Expert Systems with Applications 39 (2012) 202–209

Contents lists available at ScienceDirect

Expert Systems with Applications

journal homepage: www.elsevier.com/locate/eswa

Detection of epileptic electroencephalogram based on Permutation Entropy and Support Vector Machines

Nicoletta Nicolaou *, Julius Georgiou

KIOS Research Centre and Holistic Electronics Research Lab, Department of Electrical and Computer Engineering, University of Cyprus, Kallipoleos 75, 1678 Nicosia, Cyprus

ARTICLE INFO

Keywords:
Electroencephalogram (EEG)
Permutation Entropy (PE)
Support Vector Machine (SVM)
Epilepsy
Seizure

ABSTRACT

The electroencephalogram (EEG) has proven a valuable tool in the study and detection of epilepsy. This paper investigates for the first time the use of Permutation Entropy (PE) as a feature for automated epileptic seizure detection. A Support Vector Machine (SVM) is used to classify segments of normal and epileptic EEG based on PE values. The proposed system utilizes the fact that the EEG during epileptic seizures is characterized by lower PE than normal EEG. It is shown that average sensitivity of 94.38% and average specificity of 93.23% is obtained by using PE as a feature to characterize epileptic and seizure-free EEG, while 100% sensitivity and specificity were also obtained in single-trial classifications.

1. Introduction

The electroencephalogram (EEG) has proved to be a valuable tool in the study of conditions whose effects are manifest in the electrical brain activity. Epilepsy is one such condition, characterized by the occurrence of spatially well-localized or widespread transient recurrent seizures (synchronous neuronal activity) visible in the EEG (Lehnertz, 2008). Approximately 1% of the world population suffers from epilepsy, constituting the condition as one of the most common neurological disorders (Duncan, Sander, Sisodiya, & Walker, 2006). Due to the difficulty in predicting the onset of seizures, the study of epilepsy involves the continuous recording of the EEG over long periods of a few days. As a result, a large number of data must then be visually analyzed by an expert such that activity related to epilepsy can be detected. Visual analysis of such signals is not a highly subjective procedure, as a recent study of 4 human experts demonstrated that 92% inter-expert sensitivity was achieved (Wilson, Scheuer, Plummer, Young, & Pacia, 2003). However, over the years many attempts have been made to develop automated epileptic seizure detection systems in order to assist the experts in this time-consuming and tedious process. Different approaches have been taken in these systems with varying degrees of success. Features from both the time and frequency domain, such as raw EEG amplitude (Pradhan, Sadasivan, & Arunodaya, 1996), power spectrum (Kiymik, Subasi, & Ozcalik, 2004), wavelet analysis (Subasi, 2005), and relative spike amplitude and rhythmicity (Srinivasan, Eswaran, & Sriraam, 2005), have been utilized as inputs to the automated seizure detection systems; both linear and non-linear features have been investigated (McSharry, He, Smith, & Tarassenko, 2002; Mormann et al., 2003; Nigam & Graupe, 2004; Päivinen et al., 2005; van Putten, 2003; Wilson, Scheuer, Emerson, & Gabor, 2004). Different methods have also been used in the core of the systems for classification of the EEG segments, such as discriminant analysis (Murro et al., 1991), nearest neighbor classifier (Qu & Gotman, 1997), learning vector quantization (Pradhan et al., 1996), and neural networks (Gabor, Leach, & Dowla, 1996; Webber, Lesser, Richardson, & Wilson, 1996).

More recently, various entropy measures have been used to characterize normal and epileptic activity (Kannathal, Choo, Acharya, & Sadasivan, 2005; Quian Quiroga, Arnhold, Lehnertz, & Grassberger, 2000; van Drongelen et al., 2003). It was consistently observed that entropies of epileptic EEG segments are lower than those of normal EEG segments (Kannathal et al., 2005). Since entropy indicates the degree of disorder in a system, lowering of entropy values during epileptic seizures shows a reduction in intra-cortical information flow and supports evidence that epileptic seizures are emergent synchronous states whose dimensionality is reduced compared to non-epileptic activity (Lehnertz & Elger, 1988). Permutation Entropy (PE) is a recently introduced complexity measure that can be used for any type of time series (Bandt & Pompe, 2002). Its calculation is based on mapping the time series onto a symbolic sequence in order to quantify the relative occurrence of the different symbols. PE is becoming an increasingly valuable tool for analysis of EEG activity (see, for example Li, Cui, & Voss, 2008). Recently PE has also been used to characterize epileptic activity, where it was found that PE tracks the dynamics of the brain activity well (Bruzzo et al., 2008; Cao, Tung, Gao, Protopopescu, & Hively, 2004). The use of PE as a feature for automated

* Corresponding author. Tel.: +357 22893801; fax: +357 22893815.
E-mail address: nicoletta.n@ucy.ac.cy (N. Nicolaou).

0957-4174/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.eswa.2011.07.008

seizure prediction has not been investigated so far, and this is the main focus of this work. In the remainder of the paper PE is introduced as the input feature for automated seizure detection using a Support Vector Machine (SVM) and applied on segments of normal and epileptic EEG activity.

