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Subject-Independent Epileptic Seizure Prediction using Spectral Power and Correlation Coefficients

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Patientoberoende prognoser av epileptiska anfall med hjälp av spektral energifördelning och korrelations koefficienter

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Abstract

Epileptic seizure prediction algorithms with prediction rates above random have been produced, with varying success, during the last ten to twenty years. The algorithms produced have been tailored to the specific characteristics of a subject's epilepsy, referred to as subject-specific prediction algorithms. Such customization entails the training of the algorithm's classifier on the specific EEG-data pertaining to the subject. An inherent requirement is the time-intensive task of recording and labeling the subjects EEG, which will be used for the training of the classifier. As such, this thesis investigates the possibility of adjusting the training of a subject-specific algorithm's classifier to make it subject-independent. The investigation is based on whether the subject-independent version could achieve prediction rates equal to or better than that of the original subject-specific version. The methodology carried out employs a subject-specific algorithm, sourced from a Kaggle competition, which utilizes a Support Vector Machine and spectral power and correlation coefficients as its features. The training of the classifier was modified to be subject-independent and then compared to the performance of the subject-specific version. The results indicate that the subject-independent version performed worse than the original subject-specific one, in fact it performs below or equal to random prediction rates. It is concluded that: due to the dependency of epileptic seizure prediction algorithms on the strict characteristics of a subjects epilepsy, a subject-independent algorithm, produced with the adjustment of a subject-specific version, can't, at this time, achieve prediction rates equal to or higher than that of the subject-specific version.

Sammantfattning

De senaste 20 åren har algoritmer som kan förutspå epileptiska anfall utvecklats. Dessa har, med varierande resultat, kunnat förutspå epileptiska anfall med sannolikhetsestimeringar som varit bättre än en slumpmässig estimering. Algoritmerna är skräddarsydda för att användas på specifika egenskaper för epilepsin hos en specifik patient. Detta medför att en klassificerare anpassas efter träningen på den specifika EEG-datan för patienten. Att producera en ny patient-specifik algoritm är tidskrävande då det kräver både inspelning och att det sätts etiketter på ny EEG-data för varje patient. Därav undersöker denna rapport möjligheten att justera träningen av den patientspecifika algoritmens klassificerare för att göra den oberoende av patienten. För att kunna mäta detta undersöktes om en patientoberoende algoritm kunde uppnå sannolikhetsestimeringar som var lika bra eller bättre än en patientspecifik algoritm. Metoden har anpassats efter en algoritm som varit tillgänglig från en Kaggle-tävling. Algoritmens träning har ändrats för att bli patient-oberoende och resultaten har jämförts med resultaten från den patient-specifika algoritmen. Denna algoritm använder sig utav egenskaperna hos den spektrala energifördelningen, och korrelations koefficienter tillsammans med en Support Vector Machine. Resultaten visar att den patient-oberoende algoritmen presterar sämre än den ursprungliga patient-specifika versionen. Resultaten visar även att den inte överskrider en slumpmässig estimeringsmetod. Utifrån dessa resultat kan en slutsats dras; att baserat på de specifika egenskaperna hos en patients epilepsi, kan inte idag en patient-oberoende algoritm, utvecklad genom att anpassa en patient-specifik algoritm, nå sannolikhetsestimeringar som är lika bra med eller bättre än en patient-specifik.

Contents

1 Introduction

Epilepsy is a chronic neurological disease characterized by episodes of seizures [1][2]. There are various forms of epilepsy, depending on which region of the brain it is localised in [2]. The location of the epileptogenic zone determines the properties of the epilepsy: duration, severity, and syndromes. As such, the characteristics of a seizure manifests in various ways [2]. An epileptic seizure is characterised by hyperactivity in groups of neurons in the epileptogenic zone [2]. The overload of electrical stimulus in the affected area disturbs the normal voluntary function, resulting in a epileptic seizure [2].

Approximately 1% of the world population suffers from epilepsy, making it the most common brain disorder in the world [1]. It is estimated that 20-30% of people suffering from epilepsy are resistant to medication meant to suppress epileptic seizures. This form of epilepsy is referred to as refractory epilepsy [3][4]. Those afflicted with refractory epilepsy risk suffering a seizure at any time which has a significant impact on their social and vocational life, severely diminishing their psychological health, often forcing them into seclusion [5]. There are also severe physical implications to unabated episodes as they may result in permanent brain trauma [5]. Non-refractory epileptics already run a risk of a premature death three times greater than that of regular people [6].

The electric activity of the brain is characterised by frequencies at various wavelengths and their activity can be monitored and measured by placing electrodes on the scalp. This method is referred to as an Electroencephalogram (EEG) [5][7]. Machine learning and signal processing techniques have been readily applied to EEG-recordings to identify epileptic seizures with a high degree of accuracy. Seizure detection is a well established method and has been integrated into the procedure for epilepsy diagnosis. This has, as a result, increased diagnosis accuracy and reduced the amount of time required for a diagnosis [5][7]. While seizure detection is well established, the prospect of predicting incoming seizures from EEG is not. Research aiming at producing seizure prediction algorithms has yielded prediction rates with varying accuracy. However, the results support the notion that the prediction of a seizure is possible [5][7]. Seizure prediction mechanisms could facilitate the lives of those suffering from refractory epilepsy by giving them a way to participate in society and lead a normal life [8].

Historically, there was a lack of available long-term EEG data and the objective of the research was predominantly to support the possibility of predicting seizures. In the last ten years the supply and access to data has improved significantly. This lead to studies which produced algorithms which successfully predicted an upcoming seizure [9]. These algorithms were designed as subject-specific.

Subject-specific algorithms have been consistently featured in research on the topic of seizure prediction, many of which have been comprehensively reviewed [4][8][9]. The subject-specific model, however, has a great deal of overhead as it lacks automation, since each algorithm must be tailored specifically to the subject's data [4]. A generalized algorithm where data is gathered from a large population in order for the prediction mechanism to be tailored to any patient, independent from its specific data, has yet to be produced. Furthermore, the research on subject-independent epilepsy prediction is lacking in the field. Such

an algorithm would be desirable as it would enable for a general system available to many, without the need for time-intensive gathering and labeling of subject-specific data.

1.1 Problem statement

Can subject-independent epilepsy prediction achieve prediction rates equal to or higher than subject-specific epilepsy prediction?

1.2 Scope & Objective

The objective of this study is to investigate the performance of subject-independent epileptic seizure prediction as compared to subject-specific. For this purpose, available open-source, subject-specific algorithms were sought after and inspected to deem whether the training of the classifier could be adapted to a subject-independent model. It was decided to opt for a comprehensible algorithm with good (subject-specific) performance in order to see whether a similar performance could be attained with a subject-independent model. Naturally an investigation could have been comprised of multiple algorithms and a performance comparison against each other. However, due to the lack of subject-independent studies, one algorithm was deemed to be a suitable limitation for this study.

This study utilized an open-source seizure prediction algorithm from a Kaggle competition, "American Epilepsy Society Seizure Prediction Challenge" in 2014. The extent to which the subject-independent model is investigated therefore depended upon the implementation of the algorithm. This entails that the choice of features and classifier are based on the motivations of the algorithm's author. As such, the study did not investigate the impact that selecting different features and classifiers other than spectral power and a support vector machine, might have had on classification rates.

