Entropy

Permutation entropy is a measure of complexity introduced by Bandt [76]. Its application to absence epilepsy on rats indicated superiority on prediction of epileptic seizures and identification of preictal periods (54 % detection rate) comparing with sample entropy [77]. The same study achieved 98.6 % correct identification of interictal periods.

2.3.8 Order Index

Order index is another nonlinear feature that was proposed by Ouyang [78] measuring the irregularity of non-stationary time series. In a recent work [79], a comparative analysis of order index along with other linear and nonlinear features was performed.

2.4 Morphological Analysis

Most algorithms in the literature select features based on amplitude, spectral properties, and synchronization of ongoing EEG in order to identify a seizure. However, little progress has been made in order to incorporate a neurologist's experience in analyzing a waveform morphology and shape for making a decision on optimal epilepsy treatment. Some studies working towards shape analysis of epileptic seizures give quite promising results not only by their techniques themselves but also by the prospect of integrating the present and future perception of neurologists' expertise. In this way, Deburchgraeve et al. [80] extracts segments that morphologically resemble seizures by a combined nonlinear energy operator and a spikiness index. Then a detector is applied exploiting the repetitive nature of a seizure is applied. The spike and wave complexes of epileptic syndromes can also be extracted by a two-stage algorithm, the first enhancing the existence of spikes and the second applying a patient-specific template matching [81]. Interictal spikes have also been detected using Walsh transform in addition to the fulfillment of clinical criteria establishing a simulated epileptic spike [82, 83].

2.5 Vision-Based Analysis

In some cases, epilepsy monitoring is performed with synchronized video and EEG recordings. Epileptic syndromes are evaluated based not only on scalp recordings but also on human motion features extracted from video sequences. Analysis involves mainly detection of the myoclonic jerks, eye motion (eyeball doze, eyeball upwards roll, eyelid movements), head jerks and movements, facial expressions (mouth, lips malformations). However, it can be understood that a seizure specific organization and combination of motion features should be applied in order to provide better results [84]. This promising area of research helps neurologist experts have a more complete picture preventing them from false alarms and leading to decision support with increased accuracy. A thorough review can be found in [85]. Vision-based analysis in epilepsy can be divided into two categories, marker-based and marker-free techniques. Marker-based techniques track objects/markers placed in representative parts of the human body that convey information related to the epileptic manifestation. On the other hand, marker-free techniques use advanced image processing and computer vision tools to extract motion-related information directly from the image sequences in the video. Both techniques return time-varying signals, which form the basis for further feature extraction in the time- and frequency domain. The extracted features finally feed a classifier such as an ANN or a decision tree with the aim to detect epileptic seizures.

3 Seizure Prediction

Nowadays, seizure detection is considered practically an issue that has been solved with satisfactory accuracy. On the other hand, seizure prediction remains an open scientific problem in a way that there is no consistent approach for predicting a seizure accurately within a significant amount of time before it occurs. However, many algorithms have been tested in their ability to forecast seizures.

3.1 Early Approaches

The notion of seizure prediction was firstly mentioned in 1975 [86] based on spectral analysis of EEG data collected from two electrodes. In 1981, Rogowski et al. [87] investigated preictal periods using pole trajectories of an autoregressive model. Gotman et al. [88] investigated rates of interictal spiking as indicators of upcoming seizures.

3.2 Linear Methods

3.2.1 Statistical Measures

Among other measures Mormann et al. [89] investigated the statistical moment of the EEG amplitudes in order to detect the preictal state. Other linear measures like power have been used in [90] and signal variance has been used in [91] to predict seizure onset.

3.2.2 Hjorth Parameters

Hjorth parameters, namely, activity, mobility, and complexity, are time domain parameters useful for the quantitative evaluation of EEG [92]. The parameter of activity represents the variance of signal's amplitude, the mobility represents the square root of the ratio between the variances of the first derivative and the amplitude, and the complexity is derived as the ratio between the mobility of the first derivative of the EEG and the mobility of the EEG itself. Mormann et al. used Hjorth parameters among others as features for seizure prediction [89]. Mobility has been also used followed by SVM classification achieving better false positive rates (fpr) in comparison with plain spectral analysis [93].

