

NEUROPHYSIOLOGICAL AND STATISTICAL ANALYSIS OF FAILURES IN AUTOMATIC SLEEP STAGE CLASSIFICATION

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Keywords: Automatic sleep stage classification: Failure analysis: Challenges in sleep staging.

Abstract: This paper analyses some of the challenges in automatic multiclass sleep stage classification. Six electroencephalographic (EEG) and two electrooculographic (EOG) channels were used in this study. A set of significant features are selected by a minimum-redundancy maximum-relevance (mRMR) criterion and then classified using support vector machine (SVM). The system is tested on 14 subjects suspected of having sleep apnea. The automatic sleep staging showed a 77.70% (± 15.8) sensitivity and 95.49% (± 2.68) specificity. From the analysis comparing EEG records with visual and automatic classification, we found that the main cause of failures are the similarities between adjacent phases of sleep, in particular in discriminating N1 and N2. Based on the variation of the values of the features it is possible to implement some thresholds and to apply some heuristic rules to improve the performance.

1 INTRODUCTION

Sleep is an active and regulated process with an essential restorative function for physical and mental health (Zoubek *et al.*, 2007). Time courses of sleep stages, based in polysomnography (PSG), are commonly used to quantify sleep quality and diagnose sleep-related disorders. The PSG signals are segmented into epochs, and then electroencephalographic (EEG) rhythms and other parameters are estimated for each individual segment. According to new criteria based on the Rechtschaffen and Kales (R&K) rules, determined by the American Academy of Sleep Medicine (AASM) (Iber *et al.*, 2007), sleep-wake cycle is categorized into awake (W), non rapid eye movement (NREM) and rapid eye movement (REM, stage R) sleep stages. NREM sleep is further divided into three stages: N1, N2 and N3.

Automated systems have emerged in the last years to save time and to improve the agreement levels of sleep scoring, (Zoubek *et al.*, 2007; Nicolaou and Georgiou, 2011). Some publications can be found in the literature, describing problems and challenges of the automatic sleep stage classification (ASSC). In 2003, researchers concluded that the strengths of the ASSC should be the automatic removal of artifacts, a good

quantitative evaluation of delta waves, an automatic analysis similar to visual analysis regarding precision, reliability and reproducible results (Penzel *et al.*, 2003). Furthermore, the authors identified main problems in ASSC: N1 and REM sleep are difficult to distinguish due to similar EEG patterns (EOG is indispensable); wakefulness and REM sleep are difficult to distinguish because they depend heavily of the electromyographic (EMG) signal; N2 may be difficult to define, if the person has only few sleep spindles or if the spindle frequency is outside the range of normal values (Penzel *et al.*, 2003). Few years later (Zoubek *et al.*, 2007) reported that the real challenge in automatic sleep analysis was to the ability to discriminate accurately N1 from REM. Recently, (Helland *et al.*, 2010) concluded that fully ASSC is achievable if ambiguities in the assignment of sleep stages are solved. The authors verified that removing sources of sleep stage ambiguity improves classification considerably, in 10% overall, more than the improvement achieved by including features from the electrocardiogram (ECG) and respiratory signal parameters.

Sleep Apnea Syndrome (SAS) is a sleep disorder with a high prevalence which requires PSG for diagnosis, starting therapy and subsequent treatment initiation. Sometimes, first evaluations use also continuous positive airway pressure (CPAP) and multiple sleep latency test (MSLT). CPAP uses mild

air pressure to keep the airways open while the subject sleeps. MSLT is used in the assessment and diagnosis of disorder of excessive somnolence and to evaluate daytime sleepiness in relation to various therapeutic or experimental manipulations (Carskadon, 1986). SAS is clinically relevant when the breath stops during more than 10 seconds and occurs more than five times per hour of sleep, causing arousal from sleep (AASM, 1999). According to the American Sleep Disorders Association (ASDA) an arousal is defined as “an abrupt shift in EEG frequency, which may include theta, alpha and/or frequencies greater than 16 Hz but not spindles”. The arousal must last ≥ 3 seconds and it must be accompanied by an increase in chin EMG if it occurs during REM sleep (Bonnet *et al.*, 1992). Some aspects, such as rapid fluctuations of sleep and drowsiness gain importance in ASSC of apnea patients (Tsara *et al.*, 2009; Penzel *et al.*, 2003).

