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1	Improving Classification of Epileptic and Non-Epileptic EEG Events			
2	by Feature Selection			
3				
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14				
15	Abstract: Correctly diagnosing generalized epileptic from non-epileptic episodes, such as			
16	psychogenic non epileptic seizures (PNES) and vasovagal or vasodepressor syncope (VVS), despite its			
17	importance for the administration of appropriate treatment, life improvement of the patient, and cost			
18	reduction for patient and healthcare system, is rarely tackled in the literature. Usually clinicians			
19	differentiate between generalized epileptic seizures and PNES based on clinical features and video-			
20	EEG. In this work, we investigate the use of machine learning techniques for automatic classification			
21	of generalized epileptic and non-epileptic events based only on multi-channel EEG data. For this			
22	purpose, we extract the signal patterns in the time domain and in the frequency domain and then			
23	combine all features across channels to characterize the spatio-temporal manifestation of seizures.			
24	Several classification algorithms are explored and evaluated on EEG epochs from 11 subjects in an			
25	inter-subject cross-validation setting. Due to large number of features feature ranking and selection is			
26	performed prior to classification using the ReliefF ranking algorithm within two different voting			
27	strategies. The classification models using feature subsets, achieved higher accuracy compared to the			
28	models using all features reaching 95% (Bayesian Network), 89% (Random Committee) and 87%			
29	(Random Forest) for binary classification (epileptic versus non-epileptic). The results demonstrate the			
30	competitiveness of this approach as opposed to previous methods.			

1 Keywords: epileptic seizures, PNES, vasovagal syncope, classification, machine learning.

2

3 1. Introduction

One of the most common and challenging medical cases in everyday clinical practice is that of
patients reporting one or more episodes of paroxysmal loss of consciousness or altered awareness. The
management of these medical cases may be proven to be demanding, time consuming and expensive
and finally, in spite of the extensive and exhaustive investigation, the underlying diagnosis may remain
elusive [1,2,3]. The differential diagnosis that a clinician usually faces is mainly that of an epileptic
seizure, a possible psychogenic non epileptic seizure (PNES) and a probable vasovagal syncope (VVS).

10 The diagnosis of epilepsy and its differentiation from other causes of TLoC is typically based on 11 historical information and is assisted by specific tests [2]. However clinical information is commonly 12 fragmented or even missing because patients may have limited or no recall of the event and a witness 13 account might not be available to describe diagnostically decisive clinical phenomena [1,2]. Even when 14 a witness is available, diagnosis may be difficult and often remains uncertain because convulsive 15 syncope, a seizure-like reaction resulting from global cerebral hypoperfusion, can mimic epileptic 16 seizures [3,4]. Agreement between physicians as to the nature of a single event may also be limited [5]. 17 Such diagnostic uncertainty has cost both in terms of mortality and ongoing morbidity and in terms of 18 the financial burden associated with hospitalization and repeated investigations.

19 Epileptic seizures are brief episodes of abnormal excessive or synchronous neuronal activity in 20 the brain of patients suffering from epilepsy [6]. During an epileptic seizure there are several specific 21 changes recorded in the electroencephalogram (EEG) which is a sensitive and important test used to 22 evaluate patients with suspected epilepsy. There are certain characteristic ictal neurophysiological 23 patterns that support the identification and detection of epileptic events and postictal and/or interictal 24 abnormalities that can provide supplementary information. Fig. 1 shows generalized spike wave 25 abnormalities from an epileptic patient. Specifically, there is a burst of generalized 3-5 Hz spike and 26 slow wave complex lasting approximately 5 secs.

27

FIGURE 1

Pshychogenic non-epileptic seizures (PNES) are sudden paroxysmal changes in behavior or
 consciousness, that resemble epilepsy but are not accompanied by the electrophysiological changes that
 characterize an epileptic seizure [7]. Although the clinical history can help differentiate these episodes,

it is not unlikely to have inconclusive and insufficient event description by the patient and witnesses,
 not being able to confidently exclude an underlying epileptic disorder. In these cases the diagnosis of
 PNES can be supported by video-EEG monitoring, especially if a psychogenic event is captured, since
 in the case of PNES there are no specific EEG changes. Fig 2 shows an EEG fragment during a PNES.
 No EEG correlates can be seen and the recording is frequently marred by muscular artifacts.

6

FIGURE 2

7 Vasovagal or vasodepressor syncope is a common type of syncope and various mechanisms 8 have been postulated for explaining the characteristic association of hypotension and bradycardia. The 9 term "vasovagal" was introduced by Lewis [8] to indicate that both blood vessels and heart were 10 implicated and since atropine reversed the bradycardia but not the hypotension he considered 11 vasodilatation as the primary responsible factor. During a vasovagal syncopal attack there may be some 12 characteristic EEG changes starting with progressive generalized theta slowing of background rhythms 13 followed by sometimes hypersynchronous delta activity of high voltage, (beta / alpha \rightarrow theta \rightarrow delta) 14 and appearance of progressively lower voltage rhythms until isoelectric suppression [9,10] (see Fig. 3). 15 This pattern is progressively reversed after the patient's fall, during his/her recovery. These changes do 16 not include any ictal activity.