2. Methods

2.1. Dataset

The dataset contains five sets (A–E) of EEG recordings from healthy and epileptic subjects (Andrzejak et al., 2001) and is available online (''Klinik für Epileptologie, Universität Bonn''). Each set contains 100 single-channel segments of 23.6 s duration from continuous EEG recordings, which were cut out after visual selection for artifacts. Hence, each segment is free of artifacts and fulfills a stationarity criterion. The first set of EEG data (A and B) contains surface EEG recordings from 5 healthy volunteers. The data was obtained while the volunteers were awake and relaxed with eyes open (A) and eyes closed (B). The second set of EEG data (C–E) contains intracranial recordings from depth and strip electrodes implanted within the epileptogenic zones from five epileptic patients (depth electrodes were implanted symmetrically in the hippocampal formations, strip electrodes were implanted onto the lateral and basal regions of the neocortex). Sets C and D contain activity measured only during seizure-free intervals from the depth electrodes, while set E contains only seizure activity from all electrode locations. All EEG signals are recorded at a sampling rate of 173.61 Hz using a 128-channel amplifier system with an average common reference, and are band-pass filtered at 0.53–40 Hz. Fig. 1 shows examples of signals from the five sets available in the dataset, and Fig. 2 shows their corresponding spectra.

2.2. Permutation Entropy

The PE is a complexity measure for time series based on comparing neighboring values and was introduced by Bandt and Pompe (2002). The continuous time series is mapped onto a symbolic sequence which describes the relationship between present values and a fixed number of equidistant values at a given past time. This mapping is achieved by, first, embedding the time series, $x(t)$, $t = 1, 2, \ldots$, into an m-dimensional space,

$$X(t) = [x(t), x(t+\tau), \ldots, x(t+m\tau)] \quad (1)$$

where m is the embedding dimension (the number of samples included in each motif) and τ is the time lag (the number of samples spanned by each section of the motif). For a given embedding dimension there will be $m!$ possible permutations (motifs). If each permutation is considered as a symbol, the embedded time vectors $X(t)$ can be represented by a symbol sequence, j, each having probability distribution p_j. Thus, based on the Shannon entropy definition the normalized PE, H_p, of a given time series, $x(t)$, is defined as:

$$H_p(m) = -\frac{1}{\ln(m!)} \sum_{j=1}^{J} p_j \ln(p_j) \quad (2)$$

where J is the distinct number of symbols for a given embedding dimension ($J \leqslant m!$). The factor $\frac{1}{\ln(m!)}$ is a normalization factor such that $0 \leqslant H_p / \ln(m!) \leqslant 1$. PE measures the departure of the time series from a complete random one: the smaller the value of the PE, the more regular the time series. The upper bound, $H_p = \ln(m!)$ is attained when all of the possible $m!$ permutations appear in the time series with the same probability, something which is more likely to be observed when the EEG signal is dominated by high frequencies. This implies that H_p increases with the irregularity of the time series. At slower frequencies the permutations corresponding to peaks and troughs are observed less frequently, i.e. the EEG is more regular, hence the permutations appear with different probabilities, which decreases the PE of the signal. With regards to the embedding dimension, m, if this is too large then it becomes difficult to detect changes in the time series. However, if this is too small, then there are very few distinct states (symbols) and the scheme will not work. For EEG signals values of $m = 3, \ldots, 7$ have been recommended (Bandt & Pompe, 2002). For the time lag, it is adequate to use a value of $\tau = 1$ to extract most of the information in the EEG (Bruzzo et al., 2008; Olofsen, Sleigh, & Dahan, 2008), hence this value is commonly chosen in EEG analysis.

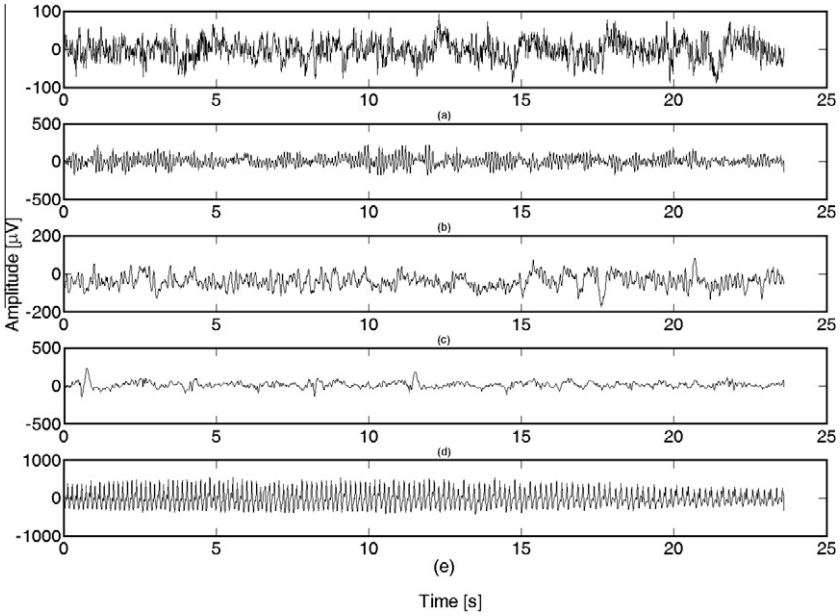

Fig. 1. Example 23.6 s EEG data from the five available datasets. (a) Set A – scalp EEG from awake healthy subject with eyes open; (b) set B – scalp EEG from awake healthy subject with eyes closed; (c) and (d) sets C and D respectively – intracranial depth EEG from epileptic subjects during no seizure; (e) set E – intracranial EEG from depth and strip electrodes from epileptic subjects during seizures. Note the different y-axis scales.

