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Epileptic seizures prediction using a machine learning approach

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Dedico este trabalho àqueles que sempre me apoiaram. Especialmente, dedico este trabalho à minha família que, mesmo longe, meu deu o apoio necessário para que eu pudesse continuar minha caminhada.

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"Limits, like fears, are often just an illusion."

- Michael Jordan

ABSTRACT

OLIVEIRA, L. F. **Epileptic seizures prediction using a machine learning approach**. 2020. 53p. Monografia (Trabalho de Conclusão de Curso) - Escola de Engenharia de São Carlos, Universidade de São Paulo, São Carlos, 2020.

This study aims to develop a seizure prediction procedure using a machine learning approach. With the electroencephalography (EEG) data collected from 3 patients, a seizure prediction pipeline was developed after experimenting with several machine learning algorithms such as random forests, gradient boosting, recurrent neural networks and logistic regression. For each patient, the EEG measurements were equally divided into 10 minute segments and labeled as preictal (prior to a seizure) and interictal (between seizures or normal activity). Therefore, the prediction task can be assumed as a binary classification problem, where we want to classify each 10 minute EEG segment as interictal or preictal. The method proposed in this work relies on dividing each segment into smaller windows of 30 seconds each. After this division, a feature extraction step takes place, retrieving the signal statistics (mean, standard deviation, kurtosis and etc) and frequency domain features, such as the the signal power between certain frequency bands. After the evaluation of several machine learning approaches, an algorithm based on a logistic regression was able to obtain significant patient-specific results, which shows that, for one given patient, a seizure prediction technique can be developed with the help of machine learning and EEG data.

Keywords: Seizure Prediction, Machine Learning, Classification, Electroencephalography, EEG

RESUMO

OLIVEIRA, L. F. **Previsão de ataques epilépticos com a utilização de aprendizado de máquina**. 2020. 53p. Monografia (Trabalho de Conclusão de Curso) - Escola de Engenharia de São Carlos, Universidade de São Paulo, São Carlos, 2020.

Este estudo tem como objetivo o desenvolvimento de um método para a previsão de ataques epilépticos utilizando uma abordagem baseada em aprendizado de máquina. Com o auxílio de dados oriundos da eletroencefalografia que foram coletados de 3 pacientes, um pipeline de previsão foi desenvolvido após a avaliação de diferentes técnicas de aprendizado de máquina. Entre tais técnicas, pode-se citar: florestas aleatórias, *gradient boosting*, redes neurais recorrentes e regressão logística. Para cada paciente, o sinal de EEG foi dividido em segmentos de iguais duração, cada um durando 10 minutos. Além disso, cada segmento foi rotulado como pré-ictal (anterior ao ataque epiléptico) ou interictal (entre ataques ou atividade cerebral normal). Sendo assim, o problema tratado neste trabalho pode ser resumido como uma tarefa de classificação binária onde deseja-se classificar cada segmento de EEG como pré-ictal ou interictal. O método proposto nesse trabalho se baseia na divisão deste segmento de 10 minutos em janelas menores, de 30 segundos cada. Após essa divisão, um procedimento de extração de características (*features*) é realizado. Algumas destas características incluem diversas estatísticas que foram calculadas do sinal (média, desvio padrão, assimetria, curtose, etc), bem como características derivadas do domínio da frequência, como por exemplo a potência do sinal em diferentes bandas. Após a avaliação de diferentes de diferentes algoritmos de aprendizado de máquina, foi possível concluir que um algortimo baseado em regressão logística foi capaz de obter resultados significantes para cada paciente, mostrando que uma técnica de previsão de epilepsia pode ser desenvolvida com o auxílio de dados de EEG e de aprendizado de máquina.

Palavras-chave: Previsão de epilepsia, aprendizado de máquina, classificação, eletroencefalografia, EEG

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LIST OF ABBREVIATIONS AND ACRONYMS

EEG	*Electroencephalography*
iEEG	*Intracranial electroencephalography*
PSD	*Power spectral density*
AUC	*Area under the curve*
ROC	*Receiver operating characteristic*
FPR	*False positive rate*
TPR	*True positive rate*
ERS	*European respiratory society*

CONTENTS

1 INTRODUCTION

The epilepsy is a chronic disease that affects the brain and is responsible for causing repetitive seizures. Recent studies show that the epilepsy affects around 70 million people in the world, being responsible for 0.7% of the global disease load (FAZEL et al., 2013). Epileptic seizures happen unexpectedly and can be classified into two categories: partial and general. In the case of a partial seizure, the attack occurs in only one half of the brain, while in the general case the seizure occurs in both parts of the brain. During a partial seizure, it is possible that the given person is conscious and does not realize that a seizure is taking place, which can lead to an aggravation of the disease (FERGUS et al., 2016), (CHAOVALITWONGSE et al., 2011).

The diagnosis of the disease is done with the assistance of the electroencephalography (EEG), a technique capable of reading the electrical potential generated in the brain with a special device called electroencephalogram (KUMAR; BHUVANESWARI, 2012). The data generated from this technique are constantly analyzed by neurologists who aim to detect indicating patterns that signalize the presence of the disease. These analyses are done in a visual fashion, which makes this work laborious and time-consuming, since neurologists need some hours in order to analyze the data recorded from only one daily session and from a single patient. Besides, there is also the fact that it is necessary to allocate a specialized doctor only for this task (ULLAH et al., 2018).

With the development of the field of machine learning along with a development in the data collection process, the automation of the seizure detection and prediction task became possible. Since the late 20^{th} and the early 21^{st} centuries, researchers have been trying to come up with different approaches to enable seizure prediction and detection, mostly relying on machine learning algorithms (KUHLMANN et al., 2018b). These algorithms are capable of exploring hidden patterns that are present in the high complex EEG signal. Some previous work obtained significant results by applying such techniques to detect the occurrence of a seizure while it is happening, (FERGUS et al., 2016), (CARNEY; MYERS; GEYER, 2011), (LI et al., 2017). However, the occurrence of an epileptic seizure can lead to the lost of consciousness and also to serious injuries. (FUJIWARA et al., 2015). Because of this, it is necessary to develop an algorithm which is capable of predicting future seizures, since its anticipation would make it possible for preventive or control measures to be taken before the seizure's onset, which could even lead to a cancellation of the seizure before its physiological manifestations start to take place (BEGANOVIC; JUKIC; KEVRIC, 2019).

A factor that plays an important role in determining the viability of the development of seizure prediction techniques with a machine learning approach is the availability of good-quality EEG measurement data. Until the last few years, only a limited amount of data was available. With the evolution of data collection systems, researchers are being able to collect even more EEG data over time. More importantly, this data is constantly being publicly available to the seizure prediction research community. Some examples of these open source databases are the ones provided by Epilepsy Ecosystem (KUHLMANN et al., 2018b), *PhysioNet* (GOLDBERGER et al., 2000) and by the *Temple University Hospital Corpus* (SHAH et al., 2018). These databases provide both intracranial and scalp EEG data.

Since the problem of developing a reliable seizure prediction method is posed, the purpose of this work is to develop an algorithm for seizure prediction based on EEG data. The main focus is to evaluate how the EEG signal can be processed so that a machine learning algorithm can be able to classify, with a certain anticipation, if a seizure is likely to happen in the next minutes. Mostly, attention will be given to the feature extraction process in order to assess which variables are important in determining the occurrence of a seizure. These features will be derived from a variety of areas, ranging from basic signal statistics to features derived from signal processing techniques. At the end of this project, the goal is to have a patient-specific system that is capable to confidently detect if there is a high chance that this specific patient has a upcoming seizure.

2 LITERATURE REVIEW

2.1 Task definition

One of the methodologies that are commonly applied by seizure prediction researchers consists of a pre-selection of a preictal (prior to seizure) duration, intending to categorize the signal in preictal and interictal states. If a pre-selected segment is labeled as preictal, this means that the given patient had a seizure in a short time interval after the moment defined as the end of this preictal segment. On the other hand, if a pre-selected segment is labeled as interictal, this means that the patient did not have any seizure activity after this event, which indicates a normal activity of the brain or a period between seizures. Therefore, the seizure prediction task can be summarized as a binary classification problem where we want to determine if a given EEG segment is preictal or interictal (TSIOURIS et al., 2018).

