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Pattern Recognition With Adaptive-Thresholds For Sleep Spindle In High Density EEG Signals

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Abstract

Sleep spindles are electroencephalographic oscillations peculiar of non-REM sleep, related to neuronal mechanisms underlying sleep restoration and learning consolidation. Based on their very singular morphology, sleep spindles can be visually recognized and detected, even though this approach can lead to significant mis-detections. For this reason, many efforts have been put in developing a reliable algorithm for spindle automatic detection, and a number of methods, based on different techniques, have been tested via visual validation. This work aims at improving current pattern recognition procedures for sleep spindles detection by taking into account their physiological sources of variability. We provide a method as a synthesis of the current state of art that, improving dynamic threshold adaptation, is able to follow modification of spindle characteristics as a function of sleep depth and inter-subjects variability. The algorithm has been applied to physiological data recorded by a high density EEG in order to perform a validation based on visual inspection and on evaluation of expected results from normal night sleep in healthy subjects.

I Introduction

Sleep spindles, together with sleep slow oscillations [1], [2] are hallmarks of non-REM (nREM) sleep. Spindles originate in the thalamus, from the mutual interactions between GABAergic neurons of the reticular nucleus (RE) and thalamocortical neurons (TC). RE elicits inhibitory postsynaptic potentials in TC neurons, which respond with a feedback on

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the RE and so on [3], [4]; this cycle of oscillations results in a sleep spindle, which reverberates in the cortex. From the electroencephalographic point of view, sleep spindles are groups of waves oscillating at a dominant frequency between 12 and 15 Hz [3] and with a peculiar waxing and waning (spindling) shape [5]. Their amplitude is highly variable, however never exceeding the peak-to-peak value of 50μV [6]. Their rate of occurrence is also highly variable among subjects, normality ranging from 200 to more than 1000 spindles per night [7].

At present, the most part of sleep specialists perform their detection manually, but firsthand experience from our lab have shown that this procedure has a low inter-rater reliability and leads to several mis-detections due to the high variability of the phenomenon. We believe that this fact accounts for the huge number of methods developed in order to perform automatic spindle detection that, depending on the nature of that main criterion for the recognition, can be grouped into three major families: methods based on Time-Frequency decomposition, on the Matching Pursuit algorithm, and, finally on pattern-recognition techniques.

Time-frequency analysis is a classical approach for evaluating the temporal evolution of the power content as a function of the frequency [8], and therefore it is particularly suitable for the analysis of non-stationary signals, like EEGs. The most used algorithms for EEGs are the Short-Time Fourier Transform and the Wavelet Transforms. However, these techniques alone are not sufficient to perform spindle detection with sufficient sensitivity and specificity. In fact, in order to create sequential detectors, they are used in combination with other criteria such as methods stemming from pattern recognition [9], [10]. Other works have integrated time-frequency analysis with the use of the Teager Operator, a measure of the instantaneous variations of the sinusoidal energy of the signal [9].

Another group of methods stems from the *Matching Pursuit algorithm*. This algorithm has been developed by Mallat and Zhang [11] and it is a sort of improvement of the Wavelet Transform, based on the adaptive fitting of the signal by using peculiar functions belonging to a wide set of waveforms, the *dictionary*. These functions, the *atoms*, can be modulated via linear transformations (translation and rescaling) in order to obtain the best linear combination in representing the signal.

The last group of methods is based on *pattern recognition*. This group of methods completely rely on the formal definition of the shape of sleep spindles, given by Rechtschaffen and Kales: *"The presence of sleep spindle should not be defined unless it is of at least 0.5 sec duration, i.e., one should be able to count 6 or 7 distinct waves within the half-second period. (…) The term should be used only to describe activity between 12 and 14 cps"*. There are several works aiming at using a pattern recognition method; among the most recent ones, we have selected the work of Andrillon and colleagues [12], since its feasibility, from normal subjects to schizophrenic patients, has been demonstrated. This method is based on a sequential process, i.e. on a number of steps: the signal is first filtered in the sigma band; its instantaneous amplitude, the so called *envelope*, is then extracted; the beginnings, the maxima and the ends of the spindles are then identified via envelope

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thresholds; A final inspection of the frequency band power of the above-threshold events is performed to discard artifactual spindles.

A common limit of many proposed method is to take into account the spindle variability only partially, where variability is intended both between subjects and nights and in time, within nights. Thus, the purpose of this work is to develop an algorithm based on pattern recognition, i.e. based on the detection of the singular spindle shape, that takes this variability into proper account. The developed method consist in selecting spindles using two thresholds that are designed to be dynamical, i.e. able to follow the physiological variations of the signal throughout the whole night. The algorithm also provides several features to characterize the different spindles. The algorithm has been applied to real sleep recordings in order to verify the expected sleep spindle spatial (distribution over the scalp) and temporal properties (time-varying rate of occurrences) and to perform a validation based on visual inspection of the detected spindles.