17

FIGURE 3

18 Several methods have been proposed for the classification of EEG captured events into epileptic 19 or normal [11,12,13,14,15]. The problem of the discrimination between ictal and interictal EEG signals 20 has been studied [16], too. However, only a few studies deal with the differentiation between epileptic 21 and other paroxysmal episodes of loss of consciousness such as PNES and vasovagal syncope. It is 22 worth to note that the discrimination between different types of non-epileptic events is considerably 23 more useful in diagnostic procedure given the semiological resemblance between the aforementioned 24 paroxysmal attacks. Furthermore, according to [7] the one third of PNES patients may have clinical 25 convincing GrandMal like seizures. This makes discrimination between PNES and epileptic seizures a 26 challenging task, especially in an online monitoring system for automatic detection of epileptic events, 27 such as [17], where false alarms caused by events similar to epilepsy are undesired.

To the best of our knowledge, only a few studies have been proposed in the literature for automated classification between epileptic and non-epileptic pathological events from EEG. Poulos et al. [18] proposed an algorithm which estimates a number of auto-correlated coefficients extracted from 1 an appropriately selected epileptic EEG segment and examines whether these coefficients are 2 correlated with the coefficients of the unknown EEG segments in order to classify the latest into 3 epileptic or non-epileptic. Their algorithm obtained a sensitivity of 83% for 90% specificity. 4 Papavlasopoulos et al. [19] trained a LVQ1 neural network on an appropriately extracted set of auto-5 correlation coefficients (codebook) and used the resulting model to classify the corresponding feature 6 vectors of the unknown EEG segments. The LVQ1 network achieved 86% accuracy. The feature 7 extraction methods of the aforementioned classification frameworks, as well as the achieved results, 8 can be found in [20]. Statistical analysis of the results based on chi-square test showed that the LVQ 9 neural network method is superior than the cross-correlation one [20].

Regarding the features used for the classification of EEG segments the relevant works in the literature are considerably more. In the majority of them, the analysis is based on the estimation of the EEG channels' spectral magnitude [11, 15, 21, 22]. Other EEG features that have been reported are the autoregressive filter coefficients, the continuous and discrete wavelet transform, as well as energy per brain wave (delta, theta, alpha, beta, gamma) bands [15,21, 23]. Finally, time domain features have been proposed, such as zero-crossing rate [24] and statistics of the EEG samples per channel [15,21].

16 In this study, we evaluate a large set of time and frequency domain features which have been 17 widely used for the analysis of EEG signals in the literature. In addition to the reported evaluations 18 found in the literature, we extend the non-epileptic class to both PNES and VVS events. The diagnosis 19 of epilepsy is more challenging compared to the detection of seizure onset due to the semiological 20 resemblance between epileptic and non-epileptic events, especially when video-EEG monitoring is not 21 incorporated [25]. Also, the classification of abnormal episodes into different types requires a broad 22 knowledge of EEG patterns across patients, while seizure detection can rely on patient-specific models 23 which are easier to learn, especially for generalized seizures [26]. For the evaluation, we examined a 24 number of different classification algorithms. Our classification methodology can be used as part of 25 our previous seizure detection architecture [26,27] in order to discriminate the detected events into 26 epileptic or non-epileptic.

In a further step, feature ranking investigation using two different strategies (one based on frequency of feature appearing in a specific rank and the other based on sum of the weights assigned by the ReliefF ranking algorithm) was performed. The classification models using subsets of N best features were evaluated and revealed the most significant features for the classification task. The rest of this paper is organized as follows. In Section 2 the classification methodology is
 presented and details about the evaluation data are provided. Section 3 describes the experimental
 protocol followed and presents the achieved results. Finally, in Section 4 we conclude this work.

4

5 2. Material and methods

6 2.1 Methodology for classification of generalized epileptic and non-epileptic events

7 The presented architecture for classification between generalized epileptic and non-epileptic 8 EEG events is part of an end-to-end system for monitoring and analysis of brain disorders, the 9 ARMOR framework [17]. Within the ARMOR framework patients suffering from seizures are 10 monitored through sensors and the multi-parametric data are processed automatically (real-time by 11 software tools) or semi-manually (offline with the support of software tools and visualizations) by 12 neurology experts [26,27].

The proposed classification methodology can be used as additional module after the seizure detection and focal-vs-generalized events classification components [26,27] in order to discriminate the detected events into generalized epileptic, manifested by Generalized Spike Wave discharges (GSW) or non-epileptic, such as PNES and VVS. The block diagram of the overall architecture is illustrated in Figure 4.

18

FIGURE 4

19 Initially, the multidimensional EEG data are preprocessed by applying notch filtering (at 50Hz), 20 baseline correction and re-sampling at 250 Hz (in order to obtain a common resolution level for all data 21 coming from different patients and acquisition systems). Frame blocking of the incoming EEG streams 22 to epochs of constant length w (= 2 seconds) is performed with constant time-shift and without time-23 overlap between successive epochs. Each epoch is a $N \times w$ matrix, where N is the number of selected 24 EEG electrodes. A large number of features is extracted for each one of the N electrodes to 25 characterize the temporal patterns and frequency content of each epoch. The extracted time domain and 26 frequency domain features from all electrodes are concatenated to a single feature vector as a 27 representative signature for each epoch. Details on the type of extracted features are provided in section 28 2.3.

All epochs are used as input to ARMOR's seizure detection module which detects paroxysmal
 events. The epochs classified as normal are ignored whereas epochs classified as seizure are further

entered to the seizure type classifier. In this final step, models for binary classification between generalized epileptic or non-epileptic events (PNES or VVS), which have been previously built in a training phase, are used in order to label the epochs. Each epoch is classified independently and no temporal constraints (across epochs) are applied, such as taking into consideration the class label of the precedent or subsequent epoch or the total event duration.