2.2 Nature of EEG Data

EEG mainly reflects the summation of postsynaptic potentials at the dendrites of groups of neurons. As the ion channels on the brain cell membrane are activated by neurotransmitters, ions flow into and out of the neuron. This change in potential generates electrical fields that surrounds the neuron. With this phenomenon happening synchronously in a net containing thousands of neurons, the electrical fields generated by individual neurons end up being summed, creating a resulting electric field that is powerful enough to be measured by the EEG electrodes, which can be placed inside the head (intracranial EEG) or above the scalp. After the signal is captured by the electrodes, proper instrumentation circuits are used in order to amplify and filter the signal so it can be later processed (COHEN, 2014). An illustration of the EEG data acquisition process is illustrated in Figure 1.

In order to capture the electrical activity inside the brain, different types of EEG montages were proposed by previous work. These montages define a certain configuration in which electrodes are placed inside the cranium or above the scalp. One very commonly used montage, which is also the montage in which the data used in this work was acquired, is the 10-20 system, which is displayed in figure 2. With this montage, it is possible to receive EEG signals from 16 electrodes, in total (SAZGAR; YOUNG, 2019). An example of the measured generated signal can be visualized in figure 3. At the end, this configuration provides 16 EEG time series, one for each electrode, as shown in figure 3

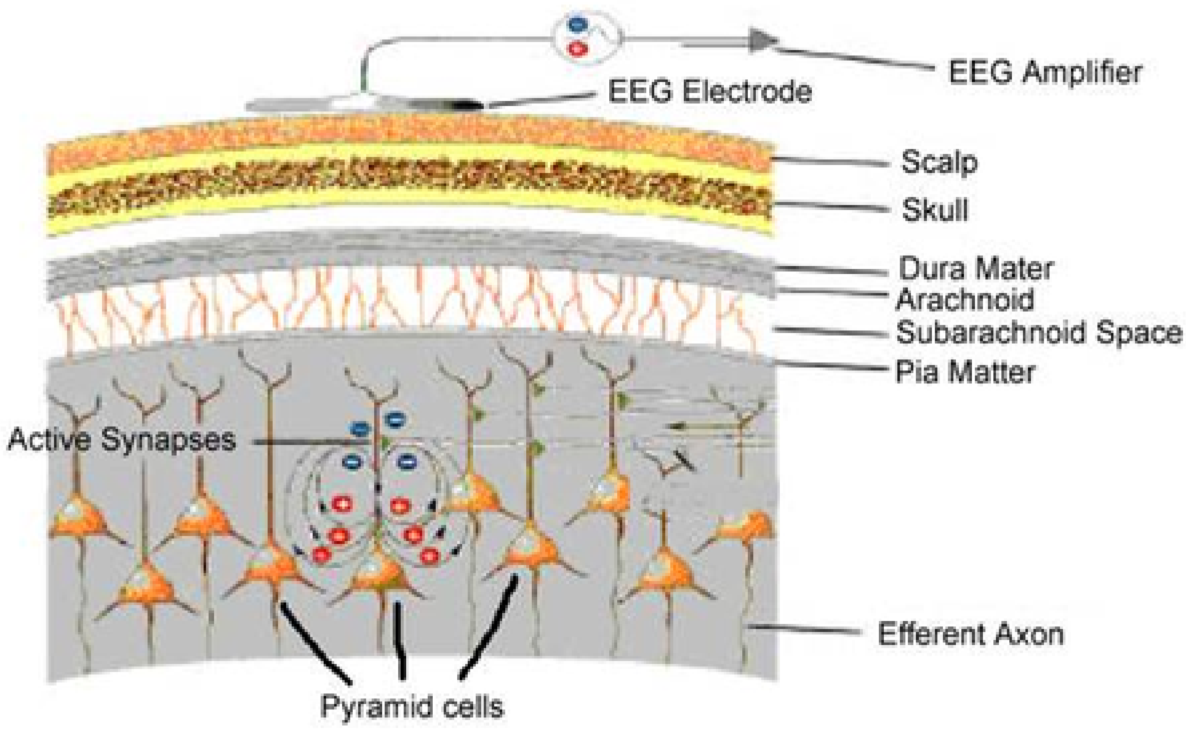

Figure 1 – Nature of EEG data - Source: Epilepsy Foundation

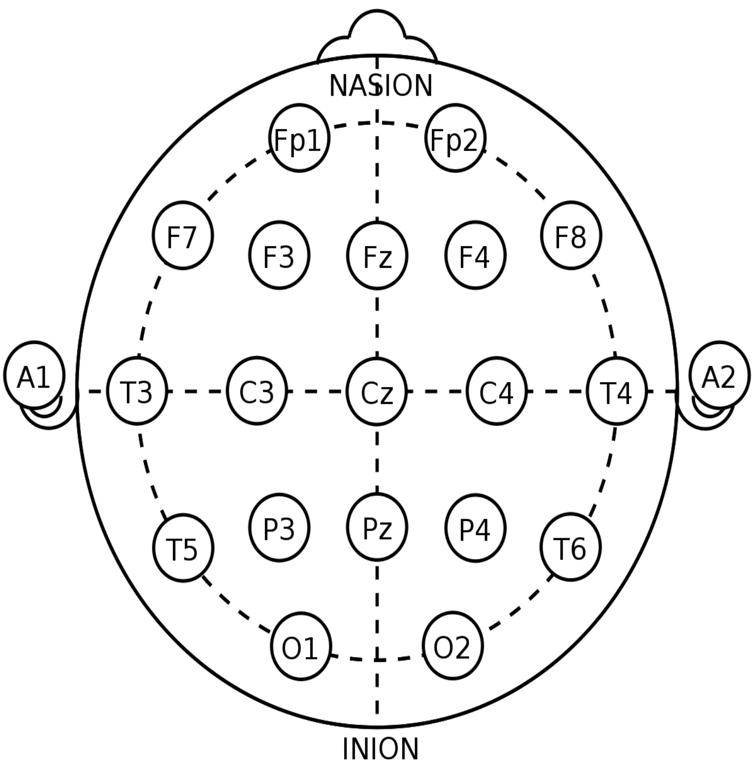

Figure 2 – EEG 10-20 system montage configuration - Source: ERS

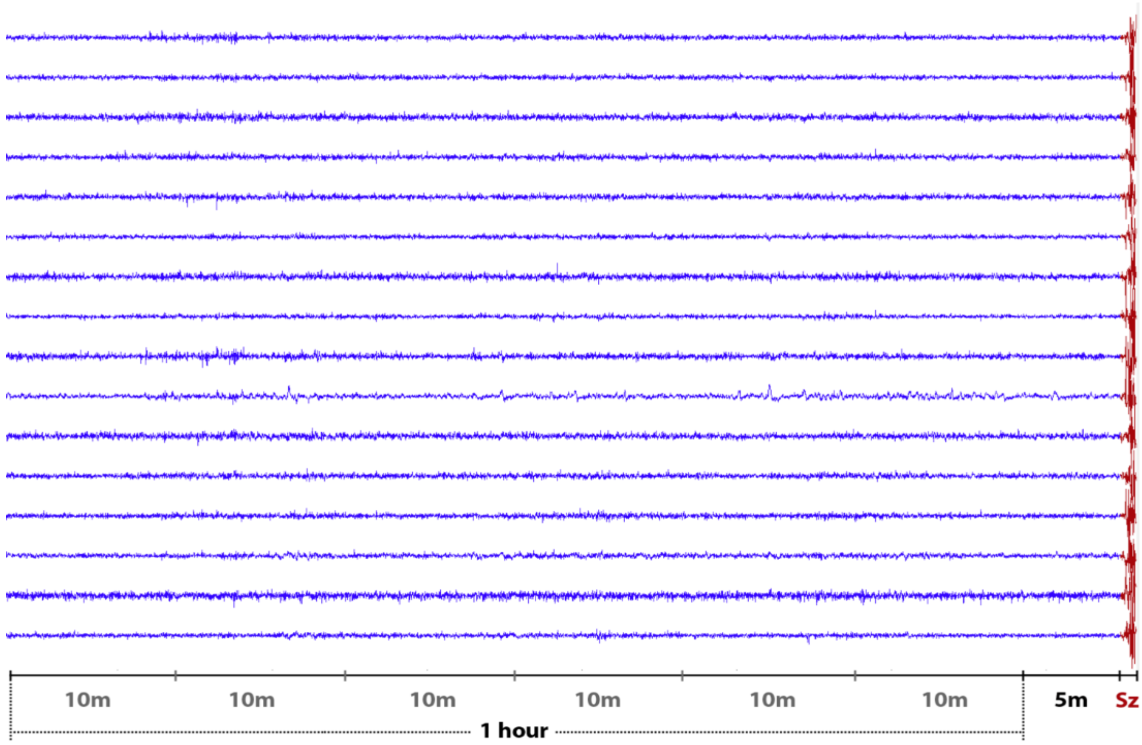

Figure 3 – EEG 16-channel time series data - Source: Epilepsy Ecosystem

2.3 EEG Features

In order to process the raw EEG signal segment, it is common to split the raw segment into segments of smaller duration (or windows) that are later used for feature extraction. This provides a reduction in the complexity of the EEG data as seen by the machine learning algorithms, which can provide more classification power during the task (DIREITO et al., 2011). In the next sections, a theoretical basis for the features used in this work will be presented.

