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A robust methodology for classification of epileptic seizures in EEG signals

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Abstract

Drug inefficiency in patients with refractory seizures renders epilepsy a life-threatening and challenging brain disorder and stresses the need for accurate seizure detection and prediction methods and more personalized closed-loop treatment systems. In this paper, a multicenter methodology for automated seizure detection based on Discrete Wavelet Transform (DWT) is presented. A decomposition of 5 levels is applied in each EEG segment and five features are extracted from the wavelet coefficients. The extracted feature vector is used to train a Random Forest classifier and discriminate between ictal and interictal data. EEG recordings from the database of University of Bonn and the database of the University Hospital of Freiburg were employed, in an attempt to test the efficiency and robustness of the method. Classification results in both databases are significant, reaching accuracy above 95% and confirming the robustness of the methodology. Sensitivity and False Positive Rate for the Freiburg database reached 99.74% and 0.21/h respectively.

Keywords Bonn EEG database · Discrete wavelet transform (DWT) · Electroencephalogram (EEG) · Epileptic seizure · Multicenter · Freiburg EEG database

1 Introduction

Epilepsy is a brain disorder caused by recurrent episodes of abnormal electrical discharges of the neurons, called seizures. This neurological disorder engrossed much of the research attention over the last decades owing to the complexity and the severity of the seizure events. Despite the enormous breakthroughs that have been achieved, there are more than 30% of the epileptic patients who experiences uncontrolled seizures, even with the use of anticonvulsant medications [1]. Therefore, epilepsy is a dreadful neurological disorder, considered as significant culprit of mortality in developed as well as developing countries [2].

Generally, epileptic seizures are divided into two fundamental types based on the brain areas that are activated during seizures: partial and generalized. Partial seizures arise from a single brain area and remain only to one cerebral hemisphere, whereas generalized seizures involve the entire brain [3]. The diagnosis and monitoring of the seizures is done through the electroencephalogram (EEG), which records the brain activity through electrodes that are either attached to the scalp (scalp EEG - sEEG) or placed invasively inside the brain (intracranial EEG -iEEG). In general, the clinical EEG recording is performed between two seizures (interictal period) and seldom during a seizure (ictal period).

Experienced epileptologists have to examine a vast amount of data for the diagnosis of epilepsy. The visual analysis of the EEG recording that often lasts several hours is usually a time-consuming and eventually a laborious undertaking. In the literature, there is an abundance of methodologies for automated seizure analysis, aiming to assist in the epileptologist's task. The main groups of studies focus on automated seizure detection, automated seizure prediction and seizures origin localization [4], towards developing novel intervention systems.

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The majority of these methodologies concur with a two-stage procedure, following a pattern recognition approach: feature extraction and classification.

Methods for automated seizure detection have been evaluated in databases from various epilepsy centers. The most well-known databases that have been widely utilized throughout the years are the database of the University of Bonn and the database of the Epilepsy Center of the University Hospital of Freiburg. The database of the department of Epileptology of the University of Bonn is the most common dataset and consists of scalp and iEEG signals that have been recorded from 5 healthy and 5 epileptic patients. These long-term EEG recordings were cut off forming 5 different sets of 100-single signals of 23.6 s duration each. On the other hand, the database of the Epilepsy Center of the University Hospital of Freiburg is a high-quality dataset that contains continuous long-term iEEG recordings (1 h) acquired with 6 channels from 21 patients during pre-surgical examination. This database provides more information about the patients (age, sex, seizure origin) and is closer to clinical EEG recordings. The databases are thoroughly described in section III.

In this paper, a multicenter, wavelet-based method for automated seizure detection is proposed. The Discrete Wavelet Transform is used to divide EEG recordings to specific bands of interest and extract several features. Then, these features are used as input to a Random Forest classifier. The method is evaluated on the database of the University of Bonn and the database of the Epilepsy Center of the University Hospital of Freiburg, and the obtained results indicate the robustness of the proposed approach.