During the training phase of the classification architecture, epochs with known class labels
(labeled manually by medical experts) are used to train binary classification models, i.e. generalized
epileptic (GSW) vs non-epileptic (PNES and VVS).

9 During the test phase the unknown multidimensional EEG signal is preprocessed and
10 parameterized with similar setup as in the training phase. Each extracted feature vector is provided as
11 input to the seizure detector and according to the decision to the seizure classifier.

12

13 2.2 Data

14 The previously described classification methodology was evaluated on multi-parametric 15 recordings performed within the ARMOR project [17]. The recordings were performed in the 16 Department of Clinical Neurophysiology and Epilepsies in St Thomas' Hospital in London and 17 acquired from 11 patients in total. All participants had at least one of their typical epileptic or non 18 epileptic events captured during the recording procedure. The epileptic group, consisted of patients 19 with known diagnosis of idiopathic generalized epilepsy, manifested clinically with absence seizures 20 and they had at least one clinical episode captured during the recording associated with generalized 21 spike wave discharges on the EEG. The non epileptic group included patients who had sustained a 22 vasovagal syncope (2 participants) or a psychogenic non epileptic attack (5 participants) during their 23 monitoring. The epilepsy group contains 105 generalized seizures while the non-epilepsy groups 24 include 21 events (19 PNES and 2 VVS). Patients with focal seizures were excluded from this analysis. 25 The recordings were performed using conventional AgCl EEG electrodes positioned according to 26 the extended international 10-20 system. A subset of the main EEG channels was selected for analysis 27 which included the following channels: Fp2, F8, F4, T4, C4, A2, P4, T6, O2, Fp1, F7, F3, A1, C3, T3, 28 P3, T5, O1, Fz, Cz, Pz. The recordings were manually annotated by expert Neurologists of the King 29 College London. Only epochs during paroxysmal events were considered for training and for testing. 30 All data were stored in EDF+ formatted files [28].

2

2.3 Feature Extraction and Classification Algorithms

3 After preprocessing, time domain and frequency domain features were extracted for each epoch. 4 In particular, each of the EEG channels was parameterized using the following features: (i) time-5 domain features: minimum value, maximum value, mean, variance, standard deviation, percentiles 6 (25%, 50%-median and 75%), interquartile range, mean absolute deviation, range, skewness, kyrtosis, 7 energy, Shannon's entropy, logarithmic energy entropy, number of local maxima and local minima, 8 zero-crossing rate, and (ii) frequency-domain features: 6-th order autoregressive-filter (AR) 9 coefficients, power spectral density, frequency with maximum and minimum amplitude, the power of 10 continuous wavelet transform using symlet 5 mother wavelet of scale 25 and 32, the power of discrete 11 wavelet transform with mother wavelet function Daubechies 16 and decomposition level equal to 8. 12 This resulted to 55 variables for each of the N=21 EEG channels producing a feature vector of 13 dimensionality equal to 1155 in total.

14 The computed feature vectors, V, were used to train classification models. In order to evaluate the 15 ability of the above features to discriminate between epileptic and non-epileptic epochs we examined 16 several classification algorithms, including BayesNet [29,30], RandomCommittee, Random Forest 17 [31], IBk [32] and SMO [33,34] with RBF kernel, which were implemented by the WEKA machine 18 learning toolkit [35]. The classifiers in our study were selected in an attempt to evaluate representative 19 algorithms for each one of the main categories of machine learning classification methods including 20 probabilistic networks (BayesNet), decision trees (RandomForest), support vector machines (SMO), 21 ensemble classifiers (RandomCommittee and RandomForest) but also simple methods such as k 22 nearest neighbors (IBk).

During the test phase, the EEG recordings were pre-processed and parameterized as during training. Each classification model was used to label each of the detected seizure epochs. In the present evaluation no additional rules (e.g. knowledge based rules regarding events duration) were applied on the classification decision .

Evaluation was performed in a leave-one-out cross-validation setting. Specifically, each time one
subject was left-out for testing, while the rest of the subjects were used for training. For the left-out
subject, all epochs between seizure onset and offset were used as testing samples. Table 1 shows the
number of epochs that were extracted from each subject during the seizure(s).

TABLE 1

2 The purpose of this study was to evaluate the seizure classification module, thus only paroxysmal
3 events were used for training and testing of the classifiers. Evaluation of the total ARMOR framework
4 may include the combined use of seizure detection and seizure classification in future work.

- 5
- 6

2.4 Feature Ranking and Feature Subsets Evaluation

7 In a further step we examined the discriminative power of the extracted features for the 8 classification of epileptic and non-epileptic EEG events. The ReliefF algorithm [36] (which is an 9 extension of an earlier algorithm called Relief [37]) was used for estimating the importance of each 10 feature in binary classification (generalizing to polynomial classification by decomposition into a 11 number of binary problems). In the ReliefF algorithm the weight of any given feature decreases if the 12 squared Euclidean distance of that feature to nearby instances of the same class is more than the 13 distance to nearby instances of the other class. ReliefF is considered one of the most successful feature 14 ranking algorithms due to its simplicity and effectiveness [38, 39,40] (only linear time in the number of 15 given features and training samples is required), noise tolerance and robustness in detecting relevant 16 features effectively, even when these features are highly dependent on other features [38,41]. 17 Furthermore, ReliefF avoids any exhaustive or heuristic combinatorial search compared with 18 conventional wrapper methods and usually performs better compared to filter methods due to the 19 performance feedback of a nonlinear classifier when searching for useful features [40].