2.3.1 Signal processing techniques

2.3.1.1 Fourier transform

The Fourier transform is a mathematical transformation that takes a signal $x(t)$ defined in the time domain and converts it to a representation in the frequency domain $X(\omega)$. This is done by writing the signal as a linear combination of an infinite amount of sines and cosines and its computation is shown in the equation 2.1.

$$X(f) = \int_{-\infty}^{+\infty} x(t)e^{-j2\pi ft} \tag{2.1}$$

Which can be also written in its discrete form:

$$X[k] = \sum_{n=0}^{N-1} x[n]e^{-j2\pi kn/N} \tag{2.2}$$

The Fourier transform has been widely used in many scenarios, ranging from data compression (REDDY; MURTHY, 1986) to image noise filtering (FIALKA; CADIK, 2006). When it comes to EEG data, the Fourier transform is not widely applied because of its stationarity assumption. The stationarity assumption states that the signal for which the transform is being computed maintain its statistical properties through the whole period of analysis. Since EEG data is non-stationary (KRYSTAL; PRADO; WEST, 1999), the application of the Fourier transform results in a very noisy spectrum $X(\omega)$, which is undesired while developing seizure prediction techniques.

2.3.1.2 Spectral density estimation

In order to deal with the non-stationarity of signals, several methods were recently developed. These methods try to, given data that are non-stationary, obtain a smoother estimation for the frequency spectrum $X(\omega)$ of the signal $x(t)$. One estimation method that is widely used is the Welch's method. The main idea behind this technique is to assume that although the signal is non-stationary, it can be assumed stationary if small time windows of size W of this signal are taken. Therefore, this method isolates the signal in windows, applying the Fourier transform in each separated window. In order to obtain the final spectrum, an average of the spectrum of each window is computed (COHEN, 2014). To compute the Welch's periodogram, the following steps must be taken:

1. Compute the periodogram for each individual defined window

$$\hat{P}_x^{(k)} = \frac{1}{N} \sum_{n=0}^{L-1} w[n]x^{(k)}[n]e^{-j2\pi kn} \tag{2.3}$$

   Where $w[n]$ represents the value of the signal window function and $x^{(k)}$ represents the k^{th} segment of the divided signal.

2. Compute the averaged periodogram across all segments

$$\hat{P}_x = \frac{1}{K} \sum_{k=1}^{K} \hat{P}_x^{(k)} \tag{2.4}$$

2.3.1.3 Energy of a signal

The energy of a signal can be computed based on its periodogram $X(f)$, which can be computed with the Fourier transform or with a spectral density estimation technique

(COHEN, 2014).

$$E = \int_{-\infty}^{\infty} |X(f)|^2 df \tag{2.5}$$

In its discrete form, the energy of a signal can be computed by taking a discrete integral of the spectrum in predefined frequency bands.

2.3.1.4 Signal differentiation

Signal differentiation is a widely applied technique in order to process and understand digital signals. The differentiation of a signal gives information about the rate of change of a signal, which can be an important information about its dynamic and therefore can be used as another step of a possible feature extraction process. The differentiation $\dot{x}[n]$ of a discrete signal $x[n]$ can be computed as follows:

$$\dot{x}[n] = \frac{x[n] - x[n-1]}{T_s} \tag{2.6}$$

Where T_s is the sampling period of the given signal.

2.3.2 Frequency related features

2.3.2.1 EEG energy bands

While studying EEG signals, researchers have found that the amount of energy contained in specific bands were descriptive of the cerebral brain activity. Relative power differences in the delta ($\leq 3Hz$), theta (4-7 Hz), alpha (8-13 Hz), beta (14-30 Hz) and gamma ($\geq 30Hz$) have shown great potential in characterizing preictal behavior in scalp and intracranial EEG measurements (PARK et al., 2011; ZHANG; PARHI, 2015; BANDARABADI et al., 2015). An example of such EEG bands is shown in figure 4, where each different color represent a respective frequency band range.

2.3.2.2 Spectral edge frequency

Another common feature that is extracted from EEG signals while working with seizure prediction is the spectral edge frequency (RASEKHI et al., 2013). The spectral edge frequency f_{edge} is defined as the frequency value for which a fraction f_q of the total amount of signal power is below f_{edge}. It can be understood as a frequency quantile if one visualizes the frequency spectrum as a distribution. Figure 4 shows an example of the spectral edge frequencies computed for values of f_q equal to 0.8, 0.9 and 0.95, respectively.

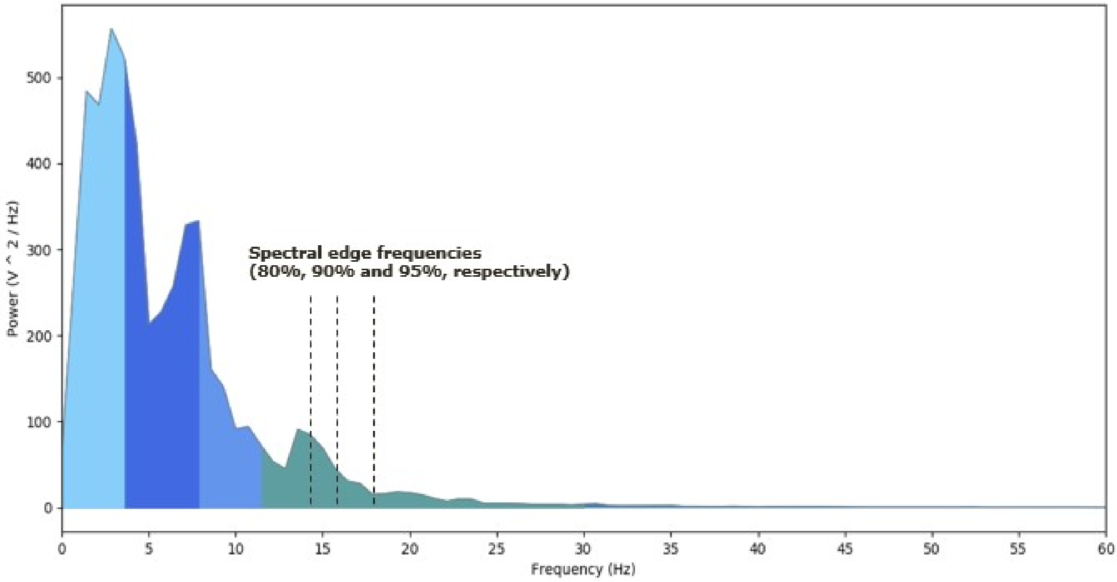

Figure 4 – EEG bands and spectral edge frequencies

2.3.3 Time related features

2.3.3.1 Number of zero crossings

One commonly extracted feature from EEG signals while working with seizure prediction algorithms is the number of zero crossings in the given signal. This feature gives information about the dynamic and about abrupt changes happening in the EEG data (TSIOURIS et al., 2018).

2.3.3.2 Maximum peak to peak difference

The maximum peak to peak difference is another feature that is commonly extracted from EEG signals. This gives information about the overall magnitude of the signal and about the magnitude of the changes happening in the signal. It can be computed as given below:

$$PP_x = max(x[n]) - min(x[n]), n = 1...N \tag{2.7}$$

2.3.3.3 Complexity and mobility

Formulated by (HJORTH, 1970), the complexity and mobility are also two factors that can be computed from a digital signal, that also gives information about the dynamical behavior of the signal. The mobility parameter represents the mean frequency or the proportion of standard deviation of the power spectrum and can be computed as shown in equation 2.8.

$$Mobility = \sqrt{\frac{var(\frac{dx(t)}{dt})}{var(x(t))}} \tag{2.8}$$

The complexity parameter represents the change in frequency and can be computed as shown in equation 2.9.

$$Complexity = \frac{Mobility(\frac{dx(t)}{dt})}{Mobility(x(t))} \tag{2.9}$$

2.3.4 Basic statistics

Let x be an arbitrary signal as seen as a function of time and $x[n]$ the n^{th} sample of the signal, where $n = 1...T$, being T the duration of the signal. It is possible to compute several basic statistics for this given signal. Those statistics can later be seen as features that will serve as inputs to the machine learning algorithm. In order to get a sense of the ideas behind these features, they will be mathematically formulated in the following sections.

