Automatic epileptic seizure prediction based on scalp EEG and ECG signals

Keider Hoyos-Osorio
Universidad Tecnológica de Pereira
Pereia, Risaralda, Colombia
jkhoyos@utp.edu.co

Jairo Castañeda-González
Universidad Tecnológica de Pereira
Pereira, Risaralda, Colombia
jhojaicastaneda@utp.edu.co

Genaro Daza-Santacoloma
Instituto de Epilepsia y
Parkinson del Eje Cafetero
Pereira, Risaralda, COlombia
research@neurocentro.co

Abstract

The epilepsy is a common neurological disease caused by a neuronal electric activity imbalance in any side of the brain, named epileptic focus. The epilepsy is characterized by recurrent and sudden seizures. Recently, researchers found that approximately 50% of epileptic patients feel auras (subjective phenomenon which precedes and indicates an epileptic seizure onset) associated to a physiological anomaly. In this research, a non-invasive seizure prediction methodology is developed in order to improve the quality of life of the patients with epilepsy, alerting them about potential seizure and avoiding falls, injuries, wounds or even death. The research addresses the recognition of patterns in electroencephalographic (EEG) and electrocardiographic (ECG) signals taken from 7 patients with focal epilepsy whom are treated at the Instituto de Epilepsia y Parkinson del Eje Cafetero–NEUROCENTRO–. The biosignals were independently analyzed, at least 15 minutes before the seizure onset and in periods with no seizure were considered. The methodology considers the generation of features computed over the discrete wavelet transform of the EEG signal and others related to the heart rate variability in the ECG signal. Using feature selection techniques such as Sequential Forward Selection (SFS) with classification algorithms as cost functions (linear-Bayes and k-nearest neighbors classifier), we found which features have the most relevant information about pre-ictal state and which of them are the most appropriated for seizure forecasting, therefore we found that ECG signal could be a potential resource for predicting epileptic seizures, and we concluded that there are patterns in EEG and ECG signals that, via machine learning algorithms, can predict the epileptic seizure onset with a total average accuracy of 94%.

1. Introduction

The epilepsy is one of the most common and devastating neuronal disease, affecting more than 50 million of people around the world. The World Health Organization defines it as a chronic disorder of the brain characterized by recurrent seizures, which are brief episodes of involuntary movement that may involve a part of the body (partial) or the entire body (generalized), and are sometimes accompanied by loss of consciousness.

One of the most disabling aspect of epileptic seizures is their sudden and unpredictable nature. For a long time it was thought that epileptic seizures were manifested abruptly and without any kind of alarm, but recently, researchers found that approximately 50% of epileptic patients feel auras (subjective phenomenon which precedes and indicates an epileptic seizure onset). The study of the Electroencephalograms (EEG) and Electrocardiographic signals (ECG) and the advances in computer science have allowed identify pre-ictal states (time previous to seizures) that can forecast a seizure onset.

Due to the susceptibility of scalp EEG (sEEG) to different types of artifacts and noise, the most seizure prediction researches have studied intracranial recordings (iEEG) [1], [3], [7], [16]. To develop seizure forecasting methodologies that are more clinically applicable, methods based on sEEG become relevant [24].

The recording of the brain electrical activity is usually difficult, therefore, several researches have employed ECG signals [5], [10], because clinical evidence shows that the heart rate pattern changes prior to an epileptic seizure, be-

978-1-5090-3797-1/16/$31.00 ©2016 IEEE

cause excessive neuronal activities affect the autonomic nervous system [15].

An efficient non invasive seizure prediction system could decrease the risks associated to the seizure occurrence, warning the patient to suspend the activities and take a suitable position, thus avoiding any kind of consequence like falls, burns or even death.

Despite the existence of many types of seizure prediction algorithms, yet there is not one that have clinical applicability, in other words, the developed methods don't have high performances for practical uses. The most difficult problems are to provide a good trade-off between a high sensitivity (predictive capability of seizures) and a low false-positive rate (false pre-ictal alarms), also the method invasiveness, the intolerance to noise and artifacts and the high computational costs.

One challenge is to find the key features which are appropriated to anticipate a seizure onset. Several linear and nonlinear measures have been reported in the literature to forecast seizures from EEG and ECG time series. Autoregressive (AR) coefficients [1], accumulated energy [4], maximum linear cross-correlation [17] are among the linear measures. Several nonlinear features have also been employed, like the correlation dimension [9], largest Lyapunov exponent [13], dynamical similarity measure based on zero-crossing intervals [24], measures of phase synchronization [16] and ECG features related to the heart rate variability (HRV) [5], [10].