In this paper the failures of an ASSC algorithm were studied relating neurophysiologic patterns with possible causes of machine pattern classification failing, aiming to identify ways to improve ASSC. The proposed classification algorithm uses temporal, parametric and time-frequency features extracted from six EEG and two EOG channels. A maximal overlap discrete wavelet transform (MODWT) is used to decompose EEG and EOG signals at different resolutions. A support vector machine (SVM) classifies transformed and normalized features previously selected by a minimum-redundancy maximum-relevance (mRMR) algorithm (Peng *et al.*, 2005). Furthermore, a median filter is used to enhance the classification accuracies.

2 MATERIALS AND METHODS

The proposed system consists of six consecutive steps, as depicted in Figure 1 (Khalighi *et al.*, 2011).

2.1 Data Acquisition and Preprocessing

A Laboratory of Sleep provided data from all-night PSG records acquired by SomnoStar Pro (Viasys SensorMedics), each with duration of almost 8 hours. Our dataset comprises data from fourteen subjects with ages between 22 and 79 years old (mean = 56 years; std = 17.11 years; four females). The six EEG channels (F3-A2, C3-A2, O1-A2, F4 A1, C4-A1, O2-A1) and two electrooculographic (EOG) channels (right EOG – R- EOG-A1; and left EOG – L-EOG-A2) used in our evaluation were

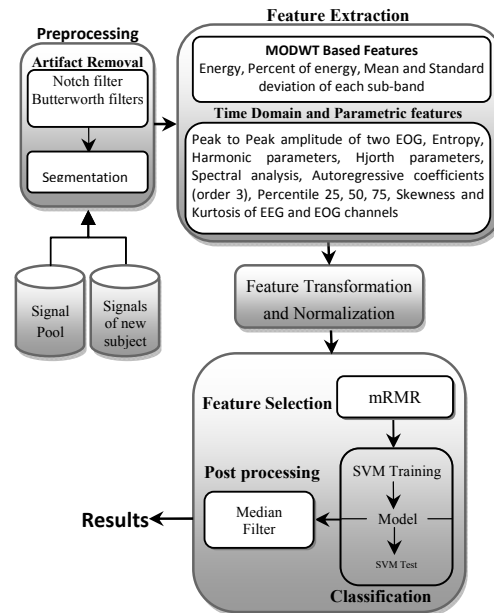


Figure 1: ASSC System Architecture.

recorded at a sampling frequency of 200 Hz. A notch filter at 50 Hz and a bandpass Butterworth filter with lower cutoff of 0.5 Hz and higher cutoff of 45 Hz were used. The sampled EEG and EOG signals are divided into segments of 30 seconds each (epoch).

From the 14 subjects, 9 are analyzed with *PSG basal*, 3 with *PSG CPAP* and the last 2 with *MSLT*. SAS has been diagnosed in 50% of the subjects.

2.2 Feature Processing, Classification and Post Processing

After preprocessing, features are extracted using several methods in the time-frequency, temporal and frequency domain as illustrated in Figure 1. The extracted features are transformed in order to change the distribution of the features. Each feature of the transformed matrix is independently normalized to the [0, 1] range to avoid features in greater numeric ranges dominating those in smaller numeric ranges, and to avoid numerical issues during the classification. Moreover, a reduction in the dimension of the raw input variable is done by mRMR algorithm (Peng *et al.*, 2005). In our algorithm the SVM (Burges, 1998) was adopted to handle the classification process. Non-stationary transients were eliminated by a post processing median filter as described in (Doroshenkov *et al.*, 2007).

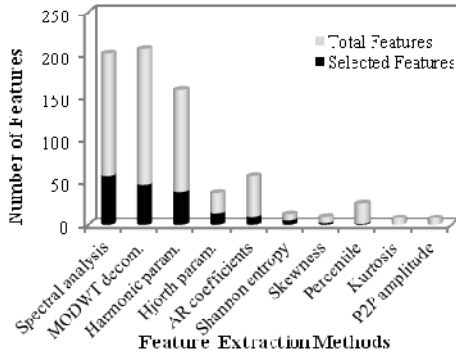


Figure 2: Selected features by mRMR. All features are extracted from 6 EEG and 2 EOG channels except the peak to peak (P2P) amplitude that was extracted only from the EOG channels.