2.3.4.1 Mean

The mean $\bar{x}$ of a signal can be computed as given below.

$$\bar{x} = \frac{1}{T}\sum_{i=1}^{T} x[i] \tag{2.10}$$

2.3.4.2 Standard deviation

Let x be a signal and $\bar{x}$ be its computed mean. We can compute its standard deviation σ as given below.

$$\sigma = \sqrt{\frac{\sum_{i=1}^{T}(x[i] - \bar{x})^2}{T - 1}} \tag{2.11}$$

2.3.4.3 Skewness

The skewness of a sample is a measure of assimetry of the data. If the data points in the sample tend to be concentrated towards values that are lower or higher than the median, the value of the skewness of this sample will change based on this variation.

The sample skewness can be computed as the Fisher-Pearson coefficient of skewness (KOKOSKA; ZWILLINGER, 2000), as shown below:

$$g_1 = \frac{m_3}{m_2^{3/2}} \tag{2.12}$$

Where m_3 and m_2 represent the third and second statistical moments, respectively. A statistical moment m_i can be computed as:

$$m_i = \frac{1}{N}\sum_{n=1}^{N}(x[n] - \bar{x})^i \tag{2.13}$$

2.3.4.4 Kurtosis

The kurtosis is the fourth central moment divided by the square root of the variance and it also gives information about the shape of the distribution of the sample values (KOKOSKA; ZWILLINGER, 2000). It can be computed by using taking the result of equation 2.13 with $i = 4$ and dividing it by the result of equation 2.14.

2.3.4.5 RMS Value

The RMS (root mean square) value of a signal gives the information about the overall magnitude of a signal without considering the difference between positive and negative value. It can be computed with the equation shown below.

$$RMS = \sqrt{\frac{\sum_{i=1}^{T} x[i]^2}{T}} \tag{2.14}$$

2.4 Machine Learning Overview

In this work, some machine learning techniques were applied in order to try to accomplish the seizure prediction task. Because of this, this section contains a brief introduction to the most important aspects of machine learning and to the most important algorithms that were applied in this project.

2.4.1 Supervised learning

In a supervised learning scenario, the main goal is to map some observed input variables X to some outputs y. The whole field of supervised machine learning aims to find different and efficient ways on how to learn a function $f(X)$ that performs the mapping of the input data space X to the output space $f(X) = \hat{y}$. Across all machine learning methods, this mapping is done with an optimization procedure that tries to find the best mapping according to some error measure, which is always conditioned on the training data at hand and is computed comparing the observed inputs y and the estimated outputs $\hat{y} = f(X)$ (BISHOP, 2006).

2.4.1.1 Classification and regression

While working in a supervised learning scenario, machine learning problems are divided into two types of tasks: classification and regression. Both of these tasks demand different approaches, which can be sumarized as follows:

1. **Classification:** A classification task consists in predicting to which class a certain instance of the input space belongs to. For example, given inputs of a variable vector $X = \{x_1, x_2, x_3, ..., x_n\}$, it is desired to determine, based on a group of classes $c = \{c_1, c_2, c_3, ..., c_n\}$, to which class c_j a certain pattern x_i can be mapped. Examples from classification tasks are image object detection (KRIZHEVSKY; SUTSKEVER; HINTON, 2012) and handwritten digits recognition (LECUN et al., 1990). In this work, our seizure prediction problem is formulated as a binary classification task, since we wish to classify an EEG segment as preictal or interictal.

2. **Regression:** A regression task differs from a classification in the sense that the desired output y is a continuous value. Having a certain input pattern $X = \{x_1, x_2, x_3, ..., x_n\}$, it is then desired to predict a continuous output $y \in (R)$. An example of this kind of machine learning task is the estimation of the value of a real state property based on the number of rooms, location neighborhood, local average income, etc (COCK, 2011).

2.5 Logistic Regression

With the objective of modelling a binary classification problem, a logistic regression tries to estimate the probabilities of each class $p(c_i)$ by applying a logistic function to the linear regression coefficients. The logistic function is described in the equation 2.15.

$$p(c_i) = \frac{1}{1 + e^{-z}} \tag{2.15}$$

Where $z = \mathbf{X}\beta$, being $\mathbf{X}$ a matrix of input variables (the inputs of the supervised learning task) and β a vector of parameters that are estimated from the data (JAMES et al., 2013). Mostly, the search for the vector of parameters β can be done using an optimization procedure called gradient descent (GASSO, 2019). Figure 5 shows the behavior of the logistic function, given that its inputs are varying linearly.

One important advantage from the logistic regression is that it is a very good probability estimator. This happens mainly because of its link logistic function. This function has saturation points in both ends, which makes sense when thinking about

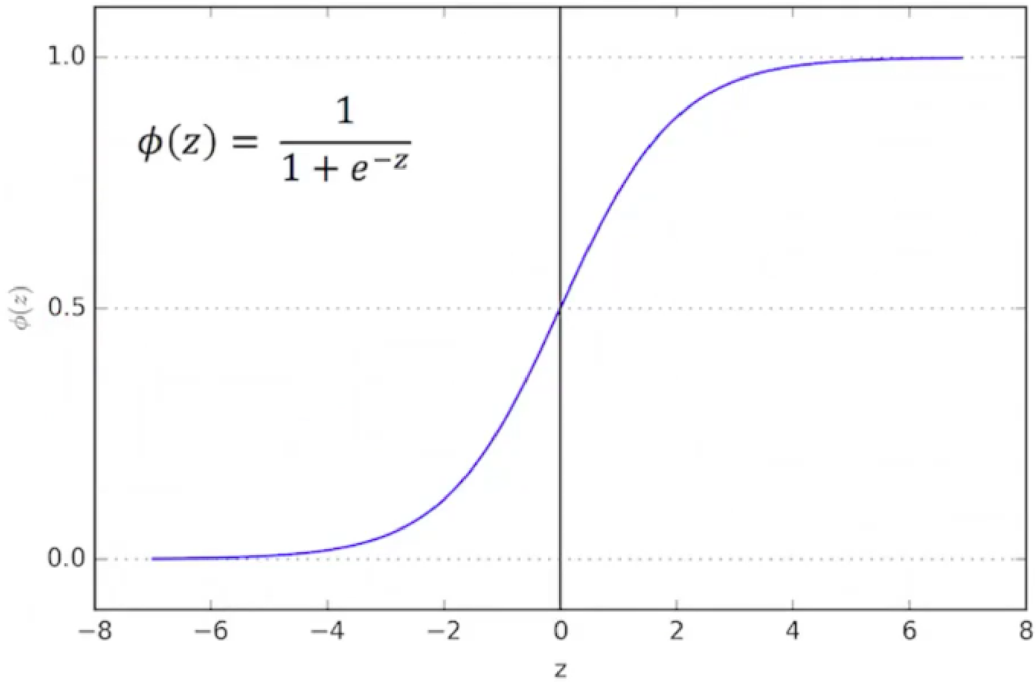

Figure 5 – Logistic regression link function - Source: TowardsDataScience

probabilities estimation. In the negative end, the smaller the value of $\mathbf{X}\beta$ gets, the derivative of this function approaches zero. The same thing happens on the other end of the function domain. The bigger the value of $\mathbf{X}\beta$, it becomes more difficult to obtain a larger probability value as an output. This makes sense because the more certain we are about the chance of a specific event happening, the more difficult it will be for us to become even more certain about it. The same explanation applies to the other end of the function: the more certain we are about a specific event not happening, the more difficult it is for us to say that the chance of this event happening is smaller. For this reason, this makes the logistic regression technique a good probability estimator in comparison with other machine learning methods (MCELREATH, 2020). This is a property of the logistic regression that will be explored in this work.

2.6 Validation methods for classification

When working with classification methods in machine learning, it is a common practice to use different classification metrics and methods in order to evaluate the performance of the obtained classifiers. This section will be dedicated to giving an overview about the evalution metrics and methods that were applied in this work.

2.6.1 ROC curve and AUC Score

An ROC (receiver operating characteristic) curve is a common tool used with binary classifiers. The ROC curve plots the true positive rate (TPR) against the false positive rate (FPR). The FPR is the proportion of instances classified as the positive class when they belong to the negative class. The TPR is the proportion of instances predicted as the positive class when they indeed belong to the positive class. By plotting the ROC curve, one can get a sense of the performance of the binary classifier (GÉRON, 2019). Figure 7 shows an example of a ROC curve of a binary classifier.