This research considers develop a non-invasive seizure prediction methodology to find which features extracted from sEEG and ECG signals offer more information about pre-ictal state and the most proficient to predict the occurrence of a seizure by using machine learning algorithms. The proposed methodology employs 2 electrophysiological signals (sEEG and ECG) to make seizure prediction.

Most current seizure prediction approaches can be summarized into (1) pre-processing the bio-signals (2) extracting measurements from this ones over time and (3) classifying them into a preictal or interictal state (period with no seizure activity) using machine learning theory. The method described in this article follows a similar methodology.

This paper has the following structure: A brief description of feature extraction, dimensionality reduction and classification techniques, the section 3 present the experimental framework and tests are specified, finally the results are discussed and the conclusions are presented.

2. Conceptual Framework

2.1. Feature extraction from EEG

Seizure prediction methods have in common an initial building block consisting of the extraction of EEG features. All EEG features are computed over a short time window of a few seconds or minutes. There are two types of measures; univariate measures, computed on each EEG channel separately, and bivariate (or multivariate) measures, which quantify some relationship, between two or more EEG channels.

A great amount of univariate features have been investigated for seizure prediction [4], [8], but non of them have obtained high performances, moreover, according to an extensive study comparing most univariate and bivariate techniques [18], they confirmed the superiority of bivariate measurements for seizure prediction.

EEG signal analysis aims to extract appropriated information from the signal. This can be done trough a transformation which enables a detailed study of relevant properties [11]. One of these transformations is the wavelet transform [11], [14], [21].

2.2. Feature extraction from ECG

2.2.1 Wave R detection and RRI obtaining

R-wave detection is an important element in this research. Features based on heart rate variability (HRV) are the main resource for epilepsy seizure prediction, an efficient detection of R-waves could guarantee a R-R Interval (RRI) signal with the most relevant information about HRV. The RRI fluctuation of ECG, is a well-known phenomenon which reflects the autonomic nervous functions, and some HRV features has been proposed for analyze the variation produced by alterations, in this case due to epileptic seizure. The RRI is the time between a R-wave and next, when all R-waves are detected in ECG a RRI signal is obtained and later processed to extract interesting features. This detection of R can be implemented based on the classical algorithm proposed by J.Pan and W.Tompkins [20]. Once all R waves are detected the full RRI signal is obtained and features like mean, standard deviation, value RMS, and some others temporal can be calculated [10] [5].

2.3. Dimensionality reduction techniques

In the seizure prediction task, usually, a lot of features are extracted from the raw EEG. Bearing in mind that in the 10-20 international system of electrode placement for EEG signal recording there are 21 channels, and that features are extracted from each channel individually, combining this large number of features would yield very high-dimensional inputs. Secondly, the computational cost of the features could make it impractical for a real time setting.

In order to reduce the dimensionality of the features space, the features selection and extraction techniques are useful.

The feature selection, is the process of selecting a subset of relevant features for use in model construction. Feature selection techniques are employed to find features that are either redundant or irrelevant, and can thus be removed without loss of information.

Feature selection schemes generally fall into three categories: filters, wrappers, and embedded methods [6], [12].

Feature selection techniques should be distinguished from feature extraction. Feature extraction creates new features by combining the original features, whereas feature selection returns a subset of the features.

2.4. Feature classification for seizure prediction

Once univariate or bivariate, linear or nonlinear measurements are derived from EEG, the most common approach for seizure prediction is to use a simple binary classification [1], [3], [5], [7], [16], [22], [24].

The principal aim of classifiers is to find a function from a training data set, which can predict the output value (preictal or interictal in this case) corresponding to any input value after having been trained. Thus, the available data set is divided into a training set ("in-sample") and a testing set ("out-of-sample").

3. Experimental framework

This seizure prediction methodology can be decomposed as following: selection of the dataset (Section 3.1), sEEG and ECG filtering (Section 3.2), computation of features from bio-signals (Section 3.3), outliers removal (Section 3.4), feature selection (Section 3.5) and binary classification for seizure prediction (Section 3.6).

3.1. Dataset

This methodology was developed and evaluated over the sEEG and ECG database of the Instituto de Epilepsia y Parkinson del Eje Cafetero–NEUROCENTRO.