2 Related work

The database of University Hospital of Bonn is the most widely used database in the literature. Time-Frequency analysis methods [5] like Wigner-Ville distribution [6], Empirical Mode Decomposition [7, 8] and Local Mean Decomposition [9] have been proposed to analyze the EEG signals in frequency bands of interest and then, to calculate linear and non-linear features. Wavelet Analysis is constantly gaining ground and a majority of studies have preferred to develop their methodology based on Wavelet Analysis. Discrete Wavelet Transform [10–12], Wavelet Packet Decomposition [13, 14], Dual-Tree Complex Wavelet Transform [15, 16] and Tunable-Q Wavelet Transform [17, 18] have been used extensively during the last decade. Apart from Time-Frequency Analysis studies, methods for extracting features based on Information Theory [19] and Entropies [20] have also been proposed.

A wide group of methods have been evaluated with the database of the University Hospital of Freiburg. Different methodologies have been proposed and the Wavelet Analysis has been adopted by many researchers. Particularly, the Discrete Wavelet Transform was preferred among other techniques [21–24]. Empirical Mode Decomposition [25], Fractal Analysis [26] and Fuzzy systems [27] have also been employed in many scientific studies and have reported adequate results in the detection of the subtle changes of the EEG recordings. Furthermore, Independent Component Analysis (ICA) and Principal Component Analysis (PCA) [28] have also played a significant role on seizure detection studies.

Despite the fact that there is a tremendous number of research studies, which have been validated on EEG signals from one epilepsy center, there are still few methodologies evaluated on more than one database. In 2012, a wavelet-based sparse functional linear model was proposed by Shengkun Xie and Sridhar Krishnan [29]. The EEG signals from the database of the University of Freiburg were initially segmented in epochs of 4096 samples and then the wavelet variances were calculated. Three classifiers namely k-Nearest Neighbor, Fisher's linear discriminant (FLD), and Support Vector Machines (SVM) were tested. The proposed method was evaluated on the database of University of Bonn and on 4 patients (8 h of analysis) of the database of Epilepsy Center of University Freiburg, reaching high levels of accuracy for six classification problems and 0.9789 of the geometric mean for the ictal-interictal problem, respectively.

Recently, the same group of researchers proposed a different approach for epilepsy diagnosis and epileptic seizure detection [30], based on dynamic principal component analysis (DPCA) and nonoverlapping moving window. PCA was used as a dimension reduction method and applied to both short-term and long-term EEG recordings. Initially the non-overlapping moving window technique was applied. The authors estimated various time lengths of EEG segments and resulted in 512 samples length for the database of University of Bonn and 1280 samples for the database of University of Freiburg. The first few principal components combined with the signal energy was used as the feature extraction technique and the one Nearest Neighbor (1-NN) classifier was chosen to discriminate the 3 classification problems: two (Z-S, ZONF-S) for the Bonn database and one (ictal-interictal) of 2 patients (Patient 1 and Patient 3) for the Freiburg database.

A comprehensive study [31] proposed in 2014 to discriminate ictal from interictal recordings. The authors tested the effectiveness of four feature extraction methods (Discrete Cosine Transform (DCT) with energy and entropy, Discrete Wavelet Transform (DWT) with STD, Empirical Mode Decomposition (EMD) with STD, Singular Value Decomposition (SVD) with energy and STD) in the Freiburg database. The features were extracted from the higher frequency components and the feature vector (of each approach) was given as input to a Least Square Support Vector Machines (LS-SVM). Ictal (200 signals) and interictal (800 signals) recordings that obtained from temporal and frontal lobe, were used to evaluate the proposed methods. In order to validate their results, the authors applied the method proposed by Varun Bajaj and Ram Bilas Pachori [32] on the Freiburg database. In this method, the EMD was applied on the EEG segments of the Bonn database. Bandwidth features namely amplitude modulation bandwidth and frequency modulation bandwidth were extracted and was used to train a LS-SVM classifier. Results in terms of accuracy, sensitivity and specificity for the two-class problem (ZONF-S) were above 94%. However, the method was evaluated on the Freiburg database by Parvez & Paul and the obtained results were not so promising.