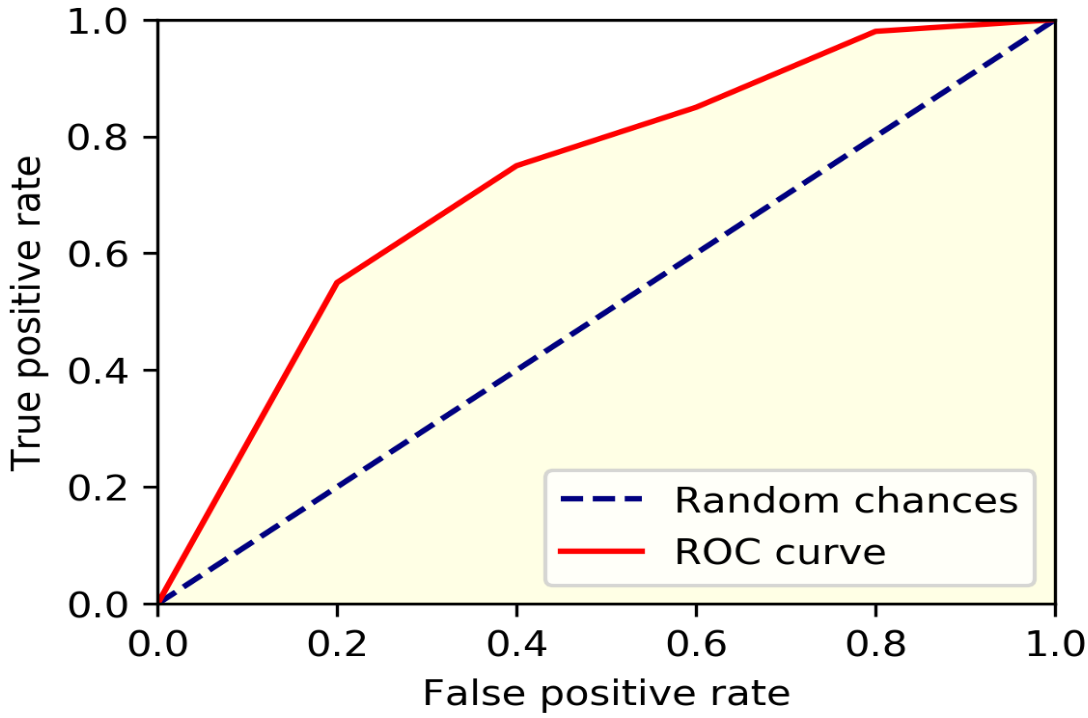

Figure 6 – ROC curve and AUC score - Source: Towards Data Science

The performance of a classifier can be assessed by looking at the ROC curve or by taking the area under it. This score obtained as the area is called AUC (area under the curve) score and is highlighted as the yellow region in figure 7. Seizure prediction techniques can be reasonably well evaluated using the ROC curve and the AUC score, since we are mostly worried about the false alarms that a seizure prediction scheme may generate.

2.6.2 Stratified K-Folds cross validation

One way to evaluate machine learning classification algorithms is the Stratified K-Folds cross validation. It consists of randomly dividing the training sets into K smaller subsets, called folds. After this division is done, the machine learning algorithm is trained using K-1 folds, while using the remaining fold to evaluate the quality of the algorithm predictions. This last fold contains datapoints that were never seen by the model, since the model must be evaluated with data coming from outside the training set in order to simulate a scenario where the model would be put into production, making its predictions on never seen data. This process is done K times, where each time a performance score (e.g AUC score) is computed for each fold. In the end, the final score is taken as a statistic of the set of scores obtained in each fold, such as the mean (GÉRON, 2019). By doing this, the K-Fold cross validation method guarantees better estimates for the true error of the classifier, since it is computed based on more than one evaluation subset.

If we are working with a classification problem, it is possible that the dataset that is being used is imbalanced with respect to the class labels (the desired output values). In order to prevent this class imbalance to be extreme within each fold, another technique that it is applied is the subset stratification. This consists in sampling the data points in a way that keeps the class proportion in each individual fold. This is a way to obtain less unbiased estimates of the true value of the error that the applied model makes when working with real world data. This a widely used approach when evaluating classifier models and that is also used in this work.

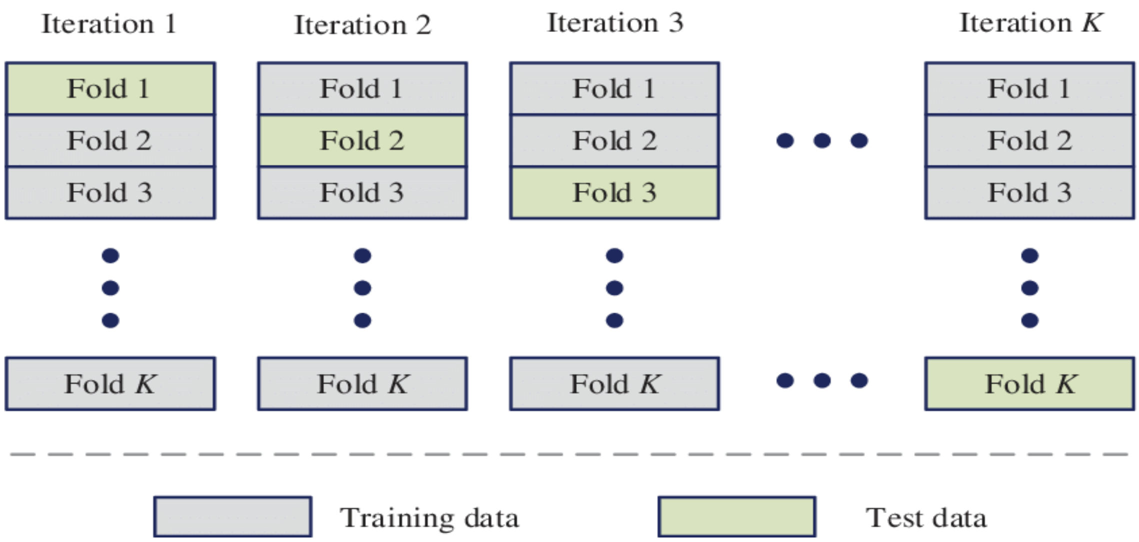

Figure 7 – K-folds cross validation - Source: Taken from (REN; LI; HAN, 2019)

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3 MATERIALS AND METHODS

3.1 EEG Data

In 2016, the Melbourne University AES-MathWorks-NIH Seizure Prediction Challenge was hosted on Kaggle. In this challenge, labeled EEG measurements from three patients were made available for users of the platform to try to come with algorithms for seizure prediction. In a previous trial conducted by *NeuroVista*, these three patients were identified as the ones for whom it was considered to be very difficult to develop a seizure prediction procedure, which is why this competition was hosted on Kaggle and why the data was lately made available at *Epilepsy Ecosystem* (KUHLMANN et al., 2018a). This is the data that is going to be used in this study.

The data consists of intracranial electroencephalogram (iEEG) measurements that were sampled with 16 channels at a sampling frequency of 400 Hz and referenced to the average voltage value. The measurements were divided into 10 minute segments and shuffled randomly. According to (KUHLMANN et al., 2018a), this is done in order to help the seizure prediction methodology generalize to a 10-minute EEG segment that was selected at an arbitrary point in time. In doing so, the seizure prediction algorithm can learn more general preictal patterns instead of relying itself on a long-term continuity of the signal. The dataset was also previously divided into train and test sets. The number of available segments varies per each patient and are displayed in table 1.