For this research, 7 patients with focal epilepsy were selected, whose information are registered in table 1.

Patient No.	Epileptic Focus
P1	Left Fronto-Temporal
P2	Mesial Temporal
P3	Left Frontal
P4	Left Fronto-Temporal
P5	Temporal
P6	Left Temporal
P7	Extra-Temporal

Table 1: NEUROCENTRO Database

Each patients' recording contains 4 seizures, which are analyzed in this paper.

The EEG signal was acquired according to the 10-20 international system of electrode placement at a 500 Hz sampling rate. The recordings include 2 channels with the electrical activity of the heart.

The manipulation, visualization and analysis of these signals were made with the assistance of the programming software Matlab®.

3.2. Pre-processing

3.2.1 sEEG pre-processing

The EEG signals are very susceptible to artifacts and noise, then it was established a pre-processing methodology using Infinite Impulse Response (IIR) elliptical filters according to [16], redesign the signal: a 49–51Hz band-reject was used to remove the power line noise, a 120 Hz cutoff low-pass , and a 0.5 Hz cutoff high-pass filter was used to remove the dc component.

3.2.2 ECG pre-processing

The ECG signal is an ionic current flow taken by electrodes placed in body, causing the cardiac fibers to contract and relax and generating a variant period signal. The interpretation of ECG signal is an essential proficiency for medical professionals and researches, errors in ECG analysis could lead to serious consequences or ineffective applications [25]. The detection of PQ, QRS and ST segments could be wrong in noisy ECG signals. Denoising any signal is a task very common in signal processing, but depending of application the remotion of noise can need some requirements. Wavelets are the best and simple technique for ECG denoising [23], [19], besides this kind of denoising allows to fix baseline errors. A Daubechies-4 wavelet was selected as mother wavelet basis due to the result reported in [25], Daubechies-4 retain important characteristics such as the form of the ECG spikes and allows to remove noise from instruments and ambient.

3.3. Feature extraction

3.3.1 sEEG feature extraction

The EEG signal in each channel is segmented into non-overlapping 5 seconds window (N=2499 samples at 500 Hz). Then, the Discrete Wavelet Transform (DWT) is computed for each window.

The wavelet transform decompose a signal in a set of basis functions obtained by expansions, contractions and displacements of a prototype wave known as the mother wave. This wave must be chosen carefully; in this case the Daubechis-4 (DB4) was selected with 8 decompositions (level 8). The DWT carries out 9 coefficient vectors of the same size of the window (2499), known as Approximation

(A8) and Detail coefficients (D1, D2, D3, D4, D5, D6, D7, D8).

The sub-band frequencies are related to the sampling rate. In the Table 2, is shown the corresponding frequencies for each level decomposition.

Coefficient	Frequency	Brain Rhythm
D1	250-500 Hz	Noise
D2	125-250 Hz	Noise
D3	62.5-125 Hz	Noise
D4	31.25-62.5 Hz	Gamma
D5	15.6-31.25 Hz	Beta
D6	7.8-15.6 Hz	alpha
D7	3.9-7.8 Hz	Theta
D8	1.95-3.9 Hz	Delta 1
A8	0-1.95 Hz	Delta 2

Table 2: DWT level decompositions and frequencies

D1, D2 and D3 coefficients were discarded ($f > 60Hz$), due to they represent non relevant frequency intervals and can be interpreting as noise.

The extracted coefficients offer a compact representation of the time and frequency of energy distribution of the EEG signal. In order to reduce the dimensionality of each set of coefficients, severals statistical features such as the minimum and maximum value, the mean, standard deviation, the energy and the entropy are computed for each sub-band.

The energy and entropy are computed according to (1) and (2) respectively:

$$ED_i = \sum_{j=1}^{N} |D_{ij}|^2, \tag{1}$$

$$ENT_i = -\sum_{j=1}^{N} D_{ij}^2 log(D_{ij}^2), \tag{2}$$

$i = 1, 2, ...l + 1$ correspond to the wavelet decomposition levels, and the $l + 1$ correspond to the approximation coefficients set, which was added to the matrix with the others coefficients, N is the amount of coefficients into each level decomposition.