In a more recent approach [33], the aforementioned group of researchers proposed two methods: i) based on DCT and energy and ii) based on EMD and STD. In the first method, the energy of high-frequency coefficients was calculated whereas in the second the standard deviation. In both cases the set of features was fed into a LS-SVM classifier. To evaluate their method on Freiburg database, 3 min from ictal and 3 min from interictal activity were acquired from 12 patients suffering from temporal and frontal lobe seizures. In some cases, the authors included the pre-ictal activity to cover a 3-min ictal period. The evaluation on the Bonn database was done for the classification problem ZONF-S and results in terms of accuracy, sensitivity and specificity was above 94% for both of the databases.

3 Method

The proposed methodology consists of three main steps: (i) signal analysis with Discrete Wavelet Transform, (ii) feature extraction, and (iii) classification with Random Forests. In the first step, a Discrete Wavelet Decomposition of 5 levels was applied, dividing each signal into several frequency sub-bands. Subsequently, five linear and non-linear features were extracted from each wavelet sub-band forming the feature vector. Finally, the set of features was used to train a Random Forest classifier. The method was evaluated using the University of Bonn database and the University of Freiburg database.

3.1 Wavelet analysis

Wavelet Transform is a Time-Frequency technique that employs mathematical functions to detect sharp signal transitions like epileptic spikes. Over the past few years, various research groups have shown a rising preference among other techniques due to its attractive properties in both frequency and time domain.

According to the Wavelet Analysis [34], the signal can be decomposed into sub-signals of half size and spectrum over dilating and translating a single function, usually in powers of two to ensure orthogonality. This function is called mother wavelet. The Discrete Wavelet Transform (DWT) is implemented with a pair of quadrature mirror filters, described as conjugate high-pass and low-pass filters. A series of decomposition levels is required to analyze the entire signal. In the first level, the input signal is simultaneously passed through the pair of filters. The obtained sub-signals are called wavelet coefficients. The coefficient of the low-pass filter is named approximation and is sub-decomposed, whereas the coefficients of the high-pass filter, namely detail, are not. The procedure is recursively repeated until the entire signal is decomposed, forming a single-side, pyramid-like architecture.

The number of decomposition levels and the mother wavelet is of high importance in DWT. In this work, a 5-level decomposition was chosen based on the dominant frequency, aiming to separate and reveal the frequency bands of importance that cover the seizure activity. The mother wavelet was selected after manual examination mainly among the Daubechies wavelets and the Daubechies of order 4 was the most appropriate to analyze the EEG recording. The resulting decomposition levels with the corresponding frequencies for both databases are presented in Table 1.

3.2 Feature extraction

In the literature, a variety of linear and non-linear detection methods have employed one or more features to acquire different attributes of the signal. In this study, the feature vector as extracted from each of the wavelet sub-bands consists of:

- The energy of the coefficients in each wavelet sub-band,
- The entropy of the coefficients in each wavelet sub-band as calculated from the signal histogram and the Probability Density Function (PDF)
- The standard deviation, the variance and the mean of the absolute values of the coefficients in each wavelet sub-band

The feature vector was subsequently used to train a Random Forests classifier. This low-dimensional feature vector showed great performance in detecting seizures in a previous study [35].

Table 1 Wavelet decomposition levels with the corresponding frequencies for the database of the university of Bonn (173.61HZ) and the database of the university of Freiburg (256HZ) – (D1-D6: Details, a: approximation)

Decomposed signal	Frequency range for the Bonn database (Hz)	Frequency range for the Freiburg database (Hz)
D1	43.4–86.8	64–128
D2	21.7–43.4	32–64
D3	10.8–21.7	16–32
D4	5.4–10.8	8–16
D5	2.7–5.4	4–8
A5	0–2.7	0–4

3.3 Classification with Random Forests

The classification with Random Forests was chosen based on recent findings from a previous study, wherein the Random Forests showed better classification results compared to Naïve Bayes, Decision Tree, k-Nearest Neighbor and Support Vector Machines [36].

