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EPILAB: A software package for studies on the prediction of epileptic seizures

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ABSTRACT

A Matlab®-based software package, EPILAB, was developed for supporting researchers in performing studies on the prediction of epileptic seizures. It provides an intuitive and convenient graphical user interface. Fundamental concepts that are crucial for epileptic seizure prediction studies were implemented. This includes, for example, the development and statistical validation of prediction methodologies in long-term continuous recordings.

Seizure prediction is usually based on electroencephalography (EEG) and electrocardiography (ECG) signals. EPILAB is able to process both EEG and ECG data stored in different formats. More than 35 time and frequency domain measures (features) can be extracted based on univariate and multivariate data analysis. These features can be post-processed and used for prediction purposes. The predictions may be conducted based on optimized thresholds or by applying classifications methods such as artificial neural networks, cellular neuronal networks, and support vector machines.

EPILAB proved to be an efficient tool for seizure prediction, and aims to be a way to communicate, evaluate, and compare results and data among the seizure prediction community.

1. Introduction

Between 30% and 40% of the epilepsy patients cannot be treated successfully either by anti-epileptic drugs or by resective surgery (Kwan and Brodie, 2000). The life of these patients is extremely affected by the occurrence of sudden and apparently unpredictable seizures, which are a cause of disability (Devinsky et al., 1995) and mortality (Cockerell et al., 1994). Hence, the development of a reliable seizure prediction method could improve the quality of life of those patients considerably.

In recent years, several time series analysis techniques were developed (Mormann et al., 2007) in order to identify a pre-seizure state, the so-called preictal state. Aiming to detect this preictal state, a large number of methods to analyze electroencephalogram (EEG) and electrocardiogram (ECG) time series were developed (Mormann et al., 2005; Valderrama et al., 2010). These methods are based on single- and multi-channel analysis, and enable the extraction of measures, i.e., features, in the time and frequency domain. The first methods were based on thresholds optimized for a given feature. Here, an alarm is triggered when a predefined feature crosses some predefined threshold (Schelter et al., 2006a). More recent studies suggested circadian dependencies. It was found that more false predictions per hour occur during night times (Schelter et al., 2006b). Hence, different thresholds for night and day were introduced. The seizure prediction challenge has also been faced as a classification problem during the past decade (Dourado et al., 2008; Costa et al., 2008; Mirowski et al., 2008; Chisci et al., 2010). The application of classification techniques has been based on the assumption that the different features extracted over time can be separated into two or more classes corresponding to

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different cerebral states. Computational intelligence methods such as support vector machines (SVMs) (Cortes and Vapnik, 1995) have been applied to address this classification problem (Mirowski et al., 2008; Chisci et al., 2010).

Several Matlab® toolboxes for EEG processing are available, for example: EEGLAB (Delorme and Makeig, 2004), BSMART (Cui et al., 2008), MEA-Tools (Egert et al., 2002), ERPWAVELAB (Mörup et al., 2007), and eConnectome (He et al., 2011). EEGLAB is an open-source Matlab® platform developed for researchers interested in event related potentials, to process collections of single EEG data epochs. ERPWAVELAB (Mörup et al., 2007) is an extension of EEGLAB and enables data analysis and visualization of the most common event related measures, e.g., evoked spectral perturbation (ERSP) and inter-trial phase coherence (ITPC), and data decomposition through non-negative matrix and multi-way factorization. The toolbox MEA-Tools (MicroElectrode Array tools) is a Matlab®-based open source toolbox developed for the analysis of multi-channel microelectrode data. BSMART (Brain-System for Multivariate AutoRegressive Timeseries) (Cui et al., 2008) is a Matlab®/C software developed for brain connectivity analysis based on EEG, magnetoencephalography (MEG) or functional magnetic resonance imaging (fMRI) data. The recently released eConnectome toolbox (He et al., 2011) was developed for brain connectivity studies based on Granger causality measures (Granger, 1969).