Discarding the 3 first detail coefficients, the group was reduced to 6 coefficient sets, and just 36 features are computed every 5 seconds window for each channel, for a total of 756 features per observation. These measurements was realized during 15 minutes (900 seconds = 180 observations) before everyone of the 4 seizures onset of each patient, and 1 hour (720 observations) of interictal period was also considered.

3.3.2 ECG feature extraction

Once all R-waves were detected, the full RRI signal is obtained, outliers have been detected and noise was removed, a sliding window with one heartbeat overlapping width of N=158 samples corresponding to 3 minutes. The width of window was determinate by trial and error. For each part of the windowed signal 9 features were calculated, 6 of them correspond to time-domain; mean of RRI (meanNN), standard deviation of RRI (SDNN), RMS value of SDNN (RMSSD), number of pairs of adjacent RRI whose difference is more than 50 ms (NN50) and the NN50 divided by total of RRI (pNN50). The remaining 3 features correspond to frequency-domain, obtained through the power spectral density (PSD) over the RRI; the low frequency power of RRI (LF). LF reflects the modulations of the sympathetic and the parasympathetic nervous system (0.04 Hz – 0.15Hz), the high frequency power of RRI (HF). HF reflects the parasympathetic nervous system activity (0.15Hz – 0.4Hz) and the ratio of LF to HL (LF/HF). LF/HF expresses the balance of the sympathetic nervous system activity with the parasympathetic nervous system activity [10] [5].

3.4. Outliers removal

Outliers are understood as observations that has been generated by different distributions to the remaining data, and may result in undesired effects on the analysis to be performed from the observations [2]. The estimation of any characteristic from biosignals, is very sensitive to factors such as recording or electronic conditions (background noise, hardware disturbances, emotional state, etc.). When this conditions are adverse, often appear observations with measured values which clearly no correspond to the structure of the assumed randomness; such observations are known as outliers.

There are multiple ways to detect outliers. In this research is used an outlier removal technique based on the calculation of the median.

Let **X** be the original matrix data of $n \times p$ dimension, where rows correspond to observations and columns to variables. Let x_{ij} be the generic element of this array. A rule for the detection of outliers in a univariate way, is to determine as outliers those points that satisfying the following condition

$$\left| \frac{x_i - Med\,(x_j)}{MEDA\,(x_j)} \right| > 4.5 \tag{3}$$

3.5. Feature selection

In order to remove redundant information, it was calculated the Pearson's Correlation between all the sEEG features and those characteristics with correlations greater than

0.95 were eliminated. Figure 1 shows that there are a lot of features which are highly correlated.

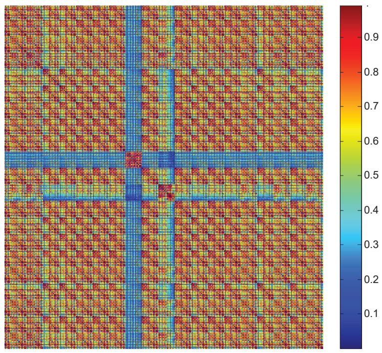

Figure 1: Pearson's correlation matrix of the sEEG original features of patient 1.

After eliminate the redundant information, the features space was reduced to 119 features as can be seen in Figure 2.

Since the range of values of raw EEG features varies widely, it should be normalized by dividing each column (features) by the maximum value, so that each feature approximately contributes the same proportion to the final decision of the classifiers.

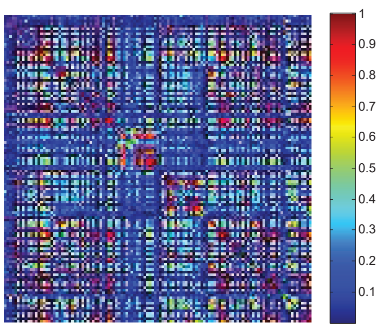

Figure 2: Pearson's correlation matrix of the sEEG reduced features of patient 1.

To find which features have the most relevant information about pre-ictal state and which of them are the most appropriated for seizure forecasting, a wrapped feature selection technique, Sequential Forward Selection (SFS), is applied.

SFS is a bottom-up searching technique. It first selects the best feature according to a cost function, after it is combined with every remaining features, then it searches the couple who bring the greatest value evaluation and they are chosen as the starting new set. Below this couple is combined with each of the remaining variables, forming triads, the triad that offer greater value in the evaluation criteria is selected. The process is repeated any times as it requires. The search stops when a set of variables does not improve the results of the cost function.