1.3 Thesis outline

The thesis is made up of 5 sections with several subsections. Section 2 is the background, where the notion of epilepsy prediction will be outlined. Moreover, all the entailing machine learning and signal processing aspects will be also be covered, from feature extraction, to classification and evaluation methods for the results. Section 2 also contains a related works section which has a retrospective look at what has been done in the field of seizure prediction and related areas. The method is in section 3, where the used data, feature extraction, classification and evaluation methods are detailed. Section 4 presents the results of the carried out method. Lastly, section 5 analyses the results and discusses their implication for the problem stated while also accounting for limitations and errors, future research and ending with the study's conclusion.

2 Background

2.1 Epilepsy prediction

Epilepsy prediction algorithms are based on two primary processes; feature extraction and classification. Feature extraction processes and transforms the EEG-data into a format which amplifies certain characteristics from which a classification into classes can be made [2][7]. The classification of the transformed data is meant to separate data into classes representing states for regular neural activity (interictal) and activity just before a seizure (preictal). As such, the algorithms designed for seizure prediction are aimed at detecting the transition from the interictal to preictal state by correctly classifying data as preictal or interictal [9]. In the subsequent sections the methodology of EEG, feature extraction and classification as pertained to seizure prediction will be elaborated upon.

2.1.1 The role of EEG in epilepsy treatment

EEG is a technology used to measure and visualize brain activity. When activated neurons generate magnetic and electrical fields and an electric current passes through a neuron it produces waves which are recorded by the EEG. The brain's activity is reflected in the range of frequencies that the electrical activity, i.e brain waves, produce. By attaching electrodes to the patient's scalp at differing locations the various frequencies of the brain waves can be recorded. This form of EEG setup is referred to as (non-invasive) scalp EEG while some treatments require surgical insertion of electrodes into the brain, referred to as (invasive) intracranial EEG [7].

The analysis of EEG recordings across multiple sessions is a well established methodology for EEG-based diagnosis and epilepsy in particular. With time consuming manual evaluation of scalp EEG recordings, it is possible to establish whether the subject has epilepsy, in which region of the brain as well as viable treatments [10].

EEG data meant for seizure prediction is characterised by separation into four states of neural activity. The states are comprised of: normal activity, the interictal state, the preictal state which is the time interval preceding a seizure, the ictal state during the epileptic seizure and lastly the postictal state after a seizure has ran its duration [2][10]. The separation of raw EEG data into the four states is achieved by manual labeling of data, an exhaustive and time consuming task [9]. Successful prediction algorithms identify and classify the preictal state from the stream of otherwise interictal data.

2.1.2 Invasive EEG

For the majority of epileptics, regular scalp EEG is sufficient for diagnosis and primarily for localisation of the epileptogenic zone. Localisation is integral in discerning the characteristics of the epilepsy and thus also treatment viability [10]. For certain epileptics, the EEG recordings are incoherent to the degree that the epileptogenic area can not be localised. For this minority invasive intracranial EEG may be warranted. However, before the surgical procedure can be performed there are strict criteria which must be fulfilled [10]. Surgically

implanted electrodes for intracranial EEG serve to reduce the noise that is perpetually present in scalp EEG. The improvement is significant to the degree that an intracranial EEG recording can register an epileptic activity which a scalp EEG would not detect [10]. Retrospectively, seizure prediction mechanism have employed data gathered from invasive EEG setups. A conceptualization of what an epileptic seizure prediction mechanism using intracranial EEG setup, in a dog, can look like can be seen in figure 1.

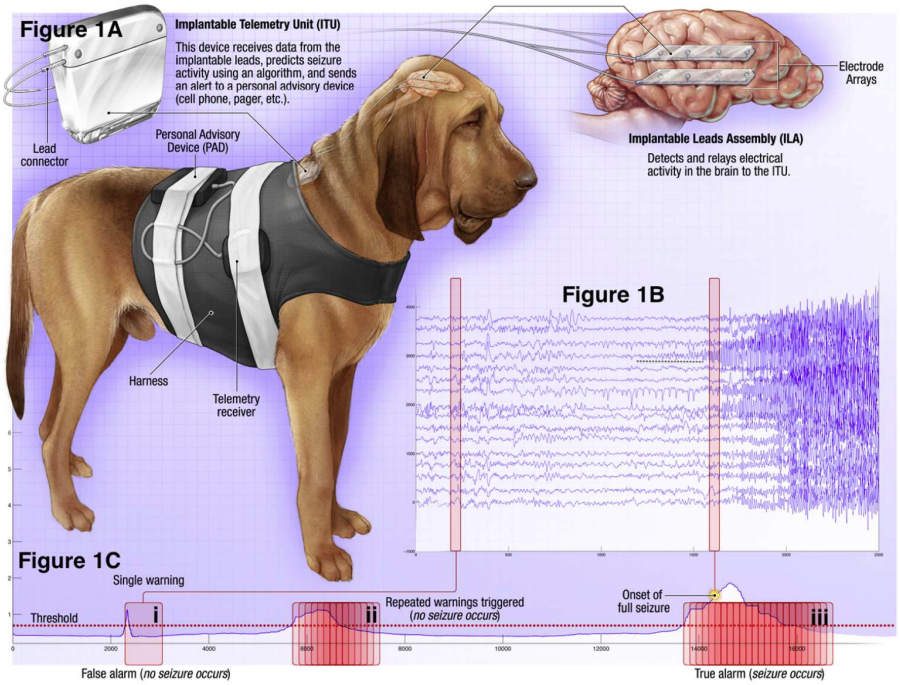


Figure 1: A conceptualization of an epileptic seizure prediction mechanism using intracranial EEG
Source: From [8]

2.2 Pattern Recognition approach to EEG analysis

The process of manual evaluation of EEG signals is a time-intensive task but also has a tendency to be inaccurate [12]. The complexity is a consequence of signals being noisy, non stationary, complex and of high dimensionality [11]. As such, signal processing and machine learning tools have been readily adopted for the task of EEG analysis to automate and standardize the process for improved interpretation accuracy and reliability [12]. For patients with refractory epilepsy, automated real time EEG signal processing and classification is an inherent approach for seizure prediction techniques. Prediction techniques rely upon the ability to evaluate a continuous stream of EEG signals to identify the preictal state and warn of an approaching seizure [9].

The research and development of seizure prediction techniques is based on linear and/or nonlinear transformations of EEG signals by applying various mathematical measures. Automated EEG signal analysis for seizure prediction

involves applying a combination of machine learning tools and mathematical transformations [13]. This method is a pattern recognition approach and is comprised of two processes; feature extraction and classification [11]. The two subsequent sections describe feature extraction and classification, and lastly one approach for evaluating the results of binary classification is introduced.