3 EXPERIMENTAL RESULTS AND DISCUSSION

The performance of the algorithm was assessed using the datasets of the fourteen-subjects mentioned in section 2.1. In the experiments, a fourth-order Daubechies with MODWT decomposition was adopted. Libsvm toolbox (Chang and Lin, 2011) with sigmoid kernel degree and C parameters were set to 0.13 and 1.25 respectively, as they produced the best empirical results. The classification accuracy was determined by using Leave-One subject-Out Cross-Validation (LOOCV). Extracted features and respective number of selected features by mRMR, are presented in Figure 2. The most relevant features were extracted from spectral analysis (58 selected features) and MODWT decomposition (47 selected features); the least effective ones were kurtosis and peak to peak amplitude.

Figure 3.a shows the hypnogram of one subject obtained from visual scoring (VS), and Figure 3.b the hypnogram obtained from automatic scoring (AS) through the optimal set of features and without applying the median filter. After median filtering (Figure 3.c), the hypnogram presents a percentage of agreement with VS 12% higher than that achieved without median filter. The confusion matrix obtained for all datasets after filtering is presented in Table 1. The columns (j) represent the stages classified by the SVM classifier and the rows (i) represent the stages determined by the experts. The misclassification occurs essentially between adjacent stages, as reported before by (Zoubek *et al.*, 2007). In the classification of stage REM, the errors were mainly

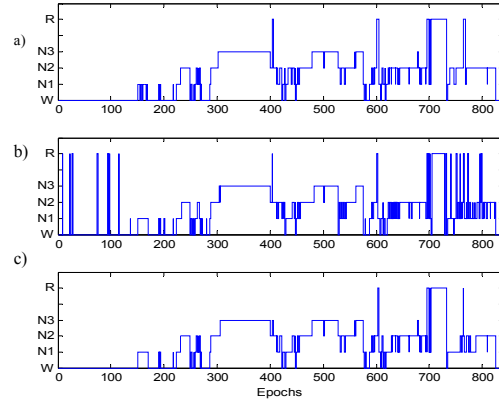


Figure 3: Hypnograms resulting from a) VS; b) AS without median filter (MF) and c) AS with MF.

Table 1: Confusion matrix obtained with SVM classifier after post processing using the optimal set of features. Each case (i, j) corresponds to the number of examples classified as i by experts and j by the ASSC algorithm, expressed as a percentage of the examples classified as i by the experts.

| (i, j)% | W | N1 | N2 | N3 | R |
|-------------|-------|-------|-------|-------|-------|
| W | 92.56 | 5.66 | 0.28 | 0.00 | 1.49 |
| N1 | 11.59 | 53.01 | 26.47 | 0.00 | 8.92 |
| N2 | 0.03 | 6.09 | 86.04 | 7.09 | 0.75 |
| N3 | 0.85 | 0.12 | 13.44 | 85.59 | 0.00 |
| R | 8.78 | 11.74 | 6.93 | 1.27 | 71.28 |

due to a wrong assignment to N1 followed by stage W. This observation can be explained by the transitions between stages that commonly occur during sleep (Kim *et al.*, 2009). Figure 4 contains the transition probabilities (a_{ij}) from stage i to stage j , extracted from a representative dataset, calculated according to

$$a_{ij} = \frac{P[q_{t+1} = j | q_t = i]}{P[q_t = i]} \quad (1)$$

The probability of transition from stage REM to N1 is higher (4.65%) than from REM to the other stages. Therefore the misclassification of REM sleep has a higher probability to be associated with a wrong attribution of N1. Furthermore, from Table 1 it is verified that the method fails particularly in N1, namely 46.98% of the epochs visually labelled as N1 were misclassified as N2 (26.47%) and as stage W (11.59%), which leads to a very low sensitivity (53%). This is due to the fact that, the classifier fails in discriminating stages with similar neurophysiologic patterns. For instance, stage W and N1 can have both alpha rhythms.

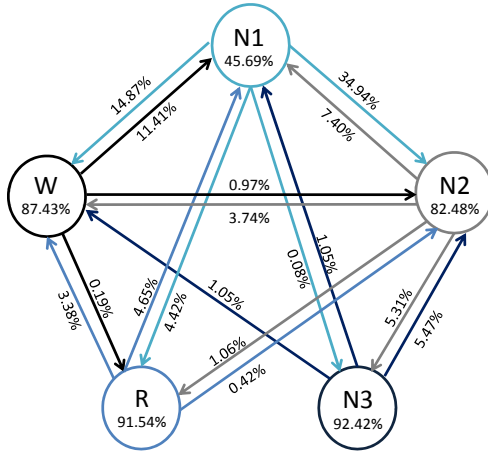


Figure 4: Sleep stages transitions probabilities for a representative dataset.