3.2.3 Accumulated Energy

The accumulated energy is computed from the average energy across all values of the signal x of a window k

$$E_k = \frac{1}{N_w} \sum_{i=1}^{N_w} x_k{}^2(i),$$

where N_w is the window length.

Then, the average of ten values of average energies are added to the running accumulated energy.

$$\mathrm{AE}_m = \frac{1}{10} \sum_{k=10m-9}^{10m} E_k + \mathrm{AE}_{m-1},$$

where $m = 1,2,\ldots,N/N_w$ and $\mathrm{AE}_0 = 0$.

This measure can be considered as the running average of average window energies. Accumulated energy has been used in various studies of seizure prediction [94–96].

3.2.4 AR Modelling

In [97], a feature extraction and classification system was proposed based on Autoregressive Models, SVM and Kalman Filtering. Its performance regarding false positives rates per hour is quite promising with a mean prediction time ranging from 5 to 92 min.

3.3 Nonlinear Methods

Most of the nonlinear methods exploit the reconstruction of a time series $x(i)$, $i = 1, 2, \ldots, N$ in phase space domain forming the m - dimensional time delayed vectors

$$X_m(i) = \{x(i), x(i + 1 \cdot \tau), \ldots, x(i + (m - 1) \cdot \tau)\},$$

where m is the embedding dimension and τ is the time delay.

This reconstruction conveys important information about the nonlinear dynamics of a signal and it is used to many methods some of them described below.

3.3.1 Lyapunov Exponent

The calculation method of Lyapunov exponents was analyzed in the previous section of this chapter. Iasemidis et al. [98–100] applied for the first time nonlinear analysis to seizure prediction. The idea behind this approach is that the transition from normal to epileptic EEG is reflected by a transition from chaotic to a more ordered state, and therefore, the spatiotemporal dynamical properties of the epileptic brain are different for different clinical states.

3.3.2 Dynamical Similarity Index

Dynamical similarity index is a method introduced in [101] which calculates brain state dynamics through phase state reconstruction and compares a running window state against a reference window with the use of the cross correlation integral. Various studies using this index have shown promising results even in the detection of preictal states of temporal lobe epilepsy [102, 103] and neocortical partial epilepsy [104].

3.3.3 Correlation Dimension

In order to calculate the correlation dimension, the correlation integral defined by Grassberger and Procaccia [105] is needed

$$C_m(\varepsilon, N_m) = \frac{2}{N_m(N_m - 1)} \sum_{i=1}^{N_m} \sum_{j=i+1}^{N_m} \Theta\left(\varepsilon - \left\|x_i - x_j\right\|\right),$$

$$N_m = N - (m - 1) \cdot \tau,$$

where Θ is the Heaviside function. This integral counts the pairs (x_i, x_j) whose distance is smaller than ε. Then, the correlation dimension D is defined by

$$D = \lim_{\substack{\varepsilon \to 0 \\ N \to \infty}} \frac{\partial \ln C_m(\varepsilon, N_m)}{\partial \ln \varepsilon}$$

In preictal states, drops in correlation dimension were observed making this measure able to identify states preceding seizures [95, 106, 107].

3.3.4 Entropies

Zandi et al. [108] used entropic measure of positive zero-crossing intervals achieving 0.28 false positive rate and average prediction time 25 min.

Kolmogorov entropy (KE) is a nonlinear measure of the rate at which information about the state of a system is lost [109] and defined as

$$\mathrm{KE} = \lim_{\substack{\varepsilon \to 0 \\ m \to \infty}} \frac{1}{\tau} \ln \frac{C_m(\varepsilon, N_m)}{C_{m+1}(\varepsilon, N_m)}$$

where C_m, C_{m+1} are the correlation integrals of embedding dimensions m, $m + 1$, respectively and τ the time delay.

In time-varying EEG signal the temporal evolution of KE is required. Time series can be divided in N_w windows, and the mean KE [110] can be calculated as

$$\mathrm{KE} = \frac{1}{N_w} \sum_{k=1}^{N_w} \mathrm{KE}(k)$$

Higher positive values of KE suggest a chaotic behavior of the system, whereas lower values suggest a more ordered system. KE has been applied to seizure anticipation in infant epilepsy [90].