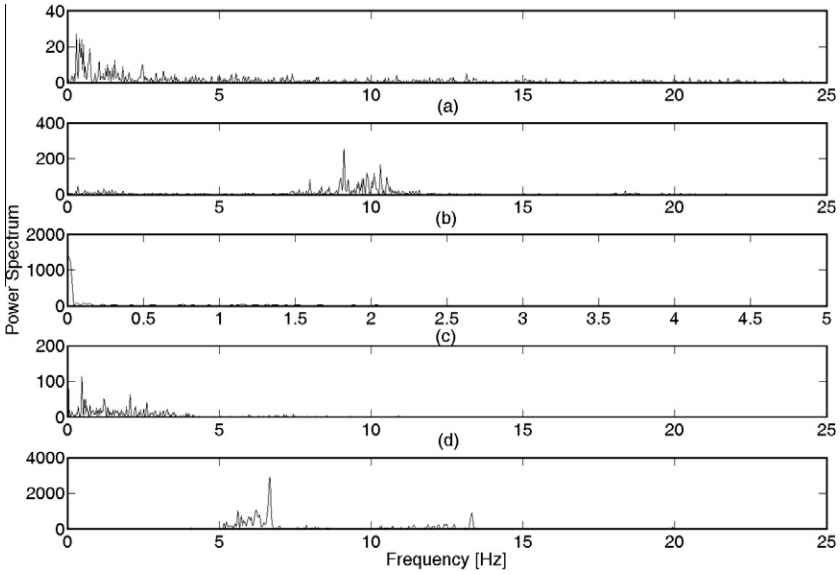

Fig. 2. Power spectrum of signals shown in Fig. 1. (a)–(e): Datasets A–E respectively. Spectra are shown for frequencies up to 25 Hz as higher frequencies displayed little, if any, power (signals contained in the dataset are band-pass filtered to 40 Hz). Note the different frequency axis scale for dataset C.

2.3. Support Vector Machines

SVMs belong to the family of kernel-based classifiers and are very powerful classifiers as they can perform both linear and non-linear classification simply by changing the "kernel" function utilized (Burges, 1998). The main concept of SVMs is to implicitly map the data into the feature space where a hyperplane (decision boundary) separating the classes may exist. This implicit mapping is achieved via the use of Kernels, which are functions that return the scalar product in the feature space by performing calculations in the data space. The simplest case is a linear SVM trained to classify linearly separable data. After re-normalization, the training data, $\{x_i, y_i\}$ for $i = 1, \ldots, m$ and $y_i \in \{-1, 1\}$, must satisfy the constraints

$$\mathbf{x}_i\mathbf{w} + b \geqslant +1 \text{ for } y_i = +1 \quad (3)$$

$$\mathbf{x}_i\mathbf{w} + b \leqslant -1 \text{ for } y_i = -1 \quad (4)$$

where $\boldsymbol{w}$ is a vector containing the hyperplane parameters and b is an offset. The points for which the equalities in the above equations hold have the smallest distance to the decision boundary and they are called the support vectors. The distance between the two parallel hyperplanes on which the support vectors for the respective classes lie is called the *margin*. Thus, the SVM finds a decision boundary that maximizes the margin. Finding the decision boundary then becomes a constrained optimization problem amounting to minimization of $\|w\|^2$ subject to the constraints in (3) and (4) and is solved using Lagrange optimization framework. The general solution is given by

$$f(x) = \sum_i a_i y_i \langle x_i, x \rangle \quad (5)$$

In the case of non-linear classification, Kernels (functions of varying shapes, e.g. polynomial or Radial Basis Function) are used to map the data into a higher dimensional feature space in which a linear separating hyperplane could be found. The general solution is then of the form:

$$f(x) = \sum_i a_i y_i K \langle x_i, x \rangle \quad (6)$$

Depending on the choice of the Kernel function SVMs can provide both linear and non-linear classification, hence a direct comparison between the two can be made without having to resort to utilization of different classifiers.

2.4. Performance Evaluation

Each of the 5 datasets contains 100 single-channel EEG segments of 23.6 s duration. Each 23.6 s-segment is split in non-overlapping windows of 1 s length, for which the PE is estimated, thus resulting into a total of 2300 PE values for each dataset. The PE is estimated for embedding dimensions $m = 3, 4$. Classification of epileptic activity (set E) is then performed against activity from healthy subjects (sets A and B) and seizure-free activity from epileptic subjects (sets C and D), i.e. 4 different 2-class classification problems were formed. Both linear and non-linear classification is investigated using a SVM. The performance is assessed for different training set sizes ($numtr = 10, 20, 40, 80, 100$). The number of test sets used in each case was 40% of the training size, i.e. $numtst = 4$, 8, 16, 32, and 40 respectively.

The performance is evaluated using the sensitivity, specificity, and overall accuracy, averaged over $B = 100$ bootstrap repetitions. In each bootstrap repetition (single-trial) the training and test sets were selected randomly out of all available features. Features used for training were not used for testing. Sensitivity, SE, is defined as the total number of true positives, TP, (correctly classified seizures) as a percentage of the total number of actual positive patterns, TN_p:

$$SE = \frac{1}{B}\sum_{b=1}^{B}\frac{TP}{TN_p} * 100\% \quad (7)$$

Specificity, *SP*, is defined as the total number of true negatives, *TN*, (correctly classified non-seizures) as a percentage of the total number of actual true negative patterns, TN_n:

$$SP = \frac{1}{B}\sum_{b=1}^{B}\frac{TP}{TN_n} * 100\% \quad (8)$$

The overall accuracy, *Acc*, is estimated as the average of *SE* and *SP*:

$$Acc = \frac{1}{2}(SE + SP) \quad (9)$$

3. Results

Fig. 3 shows the corresponding estimated PE values ($m = 4$) for the entire 23.6 s EEG segments depicted in Fig. 1 (for $m = 3$ similar

patterns are obtained). Seizure segments display the lowest PE out of all the available datasets, as also seen in Fig. 4.