2.2.1 Feature Extraction

The feature extraction process is comprised of artifact removal and signal transformation. As stated previously, there are multiple sources of disturbance which result in erratic, noisy signals, there are various established signal processing techniques for removing the undesirable disturbance. Feature extraction is then the transformation of signals into values which are representative of the state to be identified, in the case of seizure prediction; ictal and preictal [13][14]. These features are calculated over time slices of the EEG recordings, referred to as "moving-window analysis", wherein within each window features are extracted by calculations with regard to different measures. The results from the analysis are called time profiles [9]. There are several different feature extraction methods used within the field of seizure prediction. Performance, i.e prediction accuracy, is directly dependent on the selection of features and is therefore critical in the assessment of statistical validation [13][14]. The following sections will provide a description of the features used for the purposes of this thesis.

2.2.1.1 Spectral Power & Fast Fourier Transform

A Fourier transform decomposes a varying time signal into its frequency components, i.e sine and cosine waves, which indicates the variance in their magnitude, referred to as the spectral power. Fourier Transforms are applied on a signal that is assumed to be stationary. The abstracted spectral power is measured in the voltage of the EEG-signal, represented at each frequency. This makes it possible to gauge the strength of a signal at a specific frequency. It can further be summated on intervals of signal frequencies, e.g. the normal brain signals: alpha, beta, etc, this is usually referred to as the Spectral Power Bands [15]. A normal Discrete Fourier Transform requires $O(N^2)$ operations. Fast Fourier Transform uses the fact that in the (NxN) matrix, used in DFT, there are only N distinct elements [16].

By performing an FFT on signals from one or more EEG channels it is thereby possible to analyze the most prominent amplitudes which indicate a signature. This signature distinguishes whether the frequency is characteristic of a preictal or interictal state. The assumption that signals are stationary is unrealistic, in regards to seizure prediction, and as a consequence, its applicability has been challenged. However, it has shown prominent and successful use in diagnosis of epilepsy and the localisation of the epileptogenic zone [13].

2.2.1.2 Correlations Coefficients

About 60% of patients have, so called, partial seizures that originate from a certain part of the brain [17]. By comparing the EEG-signals from the focal areas with the signals in areas in a normal state, finding differences of high significance is likely [15]. One popular approach is using the correlation coefficients to find the correlation both over different channels and also different windows [17]. In

the algorithm used in this study, the Pearson correlation coefficients are used extracted by the following formula:

$$\rho_{X,Y} = \frac{cov(X,Y)}{\sigma_X \sigma_Y} \tag{1}$$

Which in short can be explained as dividing the covariance between two variables and the product of their standard deviations. The eigenvalues are calculated and sorted creating a spectrum of correlations. This shows how the dynamics of the EEG channels are affected when a seizure occurs [17].

2.2.2 Classification: Support Vector Machine

The subsequent step of the seizure prediction technique utilizes machine learning tools to classify the extracted features (data). Classification, as the name implies, is the classification of data into one or several categories dependent on the attributes of the data, i.e whether the data fits into a certain class [11]. In utilizing machine learning tools the EEG signal processing achieves robust adaptability as the classifier learns depending on the data it gathers and adjusts thereafter, a desirable attribute for generalized seizure prediction [9][11].

The basic idea behind an support vector machine (SVM) is creating a hyperplane, that distinguishes between two classes with the largest margin between the data from the two classes. The hyperplane is based on the nearest feature vectors also called support vectors, resulting in the term support vector machine [18][19]. A hyperplane is usually defined in n-1 dimensions, where the n dimension is dependent on the n features used as input on the classifier. It can be visualized as two clusters of data in 2-dimensions with a straight line separating them, where the line is the hyperplane. In this case the hyperplane is said to be linear. When more complex features are analyzed a linear hyperplane may not be able to distinguish the two classes. Two commonly used algorithms are radial basis function kernel(RBF-kernel) and polynomial kernel [20][21]. The formula for the RBF-kernel is as follows:

$$K(x_i, x_{i'}) = exp(-\gamma \sum_{j=1}^{p} (x_{ij} - x_{i'j})^2)) \tag{2}$$

There are two parameters that can be set in the RBF-kernel SVMs to attain different results, the constant gamma, and the constant C. The gamma constant affects how much influence a single training example has on the overall training. The C constant acts like a constraint on the summation part of the formula. This constraint deems which features are included in the support vector, an example of the RBF-kernel SVM classification can be seen in figure 2 [21][22].

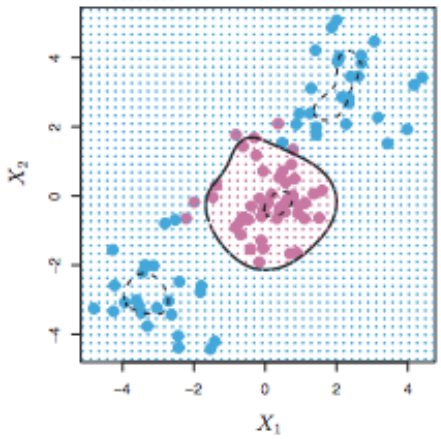


Figure 2: An example of classification with RBF-kernel SVM
Source: From [21]

For a diagnostics test, it is appropriate that the result is a probability. Such a probability represents the chance for a data point to either be 0/1, "yes"/"no", interictal/preictal. It is important to note that this is common when utilizing/implementing SVM for seizure prediction. Due to risk of the SVM overfitting the probability distribution, a common method is to fit a logistic regression (LR) model to the result. This improves the calibrations of probabilities for a given classification, hence, giving a better probability estimate for the data points. This method, where LR is fitted to the classification results, is referred to as platt scaling[23][24].

Compared with other classifiers, SVM perform particularly well on high dimensional problems which is one key problem with EEG-signal data. The downside being that the algorithm has a high demand on computational power, which makes it less favorable when applied to large data sets [25].

2.2.3 Evaluating binary classification

One approach for statistical analysis of results from a binary classifier is the receiver operating characteristic, ROC, curve. The ROC-curve is built up by plotting the sensitivity opposing (1 - specificity). Sensitivity measures the ratio of predictions that are correctly identified as positive divided by the total amount of cases. It is also referred to as the true positive rate(TPR). While specificity is the opposite, i.e. the ratio of correct predictions of negative cases divided by the total amount of cases. The false positive rate(FPR) refers to (1 - specificity). These rates are used in the ROC-curve where each point on the ROC-curve is dependent on a specific threshold. This threshold value is used to assess which probability estimates are true/false. When all the probability estimates have been categorized as true/false, the TPR and FPR can be calculated for the specific threshold. Thus, by visual inspection the best result would be a ROC-curve which reaches the top left corner, see figure 3.