	Patient 1	**Patient 2**	**Patient 3**
Number of segments in train set	450	1066	1530
Number of segments in test set	151	356	511

Table 1 – Number of segments in train and test sets

3.2 Seizure prediction methodology

3.2.1 Overview

In order to translate the raw EEG data into a format that a machine learning algorithm could understand, a signal processing and a feature extraction needed to be developed. Since each EEG segment contains recordings of 10 minutes of duration, a moving window strategy was adopted in order to be able to capture the dynamic and development of possible preictal patterns. Given an input segment, each signal from each channel is divided into 30 seconds windows with an overlap of 5 seconds each. After this step, feature extraction is performed on each window, separately. A logistic regression classification algorithm is applied to these extracted features, which estimates

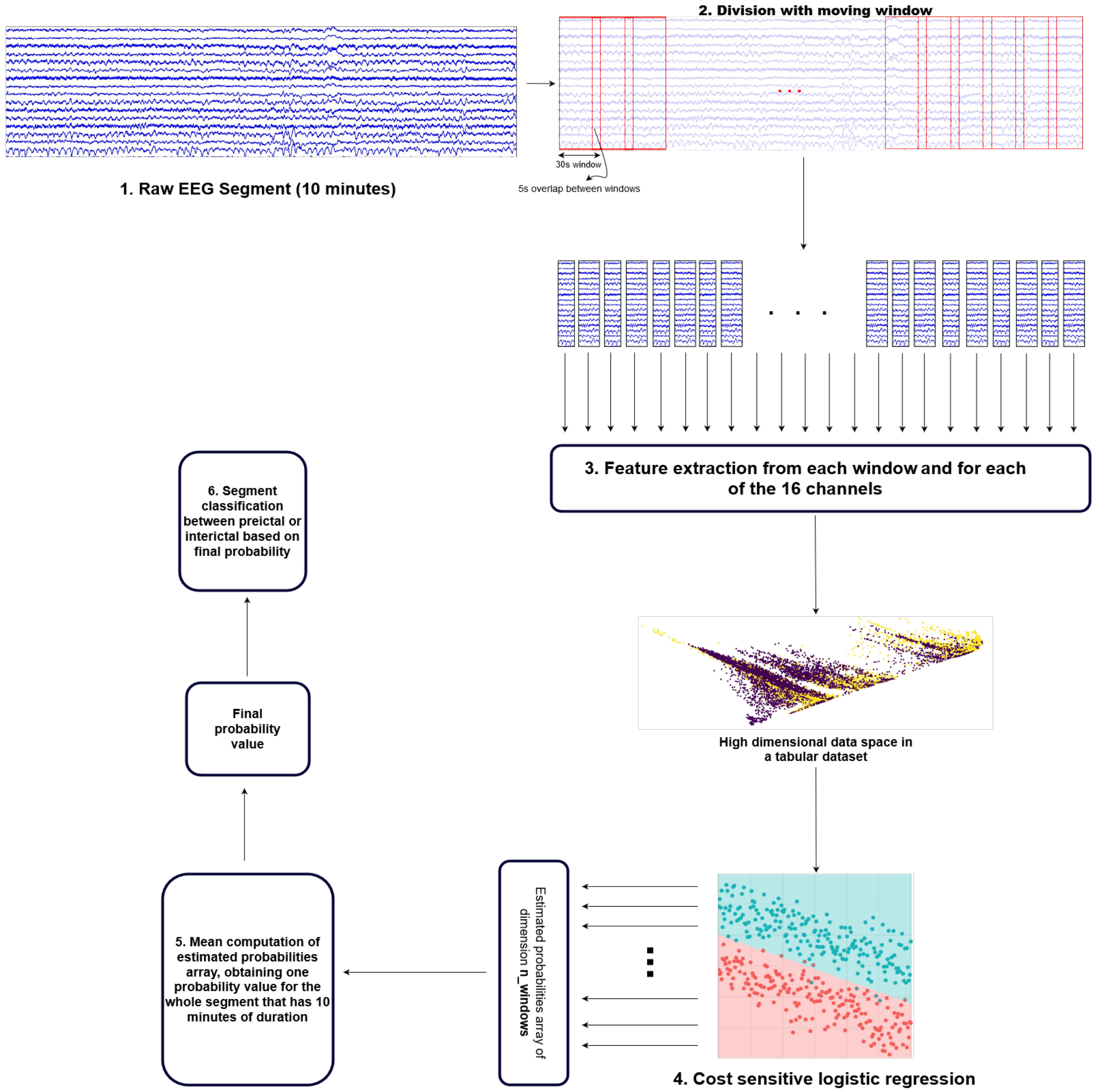

Figure 8 – Overview of the seizure prediction methodology

the probability of a certain window representing a preictal or interictal pattern. At the end of the pipeline, each segment will contain one probability value for each extracted window. These probabilities are then aggregated by taking the mean across all different windows, generating a final probability value which is then used to classify the whole segment as preictal or interictal. An illustration of the whole process is displayed in Figure 8.

3.2.2 Feature extraction

In order to abstract the raw EEG signal into a form where a machine learning algorithm could be applied, several features were extracted from each segmented window and for each channel. The features were later merged in order to form a high dimensional dataset with which the learning algorithm was used. These features contemplate a frequency and time domain analysis as well as the extraction of spatial features.

3.2.2.1 Frequency domain features

For each segmented window from each channel, the PSD (power spectral density) was estimated using the Welch's method with a window containing 4 times the sampling frequency ($4 * f_s$). After the PSD estimation, the following frequency domain features were computed:

1. Total signal power
2. Relative energy in the EEG bands: delta ($\leq 3Hz$), theta (4-7 Hz), alpha (8-13 Hz), beta (14-30 Hz) and gamma ($\geq 30Hz$).
3. Spectral edge frequencies of 75%, 80%, 85%, 90% and 95%.

3.2.2.2 Time domain features and signal statistics

Time domain and signal statistics were also computed for each segmented window and for each channel. The following features were extracted from the original signal and its first two derivatives, that were computed using signal differentiation.

1. Number of zero crossings.
2. Mean, absolute mean, standard deviation, skewness, kurtosis and RMS value.
3. Maximum peak difference.
4. Mobility and complexity

3.2.2.3 Spatial features

With the objective of investigating if the relationship between different EEG channels could describe an EEG pattern through the spatial configuration of the montage, the correlation matrix was computed. After the computation, it is possible to obtain correlation coefficient for all channel pairs. Figure 9 shows an example of a channel correlation matrix for one extracted window. The element in row i and column j of this matrix represent the computed correlation in time domain between channels i and j. Since EEG channels are distributed in different regions of the brain, the correlation values provided by this matrix try to capture the relationship between different channels that can highlight preictal or interictal patterns.

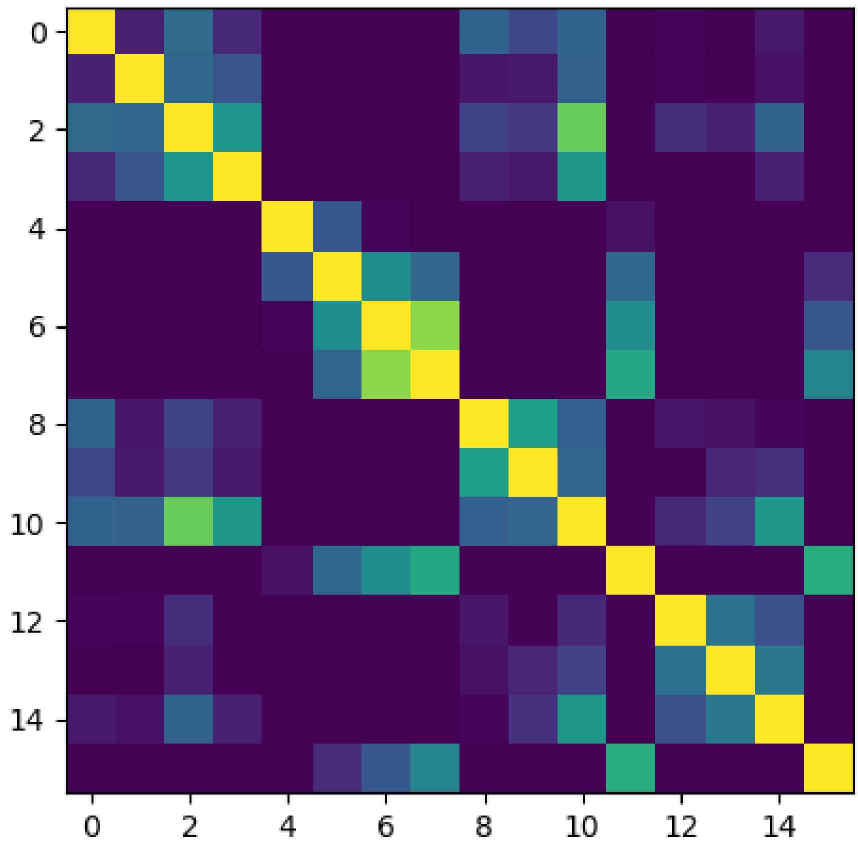

Figure 9 – Example of a correlation matrix between the 16 EEG channels for one extracted window

3.2.3 Logistic regression considerations

The extracted features were fed to a logistic regression classifier in order to be able to learn the preictal and interictal patterns. But before this was done, one small adaptation needed to be done in order to enhance the performance of our classifier. Seizure prediction datasets are always imbalanced (ULLAH et al., 2018). This means that, most of the times, there is considerably less seizure events than other types of activity in the EEG data. This poses a difficulty when working with traditional machine learning algorithms, since machine learning techniques always learn from the data by basing themselves on the optimization of some cost function. Traditionally, this learning process does not take into account the importance of certain instances of the dataset. This means that if no action is taken in order to make the algorithm handle the imbalanced dataset, it is possible that the chosen technique will be very good in getting one class right but, on the other hand, very bad at predicting instances from the other class.