In the classification of 1 s segments of seizure and non-seizure activity using the 1-dimensional PE features, a maximum average sensitivity of 94.38% (linear kernel, PE for $m = 3$) and maximum average specificity of 93.23% (linear kernel, PE for $m = 3$), 82.73% (RBF kernel, PE for $m = 3$), 91.25% (RBF kernel, PE for $m = 4$), and 87.53% (RBF kernel, PE for $m = 4$) were obtained for sets A-D respectively. Figs. 5 and 6 show the average sensitivity and specificity respectively, obtained for each dataset, as a function of training set size, for linear and non-linear kernels and for both embedding dimensions of PE. Fig. 7 shows the average accuracy obtained for each dataset, as a function of training set size, for linear and non-linear kernels and for both embedding dimensions of PE. For all parameter combinations, dataset A achieves the best sensitivity, specificity and accuracy, followed by dataset D, dataset C and dataset B.

The maximum overall classification obtained was 93.55%, 82.88%, 88.83%, and 83.13% for sets A–D respectively (Table 1). The former two were obtained with linear SVM and PE $m = 3$, while the latter two were obtained with non-linear SVM and PE $m = 3$. The best results were obtained mostly with training sample sizes of 80 and 100. The maximum overall accuracy pooled over all datasets was 86.10% (linear SVM, PE $m = 3$). Considering all classifications performed, the classification accuracy obtained was greater than 95% in 52.3% of all single-trial classifications.

4. Discussion

The Permutation Entropy (PE) is introduced as a feature for automated seizure detection using a Support Vector Machine (SVM). Even though some studies have been performed where PE is applied to epileptic EEG activity from rats (Li, Ouyang, & Richards, 2007) and humans (Bruzzo et al., 2008; Cao et al., 2004), the feasibility of PE as a feature for automated seizure detection has not been investigated so far. Our findings with regards to the estimated PE patterns are in agreement with these previous studies, where a decrease of the PE values during a seizure is observed. This implies that brain activity during a seizure has a more regular pattern than normal EEG activity as it is composed of repetitive activity with similar patterns.

Using the PE as a feature for automated seizure detection, the best average discrimination of 93.55% is obtained for seizure activity (dataset E) versus activity obtained from awake healthy volunteers with eyes open (dataset A). The average accuracy for seizure (dataset E) versus non-seizure activity pooled for all datasets (dataset A–D) is 86.10%. Both are obtained with a linear classifier and PE for $m = 3$. This supports the findings that using a low embedding dimension for the estimation of PE is appropriate for EEG signals, and PE features are linearly separable, thus decreasing the computational complexity of the classifier. In addition, considering all classifications performed, the classification accuracy obtained was greater than 95% in 52.3% of all single-trial classifications. Thus, the characteristics of the training set are very important in achieving high accuracy.

For all parameter combinations, dataset A achieves the best sensitivity, specificity and accuracy, followed by datasets D, C and B. This is expected considering the spread of PE values estimated for each dataset (Fig. 3). The largest overlap of the estimated PE values is observed for datasets E (seizure activity) and B (non-epileptic activity with eyes closed), thus making the classification between them a more difficult problem. The overlap observed is due to the fact that dataset B has lower PE values compared to those estimated for the other non-seizure datasets (A, C and D). This is due to the fact that the EEG activity in dataset B was obtained from awake volunteers with eyes closed. Closing one's eyes results into the appearance of more regular and slower (10 Hz) α rhythms. Thus, the presence of these regular rhythms decreases the PE values with a direct result of increasing the overlap between the two types of signals. The order of best results obtained here is also supported by previous work on the same data, whereby only datasets A, D and E were used as performance degraded when more detailed classification between all datasets was performed (Güler, Übeyli, & Güler, 2005; Übeyli, 2009).

The same dataset has been analyzed in a number of previous studies, with single-trial classification accuracies ranging from