The basic idea underlying Random Forests is that a combination of decorrelated decision trees can produce improved accuracy. Trees are grown in binary partitioning using randomly selected features at each node to determine the split. In detail, the feature set is sub-divided into individual subsets of instances with random values, creating the training and testing set for each decision tree, rendering each tree responsible for its own prediction. After a large number of trees is generated, they vote for the most popular class [37]. In the experiments, 100 decision trees were selected and the 10-fold cross-validation technique was employed. Different number of trees was also tested; however, the classification accuracy was not significantly improved.

On the basis of the previous study [35], which has been evaluated on the database of the University of Bonn, the high frequency bands that correspond to the detail coefficients of the 1st and the 2nd level of decomposition (D1 and D2), were included in the final feature vector. However, the database of the University of Freiburg is more complex and with enormously more data instances. In an attempt to decrease the complexity and the computational time, the high frequency bands D1 and D2 of secondary importance were excluded from the final feature vector.

4 Datasets and results

4.1 University of Bonn database

The database of University of Bonn [38] consists of five subsets, denoted as Z, O, N, F and S obtained from five healthy volunteers and five individuals suffering from epilepsy. Subsets Z and O are composed of scalp EEG segments acquired from healthy volunteers, who were relaxed and awake with eyes closed and opened, respectively. The subsets N, F and S are composed of intracranial EEG segments taken from five epileptic patients during evaluation before surgery. In detail, subset N includes interictal iEEG segments derived from the epileptogenic zone of the opposite hemisphere whereas subset O includes interictal iEEG segments acquired from the epileptogenic zone. The subset S comprises iEEG acquired from the epileptogenic zone during seizure activity. Each subset contains 100 single-channel EEG segments of 23.6 s duration (4096 samples). The sampling frequency of the data is 173.61 Hz and any artifacts due to muscle activity or eye movement were isolated and removed by the database owners after visual inspection. The epileptogenic zone was the hippocampal formation and no further information about the patients is provided.

To evaluate our methodology, each recording was segmented in epochs of 2 s (347 samples) with no overlap, leading to 1100 segments for each subset (5500 in total). Seven different classification problems were conducted as suggested in [39] to discriminate different brain states. These seven classification problems (ZONF-S, Z-S, NF-S, F-S, ZO-NF-S, Z-F-S and Z-O-N-F-S) are addressed in the majority of epileptic seizure studies when the Bonn database is involved.

4.2 University hospital of Freiburg Epilepsy Center database

The database of Epilepsy Center of University of Freiburg [40] comprises invasive long-term continuous EEG recordings obtained from 21 patients (8 male – 13 female) suffering from uncontrolled partial epilepsy. Each EEG recording is sampled at 256 Hz and is acquired from six intracranial EEG channels (three focal and three extra-focal electrodes). The data are discriminated into ictal (seizure onset and end are provided), preictal and interictal activity. In most cases, the recording duration is one hour. For each patient, two to five seizure episodes are recorded, lasting from some seconds to a few minutes, composing a dataset of 88 seizures.

In this work, an equal number of ictal and interictal recordings from all 21 patients were utilized. Two seizures from Patient 1 and one seizure from Patient 7 were excluded from the analysis due to technical issues: from Patient 1, the first seizure is interrupted during recording and the second has incorrect seizure end, while the seizure from Patient 7 was excluded due to corrupted data in the 5th channel. Thus, the total number of seizures included in the analysis is 85 (from 88 total).

Initially, the ictal and interictal EEG recordings of each patient were divided into epochs of 2 s (512 samples) with no overlap, leading to 1800 segments for each period per patient. Since the seizure duration ranges from 4.21 s to 1071.5 s, a 2-s-long window was chosen, aiming to accurately capture the seizure activity of all patients. The ictal segments between the seizure onset and seizure end, were selected, while the two segments for each seizure, that contain the seizure onset and end, were excluded from the analysis. The selected segments formed the "ictal" class, which contains the total seizure activity of each patient.