The SFS was applied with classification algorithms as cost functions and was tested the best features in 10 rotations of the original matrix. The best sEEG Channels, subbands and features for seizure forecasting were found.

For all patients the best 2 ECG features were NN50 and pNN50.

Patient	Statistic	sEEG	ECG
P1	Accuracy (%)	89.35± 3.10	99.64 ± 0.30
	Sensitivity (%)	88.66 ± 4.31	99.71 ± 0.23
	FPR	0.095	0.0048
P2	Accuracy (%)	78.44 ± 4.97	99.99 ± 0.01
	Sensitivity (%)	79.65 ± 5.09	99.99 ± 0.01
	FPR	0.2228	0
P3	Accuracy (%)	99.21 ± 0.25	99.84 ± 0.09
	Sensitivity (%)	98.61 ± 0.44	99.98 ± 0.07
	FPR	0	0.0048
P4	Accuracy (%)	84.4 ± 2.12	99.14 ± 0.03
	Sensitivity (%)	82.92 ± 1.75	99.14 ± 0.0051
	FPR	0.1250	0.0048
P5	Accuracy (%)	71.39 ± 1.87	99.99 ± 0.0008
	Sensitivity (%)	65.17 ± 2.14	99.99 ± 0.0011
	FPR	0.2224	0
P6	Accuracy (%)	96.67 ± 1.46	99.12 ± 0.32
	Sensitivity (%)	95.30 ± 0.44	98.54 ± 0.45
	FPR	0.0142	0.0044
P7	Accuracy (%)	97.59 ± 1.25	99.82 ± 0.15
	Sensitivity (%)	96.92 ± 1.91	99.78 ± 0.0031
	FPR	0.014	0.0015

Table 3: Seizure prediction results

3.6. Binary classification for seizure prediction

The sEEG was classified with a linear Bayes classifier and the ECG with a k-Nearest Neighbors (kNN) classifier. The accuracy, sensitivity and the false positive rate (FPR) of the classification for all patients are presented in Table 3.

From results shown in Table 3, between both signals, the total average of the accuracy was 94%, of the sensitivity was 93% and the FPR was 0.051. For patient 3 was achieved the highest sEEG performance. The best 2 features was plotted in the Figure 3.

The ROC curve (receiver operating characteristic) presented in Figure 4 illustrates the performance of the Linear Bayes classifier for patient 1 and its area under curve was 0.9473.

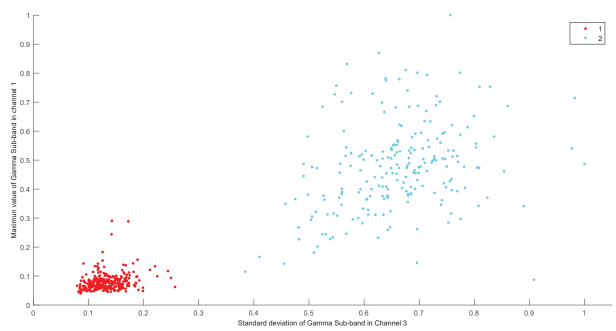

Figure 3: Binary classification into preictal state (class 1) and interictal state (class 2) with 2 features using sEEG features

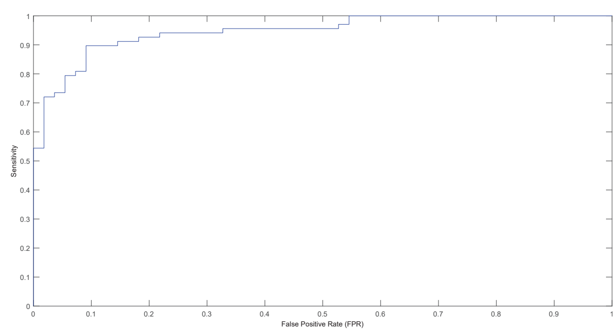

Figure 4: ROC curve for linear Bayes classifier for patient 1

4. Discussion

The total average accuracy achieved in this research was 94%. As it can be seen in Figure 3 the separability of the the 2 classes for patient 3 is great, which explains the results achieved for this patient. The sEEG recording of the patient 2, presented some abnormalities like electrodes disconnection, which is reflected in the results for this patient.

It is important remark that all the classification results were reached with less than 6 features, which make this methodology a low computational costs seizure prediction methodology regarding to the initial feature set (756 features).