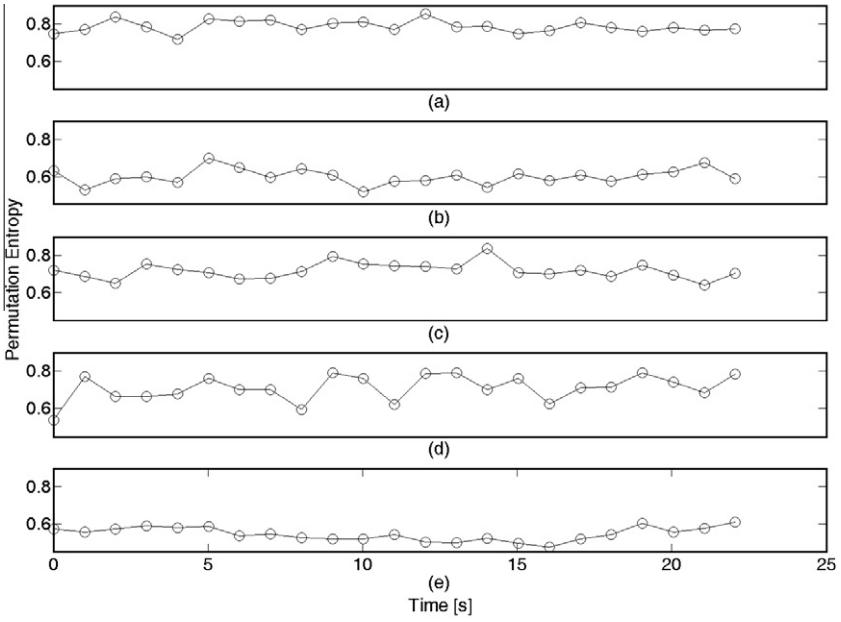

Fig. 3. Permutation Entropy (for $m = 4$) estimated for 1 s non-overlapping segments of the data depicted in Fig. 1. Each PE value corresponds to the PE value of the 1 s segment starting at the time point indicated by the PE value. The PE for the segment corresponding to the seizure (e) is much lower and non-overlapping with the PE values corresponding to seizure-free segments from both healthy (a)–(b) and epileptic (c)–(d) volunteers.

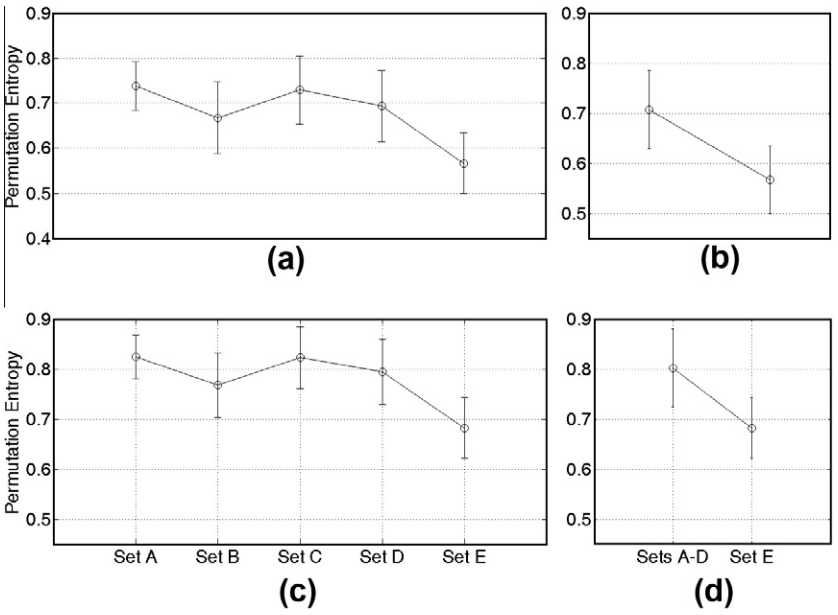

Fig. 4. Average PE values for the five datasets, plotted as (mean PE value) ± (standard deviation). Top: $m = 4$, bottom: $m = 3$. Plots (a) and (c) show the average PE values for each dataset separately. In (b) and (d) the PE values for sets A–D have been pooled together. Seizure segments display the lowest PE value. In general, similar shapes are obtained in both cases, with the actual PE values being higher for $m = 3$. For $m = 4$ there is less overlap of the PE values for seizure and seizure-free segments.

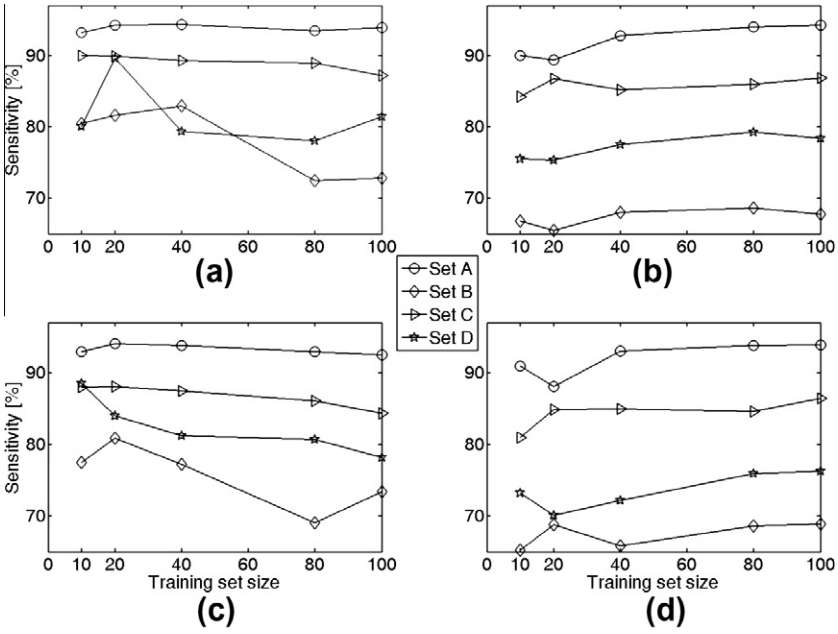

Fig. 5. Average sensitivity, as a function of training set size, estimated for PE with $m = 3$ (top) and $m = 4$ (bottom). (a) and (c): Linear SVM; (b) and (d): non-linear SVM (RBF). In general, increasing the size of the training set improves the sensitivity obtained, except for the linear SVM where for some datasets the sensitivity is decreased for larger training sets.