With regard to the interictal segments, a certain number of segments from different interictal recordings of each patient was chosen: for each patient a number of interictal segments were chosen so as the ratio of interictal to ictal segments being 10 to 1. This was made since interictal activity is dominant, and the dataset would be greatly unbalanced if all interictal segments were included in the study. These segments were used to form the class "interictal" for each patient. Table 2 presents the EEG data for each patient. In total, 28.6 h of data, being 2.6 h ictal and 26 h interictal, from the database were included in the analysis.

To evaluate the detection performance of the proposed methodology sensitivity, specificity and accuracy were calculated. For multiclass problems (from Bonn database), sensitivity and specificity are the average values for all classes. The obtained results in terms of overall accuracy, sensitivity/average sensitivity and specificity/average specificity, for the Bonn and Freiburg databases are described in Table 3.

5 Discussion

In this work, a wavelet-based methodology that has been evaluated on two well-known EEG databases, is presented. Discrete Wavelet Transform of 5 levels were applied to EEG data to decompose the signals in six bands of interest. Five typical characteristics namely energy, entropy, standard deviation, variance and mean of the absolute values were calculated from each wavelet coefficient, creating the feature vector that trained a Random Forest. EEG recordings from the database of University Bonn and the University Hospital of Freiburg were employed to test the robustness of the method.

The proposed multi-dataset methodology shows significant results in the detection of seizure activity for both databases. As the work by Parvez & Paul [31] indicated, a methodology designed and successfully tested into a specific database does not guaranty its robustness into a different dataset; in [31], the methodology presented by Bajaj & Pachori [32], which showed excellent results when applied to Bonn database, was validated in the Freiburg database, indicating significant reduction in the obtained results. A comparative study with other approaches that used both the Bonn and the Freiburg database proposed in the literature is presented in Table 4; for a direct comparison to be feasible, only methods tested in both databases are included, since approaches validated with one of the two databases have yet to demonstrate their robustness with other datasets.

The ZONF-S classification problem is the only common from the Bonn database, in all approaches presented in Table 4. For this problem, all researchers reported outstanding results, ranging from 95 to 100% for classification accuracy. The methodology presented by Xie & Krishnan [29] performs better in terms of classification accuracy, however this work has been tested in a small part of the Freiburg database (data from 4 patients with overall duration of 8 h) and thus no clear conclusions can be drawn for the generality of the method. The same applies for the approach proposed in [30] from the same authors, which achieved 100% classification accuracy for the ZONF-S problem of the Bonn database, however has been tested using data from only 2 (out of the 21) patients from the Freiburg database. Furthermore, in both cases, the proposed methodology obtained better classification accuracy results (being 97.74%) for a much larger dataset obtained from the Freiburg database (data from all 21 patients with overall

Table 2 patient characteristics, number of seizures and number of EEG segments (Ictal and Interictal) for each patient in the Freiburg database

Patient	Sex	Age (years)	Number of Seizures	Number of Ictal segments	Number of Interictal segments
1	F	15	3	14	140
2	M	38	3	174	1740
3	M	14	5	226	2260
4	F	26	5	207	2070
5	F	16	5	103	1030
6	F	31	3	89	890
7	F	42	2	188	1880
8	F	32	2	160	1600
9	M	44	5	276	2760
10	M	47	5	1019	10,190
11	F	10	4	307	3070
12	F	42	4	103	1030
13	F	22	2	155	1550
14	F	41	4	426	4260
15	M	31	4	284	2840
16	F	50	5	294	2940
17	M	28	5	207	2070
18	F	25	5	25	250
19	F	28	4	19	190
20	M	33	5	205	2050
21	M	13	5	199	1990
Total			85	4680	46,800