In order to deal with this problem, a cost-sensitive logistic regression was applied. The basic idea of this method is to punish the model more severely when it fails to predict one of the classes correctly. With a logistic regression classifier, this can be done by modifying the cost function in a way that takes into account the desired behavior, that is handling the imbalanced binary classification task. Mathematically, this can be done by adding one more term to the gradients updating function which, for each instance, adds a weight as a penalty in the cost function. Fortunately, the *scikit-learn* Python package offers a out-of-the-box implementation of a cost-sensitive logistic regression. In this work, the weight of each instance was defined based on the classes proportion in the training set.

3.2.4 Validation strategy

Since several variants of the seizure prediction methodology were tested, a validation strategy needed to be adopted. The adopted strategy was a 5-fold cross-validation procedure, where the performance scores in each fold were computed based on the predictions that are obtained per segment. This means that the seizure prediction methodology was applied to the full EEG segments and, after obtaining the predicted label for all segments within each fold, the overall AUC score was computed. This whole procedure was done using data only from the training set. Finally, after the experimentation with the chosen approaches, a final AUC score was obtained by applying the methodology on the isolated test set. This evaluation procedure as applied to data related to each patient, since the purpose of this work was to build a patient-specific seizure prediction methodology.

4 RESULTS

4.1 Seizure prediction methodology

By using the explained seizure prediction methodology and the evaluation method as previously described, it was possible to obtain the following results shown in table 2 for the K-folds cross validation AUC scores. This was done before testing the methodology on a held-out test set in order to get previous estimates about the performance of the developed patient-specific models. In addition, other sliding window sizes were tested before setting the final window size as 30 seconds, as also shown in table 2.

Window duration in seconds	Patient 1	Patient 2	Patient 3
30	0.895	0.842	0.895
150	0.887	0.778	0.881
300	0.879	0.782	0.876
600 (full segment)	0.856	0.699	0.802

Table 2 – Obtained AUC scores using the adopted validation strategy.

It is possible to notice that the seizure prediction strategy was able to perform reasonably well during the validation phase. In addition, it was also possible to see that the the overall performance mostly drops when the window size gets larger. When the window size is small, the extracted features end up representing short-term preictal patterns, which shows to be beneficial for the classification task. Besides, the division of the EEG segment into smaller windows helps capture a developing pattern along the segment, which can also be an indicator of a incoming seizure. This developing pattern would be captured by the change in features values in the consecutive rolling windows.

After applying this evaluation methodology, the whole pipeline was applied to a held-out test dataset. In this test set, the chosen rolling window size for the feature extraction step was of 30 seconds, since it was the window size that better performed during the evaluation phase. The results for each patient are shown in tables 3, 4 and 5. These tables also show the count of segments that were classified as being preictal/interictal with regard to the ground truth value. For example, in table 3, we have that 98 segments were correctly classified as interictal and 42 segments were correctly classified as preictal. On the other hand, the table also shows that 8 segments were mistakenly classified as preictal while being, in fact, interictal (false positives). Finally, the table also shows that 3 segments were mistakenly classified as interictal while being preictal (false negatives).

Patient 1 - AUC Score: 0.928		
	Interictal	**Preictal**
Interictal	98	8
Preictal	3	42

Table 3 – Test set scores for patient 1

Patient 2 - AUC Score: 0.809		
	Interictal	**Preictal**
Interictal	269	45
Preictal	10	32

Table 4 – Test set scores for patient 2

Patient 3 - AUC Score: 0.917		
	Interictal	**Preictal**
Interictal	416	36
Preictal	5	54

Table 5 – Test set scores for patient 3

4.2 Discussion

After the evaluation of the results, it was possible to see that the adopted strategy for seizure prediction worked reasonably well with data from all three patients. However, it is necessary to highlight that there was some variation in the performance across patients. The methodology showed its best results with patient 1, obtaining an AUC score of 0.928 and missclassifying only 11 of a total of 151 EEG segments. On the other hand, the methodology showed its worst results when it was applied to data coming from patient 2. It obtained an AUC score of 0.809 and it missclassified 55 of a total of 356 segments. Finally, the developed seizure prediction technique showed a good performance when working with data from patient 3, obtaining an AUC score of 0.917 and missclassifying only 41 of 511 segments.

Another point that needs to be highlighted in the results is the greater amount of false positives when compared to the false negatives. This means that a embedded seizure prediction system using this methodology would raise a considerable amount of false alarms, especially when we analyze the case of patient 2. This behavior shows that, given the extracted features, it is easier to recognize a seizure when it will really occur, while interictal patterns get often confused with preictal ones. Nevertheless, it was possible to show that developed technique works better than chance, which means that seizure prediction can be done with the help of machine learning and EEG data.

5 CONCLUSION

In this work, a seizure prediction methodology was developed with the help of EEG data and with a machine learning approach. The main motivation to develop a seizure prediction seizure technique is to improve the life quality of affected patients through the development of an EEG monitoring device that is equipped with embedded seizure prediction software. After a literature review of actual seizure prediction research in chapter 2, the seizure prediction task was formulated as a binary classification task where different EEG segments must be classified between interictal and preictal.

Using data coming from 3 patients that was open-sourced and provided by EpilepsyEcosystem, the first step of the patient-specific seizure prediction methodology consisted of dividing the 16-channel and 10-minutes long EEG Channels into smaller windows of 30 seconds. After this, the next step in the methodology was to extract several features from each divided window and from each channel. These features consisted of variables extracted from time, frequency and spatial domain. Among the time features, one can mention the basic signal statistics, number of peaks, peak-to-peak voltage, etc. The frequency features consisted of the total signal power, the relative energy contained in several known EEG bands and the spectral edge frequencies. All of these frequency domain extracted features were computed after obtaining a power spectral density estimation (PSD) by using the Welch's method. Finally, the time domain correlation between each channel were extracted in order to account for possible relationships between different channels that can characterize a preictal or interictal pattern.

In order to learn from the extracted features, a cost-sensitive logistic regression classifier was trained. The main reason behind this choice was that the proposed method relied itself on the prediction of the preictal probabilities for each divided window. The logistic regression classifier provided a good probability estimation, as it was shown by the results. Also, the need to choose a cost-sensitive classifier was justified due to the big class imbalance present in the dataset for the three chosen patients. In order to evaluate the optimal window size and the classifier performance with respect to other classification algorithms, a K-Folds cross validation was implemented and the chosen evaluation metric was the AUC score.

The proposed method was able to obtain significant results for all three patients despite the considerable variation in the performance across patients and the obtained number of false negatives. For patient 1, it was possible to obtain an classifier that provided an AUC score of 0.928, missclassifying only 11 of a total of 151 EEG segments. For patient 2, the classifier obtained an AUC score of 0.809 and it has missclassified 55 of a total of 356 segments. Finally, the developed seizure prediction technique showed a good performance when working with data from patient 3, obtaining an AUC score of 0.917 and missclassifying 41 of 511 segments.

Along with others, this work showed that it is possible to develop a seizure prediction methodology using EEG data. Naturally, there is still a lot of work to be done in this field in order to enable patients to have an EEG monitoring device that is able to predict if the patient will have a seizure in the following moments or not, since EEG devices and seizure predictions algorithms, like the one developed in this work, are often prone to errors. However, with the development of this research topic, scientists can be able of developing such a device in the future, which could improve the lives of people affected by this disease in a great amount.

BIBLIOGRAPHY

BANDARABADI, M.; TEIXEIRA, C. A.; RASEKHI, J.; DOURADO, A. Epileptic seizure prediction using relative spectral power features. **Clinical Neurophysiology**, Elsevier, v. 126, n. 2, p. 237–248, 2015.

BEGANOVIC, N.; JUKIC, S.; KEVRIC, J. Anticipation of epileptic seizures using distributed eeg signal processing. In: . [S.l.: s.n.], 2019.

BISHOP, C. M. **Pattern recognition and machine learning**. [S.l.]: springer, 2006.