92.2% to 100% (Kumar, Sriraam, Benakop, & Jinaga, 2010; Polat & Güneş, 2008; Srinivasan, Eswaran, & Sriraam, 2007; Subasi, 2005; Tzallas, Tsipouras, & Fotiadis, 2007; Übeyli, 2009). The use of PE as a feature for epilepsy detection has a number of important advantages over other methods proposed so far, despite some differences in classification obtained in some cases. Firstly, PE is a feature with only 1 dimension which is simple and quick to estimate. Secondly, using PE most datasets can be separated using linear classification. These two factors decrease the computational complexity of the problem. Thirdly, PE has been estimated for 1-s segments of EEG. All these factors constitute the proposed method highly appropriate for online and real-time analysis.

In addition, the use of PE appears to have another important advantage. It is commonly believed that PE analysis provides the same information as frequency analysis of the signals. In some cases PE and frequency analysis will give similar information, e.g. a signal which contains higher frequencies usually displays larger PE. If we now consider the activity studied here, it can be seen from Fig. 2 that the frequency content of seizure activity (dataset E) includes higher frequencies than non-seizure activity, whereas data-

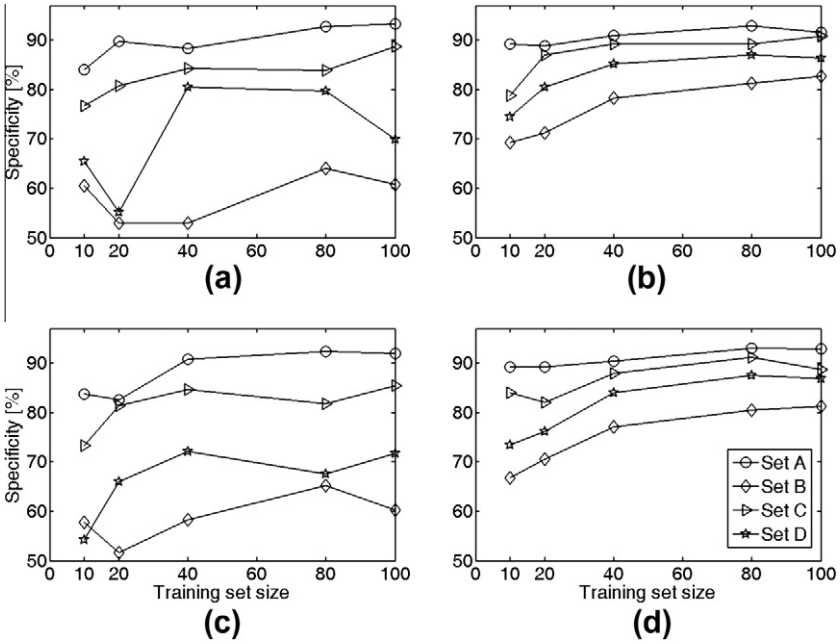

Fig. 6. Average specificity, as a function of training set size, estimated for PE with $m = 3$ (top) and $m = 4$ (bottom). (a) and (c): Linear SVM; (b) and (d): non-linear SVM (RBF). In general, increasing the size of the training set improves the specificity obtained.

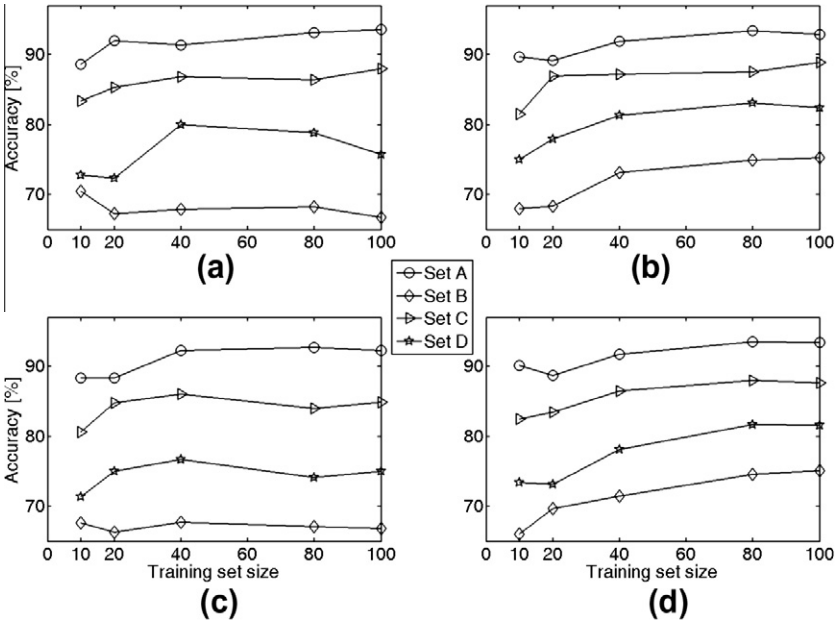

Fig. 7. Overall accuracy, as a function of training set size, estimated for PE with $m = 3$ (top) and $m = 4$ (bottom). (a) and (c): Linear SVM; (b) and (d): non-linear SVM (RBF). In general, increasing the size of the training set improves the classification accuracy obtained.

Table 1
Overall classification accuracy of dataset E versus datasets A, B, C and D, for linear and nonlinear SVM (RBF), and PE for $m = 3$ and $m = 4$.