Table 3 Results for different classification problems for the database of Bonn and the database of Freiburg, in terms of accuracy, sensitivity and specificity

	Classification problem	*Accuracy* (%)	*Sensitivity* (%)	*Specificity* (%)
Bonn database	ZONF-S	99.16	99.52	91.56
	Z-S	99.95	100	91.66
	NF-S	98.15	98.64	97.18
	F-S	97.77	97.64	97.91
	ZO-NF-S	95.84	96.04*	97.75*
	Z-F-S	96.09	96.09*	98.01*
	Z-O-N-F-S	82.25	82.25*	95.00*
	Average	95.60	95.74	95.58
Freiburg database	Ictal-interictal	97.74	99.74	97.30

*Average for all classes

Table 4 Comparative study of methods for epilepric seizure detection that have been validated in both bonn and freiburg EEG databases

Authors	Feature extraction	Features	Classifier	Validation	Database	Classification problem	Classification Metrics		
							Accuracy	Sensitivity	Specificity
*Bajaj & Pachori [32] 2011	EMD	Amplitude modulation bandwidth (B_{AM}) and frequency modulation bandwidth (B_{FM})	LS-SVM	10-fold cross-validation	Bonn 500 signals	ZONF-S	95.00% - 96.00%	94.12% - 94.44%	95.17% - 96.34%
Parvez & Paul [31] 2014					Freiburg 21 patients	Ictal-interictal	80.70%	59.22%	82.28%
Xie & Krishnan [29] 2012	Wavelet-based sparse functional linear model	Wavelet variances	1-NN	10-fold cross-validation	Bonn 500 signals	ZONF-S Z-S	100% 100%		
					Freiburg 4 patients (8 h)	Ictal-interictal	99.00%		
Parvez & Paul [33] 2015	ICA and DCT	Energy	LS-SVM	Percentage Split (80%–20%)	Bonn 500 signals	ZONF-S	95.00%	98.91%	94.35%
					Freiburg 12 patients (1.2 h)	Ictal-interictal	97.59%	100%	97.00%
Xie & Krishnan [30] 2014	DPCA	First two PCs and energy	1-NN	10-fold cross-validation	Bonn 500 signals	ZONF-S Z-S	100% 100%		
					Freiburg 2 patients (7 h)	Ictal-interictal	93.80%		
This work	DWT	Energy, entropy, STD, variance, mean of the absolute values	Random Forest	10-fold cross-validation	Bonn 500 signals	ZONF-S	95.23%	99.74%	97.42%
						Z-S	99.95%	100%	91.66%
						NF-S	98.15%	98.64%	97.18%
					Freiburg 21 patients (28.6 h)	Ictal-interictal	97.74%	99.74%	97.30%

*The evaluation on Bonn database was made by Bajaj & Pachori [32] and the evaluation on Freiburg database by Parvez & Paul [31]

Table 5 A comparison of performances of various methods that have utilized the database of the university of Freiburg for seizure detection

Authors	Year	Database/ Number of patients	Feature extraction	Features	Classifier	Learning Process	Performance Metrics
Liu et al. [22]	2012	Freiburg/21	DWT (db4)	Relative energy, relative amplitude, fluctuation index, coefficient of variation	Support Vector Machines	Training: 0.3% Testing: 99.7%	Sensitivity: 96.34% False Positive Rate: 0.58/h
Zhou et al. [41]	2013	Freiburg/21	DWT (db4)	Lacunarity and fluctuation index	Bayesian Linear Discriminant Analysis	Training: 0.1% Testing: 99.9%	Sensitivity: 96.25% False Positive Rate: 0.13/h
Yuan et al. [23]	2014	Freiburg/21	DWT	Diffusion distances	Bayesian Linear Discriminant Analysis	Training: 13% Testing: 87%	Sensitivity: 95.1% False Positive Rate: 0.24/h
Yuan et al. [24]	2016	Freiburg/21	DWT (db4)	SPD matrices	Log-Euclidean Gaussian kernel SRC	Training: 28.74% Testing: 71.26%	Sensitivity: 96.77% False Positive Rate: 0.211/h
Alickovic et al. [42]	2018	Freiburg/21 8 h	DWT (db4)	Mean of absolute values, average power, standard deviation, ratio of absolute mean values of adjacent sub-bands, skewness, kurtosis	Random Forest	10-fold cross-validation	Sensitivity: 99.95%
This work	2018	Freiburg/21	DWT	Energy, entropy, STD, variance, mean of the absolute values	Random Forest	10-fold cross-validation	Sensitivity: 99.74% False Positive Rate: 0.21/h