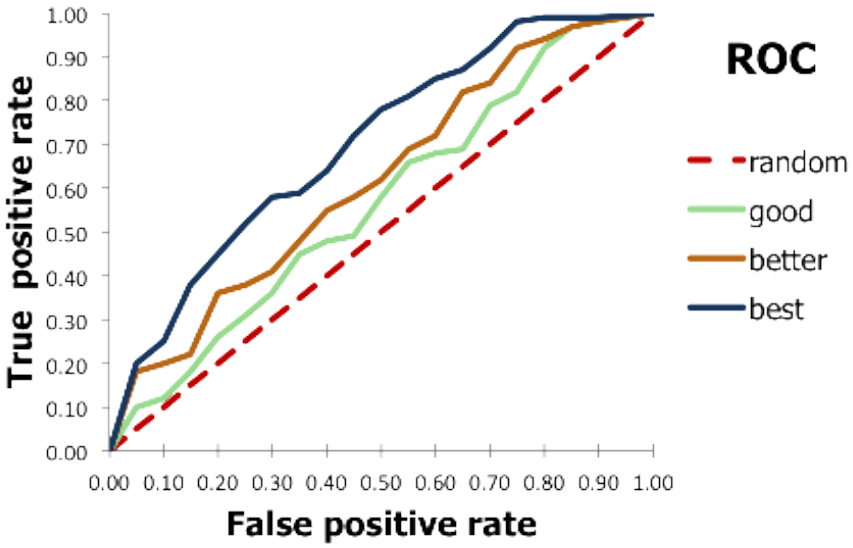


Figure 3: A conceptualization of how the ROC-curve works
Source: From [27]

Besides the ROC-curve the area under the curve, AUC, is commonly used to summarize the result. The AUC value is the probability that the classifier will predict a true/false case positively. In this study there will also be graphs based on the thresholds on the x-axis opposed to the TPR and FPR on the y-axis, this shows clearly to which extent the classifier is certain, i.e, if the probability estimates are high the classification of a clip has a high degree of certainty as well [28][29].

2.2.4 Subject-Specific and Subject-Independent classification

Whether a seizure prediction algorithm is subject-specific or independent is contingent on the training of the classifier. A subject-specific algorithm would have its classifier trained on EEG-data derived from the same subject for which it will test on. On the other hand, the subject-independent algorithm's classifier would be trained on EEG-data from other subjects than the one to be tested upon. This means that subject-specific algorithms are tailored to the characteristics of that subject's epilepsy. A subject-independent algorithm aims at taking EEG-data from multiple subjects, and by training the classifier on their data, produce a classifier able to perform general classification. The term general refers to the concept of being able to abstract from the specific characteristics of a subjects epilepsy, enabling for classification (and inherently, prediction) of EEG-data from subjects which it has not been trained for [20][26].

2.3 Related work review

The field of pattern recognition in regards to epilepsy has during the recent decade been primarily centered around diagnosing epilepsy, location of the epileptogenic area and various means for epilepsy prediction. Research on epilepsy prediction has revolved around the performance of prediction mechanisms and their suitability to be employed as a treatment option for subjects with refractory epilepsy. There are few inquiries into subject-independent prediction. One study which features prominently in references regarding the selection of subject-independent vs subject-specific algorithms is a study performed in 1997 by Qu and Gotman[26]. A lack of studies could partially be due to limited supply of commercial products and therefore the possibility of online studies (as the previously referenced material are comprised of offline studies). The following sections will elaborate on the progress the study of epilepsy prediction has undergone the last decade and extrapolate to generalized EEG classification in other areas than epilepsy prediction.

2.3.1 Epilepsy prediction

Mormann et al. (2006)[9] released a review covering most of the research done in the field of epilepsy prediction up until that point in time. The review mentions many flaws in previous studies, e.g. no reproducibility of results, insufficient quantities of EEG-data, and a lack of standardized evaluation methods. The review provided guidelines for recommended evaluation methods and suggested that the next step was for algorithms to achieve prediction rates above random on out-of-sample data.

More recently, EEG-data from dogs have been applied in studies for epileptic seizure prediction to meet the demand for more long-term data. Brinkman et al.[8] mentions that epilepsy in dogs is similar clinically and neurophysiologically to human epilepsy, they are also treated with the same medications with similar dosages, thus making research on dog's EEG-data feasible.

Park et al. (2011)[30], are credited for being the first to successfully develop a patient-specific seizure prediction algorithm. The algorithm was able to predict a seizure 50 minutes prior to the onset, with the rate of correct predictions being above random [5]. The study utilized the newly standardized evaluation methods and data from the FREIBURG database, consisting of 582 hours of EEG data, with pre-ictal recordings from 88 seizures, from 21 subjects. There were still concerns regarding the fact that the results were based on the analysis of offline data.

In 2014 another review, by Gadhoumi et al.[4], was released, covering most research done on epilepsy prediction since the guidelines from the review written by Mormann et al. had been adopted. Coupled with the increase in availability of EEG-data, several successful subject-specific prediction algorithms were developed by researchers. The algorithms differed in prediction horizons (use of different EEG-data sets), use of classifiers and features which lead to various levels of successful prediction rates. These studies further corroborated the existence of the preictal state and the model of subject-specific seizure prediction. As such, the primary objectives have been to improve on the performance of subject-specific algorithms and investigating the impact that different features may have on it. It is therefore evident that the focal point of research on seizure

prediction has been the subject-specific model. The prospects of a subject-independent prediction model has not been investigated despite its potential importance and is therefore an area ripe for study.

2.3.2 Feature extraction

Mormann et al.(2004)[14] conducted a study with the objective of comparing the performance of 30 different measures in order to corroborate the existence of the pre-ictal state. The study concluded that univariate measures were sensitive to changes immediately preceding the interictal state, while bivariate measures could distinguish dynamical differences up to hours prior to the seizure. It is stated that linear measures performed equal to or better than non-linear measures. In recent years, results from both studies and competitions show that there is still no substantial support for a feature producing better results than others [14]. Based on the fact that there is no evidence for a particular feature being superior to the other, Gadhoumi et al. [4] suggest that a combination of features may lead to better results. However, a model based on combining several features may lead to the inclusion of redundant features. Furthermore the selection of features may be related to the type of epilepsy with which the patient is diagnosed with, thus a uniform combination may be difficult to assemble [4]. This may conflict with a subject-independent prediction model as features then need to be tailored to the specific epilepsy thus warranting an additional study outside the scope of this thesis.

2.3.3 Subject-independent classification

In the study by Qu and Gotman a seizure detection algorithm was developed for the onset of epilepsy and tested it with a subject-specific, semi-subject-specific and subject-independent approach. The results concluded that the patient specific approach is superior in detection accuracy as it was able to detect seizures with 100.00% accuracy while the semi-PS and non-PS scored 45.6% and 11.7% respectively [26]. These results have been cited to motivate the use of subject-specific algorithms in studies on epilepsy detection such as Shoeb et al. (2004) and Chua et al. (2011) [31][32]. Chua et al. emphasizes the lack of subject-independent studies and in their study aimed at further improving detection rates of the scheme as well as quantifying the possible benefits . As such, the contemporary value of this paper can be put in perspective. With there currently being several open-source prediction algorithms available, they can be employed in order to further the research on the subject-independent model, which has not been investigated in isolation to our knowledge [31][32].

While there may be a lack of conducted studies for subject-independent trials for epilepsy prediction there are other areas within automated EEG analysis which explore the facets of subject-independent classification [20]. For a long time, the development of brain-computer interfaces (BCI) required long training session in order to properly train the subject to their interface [22]. These issues are prime for conducting studies regarding generalization, from subject-independence to variance in classification over time [20].