Table 2: Statistic analysis results of multiclass sleep classification (Se: sensitivity; Sp: specificity).

| | W | N1 | N2 | N3 | R | Total |
|----|-------|-------|-------|-------|-------|------------|
| Se | 92.56 | 53.01 | 86.04 | 85.59 | 71.28 | 77.70±15.8 |
| Sp | 96.75 | 94.81 | 90.59 | 97.10 | 98.19 | 95.49±2.68 |

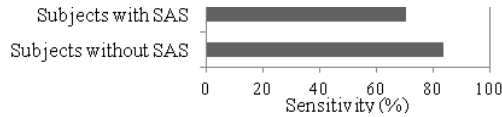


Figure 5: Sensitivity of classification in subjects with and without SAS.

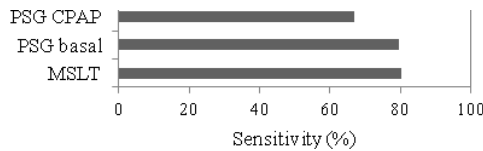


Figure 6: Sensitivity of classification in subjects analyzed with PSG CPAP, PSG basal and MSLT.

Table 2 shows that the best sensitivity value was achieved in stage W. Specificity has the highest and lowest values for REM and N2 stages, respectively. The percentage of time in N1 is about 10%. The highest number of failures related to N1 classification is maybe due to the lower number of existing epochs in this stage to train the classifier (Doroshenkov et al., 2007). Regarding the high number of epochs visually classified as W and N2 stages, the ASSC algorithm shows better performance in the classification of W (92.56%) and N2 epochs (86.04%).

Table 3: Incidence of 428 misclassified epochs in ASSC.

| Total | Related sleep stages | Incidence (%) |
|-------|----------------------|---------------|
| 428 | N1 and W | 25.47 |
| | N2 and N3 | 23.13 |
| | N1 and N2 | 21.03 |
| | W and R | 11.45 |
| | N1 and R | 8.41 |
| | N2 and R | 4.67 |
| | N2 and W | 3.97 |
| | W and N3 | 1.17 |
| | N1 and N3 | 0.70 |

Figure 5 shows the mean sensitivity of the sleep classification in subjects with and without SAS. The observed difference, almost 15%, is probably related to a large number of muscular artifacts, repetitive arousals, deep sleep fragmentation with rapid changes of sleep stages, unclear slow wave sleep and unclear REM sleep. Results in Fig. 6 show that the classification algorithm loses sensitivity, about 15%, when subjects are examined with PSG CPAP. However, as mentioned before, only 3 subjects of the dataset were analyzed with this technique, therefore the results are not conclusive.

3.2 Failures in Classification

In order to find the relation between the failures of ASSC and neurophysiologic patterns, we analysed in detail four subjects of our database, namely those presenting the best, medium and two worst values of sensitivity. Based on the first 500 epochs of each subject (2000 epochs), a total of 428 failures were found. The possible misclassification causes occur by the following order of frequency: problems related to unclear differences in frequency; non-detection of the slow activity rate; artifacts; non-apparent cause; non-detection of specific patterns of sleep (e.g., sleep spindles); arousals; complex classification even in visual scoring. From the 428 analyzed epochs, the incidence of classification failures in different groups of sleep stages is described in Table 3. The misclassification of stage W and N1 was, in 56.88% of the cases, due to problems that should be solved through spectral analysis. Moreover, between stages N2 and N3, the main cause of failures (67.68%) is related to problems that should be solved through analysis of slow activity rate. Misclassification between N1 and N2 is mainly related to two problems: cases with non-apparent reasons or cases that are visually classified based on sequence of activity (33.33%),

