



Epileptic seizure prediction using relative spectral power features



Mojtaba Bandarabadi *, César A. Teixeira, Jalil Rasekhi, António Dourado

CISUC/DEI, Center for Informatics and Systems of the University of Coimbra, Department of Informatics Engineering, Polo II, 3030-290 Coimbra, Portugal

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HIGHLIGHTS

- The proposed relative spectral power features resulted in an improved performance for seizure prediction.
- The number of selected features was 9.9 in average showing the efficiency of the introduced relative bivariate features.
- In average 75.8% of the test seizures (out-of-sample) were predicted across 1537 h of data with an average FPR of 0.1 h^{-1} .

ABSTRACT

Objective: Prediction of epileptic seizures can improve the living conditions for refractory epilepsy patients. We aimed to improve sensitivity and specificity of prediction methods, and to reduce the number of false alarms.

Methods: Relative combinations of sub-band spectral powers of electroencephalogram (EEG) recordings across all possible channel pairs were utilized for tracking gradual changes preceding seizures. By using a specifically developed feature selection method, a set of best candidate features were fed to support vector machines in order to discriminate cerebral state as preictal or non-preictal.

Results: Proposed algorithm was evaluated on continuous long-term multichannel scalp and invasive recordings (183 seizures, 3565 h). The best results demonstrated a sensitivity of 75.8% (66 out of 87 seizures) and a false prediction rate of 0.1 h^{-1} . Performance was validated statistically, and was superior to that of analytical random predictor.

Conclusion: Applying machine learning methods on a reduced subset of proposed features could predict seizure onsets with high performance.

Significance: Our method was evaluated on long-term continuous recordings of overall about 5 months, contrary to majority of previous studies using short-term fragmented data. It is of very low computational cost, while providing acceptable levels of alarm sensitivity and specificity.

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1. Introduction

Epilepsy is the abrupt occurrence of an instantaneous activity throughout a large numbers of neurons inside the brain, which can distort normal brain activity. Most treatments provided for epilepsy are in the form of anticonvulsant medication. However their side effects should be taken into account and for about 30–35% of the patients, the antiepileptic drugs are not effective (Carney et al., 2011). In such cases, brain surgery is the alternative

solution, which tries to remove the region in the brain where seizures are generated. However surgery is not always possible, and involves high risks (Spencer and Huh, 2008). Therefore about 30% of patients with epilepsy cannot be treated either by medication or by surgery, and must live with the seizures that can happen anytime, anywhere. Despite medical costs associated with the treatment of epilepsy, the injuries resulting from uncontrolled seizures represent an even higher cost to the society.

Success in predicting epileptic seizures would improve the living expectations of over 50 million patients suffering from ictal events. In (Schulze-Bonhage et al., 2010) some advantages such as avoidance of injuries, increasing the feeling of security, driving

* Corresponding author. Tel.: +351 239 790 000; fax: +351 239 701 266.

E-mail address: m.bandarabadi@gmail.com (M. Bandarabadi).

without fear, and reduction of anxiety are mentioned. Moreover, the patient has the possibility to ask for emergency help and early medications, therefore various interventions such as delivering fast-acting antiepileptic drugs, electric stimulation of vagus nerve (Shoeb et al., 2011), or deep brain stimulation could be applied to overcome the seizures (Schelter et al., 2007).

In most of the seizure prediction approaches, features are first extracted from the preprocessed windowed EEG signals, and then classified into preictal/non-preictal states. The extracted features can be univariate (from a single channel), bivariate (from pair of channels), or multivariate measures (from multiple channels simultaneously). Epileptic seizure prediction was challenged traditionally either by simply applying threshold to a given measure extracted from the EEG (Schelter et al., 2006), or by nonlinear analysis (Le Van Quyen et al., 2001; Lehnertz et al., 2003). More recently, classification methods based on high-dimensional feature spaces were used to detect the preictal state (Chisci et al., 2010; Park et al., 2011; Cabrerizo et al., 2012; Rasekhi et al., 2013; Teixeira et al., 2014).

In spite of the recent progresses and the state of the art knowledge on epilepsy, the prediction and control of epileptic seizures is still a hard problem to tackle. In fact, although around 40 years have passed from the first study made on physiology of seizures (Viglione and Walsh, 1975), and after the development of numerous prediction methods, researchers are still far from a complete and reliable approach which can practically be used in real medical applications. The main drawback with most of these studies is that they were not properly evaluated, i.e., they were not applied for long-term continuous situations close to the real conditions, making impossible to evaluate the clinical validity of the proposed approaches (Mormann et al., 2007; Andrzejak et al., 2009; Stacey, 2011).