A study by Ray et al. (2015) investigates subject-independent classification as foreground for a future study on the possibility of neurofeedback as a means to treat neuropsychiatric patients. An ensemble of data from 27 healthy patients

was created for an offline study where the ensemble was used for training and testing and achieved a mean classification rate of 75.3% when used for binary EEG classification between emotion and motor imagery. The study presents the possibility of applying a subject-independent classifiers in other niche areas where technology crosses over into medicine and supports the claim with the obtained results. There is therefore a contemporary precedence within automated EEG analysis to investigate subject-independent classification not only within the scope of epilepsy prediction but other areas as well [20].

3 Method

In order to investigate the stated problem, the decision was made to use data and an algorithm from a Kaggle competition which took place in 2014, where algorithms were made open-source to ease the progress of the field [8][33].

The suitability of the algorithm for the study of subject-independence is based on a couple of factors. The primary one is that the classifier employed is a support vector machine. As stated in section 2.2.2, SVMs lend themselves well to the task of epileptic seizure prediction due to their ability to deal with the high dimensionality of EEG data [25]. The second reason is the use of features which have shown acceptable prediction rates in several studies, and also, spectral power is the most commonly used feature [4][15][30]. Additionally, the complexity of the algorithm was at a suitable level. The method for training the subject-independent classifier was deemed appropriate after looking at other subject-independent studies for BCI's and seizure detection [20][26][personal correspondence, Benjamin H. Brinkmann].

3.1 Data

The competition data is comprised of intracranial EEGs from 2 patients and 5 dogs, and each subject's data sets are separated into sets for training and testing. The training sets contain labeled interictal and preictal data segments, while the test data is unlabeled. In this study the data from the 5 dogs will be used [33].

The EEG-signals are sampled from 16 channels, with a frequency of 400 Hz for dogs. The data is split into 10-minute segments where the interictal segments were recorded at least one week before or after any seizure, and the preictal segments are recorded one hour prior to a seizure. Table 1 shows the specific ratios between interictal and preictal states for the dogs [33].

Subject	**Seizures**	**Training clips (%interictal)**	**Testing**
Dog-1	22	504 (95.2)	502 (95.2)
Dog-2	47	542 (92.3)	1000 (91.0)
Dog-3	104	1512 (95.2)	907 (95.4)
Dog-4	29	901 (89.2)	990 (94.2)
Dog-5	19	480 (93.8)	191 (93.7)

Table 1: The number of data clips and the preictal/interictal ratio.

The format of the EEG-data are .mat files with the following format:
Dog_<1-5>_<interictal/preictal/test>_segment_<number>.mat.
Where the interictal/preictal label indicate that the segment is meant for training, the test for the testing of the classifier.

3.2 Algorithm

As described throughout the background the standard approach for seizure prediction with machine learning follows the steps: Feature extraction on the raw EEG-signals, input the features to the classifier, either as a training clip or

testing clip, and receiving a probability estimate for the testing clip. The probability estimate describing how likely a clip is preictal or interictal. See figure 4 for a brief conceptualization.

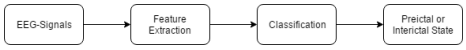


Figure 4: The process of seizure prediction with machine learning.

3.2.1 Feature extraction

Input data is resampled to 100Hz in order to reduce noise, every 10-minute segments is then split into 12 windows of about 50 seconds each. For each window, an FFT is applied which transforms it from the time domain into the frequency domain. Hence, the spectral power magnitudes have been extracted from the data. The power magnitudes in the frequency range 1-50 Hz are then converted to a logarithmic scale, for a smoother distribution. To further reduce noise the data is then resampled into 18 different partitions based on the frequency 1-50 Hz. The correlation and eigenvalue-matrices are then also added to the features; across the channels based on the reduced frequency ranges and over the time domain [33].

FFT, the correlation, and eigenvalue-matrices were selected by the author on the basis of popularity amongst the top contenders of the competitions leaderboard [33].

3.2.2 Classification

For classification, a RBF-kernel SVM with constants C and gamma set to 10^6 and 0.01, respectively, was used. The choice of classifier, and its constants, is motivated by the fact that the author tested several classifiers and settings, of which the SVM produced the best results[33].

For the subject-specific model; the interictal/preictal segments for the specific dog to be tested upon are used to train the classifier. Then the test segments for the same dog is used in the prediction. As such, each subject-specific test was performed by having trained the classifier on the interictal/preictal segments for dog<1-5>, and tested on with the same dog's test segments.

For the subject-independent model; the interictal/preictal segments of all dogs excluding the dog to be tested upon are used to train the classifier. The training data was still feature extracted for each dog independently, and then concatenated together to be used for the training of the classifier. Then the test segments for the excluded dog are used to predict on. To create the entire sample for the subject-independent model the following procedure took place:

- subject-independent model dog 1: Train on dogs<2,3,4>, test on dog-1
- subject-independent model dog 2: Train on dogs<1,3,4>, test on dog-2
- subject-independent model dog 3: Train on dogs<1,2,4>, test on dog-3
- subject-independent model dog 4: Train on dogs<1,2,3>, test on dog-4

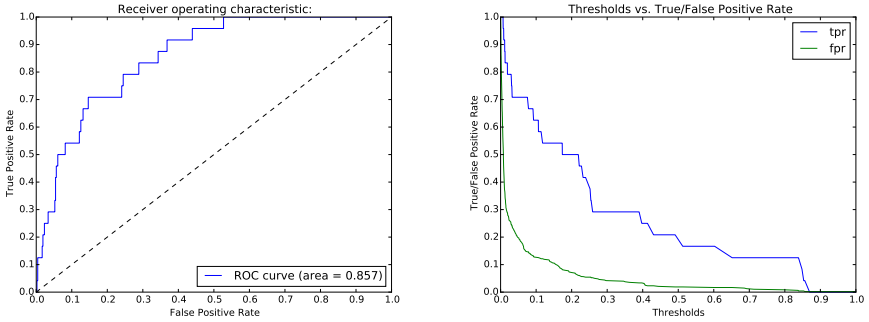
No subject-independent test was performed for dog-5, the reasoning behind this decision can be read in section 5.2.

3.2.3 Evaluation

Thus the algorithm has assigned prediction estimates to each data clip, based on the results from the classifier, and once completed the area underneath the ROC-curve is calculated. The ROC-curve was created with a built-in method which uses automated thresholds to get the different TPR and FPR values.

4 Results

The following section presents the results accumulated by running the seizure prediction algorithm with a subject-specific and subject-independent model. The section is comprised of figures 4-12a & b which present the resulting ROC-curve for the dog tested upon with a subject-specific and subject-independent model as well as the individual true and false positive rates. The area underneath the ROC-curve for all tests are summarized in table 2. In general, the subject-specific models all achieved higher areas underneath the ROC-curve with the exception of dog-5. The subject-specific model averages 0.775 ± 0.183 in area underneath the ROC-curve. As such, for all subject-specific models, except dog-5, preictal clips were more likely to receive a higher probability estimate than interictal clips, see figures <4-12>a and table 3. The subject-independent models had an average area underneath ROC of 0.467 ± 0.026, see table 3. Therefore preictal clips had a lower probability of receiving a higher probability estimate than interictal clips in the subject-independent model, corresponding to a roughly random chance. No subject-independent model was successfully produced for dog-5. Consequently the results indicate that the subject-independent-model had worse prediction outcomes than the subject-specific model.