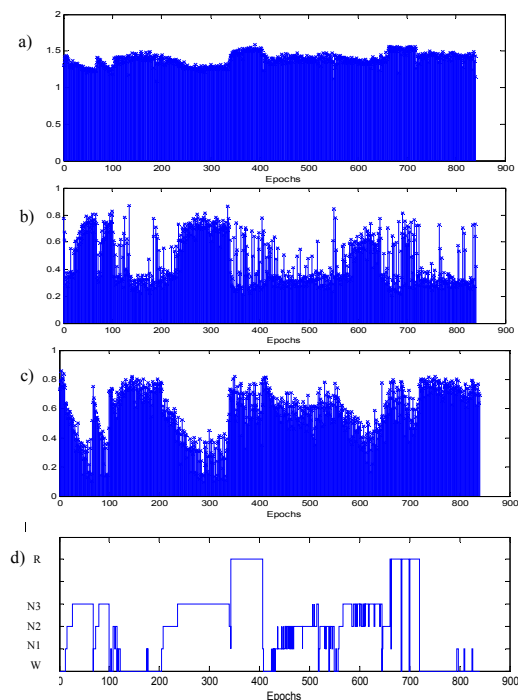


Figure 7: a) Distribution of sub-band beta 1 (16-25 Hz) during the sleep; b) Distribution of percentile 75th during one night of sleep; c) Distribution of one wavelet feature during the sleep; d) Sleep visual classification.

and cases in which the classifier is unable to detect sleep spindles and K complexes (30%). The problems in classification of stages W and REM were mainly caused by artifacts interference (63.27%). Currently, the classifier is not taking full advantage of the EOG signal and therefore new extraction methods applied to EOG should be investigated to increase detection of stage REM. In 37.04%, misclassification of stages REM and N1 did not show evident reason. Epochs with difficult VS represent 25% of the classification failing and represent 50% of the classification failing between N2 and REM. To mitigate problems in differentiating stages N2 and W, the detection of sleep arousals is crucial (41.18%). Moreover, cases in which alpha activity exists and the epoch is classified as N2 (41.18%) have to be solved. In cases of misclassification of stages W and N3 or N1 and N3 the causes are related to artifacts and sleep arousals, respectively.

In transitions between N2 and N3, the problems in AS are common. This fact is related with the percentage of slow activity in one epoch. According to R&K rules when one epoch without patterns of N2 (K complexes and sleep spindles) has more than

20% of slow activity, it should be classified as N3. Heuristic rules concerning these thresholds are not copied in our ASSC algorithm.

Figure 7 shows the behavior of some features during sleep of one night. These features have abnormal values in specific cases of misclassification. When the subject was awake or in REM sleep, spectral values of sub-band beta 1 (16-25 Hz) were higher than other stages (Figure 7.a). Furthermore, failure in the classification of stage W seems related with spectral features. Spectral values of epochs, in which stage W was misclassified as N1, were lower than in other epochs. The 75th percentile in Fig 7.b) defines the value below which 75% of the observed values fall. Comparing the distribution of percentile values during the sleep (Figure 7.b) with sleep hypnogram (Figure 7.d) we reached the conclusion that the 75th percentile is one important feature in classification of N3. The highest values of percentile are in N3, since this feature provides some information about the amplitude of the signal. Low values of this feature contributed to a misclassification of this stage as N2. In instances of misclassification of N3 as being N2, wavelet features revealed inappropriate (high values). During the sleep these features present the lowest values in N3 (Figure 7.c).

4 CONCLUSIONS

Despite the global good results, the proposed algorithm presented sensitivity 15% lower for subjects diagnosed with SAS. The main reason is related to large number of movement artifacts and repetitive arousals. To improve the robustness of the algorithms, the detection of sleep disruption such as arousals and awakenings is crucial and may be suitable for the diagnosis of SAS. Furthermore, new approaches must be investigated to solve the incorrect classification between adjacent phases.

The worst values of sensitivity occurred in classification of N1. Through neurophysiologic analysis of failures we found that false negatives in classification of N1 (Table 1) can have two main reasons: percentage of alpha activity presented in epoch and artifacts that worsen frequency analysis. High number of false positives in stage N2 lead to the worst value of specificity (Table 2), mainly due to problems in the definition of slow wave rate required to classify an epoch as N3. Regarding this analysis it was showed that the ASSC algorithm fails according to different causes, stage of the sleep, and nature of base EEG activity of the subject.

The major goal of the paper was to provide results of a failure analysis in automatic sleep stage classification and to find solutions to improve the results. Regarding the list of detected failures, there are some proposals to study and to apply in our algorithm: implement threshold levels to feature values adjusted for each patient; define some heuristic rules helping the discrimination of adjacent phases; apply artifact removal techniques; develop detection techniques of K-complexes, sleep spindles and arousals. For a more robust performance assessment, the classification algorithm has to be validated in a larger database and the manual scoring should be provided by at least two experts to be more conclusive about results.

ACKNOWLEDGEMENTS

This work has been supported by the QREN funded project SLEEPTIGHT, with FEDER reference CENTRO-01-0202-FEDER-011530.

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