

Evaluating the DoC-Forest tool for Classifying the State of Consciousness in a Completely Locked-In Syndrome Patient

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Abstract—This paper shows how the DoC-Forest method can be used for classifying the state of consciousness in a Completely Locked-In Syndrome (CLIS) patient based on electrophysiological measurements of the patients’ brain activity. The DoC-Forest is a Machine Learning (ML) based method to classify whether patients with a Disorder of Consciousness (DoC) are either in the minimally conscious state (MCS) or have the unresponsive wakefulness syndrome (UWS). As labeled training data is unavailable for CLIS patients, Stereoelectroencephalography (sEEG) data obtained from patients undergoing anesthesia was used to train an ensemble of decision trees to classify the state of consciousness. The model achieves a predictive area under the curve (AUC) of 0.73 on out-of-sample data during training. The most important features for training the model on the anesthesia dataset were determined, and an explainable ML algorithm was used to quantify how features contributed to forming the predictions for the CLIS patient. For the CLIS dataset comprising ECoG measurements from one CLIS patient, there was a time period where the CLIS patient clearly was conscious. Based on the predictions of the model trained on the anesthesia dataset, this period was clearly identifiable, indicating that despite the differences in the underlying conditions (CLIS and anesthesia) and the different measurement methods (sEEG and ECoG) the model was able to extract robust patterns predictive of the state of consciousness.

Index Terms—Completely Locked-In Syndrome, Complexity Measures, Computational Neuroscience, Consciousness, Information Theory, Machine Learning, Modeling and Prediction, Neuroscience, Signal Processing

I. INTRODUCTION

Completely Locked-In Syndrome (CLIS) is a medical condition where the patient is completely paralyzed, and therefore unable to communicate with his surroundings, while still being conscious and having a normal cognitive experience [1]. Accurately detecting consciousness in these patients is crucial for providing appropriate medical care and ensuring their quality of life.

In recent years, there has been growing interest in developing objective methods for detecting consciousness in patients with severe brain injuries [2]–[4]. Engemann et al. introduced a robust Random Forest based method called DoC-Forest to classify the state of consciousness in patients having a Disorder of Consciousness (DoC), based on EEG recordings

[2]. Minimally conscious state (MCS) and unresponsive wakefulness syndrome (UWS) are DoC that can occur in patients with severe brain injuries. In MCS patients show minimal but detectable signs of consciousness, while patients with UWS may display basic reflexes, but no signs of consciousness.

This paper evaluates whether the DoC-Forest method can be used for detecting consciousness in CLIS patients with Electroencephalography (EEG) over time. As the state of consciousness in CLIS patients is unknown, it is impossible to create a labeled training dataset which is needed for training a supervised learning model. Electroencephalography (EEG) patterns observed during slow-wave sleep are similar to those seen in the deep phase of general anesthesia [5]. Therefore, the model is trained on a Stereoelectroencephalography (sEEG) dataset obtained from patients undergoing anesthesia for surgery instead, and its predictive power is assessed. Most often, sEEG is used to localize seizures in patients with epilepsy [6].

The trained model is then used to predict the state of consciousness in a CLIS patient based on a 24-hour long ECoG recording, which includes a time period when the CLIS patient is known to be conscious, allowing an assessment of the correctness of the predictions over this time span [7]–[10].

A feature importance measure for decision trees is used to evaluate which features are most predictive of consciousness in patients undergoing anesthesia, and the TreeInterpreter method is used to assess how features contributed to forming the final predictions of the model for the CLIS patient [11] [12].

In section II of the paper the anesthesia and the CLIS datasets are described, and the DoC-Forest method is introduced. The methods for finding the most important features in the trained model and for quantifying the contributions of the features to the final predictions are also explained. Section III first analyzes how the model performed on the training dataset, and which features were most important. In the following, the predictions the model made for the CLIS patient and how each feature contributed to them was evaluated. These results are then discussed in section IV.

II. TOOLS AND METHODS

A. Data

The data used for training the ML model to classify the state of consciousness comprises Stereoelectroencephalography (sEEG) measurements (with 120 channels at 500 Hz sampling frequency), of 26 patients undergoing anesthesia [13]. The measurements were preprocessed with a 0.3 - 200 Hz band pass filter and a 50Hz notch filter. At the start of the recordings, each patient was unconscious, and the timestamp at which the first sign of reawakening could be observed was captured. Based on this information, the data could be divided in two parts, where in the first the patient was most likely unconscious and in the second one most likely conscious.