Datasets	Linear		RBF	
	$m = 3$	$m = 4$	$m = 3$	$m = 4$
A	93.55	90.13	93.42	93.45
B	82.88	72.29	75.25	75.09
C	88.00	84.14	88.83	87.94
D	79.94	77.03	83.13	81.7
Over all	86.10	80.90	85.16	84.55

set C contains activity concentrated around a few Hz only. If PE carries the same information as the frequency content of the signal, then based on the spectra observed in Fig. 2, the highest PE values should be obtained for dataset A, followed by datasets E, B, D and C. This is not the case, as the estimated PE values, in descending order, are dataset A, C, D, B and E (Fig. 3). Thus, it is not the actual frequency content of a signal that affects the PE, but how concentrated the power spectrum is. Signals with a more widespread spectrum are more likely to display larger PE values than signals whose power spectrum is more concentrated at specific frequencies. The spread of the signal along the different frequencies causes

more irregularity in the signal, resulting into the appearance of more motifs and, thus, increased PE. Thus, utilizing PE information concerning both the frequency content and signal regularity is obtained simultaneously.

In the proposed method classification is achieved using a 1-dimensional input feature estimated from a single channel of EEG, resulting into a simple feature vector and a SVM with low computational complexity. It is expected that higher classification accuracy could perhaps be achieved using more than 1 EEG channel. Nonetheless, our findings support that it could be sufficient to perform single-channel EEG analysis for seizure prediction, as was also suggested by (Cao et al., 2004). In addition, the segments analyzed here are of 1 s duration. Using longer EEG segments could also result in higher classification accuracy. However, classification of such short EEG segments is important for online and real-time seizure detection. Higher accuracy was obtained using Approximate Entropy (ApEn) (Srinivasan et al., 2007), but the higher computational complexity of ApEn compared to the low computational complexity of PE puts PE in a more advantageous position as far as real-time detection is concerned. In addition, it is not clear whether the results presented in (Srinivasan et al., 2007) are averaged over a number of trials or whether they are obtained from a single training and test cycle.

An interesting consideration is whether PE could be used as a predictor of a seizure prior to its occurrence. Li et al. showed that PE values began to gradually decrease prior to seizure onset in rats with mean seizure anticipation time of 4.9 s (Li et al., 2007). Cao et al. analyzed human depth EEG and observed a sharp drop in the PE slightly after the seizure, often preceded by an abrupt increase in the magnitude either slightly before or slightly after the seizure, indicating that the occurrence of each seizure affects the brain dynamics such that it momentarily becomes very irregular prior to becoming more regular during the seizure (Cao et al., 2004). These findings support the fact that PE tracks the brain dynamics well and encourage further investigations to numerically assess whether PE could be used as part of a system for automated seizure prediction. The development of such systems could significantly improve the quality of life for epilepsy patients and advance therapeutic possibilities through replacement of continuous with on-demand therapy.

5. Conclusions

In this paper Permutation Entropy (PE) has been employed as a feature for automated seizure detection using a Support Vector Machine (SVM). The proposed method utilizes the observation that the PE drops during a seizure. The low computational complexity of PE constitutes it a highly favorable feature to be employed as part of a system for real-time automated seizure detection. Its feasibility as a feature in such a system is supported by the high sensitivity obtained for seizure detection. The findings are also encouraging to further investigate and assess whether PE could be utilized as a feature in an automated seizure prediction system.

Acknowledgement

This work falls under the Cyprus Research Promotion Foundation's Program for Research, Technological Development and Innovation 2008 (DESMI 2008), co-funded by the Republic of Cyprus and the European Regional Development Fund (Grant: DIDAKTOR/DISEK/0308/20).

References

Andrzejak, R. G., Lehnertz, K., Rieke, C., Mormann, F., David, P., & Elger, C. E. (2001). Indications of nonlinear deterministic and finite dimensional structures in time series of brain electrical activity: Dependence on recording region and brain state. *Physical Review E, 64*, 061907.

Bandt, C., & Pompe, B. (2002). Permutation entropy: A natural complexity measure for time series. *Physical Review Letters, 88*, 174102.

Bruzzo, A. A., Gesierich, B., Santi, M., Tassinari, C. A., Birbaumer, N., & Rubboli, G. (2008). Permutation entropy to detect vigilance changes and preictal states from scalp EEG in epileptic patients. A preliminary study. *Neurological Science, 29*, 3–9.

Burges, C. J. C. (1998). A tutorial on support vector machines for pattern recognition. In U. Fayyad (Ed.), *Data Min Knowl Disc* (pp. 121–167). Boston: Kluwer Academic Publishers.

Cao, Y., Tung, W., Gao, J. B., Protopopescu, V. A., & Hively, L. M. (2004). Detecting dynamical changes in time series using the permutation entropy. *Physical Review E, 70*, 046217.

Duncan, J. S., Sander, J. W., Sisodiya, S. M., & Walker, M. C. (2006). Adult epilepsy. *Lancet, 367*, 1087.

Gabor, A. J., Leach, R. R., & Dowla, F. U. (1996). Automated seizure detection using a self-organizing neural network. *Electroencephalography and Clinical Neurophysiology, 99*, 257–266.

Güler, N. F., Übeyli, E. D., & Güler, İ. (2005). Recurrent neural networks employing Lyapunov exponents for EEG signals classification. *Expert Systems with Applications, 29*, 506–514.

Kannathal, N., Choo, M. L., Acharya, U. R., & Sadasivan, P. K. (2005). Entropies for detection of epilepsy in EEG. *Computer Methods and Programs in Biomedicine, 80*, 187–194.

Kiymik, V. P., Subasi, A., & Ozcalik, H. R. (2004). Neural networks with periodogram and autoregressive spectral analysis methods in detection of epileptic seizures. *Journal of Medical Systems, 28*, 511–522. Klinik für Epileptologie, Universität Bonn. In.