In the ROC curve the true positive rate (sensitivity) is plotted in function of the false positive rate (1-specificity) for different decision threshold, therefore the closer the ROC curve is to the upper left corner, the higher the overall accuracy of the test. The area under the ROC curve (AUC) is also a measure of how well a parameter can distinguish between the two classification groups (Preictal/Interictal), in this case was 0.9473 which indicates that the Linear Bayes classifier offers a suitable performance for epilepsy seizure prediction using univariate sEEG features.

As is shown in Table 3, the best results for ECG were obtained with a KNN classifier, but a quadratic classifier was used too, and the result for this were less than 76% for accuracy, 81% for sensitivity and 0.23 FPR. KNN classifier probably was the most effective classifier for prediction due to the distribution of data, NN50 and pNN50 showed a concentration of inter-ictal data, and pre-ictal data was distributed outside of interictal data, and this is an ideal distribution of data for KNN classifier. About why NN50 and pNN50 were the most relevant features for predicting epileptic seizures, is probably because NN50 is a direct way to measure the heart rate, to count how many R-R intervals occur in a specific time shows that there is an alteration in heart rate in states previous to a seizure, product to a reflection of the activity nervous parasympathetic/sympathetic system.

5. Conclusions

In this paper, we have presented a methodology for the prediction of epileptic seizures from the analysis of sEEG and ECG signals. The results show that the proposed methodology offers a good trade-off between sensitivity and false positive rate, besides the results make evident that ECG signal could be a potential resource for predicting epileptic seizures since electrical activity of the heart is easier to measure than of the brain. Nevertheless all the ECG signals for this research were recorded in an environment with all conditions controlled, where the patients always were in a relaxed situation and almost never they could be altered in order to keep the normal heart-rate. Even though the results for ECG were higher than sEEG results, the sEEG is an important complementing for ECG, because of the ECG methodology was based on HRV which can be affected by any quotidian activity done for the patient; here is where sEEG become relevant for this task.

Future work will be devoted to improve the methodology in terms of sensitivity and false positives rates and to implement the developed prediction methods on real-time systems that would be able to timely predict the arrival of an epileptic seizure in a fully automated way.

6. Acknowledgments

Special thanks to the SENA-COLCIENCIAS young researchers project, without their help this research could not be developed.

References

[1] L. Chisci, A. Mavino, G. Perferi, M. Sciandrone, C. Anile, G. Colicchio, and F. Fuggetta. Real-time epileptic

seizure prediction using ar models and support vector machines. *Biomedical Engineering, IEEE Transactions on*, 57(5):1124–1132, 2010.

[2] G. Daza-Santacoloma, J. F. Suárez-Cifuentes, and G. Castellanos-Domínguez. Preproceso de datos en bioseñales: una aplicación en detección de patologías de voz. *Ingeniería e investigación*, 29(3):92–96, 2009.

[3] F. Duman, N. Özdemir, and E. Yildirim. Patient specific seizure prediction algorithm using hilbert-huang transform. In *Biomedical and Health Informatics (BHI), 2012 IEEE-EMBS International Conference on*, pages 705–708. IEEE, 2012.

[4] R. Esteller, J. Echauz, M. D'Alessandro, G. Worrell, S. Cranstoun, G. Vachtsevanos, and B. Litt. Continuous energy variation during the seizure cycle: towards an on-line accumulated energy. *Clinical Neurophysiology*, 116(3):517–526, 2005.

[5] K. Fujiwara, M. Miyajima, T. Yamakawa, E. Abe, Y. Suzuki, Y. Sawada, M. Kano, T. Maehara, K. Ohta, T. Sasai-Sakuma, et al. Epileptic seizure prediction based on multivariate statistical process control of heart rate variability features.

[6] I. Guyon and A. Elisseeff. An introduction to variable and feature selection. *The Journal of Machine Learning Research*, 3:1157–1182, 2003.

[7] T. Haddad, L. Talbi, A. Lakhssassi, B.-H. Naim, and S. Aouini. Epilepsy seizure prediction using graph theory. In *New Circuits and Systems Conference (NEWCAS), 2014 IEEE 12th International*, pages 293–296. IEEE, 2014.

[8] M. A. F. Harrison, M. G. Frei, and I. Osorio. Accumulated energy revisited. *Clinical Neurophysiology*, 116(3):527–531, 2005.