3.3.5 Phase Synchronization

Phase synchronization is a nonlinear bivariate measure that has been applied widely in the field of seizure prediction. It is represented through mean phase coherence

$$R = \left| \frac{1}{N} \sum_{k=1}^{N} \mathrm{e}^{i[\varphi_a(t_k) - \varphi_b(t_k)]} \right|$$

In [111, 112] a detection of preictal state based on phase synchronization decrease is presented. This decrease can be attributed to interactions between channels that are located to epileptogenic focus (pathological synchronization) and others located out of seizure focus [113, 114].

4 Combination of Methods and Feature Selection

Detection methods can produce one or more features which are representative measures describing information needed to each problem establishment. Different features can reveal different

aspects of information a signal contains. Due to this, different features can achieve high sensitivity, some others high specificity and vice versa.

A combination of methods is necessary in order to exploit most of available information. In this case, an efficient feature selection procedure is required in order to highlight the most robust features capable to produce best results. It is reported that when using SVM as a classifier, which is considered an efficient classifier, the selected features affect the performance more than the used classifier itself [115]. Towards the same direction, omitting good features may be more detrimental for SVMs than including bad ones [116].

A study of EEG-based neonatal seizures [117] used total 55 features derived from time domain, frequency domain and information theory achieving remarkable results (good detection rate (GDR): 89 % at 1 false detection per hour (FD/h)).

In a recent study [79], nonlinear features and features derived from information theory were evaluated in surface EEG recordings. Signals were recorded from 8 epileptic patients whose seizures identified and classified by a neurologist expert as absence like seizures. The recordings were collected from 21 scalp loci of the international 10–20 system with all electrodes referenced to the earlobe. An electrode placed in the middle of the distance between Fp1 and Fp2 on the subject's forehead served as ground. For this study, 75 seizures were selected within artifact free EEG time series (without eye blinks, spikes, head movements, chewing, general discharges), as other related studies [3] indicate. Figure 2 shows an example of that study including ApEn, Order Index, and Multiscale Variance Index (MVI).

An important factor in the effectiveness of methods is the proper determination of their intrinsic parameters. In a recent study [68], a preliminary analysis of parameters used on ApEn was performed in order to ensure an improved detection rate and accuracy.

5 Decision Making and Classification

After the feature extraction, seizure detection/prediction can be evaluated using either threshold based methods or trained classifiers. The stage of thresholding can be optional or the usage of classifiers should be applied instead.

5.1 Threshold Based Analysis

Threshold based analysis focus on the determination of thresholds that can categorize feature values to ictal or non-ictal states. This can be the statistical evaluation of the variability of features' values according to the desired significance level. The most common approach is the threshold to be determined as a product of a constant and the standard deviation of the feature space distribution. The three sigma rule [118] for any unimodal probability