20 In this study, ranking is performed by following a leave-one-out strategy on the available subjects. 21 Specifically, for each leave-one-out experiment, feature ranking is performed using the ReliefF 22 algorithm in each training subset. We combine the rankings of all leave-one-out experiments and 23 calculate the total rank of features using two different strategies. The first strategy calculates the total 24 rank of features according to the frequency of a feature appearing in a specific rank. For example the 25 top-ranked feature is assumed to be the one that more frequently has the highest ranking score, 26 regardless of the distribution of the scores it receives across experiments. The second strategy 27 calculates the total rank of features according to the sum of the weights assigned by ReliefF in each 28 training set. We examined the performance of the method, in terms of accuracy, sensitivity and 29 specificity, for different number of N-best features (N =10, 20, 30, ...100, 200, 300, ..., 1100), with 30 respect to the above strategies of feature ranking.

2 3. Results and Discussion

The classification methodology presented in Section 2.1 was evaluated using the classification
algorithms and the cross-validation scheme described in Section 2.3. The accuracy, sensitivity and
specificity are defined as:

6

$$accuracy = \frac{TP + TN}{TP + FP + TN + FN}$$
(2)

8

$$sensitivity = \frac{TP}{TP + FN}$$
(3)

$$specificity = \frac{TN}{FP+TN}$$
(4)

9 where TP denotes the true positives, TN the true negatives, FP the false positives and FN the false 10 negatives. The results of the method using all features are shown on the left of Table 2. Here we 11 consider the epileptic class as the positive and the non-epileptic class (PNES or VVS) as the negative.

12

TABLE 2

As can be seen in Table 2, the overall highest accuracy of the proposed methodology for classification between epileptic and non-epileptic EEG events is 86% for BayesNet classification. RandomCommittee and Random Forest classification models follow with 83% and 74% accuracy, respectively. For the classifier with the highest accuracy (BayesNet), the sensitivity (or recall), i.e. the fraction of actual epileptic events which are correctly identified as such, is 92% and the specificity, i.e. the proportion of non-epileptic events (either PNES or VVS) which are correctly classified as such, is 78%.

In a further step, we applied feature ranking using the ReliefF algorithm and the two strategies described in Section 2.4. The performance of the classification, in terms of accuracy, for different number of N-best features (N =10, 20, 30 ..., 100, 200, 300, ..., 1100) and for each algorithm separately are shown in Fig. 5 for the 1st ranking strategy and in Fig. 6 for the 2nd ranking strategy.

24

25

FIGURE 5

FIGURE 6

As can be seen in the above figures the highest classification accuracy is achieved when a small subset of discriminative features are used. Specifically, when the 1st ranking strategy is used the highest accuracy is achieved for a subset of 10 best features with a percentage of 95% for the Bayesian Network, which is sufficiently high in comparison to the accuracy achieved when all features are used.
 Similarly, Random Committee and Random Forest achieve their highest accuracies for a subset of 300
 and 200 best features respectively. The reported accuracies for these subsets of features are 92% and
 87% for each algorithm respectively. IBk and SMO follow with an accuracy of 86% when a subset of
 40 best features is used and 87% for a subset of 200 best features, respectively.

6 The 2nd ranking strategy shows similar behavior. For the Bayesian Network the highest accuracy
7 (94%) is achieved for a subset of 50 best features. Random Committee, Random Forest, IBk and SMO
8 follow with 85% for a subset of 70 best features, 89% for a subset of 50 best features, 84% for a subset
9 of 70 best features and 90% for a subset of 60 best features, respectively.

In general, Random Forest and Random Committee seem to be the less stable algorithms, SMO
on the other hand, although not the most accurate classifier, shows a more stable behavior as function
of number of retained features, with the accuracy decreasing significantly for more than 200 features.
Tables 3 and 4 show the 50 best features according to the ranking strategy 1 and 2 respectively.

14

15

TABLE 3TABLE 4

As can be seen, in general the two ranking strategies overall agree. Both of them rank features *nmin* (number of local minima), *nmax* (number of local maxima), *aryule3* (the 3rd coefficient of 6th order autoregressive filter), *minfreq* (frequency with minimum power), *cwt25* and *cwt32* (the coefficients of continuous wavelet transform using symlet 5 mother wavelet of scale 25 and 32) in the top 50 features.

The number of local minima (*nmin*) and the number of local maxima (*nmax*) seem to be the features with the highest discriminative ability. Since these features measures the smoothness of the signal it seems that the smoothness of the epileptic epochs is different from the one of non-epileptic epochs and aids the discrimination among them. Such a claim can be verified from the distributions of the values of the *nmin* (see Fig. 7) and *nmax* (see Fig. 8) features for the epileptic and non-epileptic class.