[9] M. A. F. Harrison, I. Osorio, M. G. Frei, S. Asuri, and Y.-C. Lai. Correlation dimension and integral do not predict epileptic seizures. *Chaos: An Interdisciplinary Journal of Nonlinear Science*, 15(3):033106, 2005.

[10] H. Hashimoto, K. Fujiwara, Y. Suzuki, M. Miyajima, T. Yamakawa, M. Kano, T. Maehara, K. Ohta, T. Sasano, M. Matsuura, et al. Heart rate variability features for epilepsy seizure prediction. In *Signal and Information Processing Association Annual Summit and Conference (APSIPA), 2013 Asia-Pacific*, pages 1–4. IEEE, 2013.

[11] N. Hazarika, J. Z. Chen, A. C. Tsoi, and A. Sergejew. Classification of eeg signals using the wavelet transform. In *Digital Signal Processing Proceedings, 1997. DSP 97., 1997 13th International Conference on*, volume 1, pages 89–92. IEEE, 1997.

[12] R. Kohavi and G. H. John. Wrappers for feature subset selection. *Artificial intelligence*, 97(1):273–324, 1997.

[13] Y.-C. Lai, M. A. F. Harrison, M. G. Frei, and I. Osorio. Inability of lyapunov exponents to predict epileptic seizures. *Physical review letters*, 91(6):068102, 2003.

[14] S. Lekshmi, V. Selvam, and M. Pallikonda Rajasekaran. Eeg signal classification using principal component analysis and wavelet transform with neural network. In *Communications and Signal Processing (ICCSP), 2014 International Conference on*, pages 687–690. IEEE, 2014.

[15] P. A. Lotufo, L. Valiengo, I. M. Benseñor, and A. R. Brunoni. A systematic review and meta-analysis of heart rate variability in epilepsy and antiepileptic drugs. *Epilepsia*, 53(2):272–282, 2012.

[16] P. Mirowski, D. Madhavan, Y. LeCun, and R. Kuzniecky. Classification of patterns of eeg synchronization for seizure prediction. *Clinical neurophysiology*, 120(11):1927–1940, 2009.

[17] F. Mormann, R. G. Andrzejak, T. Kreuz, C. Rieke, P. David, C. E. Elger, and K. Lehnertz. Automated detection of a preseizure state based on a decrease in synchronization in intracranial electroencephalogram recordings from epilepsy patients. *Physical Review E*, 67(2):021912, 2003.

[18] F. Mormann, T. Kreuz, C. Rieke, R. G. Andrzejak, A. Kraskov, P. David, C. E. Elger, and K. Lehnertz. On the predictability of epileptic seizures. *Clinical neurophysiology*, 116(3):569–587, 2005.

[19] N. Nikolaev, Z. Nikolov, A. Gotchev, and K. Egiazarian. Wavelet domain wiener filtering for ecg denoising using improved signal estimate. In *Acoustics, Speech, and Signal Processing, 2000. ICASSP'00. Proceedings. 2000 IEEE International Conference on*, volume 6, pages 3578–3581. IEEE, 2000.

[20] J. Pan and W. J. Tompkins. A real-time qrs detection algorithm. *Biomedical Engineering, IEEE Transactions on*, (3):230–236, 1985.

[21] R. Panda, P. Khobragade, P. Jambhule, S. Jengthe, P. Pal, and T. Gandhi. Classification of eeg signal using wavelet transform and support vector machine for epileptic seizure diction. In *Systems in Medicine and Biology (ICSMB), 2010 International Conference on*, pages 405–408. IEEE, 2010.

[22] Y. Park, L. Luo, K. K. Parhi, and T. Netoff. Seizure prediction with spectral power of eeg using cost-sensitive support vector machines. *Epilepsia*, 52(10):1761–1770, 2011.

[23] O. Sayadi and M. B. Shamsollahi. Ecg denoising with adaptive bionic wavelet transform. In *Conference proceedings:... Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society. Annual Conference*, pages 6597–6600, 2005.

[24] A. Shahidi Zandi, R. Tafreshi, M. Javidan, G. Dumont, et al. Predicting epileptic seizures in scalp eeg based on a variational bayesian gaussian mixture model of zero-crossing intervals. *Biomedical Engineering, IEEE Transactions on*, 60(5):1401–1413, 2013.

[25] B. N. Singh and A. K. Tiwari. Optimal selection of wavelet basis function applied to ecg signal denoising. *Digital Signal Processing*, 16(3):275–287, 2006.