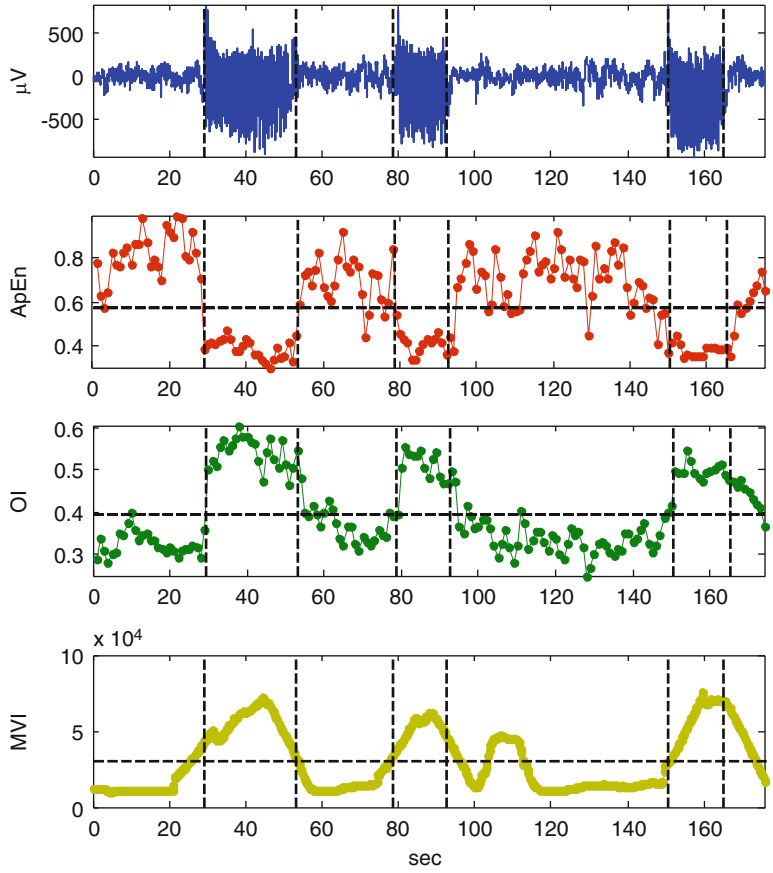

Fig. 2 EEG recording containing and the corresponding variation of approximate entropy (ApEn), Order Index (OI), and Multiscale Variance Index (MVI). The *vertical dashed lines* denote the start and end of a seizure, while the *horizontal dashed line* represents the detection threshold

density is a rule of thumb that has been applied to many problems of threshold determination. A more complex determination of threshold could be achieved using Chebyshev inequality [68].

$$P\{|\text{feature} - \mu| \geq k\sigma\} \leq \frac{1}{k^2},$$

where μ, σ are the mean value, standard deviation of the selected feature distribution and k the chosen statistical threshold.

5.2 Usage of Classifiers

Various classifiers have been employed in order to categorize data and features into classes and make conclusions about the methods performance. Classifiers like Expert Systems [118], Decision trees [119], Artificial Neural Networks (ANN) [17, 18, 30, 32, 120–122], and Support Vector Machines (SVM) [123] have been employed in order to increase a method's detection accuracy.

Although some authors [80] believe that using a classifier is not suitable for patient-independent seizure detection, they have been widely used in distinguishing between ictal and non-ictal periods.

6 Epilepsy Datasets

Some public available databases with seizure data have been used as benchmark for various studies. The most known are the Freiburg EEG database [124] contains invasive EEG recordings of 21 patients suffering from medically intractable focal epilepsy, the EPILEPSIAE database [125] that contains recordings during an invasive presurgical epilepsy monitoring at the Epilepsy Center of the University Hospital of Freiburg and the Bonn EEG database [126].

7 Performance

Performance measures in seizure detection mostly are extracted from contingency tables depicting frequencies of detected and not detected seizures by a proposed algorithm against actual and false seizures (*see* Table 1).

The most used measures include *sensitivity*, *specificity*, *accuracy*, and *precision*.

$$\text{Sensitivity} = \frac{\text{Number of correctly detected seizures}}{\text{Total number of algorithm positive outcomes}} = \frac{\text{TP}}{\text{TP} + \text{FN}}$$

$$\text{Specificity} = \frac{\text{Number of correctly normal states}}{\text{Total number of algorithm negative outcomes}} = \frac{\text{TN}}{\text{TN} + \text{FP}}$$

Table 1
Contingency table used in order to evaluate performance of a detection algorithm against experiment outcome

		Detection algorithm		
		Seizure	**No seizure (control)**	**Total**
Experiment outcome	Positive (P)	TP	FP	nP = TP + FP
	Negative (N)	FN	TN	nN = FN + TN
Total		nS = TP + FN	nNS = FP + TN	N

TP represents true positives, FP represents false positives, FN represents false negatives, and TN represents true negatives

$$\text{Accuracy} = \frac{\text{Number of correctly detected seizures} + \text{correctly normal states}}{\text{Total number of cases}} = \frac{\text{TP} + \text{TN}}{\text{TP} + \text{FP} + \text{FN} + \text{TN}}$$

$$\text{Precision} = \frac{\text{Number of correctly detected seizures}}{\text{Total number of seizures}} = \frac{\text{TP}}{\text{TP} + \text{FP}}$$

In addition, there are also positive predictive value (PPV) and negative predictive value (NPV) defined as

$$\text{PPV} = \frac{\text{Number of correctly detected seizures}}{\text{Total number of detected incidents}} = \frac{\text{TP}}{\text{TP} + \text{FP}}$$

$$\text{NPV} = \frac{\text{Number of correctly detected normal states}}{\text{Total number of normal states}} = \frac{\text{TN}}{\text{TN} + \text{FN}}$$

which address the probability of a detected seizure to be an actual seizure and the probability of a detected normal state EEG to be actual normal state EEG, respectively.