26

27

FIGURE 7

FIGURE 8

In both figures 7 and 8, the blue boxes indicate the distribution of the feature values on the epileptic class and the black boxes the distribution of the feature values on the non-epileptic class. As can be seen, there is a perfect discrimination between the epileptic and non-epileptic main boxes with the non-

1 epileptic epochs having a significantly larger number of local minima and maxima indicating less 2 smooth signal compared to the generalized spike waves. The only overlap is observed between the 3 extreme values of two classes (whiskers of the boxplots). The evaluation of our framework using only 4 these two features (*nmin* and *nmax*) extracted from all the available channels resulted in 91% accuracy 5 for 92% sensitivity and 89% specificity. The performance in terms of accuracy increases slightly when 6 nmin and nmax are extracted from the 5 best channels (Fp1, T4, T5, F7, Fp2), reaching 92%. This 7 increase indicates that the frontotemporal regions in the brain covered by the aforementioned channels 8 might be more important in discriminating generalized spike waves from PNES or VVS. The next most 9 important features for discriminating epileptic from non-epileptic events are aryule3, minfreq and 10 *cwt25* and *cwt32*. The autoregressive model specifies whether the EEG epoch depends linearly on its 11 own previous values by expressing the signal with lagged terms of itself. In particular, the AR model 12 residual (i.e. the prediction error) shows how possible is to model each sample as a linear combination 13 of its previous ones. The lower absolute values of the AR coefficients of the non epileptic class (see 14 Fig. 9 for the aryule3 feature values) indicates that the signal of the non-epileptic class is much more 15 noisy and stochastic-like compared to the epileptic signals which seem to be more structured and 16 deterministic-like. Such an experimental result is consistent with our intuition about the two types of 17 signals and the clinicians description of the events.

18

FIGURE 9

19 Differentiation is also observed on the frequency with the minimum power (*minfreq*) in the 20 spectrogram of epileptic and non-epileptic epochs (see Fig. 10), with the *minfreq* of the epileptic class 21 having a much greater range of values compared to the non-epileptic class in which the *minfreq* values 22 are clustered around 50Hz. Note that this finding is not due to notch filtering since the same 23 preprocessing was applied to all data (both epileptic and non-epileptic).

24

FIGURE 10

Finally, the expression of each epoch as a linear combination of the chosen wavelet basis functions
captures the frequency content of the epoch in a localized area of the signal which seem to highlight
the differences between the two classes (see Fig. 11 and 12).

- 28 FIGURE 11
- 29 FIGURE 12

- Finally, in order to examine the ability of the BayesNet classifier to discriminate each type of
 pathological events (GSW, PNES or VVS) from the others, we performed binary classification of all
 possible pairs of pathological events (GSW-PNES, GSW-VVS and PNES-VVS). The results in terms
 of classification accuracy for different number of N-best features (10, 20, ..50) are shown in Fig. 13.
- 5

FIGURE 13

6 As can be seen, the PNES-VVS classification problem is the most difficult case for the 7 classifier. The best classification accuracy (76%) for PNES-VVS pair is achieved when all features 8 (1155) are used. On the other hand, GSW-PNES and GSW-VVS pairs are much easier cases for the 9 classifier obtaining their maximum accuracy for the 10 best features. Specifically, GSW-PNES 10 classification achieves 96% accuracy for 96% sensitivity and 100% specificity while GSW-VVS 11 classification results in slightly lower percentages, i.e. 93% accuracy for 96% sensitivity and 87% 12 specificity. Since generalized spike waves are very specific ictal neurophysiological patterns, they 13 present much more consistent features (compared to the other types) which makes their detection an 14 easier task. On the other hand, PNES has no specific EEG patterns but is frequently accompanied by 15 muscular artifacts which present a variability across subjects. Similar variability appears even between 16 consecutive epochs of VVS examples since there are several changes that happen successively in time 17 during such an episode (beta / alpha \rightarrow theta \rightarrow delta \rightarrow lower voltage rhythms \rightarrow isoelectric 18 suppression). It seems that the variability in the feature values of the PNES and VVS epochs is high 19 (in respect to the available training data) impeding the learning of a discrimination model.

While 19 PNES appear to make a rather limited dataset, we believe that are sufficient given the lack of ictal EEG changes and the fact that their variability reflects only muscle and movement activities. The main problem is the really small sample of the 2 VVS-patients. However, VVS typically occur very rarely, in most patients annually, and only in very few patients more frequently, say monthly. It is therefore extremely unlikely to record them on standard EEG that is a 20min to one hour "snapshot" of brain activity. Still, because of the rather predictable sequence of EEG changes (alphatheta delta etc) we believe that reasonable learning of a discrimination model is achievable / possible.

The proposed methodology takes into account features extracted from all the available channels by concatenating them in a single feature vector. The spatial localization of the features is encoded in their location within the feature vector presented to the classifier. Since the seizure onset patterns in focal seizures appear over a small subset of channels close to or at the epileptic focus, a strategy to overcome the problem that different focal seizures appear on different channels is required. Such a strategy that successfully tackles the aforementioned problem has already been proposed in the literature [42]. In order to remove the information about the spatial location of the seizure from the training set, the authors in [42] proposed a sorting operation on the extracted features that reorders the features from the different channels in the feature vector before feeding it to the classifier.