duration of 28.6 h). Bajaj & Pachori [32] also reported high results for the Bonn database. However, when Parvez & Paul [31] applied their methodology in a dataset obtained from the Freiburg database, the obtained results indicated a significant reduction, being >25% for classification accuracy (from 96 to 80.7%) and > 35% for sensitivity (from 94.44 to 59.22%).

The Freiburg database is a comprehensive EEG dataset, containing continuous long-term EEG recordings that are related to clinical EEG recordings. Hence, a comparison of the results obtained by the proposed methodology with the Freiburg database with other Freiburg-based studies should be considered. Table 5 presents the most recent studies that have utilized the DWT, aiming to extract the sub-bands of interest for the identification of seizure patterns. It can be seen that the proposed method with the low-dimensional feature vector is comparable to other studies and shows great results compared to previous DWT-based methods in terms of classification sensitivity. Our method indicated high classification sensitivity (99.74%), whereas other DWT-based methods [22–24, 41], showed sensitivity results ranging from 95.10%–96.77%. The method proposed by Alickovic et al. [42] indicated the best sensitivity (99.95%), which is slightly better compared to the results of our method. Also, the False Detection Rate (FDR) of the proposed method is 0.21/h and is almost the same with the methods proposed in [23, 24]. The FDR of the method proposed by Zhou et al. [41] indicated the best FDR (0.13/h), whereas the method proposed by Liu et al. [22] showed the worst false detection rate per hour (0.58/h). Consequently, the great classification results of our method render the proposed methodology capable for clinical application in seizure prediction.

To the best of our knowledge, this is the first methodology validated on both Bonn and Freiburg databases, employing a large amount of data from all 21 patients of the later. The high levels of classification accuracy, sensitivity and specificity for both databases confirms the robustness of the proposed methodology, thus also being the only methodology that have experimentally proved its robustness for this problem. Concerning the Freiburg database, the proposed approach utilizes only the ictal EEG segments between the seizure onset and seizure end, containing only the seizure activity and not the entire ictal EEG recording provided in the database; hence, it is more appropriate to accurately capture the seizure events. However, a drawback of the proposed methodology is that the DWT is applied to decompose the signal into sub-bands of interest depending on the sampling frequency. Hence, these sub-bands correspond approximately to EEG rhythms, meaning the sub-band related to theta rhythm with DWT is the wavelet coefficient D5 (2.7–5.4 Hz) instead of the actual theta rhythm that ranges from 4 to 8 Hz. A filter-based approach may be more appropriate and would be examined in the future work.

6 Conclusion

Epilepsy remains the most challenging brain disorder worldwide. Various EEG processing methods have been proposed over the last years for automated seizure detection and prediction, with the majority of them employing EEG data from a single center. The proposed methodology has been evaluated on two of the most well-known EEG databases, showing significant classification results in discriminating seizure activity. Future research work will be towards re-evaluation on other databases to further demonstrate the generality of the method, in an attempt to predict seizures and deliver alternative intervention approaches to patients with refractory epilepsy. The ultimate research goal is to predict seizure occurrences and shed light on the underlying mechanisms of the disorder, in order to improve the patient's life and provide robust alternative solutions to patients with uncontrolled seizures. On this basis, closed-loop therapies may provide new intervention options [43] and therefore, robust seizure detection algorithms are an important issue for closing the loop.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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