Finally, tests can be evaluated by the likelihood ratio which is the probability a segment characterized as ictal classified as ictal divided by the probability a segment characterized as ictal classified as not ictal. This indicates how much likely it is a segment which tests positive is ictal compared with one who tests negative.

$$\text{Likelihood ratio} = \frac{\text{Sensitivity}}{1 - \text{Specificity}}$$

7.1 Detection Performance of Algorithms

It is understood that datasets from different sources can significantly affect a method's behavior and accuracy depending on seizure type, level of noise, patient movements, etc. Although many researchers use their own datasets, however, a public available EEG dataset [126] consisting of signals from five different states: (a) normal EEG with eyes open, (b) EEG with eyes closed, (c) EEG from interictal period (seizure free) within the epileptogenic zone, (d) EEG of interictal period from the hippocampal formation of the opposite hemisphere of the brain, (e) EEG of seizure activity, was created and used as benchmark for many researchers that evaluated their methods. The best achieved detection accuracies of these methods using this dataset are presented in Table 2.

Other studies using their own datasets have also evaluated their methods by means of detection accuracy and they are presented in Table 3.

As these datasets are heterogeneous referring to different seizure types, no safe conclusion for their comparative accuracy can be performed.

Table 2
Seizure detection accuracies for selected studies using data described in [126]

Authors	Year	Method	Dataset	Best achieved accuracy rate (%)
Gautama et al. [127]	2003	Delay vector variance	Bonn EEG database [126]	86.2
VP Nigam, D Graupe [128]	2004	Nonlinear filtering	Bonn EEG database [126]	97.2
I. Güler, E.D. Ubeyli [129]	2005	Wavelet coefficient metrics	Bonn EEG database [126]	98.68
Srinivasan et al. [120]	2005	Time and frequency features, ANN	Bonn EEG database [126]	99.6
Güler et al. [30]	2005	Lyapunov exponent, Recurrent neural networks	Bonn EEG database [126]	96.79
Kannathal et al. [32]	2005	Entropy measures, ANFIS classifier	Bonn EEG database [126]	92.22
Güler and Übeyli [130]	2006	PSD features, modified mixture of experts	Bonn EEG database [126]	98.6
Srinivasan et al. [64]	2007	ApEn, Elman network	Bonn EEG database [126]	100
Polat and Güneş [119]	2007	PSD, decision trees	Bonn EEG database [126]	98.72
Subasi [131]	2007	Wavelet coefficients metrics, mixture of experts	Bonn EEG database [126]	94.5
Tzallas et al. [17]	2007	Time–frequency analysis, ANN	Bonn EEG database [126]	96.3 (average accuracy)
Ghosh-Dastidar et al. [121]	2007	Wavelet-chaos, neural network	Bonn EEG database [126]	96.7
Polat and Güneş [132]	2008	PCA-FFT, AIRS classifier	Bonn EEG database [126]	100
Ghosh-Dastidar et al. [133]	2008	PCA, TBFNN	Bonn EEG database [126] (subset)	96.6
Ocak [65]	2009	Wavelet transform, ApEn	Bonn EEG database [126]	94.85
Tzallas et al. [18]	2009	Time–frequency analysis, ANN	Bonn EEG database [126]	100
Chandaka et al. [123]	2009	Cross-correlation, support vector machines	Bonn EEG database [126]	95.96

(continued)

Table 2
(continued)