6 However, since a seizure with focal onset (as manifested electroencephalographically) is 7 always epileptic, here we have implemented a simplified version of a focal-vs-generalized seizure 8 classification rule (as part of the ARMOR project) that automatically detects and labels the focal 9 seizures. The focal-vs-generalized seizure classification rule is part of the online seizure detector 10 [26][27] which performs a per channel analysis followed by the imposition of spatiotemporal 11 constraints before taking the final decision (clear, focal, generalized) for each tested epoch. The 12 classification rule is based on a mimetic approach requiring the seizure to be detected in at least 65% of 13 the channels in order to be characterized as generalized; otherwise it is characterized as focal. Due to 14 the different type of analysis (fusion of channel-based decisions versus fusion of features per channel to 15 reach a decision), we are not presenting results of focal seizure classification in this paper, but rather 16 focus on the classification of generalized events, which is the last component in our seizure analysis 17 framework.

18 For a clinician the differentiation between focal and generalized events is important because it 19 will play a crucial role in the medication/ treatment and general management choices. Such a rule 20 (appearance in at least 65% of channels) is mainly useful when the events are focal, since focal EEG 21 onset always indicates focal epileptic seizure activity. This rule has no clinical utility to the other event 22 types, since the EEG expression of both psychogenic non-epileptic seizures and vasovagal syncope 23 which leads to impairment of consciousness are "generalized". However, this step was introduced to 24 facilitate the solution methodologically. Upon the characterization of focal events, the method 25 presented here can be used to discriminate the remaining events into epileptic or non-epileptic.

On the clinical usefulness front, it is true that a competent seizure detection algorithm or set of algorithms should be able to detect both focal and generalized seizures, and either of these from nonepileptic events. The reason is that impairment of consciousness can be seen in temporal lobe seizures or seizures with secondary generalization. However, initial prodromal clinical symptoms and some typical EEG characteristics can be used for the differential diagnosis. Due to the big variability of

seizure presentation there needs to be a detailed analysis of adequate number of representative cases of
 different evolving patterns and this will be the part of our next work.

3 Until however we will be able to evaluate the method more extensively on a large dataset with an 4 adequate number of representative cases for focal seizures we applied the proposed methodology on a 5 dataset of 9 patients (2 subjects with focal seizures, 5 subjects with PNES and 2 subjects with VVS). 6 We developed also a different algorithm to remove the spatial content from the features. The algorithm 7 sorts the features for each channel according to feature type and then extracts the standard deviation of 8 each feature type across channels, and the difference between maximum and minimum values of each 9 feature (max-min). We introduced the standard deviation and the max-min values to the BayesNet 10 classifier and achieved 74% accuracy, 70% sensitivity and 76% specificity when the 20 best features 11 are used. The above results were obtained with a leave-one-patient-out strategy for validation. Since 12 the dataset size is small we assessed the method also in a leave-one-epoch-out strategy, as performed in 13 some other studies and achieved 90.2% accuracy, 86.7% sensitivity and 91.5% specificity. The 14 achieved accuracy in this case is much higher, as expected. However, we do not emphasize the 15 importance of these results since they might not generalize to other data.

16 Although direct comparison with other studies is not possible due to the different characteristics 17 of each dataset (e.g. different seizure types, lack of PNES or VVS examples in most studies or use of 18 single channel data), the achieved classification accuracy is higher than the one reported in the 19 literature. In particular, the achieved accuracy in [22] is 86%, lower than the accuracy of BayesNet in 20 our methodology (95%). Furthermore, in [21] the reported sensitivity (83%) and specificity (98%) are 21 lower than the sensitivity of the majority of the classification methods evaluated in our work and the 22 specificity achieved by our framework (98%) when a subset of 10 discriminative features are used with 23 respect to BayesNet classification.

Finally, although an initial work was held to reliably solve the problem of discrimination between different types of paroxysmal event and reveal the most discriminative features from a large set of time and frequency domain features given a dataset of 11 patients, there are some limitations that should be taken into account. The number of non-epileptic examples especially those of VVS) is limited and might not capture well the variability of the corresponding EEG events while the available generalized spike waves seem to be enough to describe such a consistent group of patterns. Under this scope we plan to start EEG recordings during tilt table test, which provokes VVS and therefore we shall have a substantial number for further analysis. Furthermore, we aim to perform a more in depth
analysis of focal seizures.

3 4. Conclusions

4 In this paper, we investigated the problem of classification between epileptic and non-epileptic 5 events from multi-channel EEG data using a large number of time-domain and frequency domain 6 features. The proposed methodology was evaluated in EEG data from 11 subjects. Examination of 7 several classification algorithms showed that the best accuracy is achieved by BayesNet. Feature 8 ranking investigation and evaluation of the classification models using subsets of features were 9 performed and revealed the most significant features for the classification task. The use of the most 10 discriminative features (N = 10) increased significantly the performance of BayesNet classification at 11 95% accuracy (94% sensitivity for 98% specificity). The method has been evaluated using cross-12 validation across subjects and showed that it can generalize satisfactorily providing the means for 13 diagnosis support.