The CLIS data consists of electrocorticography (ECoG) recordings (with 64 channels at 500 Hz sampling frequency) from one CLIS patient over 24 hours [7]. For the ECoG a 0 - 40 Hz 3rd order Butterworth filter was applied. Over the measured timespan there was an about 2-hour-long period when the CLIS patient was clearly conscious and responsive to questions, as a clinician was able to successfully conduct an interview with the patient [8] [10].

B. DoC-Forest method

The DoC-Forest method introduced by Engemann et al. comprises three general steps: computing markers of consciousness on neuroimaging data, applying summary statistics to the markers to get features that are independent of the specifics of the measurement process (like the number of channels in the neuroimaging technique used) and finally training an ensemble of decision trees on these features to discriminate between MCS and UWS [2]. In the following it is described how the method was applied to predict the state of consciousness in CLIS patients over time.

First, the training and CLIS datasets were loaded and divided into 8 second long epochs using the MNE python package [14].

The markers of consciousness used in this paper are a subset of those used in the original DoC-Forest paper [2]. Table I groups the relevant markers in three conceptual families: information theoretic, connectivity based, and spectral measures. Previous research has found that being conscious is associated with a more complex brain activity [15]. $PE\theta$, K , and SE are different methods for quantifying the complexity of measured brain activity. $|\alpha|$, $|\beta|$, $|\delta|$, $|\gamma|$ and $|\theta|$ describe how the total energy of the measured signal is distributed across different frequency bands. Analyzing the frequency spectrum of EEG signals is one of the longest known approaches for establishing connections between brain activity and different mental states like consciousness or sleep [16]. Connectivity based markers like $wSMI\ \theta$ aim to quantify information sharing in the brain. Research has shown, the more correlated activity in different regions of the brain is, the more likely the patient is to be conscious [17].

Engemann et al. provide an open-source python package called NICE which efficiently implements algorithms for computing the aforementioned markers of consciousness [2].

TABLE I
MARKERS OF CONSCIOUSNESS [2]

Abbreviation	Marker	Conceptual family
$PE\theta$	Permutation entropy	Information theory
K	Kolmogorov complexity	Information theory
$wSMI\ \theta$	Weighted symbolic mutual information	Connectivity
$ \alpha $	Normalized alpha PSD	Spectral
$ \beta $	Normalized beta PSD	Spectral
$ \delta $	Normalized delta PSD	Spectral
$ \gamma $	Normalized gamma PSD	Spectral
$ \theta $	Normalized theta PSD	Spectral
MSF	Median power frequency	Spectral
$SE90$	Spectral entropy 90	Spectral
$SE95$	Spectral entropy 95	Spectral
SE	Spectral entropy	Spectral

The NICE package is used to compute each marker for each epoch and each channel in the training and CLIS datasets. To obtain a set of features that is independent of the measurement protocol (e.g. independent of the number of sEEG or ECoG channels), summary statistics are applied to the time dimension (across epochs) and spatial dimension (across channels) for each patient. For each marker and distinct patient in the anesthesia and CLIS datasets, the spatial dimension is reduced to two values per epoch by computing the arithmetic mean and standard deviation over all channels, respectively. Then, to each of the two resulting series of means and standard deviations a 15-minute rolling window is applied, for which again the mean and the standard deviation are computed, resulting in a total of four feature series per marker, which sums up to a total of 48 features. The application of a rolling window constitutes a difference to the original DoC-Forest method, where the time dimension is completely reduced, giving only one value per feature and per patient. With the rolling window approach it can not only be estimated if a patient was conscious during the recording at all, but also at which point in time he may have been conscious or not.

Each feature can be described by a 3-tupel containing (*marker*, *f_{epochs}*, *f_{channels}*), where the *f_{epochs}* and *f_{channels}* functions are either the arithmetic mean (short "mean") or the standard deviation (short "std"). E.g. (SE, mean, std) would describe the feature where first for each epoch the standard deviation of the spectral entropies across all channels was computed, and then a rolling arithmetic mean was applied to the resulting series of standard deviations.

C. Explainable Machine Learning

The ML algorithm used to classify the state of consciousness of the CLIS patient is the same one used in the DoC-Forest method, called ExtraTrees (short for Extremely Randomized Trees) [2] [18]. The ExtraTrees algorithm calculates an ensemble of Decision Trees similar to the well-known Random Forest algorithm (from which the name "DoC-Forest" was derived) [19]. The difference is that when training the decision trees for the ExtraTrees ensemble, the splits are not optimized like in the Random Forest algorithm, but chosen at random, making it more suitable for neuroimaging data which generally has a low signal-to-noise ratio.