Authors	Year	Method	Dataset	Best achieved accuracy rate (%)
Altunay et al. [11]	2010	Linear prediction filter	Bonn EEG database [126]	93.33
Guo et al. [134]	2010	Discrete wavelet transform, line length feature, MLPNN	Bonn EEG database [126]	97.77
Kumar et al. [33]	2010	Entropy measures, Recurrent Elman network (REN)	Bonn EEG database [126]	99.75
Übeyli [122]	2010	Lyapunov exponents, probabilistic neural networks	Bonn EEG database [126]	98.05
Fathima et al. [12]	2011	Discrete wavelet transform	Bonn EEG database [126]	99.5
Guo et al. [135]	2011	Genetic programming features, K-nearest neighbor classifier	Bonn EEG database [126]	99.2
Martis et al. [136]	2012	EMD features	Bonn EEG database [126]	95.33

Table 3
Seizure detection accuracies for selected studies using their own datasets

Authors	Year	Seizure type	Method	Dataset	Best achieved accuracy rate (%)
Liu et al. [10]	1992	Neonatal seizures	Scored autocorrelation Moment	EEG segments (58 with seizures, 59 without seizures)	91.4
Alkan et al. [137]	2005	Absence seizures (petit mal)	MUSIC, autoregressive Spectrum, MPLNN	EEG of 11 subjects (6 normal, 5 epileptic) with 20 absence seizures (petit mal) total	92
Greene et al. [138]	2007	Neonatal seizures	Combination of EEG and ECG features, LD classifier	10 neonates, 633 seizures	86.32
Vukkadala et al. [139]	2009	No specific type	Approximate entropy, Elman neural network	Intracranial EEG of 21 subjects (12 normal, 9 epileptic) containing 30 ictal and 30 non-ictal periods	93.33

(continued)

Table 3
(continued)

Authors	Year	Seizure type	Method	Dataset	Best achieved accuracy rate (%)
Yuan et al. [13]	2012	Intractable focal seizures	Linear/nonlinear features, extreme learning machine	21 patients EEG data (81 seizures)	94.9
Zhou et al. [140]	2013	Intractable focal seizures	Lacunarity, Bayesian LDA	21 patients EEG data (81 seizures)	96.67

7.2 Prediction Performance of Algorithms

In order to evaluate the predictability and the performance of different methods, a framework called the seizure prediction characteristic [5, 141] was introduced. According to this, in a seizure prediction scheme four parameters should be taken into account: the seizure occurrence period (SOP) which is the time period during which the seizure is to be expected, the seizure prediction horizon (SPH) which is a minimum window of time between the alarm raised by the prediction method and the beginning of SOP, the false prediction rate (FPR) which is the number of false predictions per time interval and the sensitivity which is the fraction of correctly predicted seizures within total seizures. These characteristics can evaluate the effectiveness of a prediction scheme.

8 Discussion

This chapter reviews and presents a comparative presentation of the state-of-the-art methods in the area of seizure detection and prediction. Most methods are EEG-based as EEG is by far the most widely used tool for seizure detection and prediction. Besides that, the area of vision-based detection and its combination with biosignal analysis is also briefly presented as a very promising tool in clinical and research practice.

Each method presents its advantages and limitations achieving its maximum effect regarding the application and seizure type. In many cases seizure characteristics are notably varying even among different seizures of the same patient and this phenomenon is more common in small ages [144]. Therefore, a combination of these methods is, in many cases, substantial exploiting the advantages of each one maximizing the effectiveness.

An objective comparative assessment would be ideal in order to be able to choose the optimal methods for specific applications. However, in the related literature, it is difficult to define such a framework because of different datasets used in different studies. Seizure types, sample size, dataset precision (number of electrodes, sampling frequency, etc.) and adopted experiment setup are the main factors that prevent objectivity in methods' evaluation. In addition, as there are no standard guidelines with reliable standardized data, most studies apply their methods on small datasets or the collection of data is driven exclusively by their application. Hence, they often demonstrate good accuracy for selected EEG segments but it is not safe to make a generalized assumption about their performance.

Despite the intrinsic difficulties, this review aims to introduce and foster the understanding of available methods in the area of seizure detection and prediction. Its contribution is towards the construction of a consistent framework for the area of epilepsy detection/prediction that can balance computational complexity and accuracy.

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