14

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- 10
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- 12

Subject	Class	Number of Epochs	Number of Seizures
1	GSW	59	52
2	GSW	29	19
3	GSW	16	14
4	GSW	19	20
5	PNES	1	1
6	PNES	1	1
7	PNES	1	1
8	PNES	13	13
9	PNES	3	3
10	VVS	45	1
11	VVS	18	1

Table 1 Number of seizures and number of seizure epochs (2 seconds) per subject

Classification Model	Statistical Measures before Feature Selection			Statistical Measures after Feature Selection		
Widdei	Accuracy	Sensitivity	Specificity	Accuracy	Sensitivity	Specificity
BayesNet	86%	92%	78%	95%	94%	98%
RandomCommittee	83%	88%	77%	92%	89%	77%
RandomForest	74%	77%	70%	87%	92%	79%
IBk	69%	86%	43%	86%	94%	76%
SMO (RBF kernel)	68%	55%	87%	87%	85%	91%

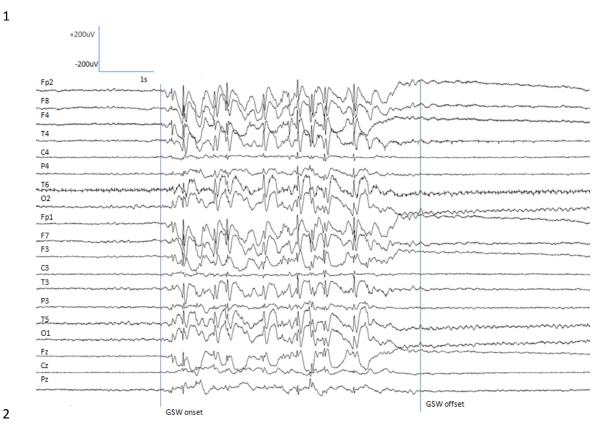
 Table 2 Classification performance before and after Feature Selection.

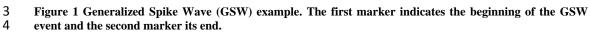
Feature	Channels		
nmin	Fp1, T4, T5, Fz, F7, Fp2, A1, T6, Cz, O1, F4, F3, F8, P4		
nmax	Fp1, T4, T5, F7, Fp2, P3, Fz, T3, T6, A1, Cz, O1, F4, F3, F8, P4		
max	Fp1		
std	Fp1		
aryule3	T6, T4, F4, C4, F7, T5		
maxfreq	T3, O2		
aryule2	T4, T5, P4, Fp1, O1		
logee	C4		
cwt25	A1		
cwt32	A1, Fp2		
minfreq	F7		

 Table 3 Best features according to the top 50 ranking of STRATEGY 1 and the channels they appear on.

Feature	Channels
nmax	T4, Fp1, T5, F7, Fp2, Fz, T3, O1, P3, T6, F3, F8, F4, A1, Cz, P4
nmin	T4, Fp1, T5, F7, Fp2, Fz, T3, O1, P3, T6, F3, F8, F4, A1, Cz, P4
aryule3	T4, F4, T6, C4, T5, F7, O1
aryule2	T4, T3, T5, Fp2, F4, P4
Minfreq	T4
cwt32	A1, Fp2
cwt25	A1, Fp2

Table 4 Best features according to the top 50 ranking of STRATEGY 2 and the channels they appear on.





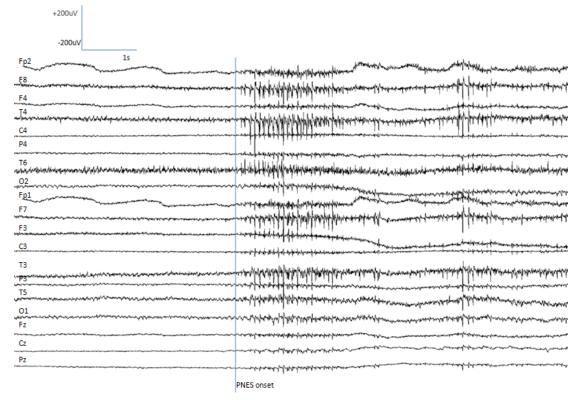
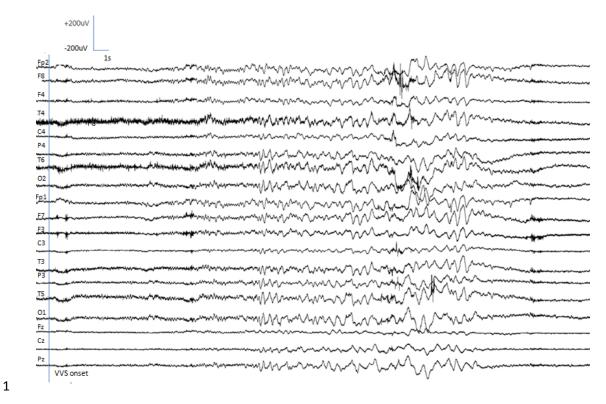
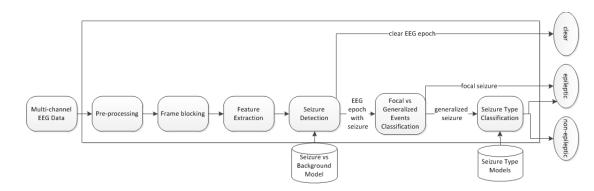


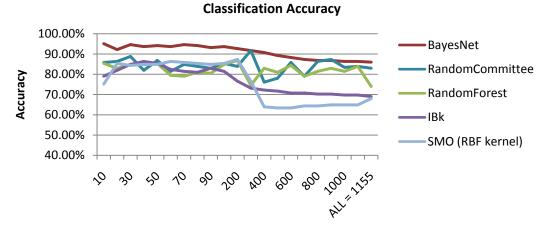
Figure 2 Psychogeninc Non Epileptic Seizure (PNES) example. The marker indicates the beginning of the
 PNES event.