The advantages of bivariate and multivariate measures over single-variate have been pointed out in several studies (Lehnertz and Litt, 2005; Mormann et al., 2005; Mormann et al., 2007). A wide study (Mormann et al., 2005) was carried out to compare most of the linear and non-linear methods involving single channel and multi-channel features, concluding that univariate measures (effective correlation dimension, Lyapunov exponents, and accumulated energy of the signal) could not produce better results than a random predictor. In contrast, they raised some evidences showing that measures quantifying the relations between recording electrodes and representing the interaction between different regions of brain exhibit a promising capability, which is beyond the chance level demonstrated by statistical validation. For synchronization criteria such as phase synchronization and lag synchronization, it has been shown that distinctively better functionality can be obtained, supporting the importance of bivariate features. Further notable works in this field include studies based on measures of spike rate (Shufang et al., 2013), nonlinear similarity index (Navarro and Martinerie, 2005), convergence and divergence of short-term maximum Lyapunov exponents (Iasemidis et al., 2003), mean phase coherence (Mormann et al., 2003), wavelet energy and entropy (Gadhomi et al., 2012), and high frequency oscillations (Pearce et al., 2013).

Among the univariate features, studies on the spectral power of raw EEG signal have proved the ability to track the transient changes from interictal to ictal states (Cerf and El Ouardad, 2000; Mormann et al., 2005; Netoff et al., 2009; Park et al., 2011), and to detect ictal state (Ayala et al., 2011; Kharbouch et al., 2011). Authors (Mormann et al., 2005) described a relative decrease in power of Delta band in preictal period in comparison with the interictal period. Additionally, this decrease was accompanied by a relative increase of power in the remaining bands. Netoff (Netoff et al., 2009) proposed a patient-specific algorithm, based on the features obtained from spectral powers in the 9 following

bands: delta (0.5–4 Hz], theta (4–8 Hz], alpha (8–13 Hz], beta (13–30 Hz], four gamma sub-bands (30–50 Hz], (50–70 Hz], (70–90 Hz], (90 Hz–), and total power of six EEG electrodes, three over the seizure focus and three distant from the focus. They reported an average sensitivity of 77.8% (predicted 35 among 45 seizures), and a false positive rate per hour (FPR) of zero. They also argued that the spectral power in certain sub-bands of the intracranial EEG (iEEG), specifically in higher frequency sub-bands, may play a key role in seizure prediction. Later (Park et al., 2011) proposed a patient-specific seizure prediction algorithm using four different methods to compute spectral power of the iEEG: raw, bipolar, time-differential, bipolar/time-differential, and used them as features. The proposed algorithm was applied on 80 seizures, and a total of 433.2-h of interictal data. The best results obtained from bipolar approach were 97.5% sensitivity and 0.27 false positives per hour in out-of-sample data.

This work compares spectral powers within different sub-bands of different electrodes, and exploits relations between them to be used as features. An approach is also introduced for selection of the best features from the high dimensional relative bivariate features space. Selected features can reflect the relationships between different frequency bands in the different regions of the brain. For instance, if spectral power of gamma band of a focal channel divided by spectral power of theta band of an opposite channel achieves the highest rank, one may conclude that this measure can better track the transient changes. Therefore, the selection of the most discriminative features plays an important role in this study, and a feature selection method is developed.

The seizure prediction is faced as a binary classification problem between preictal and non-preictal states. Preictal is the state just before the seizure, which is to be detected in order to predict the proceeding seizure; depending on the starting time of seizure symptoms, the preictal can cover from several seconds up to several hours before the seizure (Litt and Echaz, 2002; Ebersole, 2005; Mormann et al., 2007). Non-preictal class covers the three states of ictal, postictal, and interictal. Ictal state is the time period in which seizure happens. Postictal state encompasses the moments after seizure onset. Interictal state, during which the patient enjoys a normal brain activity, is the interval beginning right after the postictal state of a seizure and ending before the preictal state of the next seizure. The identification of preictal state is made using the computational intelligence SVM classifier and its output regularization by firing power (FP) (Teixeira et al., 2011) method. Results from both scalp and intracranial recordings are compared in order to examine whether the iEEG prevails over sEEG predictions or not. The advantages of the proposed approaches have been evidenced by the comparison of the results.

2. Materials and methods

2.1. Subjects

Long-term continuous multichannel EEG recordings of twenty-four patients (19 males and 5 females, aged 15–57 years, median 35.5 years) with refractory partial epilepsy from the European Epilepsy Database (Klatt et al., 2012) were used. Recordings were obtained at the epilepsy units of the University Hospitals of Coimbra, Portugal, the Pitié-Salpêtrière Hospital of Paris, France, and the University Clinic of Freiburg, Germany. Sixteen patients were monitored through scalp electrodes whereas the other eight were monitored through intracranial electrodes. The 10–20 electrode montage was used for scalp recordings. The onset times were marked by epileptologists by visual inspection of sEEG/iEEG recordings and using the video recordings of the patient during his/her stay in the hospital. Information of both electroencephalographic

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