CARNEY, P. R.; MYERS, S.; GEYER, J. D. Seizure prediction: methods. **Epilepsy & behavior**, Elsevier, v. 22, p. S94–S101, 2011.

CHAOVALITWONGSE, W. A.; POTTENGER, R. S.; WANG, S.; FAN, Y.-J.; IASEMIDIS, L. D. Pattern-and network-based classification techniques for multichannel medical data signals to improve brain diagnosis. **IEEE Transactions on Systems, Man, and Cybernetics-Part A: Systems and Humans**, IEEE, v. 41, n. 5, p. 977–988, 2011.

COCK, D. D. Ames, iowa: Alternative to the boston housing data as an end of semester regression project. **Journal of Statistics Education**, Taylor & Francis, v. 19, n. 3, 2011.

COHEN, M. X. **Analyzing neural time series data: theory and practice**. [S.l.]: MIT press, 2014.

DIREITO, B.; VENTURA, F.; TEIXEIRA, C.; DOURADO, A. Optimized feature subsets for epileptic seizure prediction studies. In: IEEE. **2011 Annual International Conference of the IEEE Engineering in Medicine and Biology Society**. [S.l.], 2011. p. 1636–1639.

FAZEL, S.; WOLF, A.; LÅNGSTRÖM, N.; NEWTON, C. R.; LICHTENSTEIN, P. Premature mortality in epilepsy and the role of psychiatric comorbidity: a total population study. **The Lancet**, Elsevier, v. 382, n. 9905, p. 1646–1654, 2013.

FERGUS, P.; HUSSAIN, A.; HIGNETT, D.; AL-JUMEILY, D.; ABDEL-AZIZ, K.; HAMDAN, H. A machine learning system for automated whole-brain seizure detection. **Applied Computing and Informatics**, Elsevier, v. 12, n. 1, p. 70–89, 2016.

FIALKA, O.; CADIK, M. Fft and convolution performance in image filtering on gpu. In: IEEE. **Tenth International Conference on Information Visualisation (IV'06)**. [S.l.], 2006. p. 609–614.

FUJIWARA, K.; MIYAJIMA, M.; YAMAKAWA, T.; ABE, E.; SUZUKI, Y.; SAWADA, Y.; KANO, M.; MAEHARA, T.; OHTA, K.; SASAI-SAKUMA, T. et al. Epileptic seizure prediction based on multivariate statistical process control of heart rate variability features. **IEEE Transactions on Biomedical Engineering**, IEEE, v. 63, n. 6, p. 1321–1332, 2015.

GASSO, G. Logistic regression. 2019.

GÉRON, A. **Hands-on machine learning with Scikit-Learn, Keras, and TensorFlow: Concepts, tools, and techniques to build intelligent systems**. [S.l.]: O'Reilly Media, 2019.

GOLDBERGER, A. L.; AMARAL, L. A.; GLASS, L.; HAUSDORFF, J. M.; IVANOV, P. C.; MARK, R. G.; MIETUS, J. E.; MOODY, G. B.; PENG, C.-K.; STANLEY, H. E. Physiobank, physiotoolkit, and physionet: components of a new research resource for complex physiologic signals. **circulation**, Am Heart Assoc, v. 101, n. 23, p. e215–e220, 2000.

HJORTH, B. Eeg analysis based on time domain properties. **Electroencephalography and clinical neurophysiology**, Elsevier, v. 29, n. 3, p. 306–310, 1970.

JAMES, G.; WITTEN, D.; HASTIE, T.; TIBSHIRANI, R. **An introduction to statistical learning**. [S.l.]: Springer, 2013. v. 112.

KOKOSKA, S.; ZWILLINGER, D. **CRC standard probability and statistics tables and formulae**. [S.l.]: Crc Press, 2000.

KRIZHEVSKY, A.; SUTSKEVER, I.; HINTON, G. E. Imagenet classification with deep convolutional neural networks. In: **Advances in neural information processing systems**. [S.l.: s.n.], 2012. p. 1097–1105.

KRYSTAL, A. D.; PRADO, R.; WEST, M. New methods of time series analysis of non-stationary eeg data: eigenstructure decompositions of time varying autoregressions. **Clinical Neurophysiology**, Elsevier, v. 110, n. 12, p. 2197–2206, 1999.

KUHLMANN, L.; KAROLY, P.; FREESTONE, D. R.; BRINKMANN, B. H.; TEMKO, A.; BARACHANT, A.; LI, F.; JR, G. T.; LANG, B. W.; LAVERY, D. et al. Epilepsyecosystem. org: crowd-sourcing reproducible seizure prediction with long-term human intracranial eeg. **Brain**, Oxford University Press, v. 141, n. 9, p. 2619–2630, 2018.

KUHLMANN, L.; LEHNERTZ, K.; RICHARDSON, M. P.; SCHELTER, B.; ZAVERI, H. P. Seizure prediction—ready for a new era. **Nature Reviews Neurology**, Nature Publishing Group, v. 14, n. 10, p. 618–630, 2018.

KUMAR, J. S.; BHUVANESWARI, P. Analysis of electroencephalography (eeg) signals and its categorization–a study. **Procedia engineering**, Elsevier, v. 38, p. 2525–2536, 2012.

LECUN, Y.; BOSER, B. E.; DENKER, J. S.; HENDERSON, D.; HOWARD, R. E.; HUBBARD, W. E.; JACKEL, L. D. Handwritten digit recognition with a back-propagation network. In: **Advances in neural information processing systems**. [S.l.: s.n.], 1990. p. 396–404.

LI, Y.; WANG, X.-D.; LUO, M.-L.; LI, K.; YANG, X.-F.; GUO, Q. Epileptic seizure classification of eegs using time–frequency analysis based multiscale radial basis functions. **IEEE journal of biomedical and health informatics**, IEEE, v. 22, n. 2, p. 386–397, 2017.

MCELREATH, R. **Statistical rethinking: A Bayesian course with examples in R and Stan**. [S.l.]: CRC press, 2020.

PARK, Y.; LUO, L.; PARHI, K. K.; NETOFF, T. Seizure prediction with spectral power of eeg using cost-sensitive support vector machines. **Epilepsia**, Wiley Online Library, v. 52, n. 10, p. 1761–1770, 2011.

RASEKHI, J.; MOLLAEI, M. R. K.; BANDARABADI, M.; TEIXEIRA, C. A.; DOURADO, A. Preprocessing effects of 22 linear univariate features on the performance of seizure prediction methods. **Journal of neuroscience methods**, Elsevier, v. 217, n. 1-2, p. 9–16, 2013.

REDDY, B. S.; MURTHY, I. Ecg data compression using fourier descriptors. **IEEE Transactions on Biomedical Engineering**, IEEE, n. 4, p. 428–434, 1986.

REN, Q.; LI, M.; HAN, S. Tectonic discrimination of olivine in basalt using data mining techniques based on major elements: a comparative study from multiple perspectives. **Big Earth Data**, Taylor & Francis, v. 3, n. 1, p. 8–25, 2019.

SAZGAR, M.; YOUNG, M. G. Overview of eeg, electrode placement, and montages. In: **Absolute Epilepsy and EEG Rotation Review**. [S.l.]: Springer, 2019. p. 117–125.

SHAH, V.; WELTIN, E. V.; LOPEZ, S.; MCHUGH, J. R.; VELOSO, L.; GOLMOHAMMADI, M.; OBEID, I.; PICONE, J. The temple university hospital seizure detection corpus. **Frontiers in neuroinformatics**, Frontiers, v. 12, p. 83, 2018.

TSIOURIS, K. M.; PEZOULAS, V. C.; ZERVAKIS, M.; KONITSIOTIS, S.; KOUTSOURIS, D. D.; FOTIADIS, D. I. A long short-term memory deep learning network for the prediction of epileptic seizures using eeg signals. **Computers in biology and medicine**, Elsevier, v. 99, p. 24–37, 2018.

ULLAH, I.; HUSSAIN, M.; ABOALSAMH, H. et al. An automated system for epilepsy detection using eeg brain signals based on deep learning approach. **Expert Systems with Applications**, Elsevier, v. 107, p. 61–71, 2018.

ZHANG, Z.; PARHI, K. K. Low-complexity seizure prediction from ieeg/seeg using spectral power and ratios of spectral power. **IEEE transactions on biomedical circuits and systems**, IEEE, v. 10, n. 3, p. 693–706, 2015.

Appendix

Link to the code repository: https://gitlab.com/leonardo.fernandes.oliv/seizure-forecasting