Kumar, S. P., Sriraam, N., Benakop, P. G., & Jinaga, B. C. (2010). Entropies based detection of epileptic seizures with artificial neural network classifiers. *Expert Systems with Applications, 37*, 3284–3291.

Lehnertz, K. (2008). Epilepsy and nonlinear dynamics. *Journal of Biological Physics, 34*, 253–266.

Lehnertz, K., & Elger, C. E. (1988). Can epileptic seizures be predicted? Evidence from nonlinear time series analyses of brain electrical activity. *Physical Review Letters, 80*, 5019–5023.

Li, X., Cui, S., & Voss, L. J. (2008). Using Permutation Entropy to measure the electroencephalographic effects of sevoflurane. *Anesthesiology, 109*, 448–456.

Li, X., Ouyang, G., & Richards, D. A. (2007). Predictability analysis of absence seizures with permutation entropy. *Epilepsy Research, 77*, 70–74.

McSharry, P. E., He, T., Smith, L. A., & Tarassenko, L. (2002). Linear and non-linear methods for automatic seizure detection in scalp electro-encephalogram recordings. *Medical and Biological Engineering and Computing, 40*, 447–461.

Mormann, F., Andrzejak, R. G., Kreuz, T., Rieke, C., David, P., Elger, C. E., et al. (2003). Automated detection of a preseizure state based on a decrease in synchronization in intracranial electroencephalogram recordings from epilepsy patients. *Physical Review E, 67*, 021912.

Murro, A. M., King, D. W., Smith, J. R., Gallagher, B. B., Flanigin, H. F., & Meador, K. (1991). Computerized seizure detection of complex partial seizures. *Electroencephalography and Clinical Neurophysiology*, 79.

Nigam, V. P., & Graupe, D. (2004). A neural-network-based detection of epilepsy. *Neurological Research, 26*, 55–60 (56).

Olofsen, E., Sleigh, J. W., & Dahan, A. (2008). Permutation entropy of the electroencephalogram: a measure of anaesthetic drug effect. *British Journal of Anaesthesia, 101*, 810–821.

Päivinen, N., Lammi, S., Pitkänen, A., Nissinen, J., Penttonen, M., & Grönfors, T. (2005). Epileptic seizure detection: A nonlinear viewpoint. *Computer Methods and Programs in Biomedicine, 79*, 151–159.

Polat, K., & Güneş, S. (2008). Artificial immune recognition system with fuzzy resource allocation mechanism classifier, principal component analysis and FFT method based new hybrid automated identification system for classification of EEG signals. *Expert Systems with Applications, 34*, 2039–2048.

Pradhan, N., Sadasivan, P. K., & Arunodaya, G. R. (1996). Detection of seizure activity in EEG by an artificial neural network: A preliminary study. *Computers and Biomedical Research, 29*, 303–313.

Qu, H., & Gotman, J. (1997). A patient-specific algorithm for the detection of seizure onset in long-term EEG monitoring: Possible use as a warning device. *IEEE Transactions on Biomedical Engineering, 44*, 115–122.

Quian Quiroga, R., Arnhold, J., Lehnertz, K., & Grassberger, P. (2000). Kulback–Leibler and renormalized entropies: Applications to electroencephalograms of epilepsy patients. *Physical Review E, 62*, 8380–8386.

Srinivasan, V., Eswaran, C., & Sriraam, N. (2005). Artificial neural network based epileptic detection using time-domain and frequency-domain features. *Journal of Medical Systems, 29*, 647–660.

Srinivasan, V., Eswaran, C., & Sriraam, N. (2007). Approximate entropy-based epileptic EEG detection using artificial neural networks. *IEEE Transactions on Information Technology in Biomedicine, 11*, 288–295.

Subasi, A. (2005). Epileptic seizure detection using dynamic wavelet network. *Expert Systems with Applications, 29*, 343–355.

Tzallas, A. T., Tsipouras, M. G., & Fotiadis, D. I. (2007). Automatic seizure detection based on time-frequency analysis and artificial neural networks. *Computational Intelligence and Neuroscience*, 80510 (80513 p.).

Übeyli, E. D. (2009). Combined neural network model employing wavelet coefficients for EEG signals classification. *Digit Signal Process, 19*, 297–308.

van Drongelen, W., Nayak, S., Frim, D. M., Kohrman, M. H., Towle, V. L., Lee, H. C., et al. (2003). Seizure anticipation in pediatric epilepsy: use of kolmogorov entropy. *Pediatric Neurology, 29*, 207–213.

van Putten, M. J. A. M. (2003). Nearest neighbor phase synchronization as a measure to detect seizure activity from scalp EEG recordings. *Journal of Clinical Neurophysiology, 20*, 320–325.

Webber, W. R. S., Lesser, R. P., Richardson, R. T., & Wilson, K. (1996). An approach to seizure detection using an artificial neural network (ANN). *Electroencephalography and Clinical Neurophysiology, 98*, 250–272.

Wilson, K., Scheuer, M. L., Plummer, C., Young, B., & Pacia, S. (2003). Seizure detection: correlation of human experts. *Clinical Neurophysiology, 114*, 2156–2164.

Wilson, S. B., Scheuer, M. L., Emerson, R. G., & Gabor, A. J. (2004). Seizure detection: Evaluation of the Reveal algorithm. *Clinical Neurophysiology, 115*, 2280–2291.