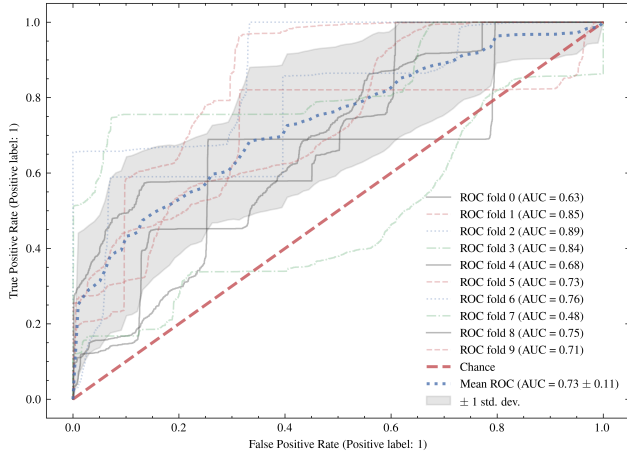


Fig. 1. The receiver operating characteristic (ROC) curves for the out-of-sample predictions on the test-sets, made with the ExtraTrees models trained on the corresponding train sets. The ten train/test splits were generated from the sEEG anesthesia dataset.

On one hand, the Mean Decrease Impurity (MDI) quantifies how important a feature is for the overall predictive power of the ensemble model [11]. It depends on how much, on average, the feature reduces the uncertainty about the observed labels in the training dataset. TreeInterpreter on the other hand, is a tool for measuring how much each feature contributes to a single prediction of a Decision Tree (Ensemble), made based on one observed data sample [12]. The contributions for each feature are computed for each Decision Tree individually, and then averaged over the ensemble. For a single Decision Tree, the predicted probability \hat{p} based on a given sample vector x_t at time t containing K feature values, can be decomposed into feature contributions:

$$\hat{p}(x_t) = c_{full} + \sum_{k=1}^K contribution(x_t, k) \quad (1)$$

where c_{full} refers to the empirical probability of the label being one in the training set (the bias), and $contribution(x_t, k) \in [-1, 1]$ is the contribution of the k -th feature in the sample vector x_t . The exact procedure for calculating the feature contributions for a decision tree ensemble is explained in [12].

III. RESULTS

To assess the performance of the approach on the anesthesia training dataset, ten random train/test data splits are generated for Cross Validation (CV), with data from 22 patients in each train split and from 4 patients in each test split. Fig. 1 shows the ROC curves the classifiers achieve for out-of-sample predictions on the CV test sets [21]. With an average Area Under Curve (AUC) of 0.73, our model consistently performs better than chance, showing that the approach is effective in classifying the state of consciousness in before unseen patients undergoing anesthesia [21].

Fig. 2 shows the MDI distributions for 20 features which were on average the most important across the different cross