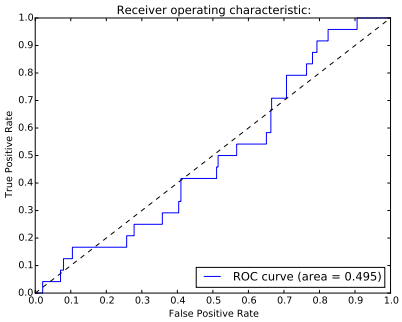


(a) Subject specific ROC-curve

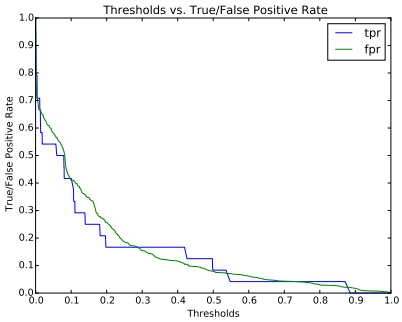
(b) Subject specific threshold

Figure 5: Results from dog 1 Subject-specific test

Figure 5 is based on the subject-specific model for dog-1; trained on the interictal and preictal clips from dog-1 and tested on the test clips from dog-1. Figure 5a shows that the area underneath the ROC-curve (AUC) is 0.857. The true and false positive rates decrease as the threshold increases. In 5b, the true positive rates have an overall higher probability estimate for all thresholds than false positive rates. There are few true predictions that are made with a higher probability estimate than 0.1 at the thresholds greater than 0.8, which corresponds with the area underneath the curve.



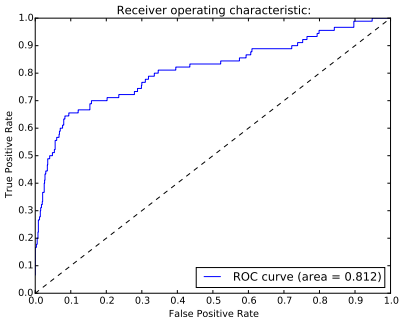
(a) Subject independent ROC-curve



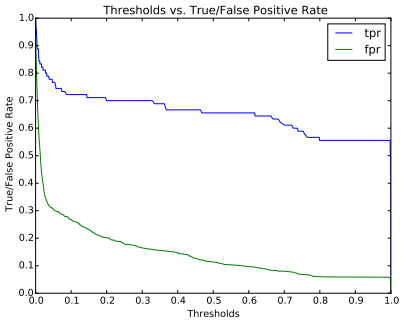
(b) Subject independent threshold

Figure 6: Results from dog 1 subject-independent test

In figure 6 the results from the subject-independent model for dog-1 is shown, based on training on preictal and interictal clips from dogs 2-4 and testing on the test clips from dog-1. Figure 6a shows that the area underneath the ROC-curve for the subject-independent model for dog-1 is 0.48. The individual true/false positive rates for the subject-independent model are represented against the thresholds in figure 6b. The trend for both rates probability estimates is a decreasing curve in the range 0.7-0.0. The estimates stabilize near the 0.6 threshold, with the probability $0=<0.05$ for both true and false positive rates until the 0.9 threshold for the true positive, and 1.0 for the false.



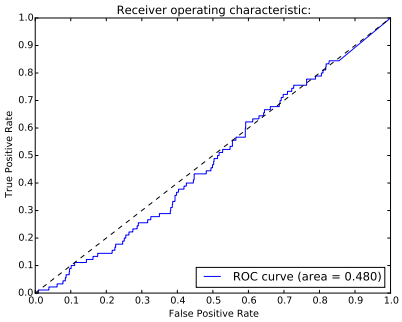
(a) Subject-specific ROC-curve



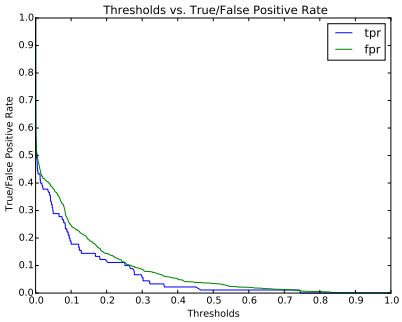
(b) Subject-specific threshold

Figure 7: Result from dog 2 subject-specific test

Figure 7 shows the subject-specific model for dog-2, i.e. trained on the interictal and preictal clips and tested on the test clips of dog-2. The area underneath ROC-curve for the subject-specific model of dog-2 is 0.812 and is displayed in figure 7a. Figure 7b shows the true positive rates are in the range of 0.7-0.6 for their probability estimates, the decrease stabilizing at threshold 0.8 and estimate 0.6. The false positive prediction rate has lower probability estimates than the true rate. The false prediction rates are in the range 0.3-0.1, decreasing from thresholds <0.1 until stabilizing at threshold 0.9 with estimates $\tilde{0}.1$.



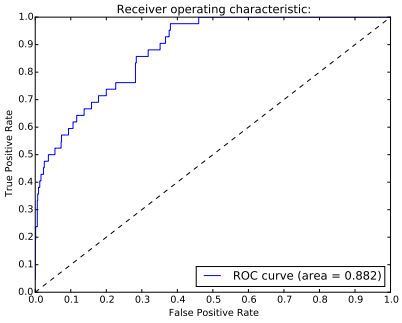
(a) Subject-independent ROC-curve



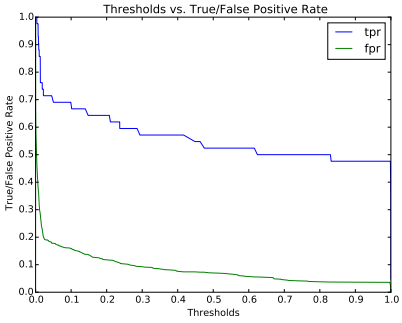
(b) Subject-independent threshold

Figure 8: Result from dog 2 subject-independent test

Figure 8 shows subject-independent model of dog-2, trained on interictal and preictal clips from dog 1,3, and 4 and tested on test clips from dog-2. The prediction outcome of the subject-independent model of dog-2 is represented in figures 8a & 8b. The ROC-curve is displayed in figure 8a, with an area underneath the curve of 0.495. The true and false positive rates are displayed in figure 8b. The probability estimates for the true positive rates are in the range 0.2-0.0 for thresholds in the range 0.1-0.8. Worth noting is that the true positive rate stabilizes at threshold $\tilde{0}.5$ with probability estimate <0.1, until eventually reaching zero at $\tilde{0}.8$. The false positive rate is approximately in the same range as the true positive, however, it ranges from 0.3-0.1 for the same threshold interval.