However, none of the mentioned toolboxes was developed specifically for seizure prediction studies. Specific software for seizure prediction should enable long-term EEG/ECG processing, encompassing long-term feature extraction and prediction. Guidelines crucial for the quality of epileptic seizure prediction studies should be considered (Mormann et al., 2007):

- algorithms should be tested on long-term continuous data covering several days, including a sufficient number of seizures and a sufficient duration of interictal data;
- a given predictor should be evaluated in terms of sensitivity and specificity for a given seizure occurrence period, i.e., the time interval after an alarm within which a seizure is expected. For specificity, the false prediction rate can be used but it should be related to only those time intervals in which false alarms are possible;
- predictors should be statistically validated to assess if a given predictor performs above chance level;
- the performance should be evaluated prospectively on out-of-sample data.

We developed EPILAB, a Matlab® toolbox, for epileptic seizure prediction that allows studying seizure prediction based on a high dimensional feature space. The software was developed for Windows (Microsoft Corporation), Linux, and Mac OS X (Apple Inc.) operating systems. Threshold- and classification-based prediction algorithms are considered and evaluated following the guidelines above. It was designed to support researchers in performing seizure prediction studies based on long-term EEG/ECG recordings in an efficient and user-friendly graphical user interface (GUI). In addition, the object-oriented base of EPILAB enables the easy integration of new methodologies.

EPILAB is a product of the European project EPILEPSIAE, and will be freely available by the end of 2011. All the documentation and code will be available at http://www.epilepsiae.eu

The first four sections describe the five main modules of EPILAB, as presented in Fig. 1. The process to create a new study is presented in Section 2. The features that can be extracted and their computation setup are described in Section 3. The possibilities to perform feature selection and dimensionality reduction on high-dimensional feature spaces are presented in Section 4. The prediction algorithms that are considered and their setup in EPILAB are described in Section 5. In Section 6, an example for an application to a long-term recording is reported. Final conclusions, limitations, and future improvements are described in Section 7.

2. Creating a new study

A new study can be created based on raw EEG/ECG data files or on previously computed features. When beginning a new study from raw data (Fig. 2A), different binary formats are supported, including Mat-Files (The Mathworks, Inc.), TRC files (Micromed S.p.A., Italy), and Nicolet Files. Raw data in a single file or dispersed in several files can be accessed. In the case of a multi-file organization, EPILAB is able to assess recursively directories of files, and create an internal mapping such that all the data can be processed as if they were in a single file. During the study creation, the information necessary for future processing is retrieved such as sampling frequencies, temporal gaps between files, events occurring during the recording (e.g., seizure times), and electrode description.

After study creation, EEG/ECG signals can be displayed using the raw data navigation tool integrated in EPILAB (Fig. 2B). The user can visualize a data window with a specified time-length. The two main modes of navigation are by time and by EEG annotation events. The latter enables the user to easily locate the events like seizure onsets and offsets marked in a given file. Optionally, the visualized data can be filtered.

A study can also be based on features computed previously. The user has the possibility to integrate more than one file of features that were computed using the same computation parameters. The user can navigate over the feature data by using a tool similar to the one developed for raw data.

3. Feature extraction

EPILAB includes several measures for raw EEG and ECG signals that have been shown to be useful in seizure prediction. Measures are either based on one channel (univariate) or on multiple channels (multivariate), and are computed in a window-by-window basis. Prior to feature computation the user may decide to apply filters. Three infinite impulse response (IIR) forward–backward Butterworth filters can be applied: low-pass, high-pass, and notch (to minimize power line interferences). Butterworth filters, or maximally flat magnitude filters, present no ripple (oscillations) in the pass- and stop-bands, producing a uniform acceptance of the wanted EEG frequencies. When compared to other IIR filters they present a larger transition band, which can be minimized by increasing the filter order.

Table 1 summarizes the features that are presently included in EPILAB, which are briefly presented below.

3.1. Univariate EEG features

The “prediction error”, derived from an autoregressive model of the EEG signal, has been suggested for both detection (Altunay et al., 2010) and prediction purposes (Rajdev et al., 2010). As seizures approach, the EEG signals are claimed to be better predictable by an autoregressive model of order p (AR(p)), i.e., the mean squared error (MSE) in the preictal phase decreases. With the onset of the seizure, this decrease in the MSE is assumed to disappear.

The “decorrelation time” is defined as the time of the first zero crossing of the autocorrelation sequence of a given EEG signal (Mormann et al., 2005). If the decorrelation time is lower, the signal is less correlated. Prior to seizures, a decrease in the power related