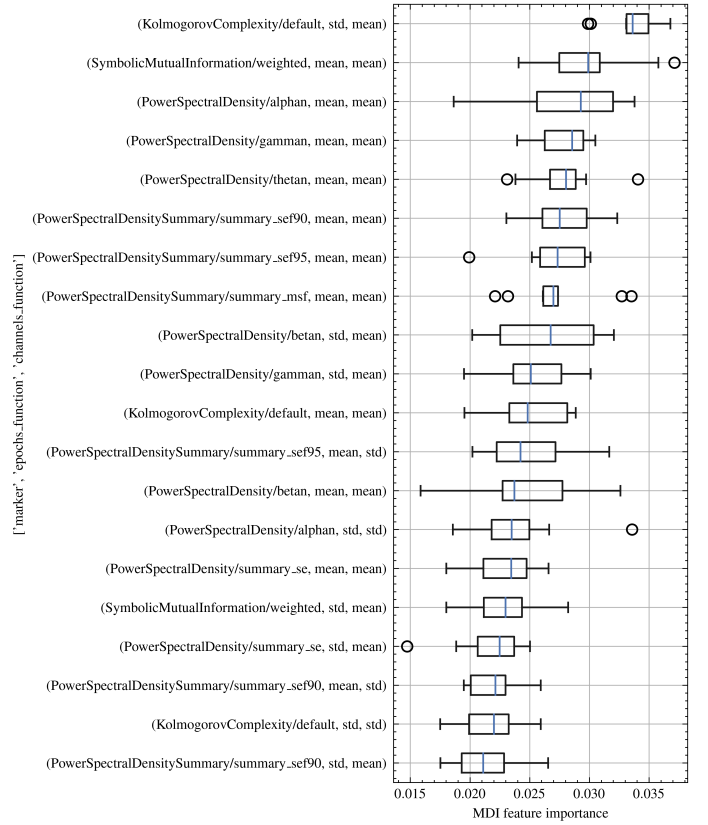


Fig. 2. Twenty most important MDI feature importance distributions for the ExtraTrees models across the ten Cross Validation splits of the sEEG anesthesia dataset. A feature is described by a 3-tuple, containing (*marker*, *fepochs*, *fchannels*), where *fepochs*, *fchannels* are the functions applied to reduce the time dimension (epochs) and spatial dimension (channels), respectively. *fepochs* and *fchannels* can either be the arithmetic mean ("mean") or the standard deviation ("std").

validation splits. In general, features describing the average expression of a marker across epochs and channels were the most important, which confirms previous findings on markers of consciousness [15]–[17]. A notable exception is the topmost feature in Fig. 2, describing how much the average Kolmogorov Complexity across channels varied in the last 15 minutes. It is the most important feature, and describes the variance of the markers' expression over time, while the seven next most important features all describe average marker expressions across channels and epochs.

The ExtraTrees model trained on the sEEG anesthesia dataset was then used to predict the state of consciousness for the CLIS patient, based on the ECoG data. The levels of the predicted probabilities for the CLIS patient being conscious in Fig. 3 nicely fit the sleep patterns of a normal human, with the probability of being conscious rising at about 8:00 AM, and decreasing back to the initial lower level only after about 8:00 PM. There is evidence that suggests that CLIS patients have normal sleep patterns comparable to healthy humans [22]. Beyond that, the predicted probability of the patient being conscious is at a high level during the period when the CLIS patient is known to be conscious [8]–[10]. This indicates, that

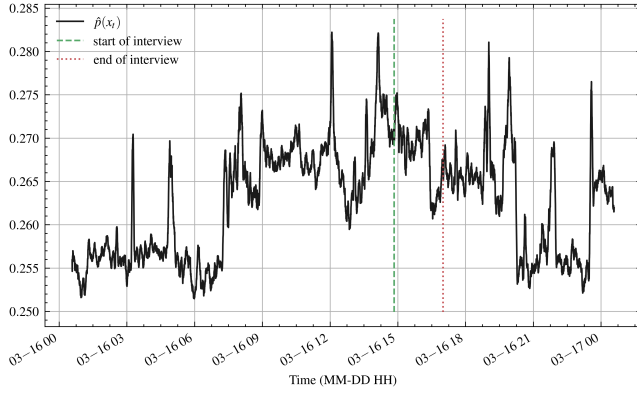


Fig. 3. Predicted probabilities for the CLIS patient, obtained from the model trained on the anesthesia dataset. A bigger value means the model considers the probability of the patient being conscious to be higher. It is clearly visible that during the interview when the patient is known to be conscious the probability level is among the highest.

there are patterns identified by the model in the brain activity of patients undergoing anesthesia which generalize to CLIS patients, therefore allowing the classification of the state of consciousness in CLIS patients.

It should be noted that the probabilities generated by the model depend on the number of positive and negative labels in the training data, which is not balanced. Accordingly, they should not be interpreted as literal probabilities, but only in a comparative fashion.

Fig. 4 illustrates the distributions of the contributions for each feature k over all feature vectors x_t , as described in Eq. (1). The box plots are sorted in descending order of the variance of the contributions over time. This is done as not merely a constant high contribution makes a feature important, but how the contributions actually explain the variance of the predicted probabilities over time.

The most important features positively influencing the predicted probabilities are all based on the marker measuring the normalized PSD in the β band. Previous research has associated high activity in the β band with increased alertness in humans [23]. What is striking is that the majority of the other important features express how much the marker values vary across channels or epochs or both, while most of the features which contributed the most (in terms of MDI) to the predictive power of the model on the training dataset, are based on the average expression of the marker values over channels and epochs.

IV. DISCUSSION

In this paper it was evaluated if the DoC-Forest method introduced to classify Disorders of Consciousness can successfully be applied to classify the state of consciousness in patients undergoing anesthesia and CLIS patients over time, based on neuroimaging data [2].