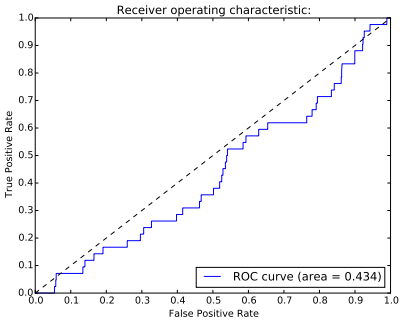
(a) Subject-specific ROC-curve



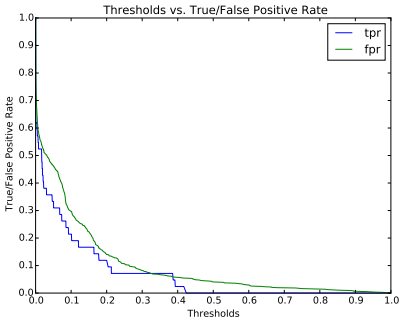
(b) Subject-specific threshold

Figure 9: Result from dog 3 subject-specific test

Figure 9 shows the subject-specific model for dog-3; both trained on interictal and preictal clips and tested on test clips from dog-3. The general prediction outcome of the subject-specific model of dog-3 is represented in figures 9a & 9b. Figure 9a shows that the area underneath the curve is 0.882. The true and false positive rates are illustrated in figure 9b. The true positive rate has decreasing probability estimates in the range 0.7-0.5 for thresholds in the range 0.1-1.0. False positive rates probability estimates decrease from 0.2 to <0.1 for thresholds 0.2-1.0.



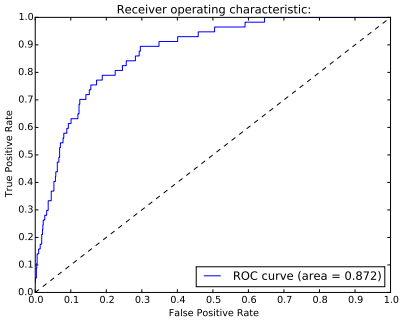
(a) Subject-independent ROC-curve



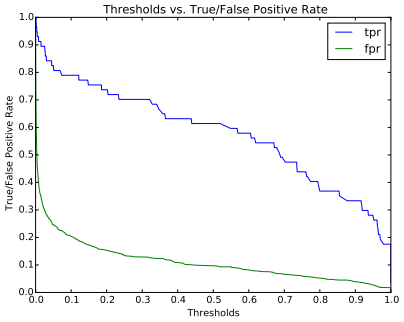
(b) Subject-independent threshold

Figure 10: Result from dog-3 subject-independent test

The figures in 10 are based on the results of the subject-independent model for dog-3, where training is done on interictal and preictal clips from dogs 1,2,4 and testing on the test clips of dog-3. Figure 10a shows the ROC-curve for the subject-independent model for dog-3, with the area underneath the curve being 0.434. In figure 10b; the true positive prediction rate has probability estimates in the range >0.2 to 0.0 for threshold 0.1 to $\tilde{0}$.4. False positive rates have probability estimates range from 0.3-0.0 for thresholds 0.1-$\tilde{0}$.95.



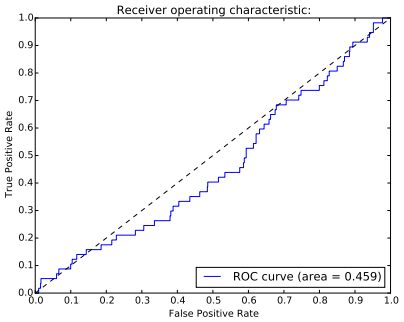
(a) Subject-specific ROC-curve



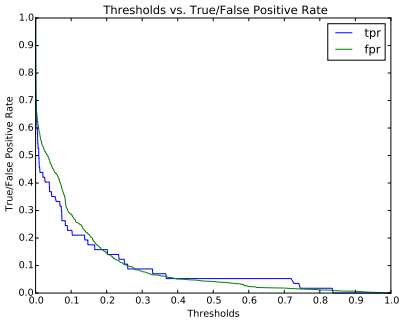
(b) Subject-specific threshold

Figure 11: Result from dog 4 subject-specific test

Figure 11 shows the subject-specific model for dog-4, trained on interictal and preictal clips of dog-4 and tested on test clips from dog-4. Figure 11a the ROC-curve for the subject-specific model for dog-4 is plotted with the area underneath the curve being 0.872. In figure 11b; the true positive prediction rate has probability estimates in the range 0.8 to $\tilde{0}$.25 for threshold 0.1 to 1.0. False positive rates have probability estimates ranging from 0.2 to $\tilde{0}$.1 for thresholds 0.1-1.0.



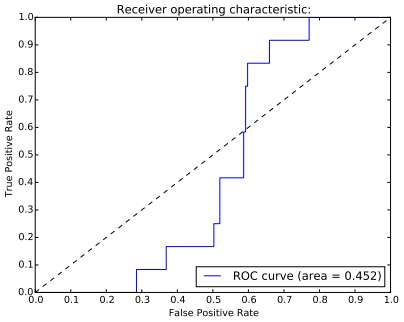
(a) Subject-independent ROC-curve



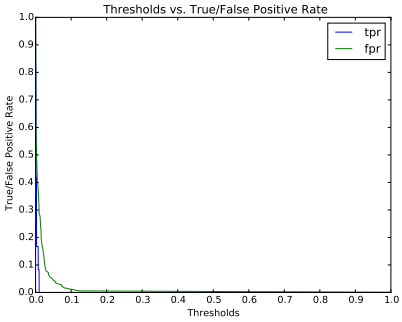
(b) Subject-independent threshold

Figure 12: Result from dog 4 subject-independent test

The figure 12 shows the results of the subject-independent model for dog-4, training on interictal and preictal clips from dogs 1,2,3 and testing on test clips from dog-4. In figure 12a the ROC-curve for the subject-independent model for dog-4 is plotted with the area underneath the curve being 0.459. In figure 12b; the true positive prediction rate has probability estimates in the range >0.2 to 0.0 for threshold 0.1 to $\tilde{0}$.9. False positive rates have probability estimates ranging from 0.4-0.0 for the same thresholds.



(a) Subject-specific ROC-curve



(b) Subject-specific threshold

Figure 13: Result from dog 5 subject-specific test

Figure 13 is the resulting subject-specific test for dog-5, training on preictal and interictal clips of dog-5 and testing on test clips from dog-5. Figure 13a shows the ROC-curve for the subject-specific model for dog-5 with the area underneath the curve being 0.452. The true and false positive rates in figure 13b are intelligible and do not provide information from which any significant prediction estimates and thresholds ranges can be derived.

Test Subject	**SS AUC(%)**	**SI AUC(%)**
Dog-1	0.857	0.495
Dog-2	0.812	0.480
Dog-3	0.882	0.434
Dog-4	0.872	0.459
Dog-5	0.452	N/A

Table 2: **Area underneath ROC** for all subjects, for both models

Table 2 has the areas underneath the ROC-curve for dogs-1 to 5 with regards to both models; subject specific and subject independent.

SS AUC avg.±stdv. (%)	**SI AUC avg.±stdv(%)**	**t-value & p-value**
0.775 ± 0.183	0.467 ± 0.026	15.024 & 0.001

Table 3: Comparative statistics: mean AUC± stdv and AUC T-Test

Table 3 has the average areas underneath the ROC-curve ± standard deviation for both subject specific and subject independent, as well as the calculated student's t-test.