2 Figure 3 Vasovagal Syncopal Event (VVS) example. The marker indicates the beginning of the VVS event.

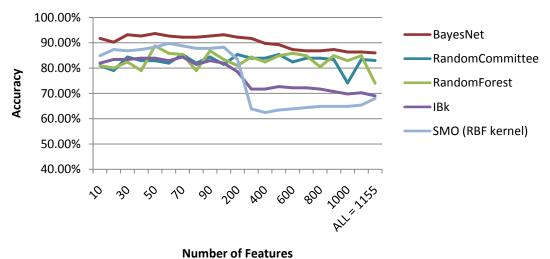


5 Figure 4. The concept of seizure detection and classification within the ARMOR framework.



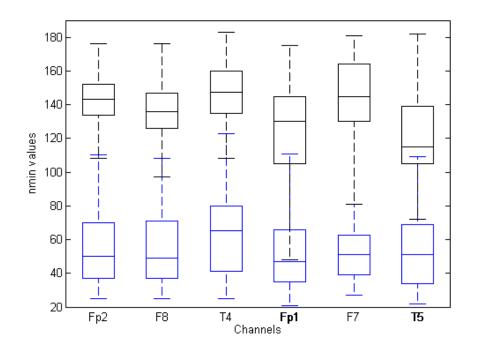
Number of Features





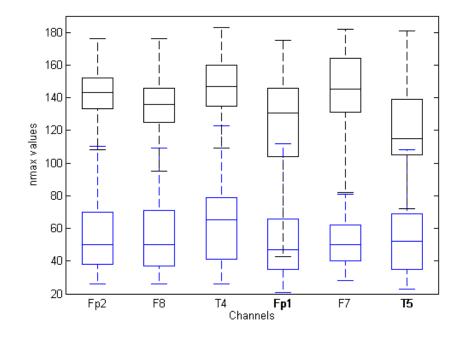
Classification Accuracy

4 Figure 6 Classification Accuracy when 2nd Ranking Strategy (based on Sum of ReliefF Weights) is used.

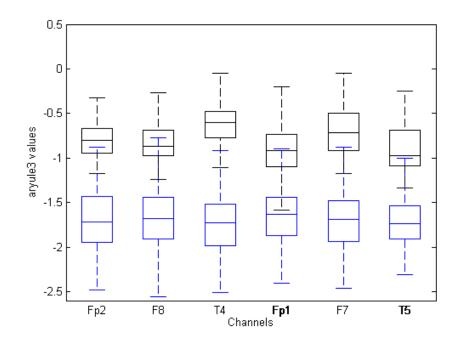




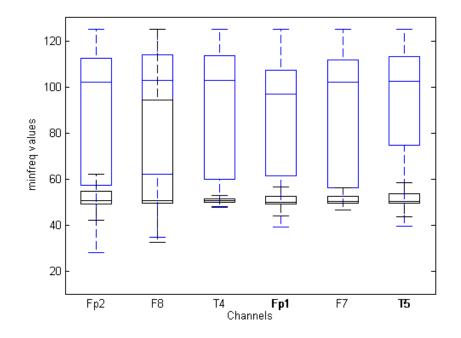
2 Figure 7 Values of the feature *nmin* of epileptic (blue boxes) and non-epileptic (black boxes) EEG epochs.



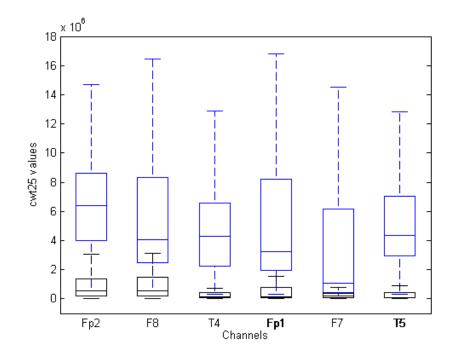
4 Figure 8 Values of the feature *nmax* of epileptic (blue boxes) and non-epileptic (black boxes) EEG epochs.



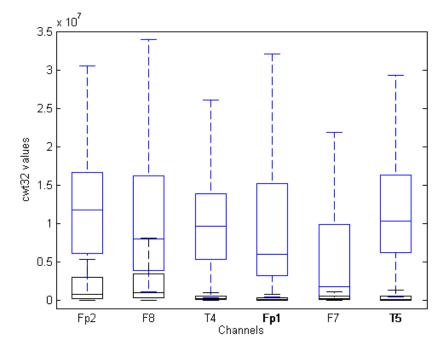
2 Figure 9 Values of the feature *aryule3* of epileptic (blue boxes) and non-epileptic (black boxes) EEG epochs.



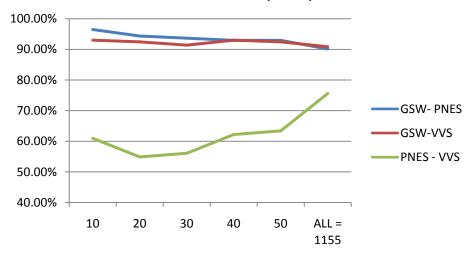
4 Figure 10 Values of the feature *minfreq* of epileptic (blue boxes) and non-epileptic (black boxes) EEG epochs.



2 Figure 11 Values of the feature *cwt25* of epileptic (blue boxes) and non-epileptic (black boxes) EEG epochs.



4 Figure 12 Values of the feature *cwt32* of epileptic (blue boxes) and non-epileptic (black boxes) EEG epochs.



Pairwise Classification Accuracy of BayesNet

2 Figure 13 Pairwise classification accuracy of BayesNet classifier for different number of best features.

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