On the anesthesia dataset, an average predictive AUC of 0.73 on data from before unseen patients was achieved,

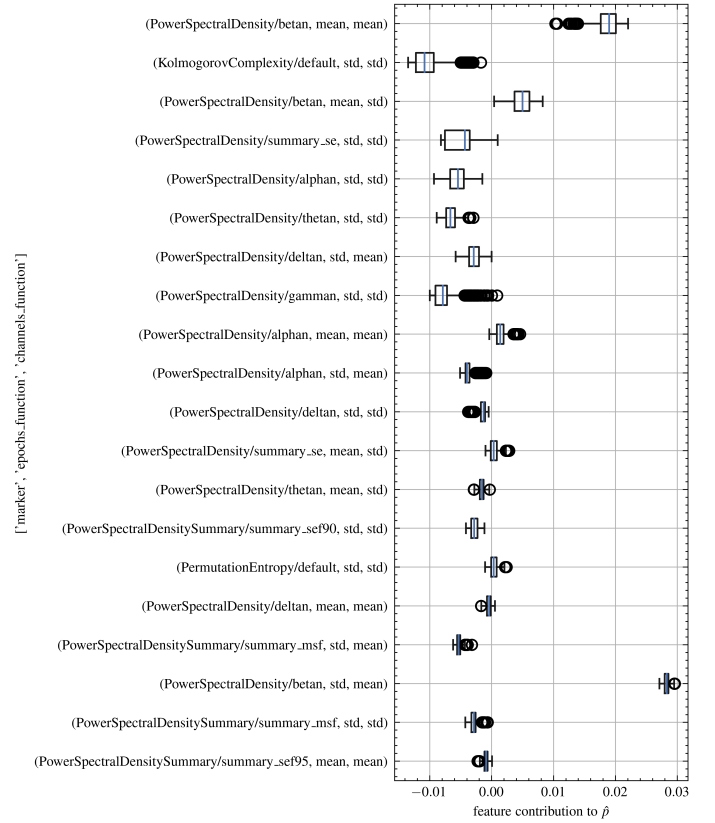


Fig. 4. Distributions of the contributions (see Eq. (1)) of the twenty features that were the most important in forming the predictions \hat{p} in Fig. 3, sorted in descending order of the variance of their contributions over the 24-hour time period. A feature is described by a 3-tupel, containing (*marker*, *f_epochs*, *f_channels*), where *f_epochs*, *f_channels* are the functions applied to reduce the time dimension (epochs) and spatial dimension (channels), respectively. *f_epochs* and *f_channels* can either be the arithmetic mean ("mean") or the standard deviation ("std").

showing that the method was able to learn patterns that predict the state of consciousness in patients undergoing anesthesia.

When the model was applied to the CLIS dataset, the predicted probabilities indicated periods of higher and lower probabilities that matched the sleep pattern of a human. They also were at a high level during the time period when the CLIS patient was known to be conscious.

Comparing the most important features (with the highest MDI) on the anesthesia dataset with the features that were most important in forming the predictions on the CLIS dataset (based on the variance of its TreeInterpreter contributions over time), one can see a striking difference. While for the anesthesia dataset, features describing the mean expression of a marker across epochs and across channels were most important, for the CLIS predictions features describing the variance of a marker (across epochs, channels or both) were most important. Unconsciousness in anesthesia is characterized by burst suppression patterns in the brains' activity [24], and so-called sleep spindles [25] are burst-like patterns of activity observed during non-rapid eye movement sleep. It is therefore plausible that during anesthesia-induced unconsciousness and

non-rapid eye movement sleep the measured variance across time of e.g. signal complexity is higher than during wakefulness. This could explain why those features robustly predict the state of consciousness for patients undergoing anesthesia and CLIS patients as well.

V. CONCLUSION

This paper demonstrates the successful adaptation of the DoC-Forest method to predict consciousness in patients under anesthesia. The obtained ML model could also be applied to classify consciousness in CLIS patients. A feature importance measure and explanation tools for the models predictions were used to identify key predictors for anesthesia and CLIS states, revealing differences between the two.

The approach outlined in this paper can be used to assess the generalizability of complex tree-based ML models to new datasets with varying characteristics, which were in this case differing neuroimaging techniques and neurophysiological differences between anesthesia and CLIS patients. It enables to state hypothesis about which features used in a model generalize well and which factors may hinder generalizability.

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