From the presented results a couple of observations can be made by examining each threshold for each dog (for the subject-independent model), in order to elaborate on the degree of accuracy for the classification per threshold. Across all subject-independent models the generalization can be made that the true positive rates are lower than false positives for most thresholds. This indicates that there are more interictal clips being classified to those thresholds than preictal clips. In turn, it implies that the probability estimates for the subject-independent model can be considered as randomly distributed along the thresholds. This random distribution and the lower number of preictal clips could explain why the TPR for certain parts are erratic and therefore higher than the FPR at certain thresholds. Consequently, the AUC value for all subject-independent models are low enough for the classifier's prediction accuracy to be considered as random.

5 Discussion

5.1 Result Analysis

The following section will give short summary of the most pertinent results and their implication using inferential statistics. The results will then be analyzed in regards to the problem statement. The analysis will be, as stated in section 1.2, centered on how various aspects of the algorithm may have lead to the results. Lastly, the analysis will then be extrapolated to a broader perspective for the field of epileptic seizure prediction.

The ROC-curves for subject-specific and subject-independent models lead to one primary observation: the subject-independent model prediction accuracy is worse than the specific one. The best results were achieved by the subject-independent classifier for dog-1 with a AUC of 0.495, the worst being dog-3 with AUC 0.434, with an average of 0.467 ± 0.026 across all subject-independent models. Consequently, such low values for the accuracy tests of the subject-independent classifiers indicate an inability to discriminate between preictal and interictal states. Thus, a mechanism using a subject-independent model with the algorithm utilized would not be able to predict epileptic seizures.

In contrast to the subject-specific model for which the best results were achieved for dog-3 with an AUC of 0.88, and the worst by dog-5 with an AUC of 0.45, and an average of 0.775 ± 0.183. Looking across all subject-specific models the accuracy test for classifiers (with the exception of dog-5) indicate a strong ability to discriminate between interictal and preictal states. Given this result, the subject-specific model of the algorithm is suited for predicting epileptic seizures. This notion has, however, been corroborated by other studies prior to this one, and the author of the algorithm, and should therefore not be considered as additive evidence [5][9]. This is due to the fact that the subject-specific results were obtained by running the algorithm with the same parameters and data as in the competition.

By examining the average area underneath the curve for both models and applying methods from inferential statistics, it is possible to establish whether the difference between the averages are significant. From table 3; the average areas underneath the curves are 0.775 ± 0.183, 0.467 ± 0.026, for subject-specific and independent, respectively. The Student's t-test, i.e, two sample t-test where the variances are equal (confirmed by performing a F-test prior to the calculation) has a p value of 0.001 (3 sig. fig.) with a 5% risk for error. From the test it is possible to infer that the perceived difference between averages is significant. This means that the difference observed is confirmed. It is therefore possible to state the that subject-independent model performed significantly worse than than the subject-specific model.

We reason that, the primary cause for the low accuracy of the subject-independent model are intricacies of the feature extraction process. The way the algorithm was designed, the subject-independent model for a dog is trained on an ensemble of features (one collection) from the feature extraction process which took place for each dog independently. That is, the training data is made up of already feature extracted data from the dogs to be used for training. To elaborate; all spectral power features from the FFT, the correlation coefficients and eigenvalues are extracted for each dog separately and are then concatenated into one training set. By performing the feature extraction on each dog sep-

arately, the model is trained on the most distinguished features for each dog (rather than for all the dogs). Based on the results presented in the previous section, we can see that using the features specific to each dog for the training of the subject-independent model did not suffice for predicting on other dogs. For possible adjustments to the feature extraction of the training data, see section 5.3

The differences in the performance between the models may be explained by the uniqueness of the brain and dependability of prediction algorithms on the strict characteristics of a subject's epilepsy [34]. A subject's unique epileptic characteristics is the unique set of pre-seizure changes in frequency and location of the epileptogenic zone [34][14]. In the scope of our results this entails that, depending on the epilepsy, the transition from the interictal to preictal state may manifest differently in the EEG-data [14]. This will affect which features are being emphasized depending on the dog's brain. This will in turn affect the classifier when dogs with different epilepsies are used for training.The classifier will be primed for pre-seizure changes specific to the dogs included in the training set. This leads to the subject-independent classifier attempting to classify epileptic seizures which manifest on different frequencies and in different locations than the dog being tested on. As such, the adaptation of a subject-specific algorithm to a subject-independent one may require the extraction of epileptic characteristics common to all dogs in the training sample. Additionally, this could indicate that the carried out method where a functioning subject-specific algorithm's training is modified to be subject-independent, is insufficient in the creation of a functioning subject-independent epileptic prediction algorithm.

5.2 Limitations and Anomalies

No results were produced for dog-5 using the subject-independent classifier. This is due to the fact that dog-5 only contained data from 15 channels. The 16th channel had no recorded physiology and was therefore omitted to save disk space. When the data for dog-5 was included in the training (or predicted on) the algorithm broke and output an error. The solution would have been to populate the vector of that channel with random noise but we opted against this. Additionally this may be the cause for the poor results for the subject-specific test on dog-5.

The author of the algorithm admitted a couple of limitations regarding its use. He emphasized that the circumstances under which the algorithm was written were not ideal. By starting too close to the deadline of the competition the author felt stressed and pressured, which lead to parts of the code being unoptimized and even non-functional. While these limitations are accounted for, the author states that several possible expansions of the algorithm that he had in mind were left unexplored. Amongst these was the code for testing on a cross model, which is the subject independent model but with the data of the subject being tested on included in the training. While this code is included in the available algorithm, it is stated that the optimization of it would require investigating the optimal setup of features.

5.3 Future research

In this study the algorithm used was developed for subject-specific purposes. Due to the lack of research on subject-independent models, a first step would be developing an algorithm focusing on subject-independent classification.

As mentioned in section 5.1 the most important factor in seizure prediction is the feature extraction. Having an algorithm that could either abstract common features between different epilepsies, or using a larger set of training data, with more dogs, to include many different kinds of epilepsy, could both possibly increase the performance. The first place algorithm in the competition used a composition of three classifiers, where different sets of features were used for each different classifier. This could be further investigated to implement a better algorithm for subject-independent prediction. Further studies should investigate how an even larger amount of dogs could cover a broader spectrum of epilepsy in subject-independent prediction.

The algorithm used in this study, uses the features of correlation coefficients and eigenvalues between the channels of one specific dog. If instead, the feature extraction process was performed on the ensemble of all raw EEG data from all the dogs, then features between the dogs could have been extracted. This could be a possible approach for an algorithm which abstracts common features between different epilepsies. Additionally, to match the common features of the training data, it could be necessary to include some of the training data as a reference, to find the common features, in the testing data.

5.4 Conclusion

Due to the inherent strict characteristics of epilepsy and seizure prediction algorithm's dependency upon them; the results do not corroborate the notion that the subject-independent model performs equal to or higher than the subject-specific model. Following the established framework, the subject-independent model did not achieve prediction rates above random, i.e performed worse than the subject-specific model. This leads to the conclusion that the subject-independent algorithm, with the adjustment of a subject-specific algorithm, can not, at this time, achieve prediction rates equal to or higher than that of the original subject-specific version.

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