II Methods

A The algorithm

Spindle detection and characterization partially follow previously published algorithms [12], [13] and are based on a sequential process described by the flow chart of Figure 1).

B Validation of the algorithm

1) Signal preparation

EEG signals were segmented in 300*s* epochs. Previously sleep-staged and artifact-free nREM EEG epochs were band-pass filtered with a Chebyshev filter, type II, using two different frequency bands: the sigma band, between 12 and 15 Hz, and the high gamma band, between 70 and 90 Hz. For each band, the instantaneous amplitude of the signal was calculated via Hilbert Transform, in order to apply the following detection step to each band.

2) Spindle detection

The detection uses two different thresholds, a lower one, which identifies the starting and the ending points of the spindle, and an upper one, for the peak value. An observation window of 2s was chosen, accordingly with the expected spindle largest duration [12].

Firstly, the upper threshold was applied to identify putative spindle peaks, then starting from the peak location, the algorithm moves to left and to right for a maximum length of half window in order to search for the starting and ending points, respectively. If the instantaneous-amplitude signal crosses the lower threshold both at left and at right within this time interval, a spindle is detected in the related frequency band (classical sleep spindles in the sigma band, gamma spindles in the gamma band).

Because of the significant variability of the signal amplitude between subjects, sleep stage and derivations, thresholds were set as a function of

the mean signal amplitude in the band, computed and applied separately from one epoch to the other. The lower and upper thresholds were set at one and four times the mean value of the envelope amplitude, respectively.

By applying the procedure 2) to both sigma- and gamma-filtered signals, we also detected spindles-like structures at high frequencies; when these gamma spindles had an overlap with sigma spindles (*broadband* spindles) we retained them. Isolated gamma spindles, whose relevance needs to be still investigated and are thus outside the purposes of this work, were discarded.

3) Feature extraction

For each detected sleep spindle, we collected the following features for analysis: peak-to-peak amplitude, dominant frequency (computed via Hilbert Transform), spindle duration, a flag indicating the simultaneous presence/absence of a gamma spindle and its corresponding amplitude.

All algorithms have been entirely developed in Matlab (MathWorks, Natick, MA, USA), graphical outputs have been produced with the EEGLAB toolbox [14].

C Application to Real Data: Sleep Recordings

Eight healthy subjects underwent night sleep recordings. Prior to the experiment, they spent a night in the laboratory, as adaptation to the experimental condition. They were requested to avoid alcoholic drinks or caffeine in the 24 hours preceding the experiment.

All participants gave their signed informed consent according to the ethical commettee of Pisa University.

Sleep high-density EEG were recorded with a 128-electrodes HydroCel Geodesic Sensor Nets and a NetAmps 300 system (GSN300; Electrical Geodesic Inc., Inc., Eugene,OR, USA). Data were continuously recorded, sampled at 500 Hz. EEG data analysis has been performed after sleep staging visually performed by a sleep specialist. This was done according to international standards, on time windows of different size from those used for the detection, namely 30s for the staging and 300s for the analysis. The EEG was previously referenced to the mastoids. After exclusion of 23 electrodes used for the recording of the muscular activity, only 105 channels per subject were retained.

The detection method has been validated by means of an a-posteriori visual inspection of the automatic-detected spindles. The visual inspection was performed by a sleep specialist that was asked to mark each automatically detected spindle as a true or false positive, based on visual inspection of the signal filtered in the sigma band. In addition, the proper functioning of the algorithm is further indirectly validated by means of the results obtained by its application to the EEG series earlier described. Nevertheless, an a-priori validation still needs to be performed in order to evaluate whether any visually-detected spindles are not detected by the algorithm.

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III Results

Examples of sleep spindles detected by the proposed method are shown in Figure 2. In the figure two opposite cases are shown: Panel A shows two full-fledged spindles, one is following a K-complex, the second is a temporally isolated one and both would be recognized by visual scoring of any sleep expert; Panel B shows a spindle warped by a slower oscillation which would be difficult to be identified during manual visual scoring.

The results of the algorithm have been a posteriori validated by a sleep specialist, achieving on average a sensitivity of 95%. Table I shows the variability of false positive spindles over the subjects.

Moreover, applying the automatic detection on the eight night EEG recordings, the visual analysis of group-averaged spindle feature distribution provided results (see Fig. 3) in line with available literature. In particular, spindles resulted more prevalent in central-parietal areas (topological map of the rate). By mapping the spindle features, we also identified a difference between the distribution of spindle rate (centro-parietal peak) and that of associated sigma amplitude (frontal peak in the topological map of the amplitude). The dominant frequency and the spindle temporal width also had specific scalp topologies: spindles were faster in the posterior areas and of less duration on the parieto-temporal areas.

IV Discussion

In this work, we originally employed dynamical thresholds that allowed us to detect sleep spindles, taking into account the physiological variations of the signal amplitude taking place throughout the night. Both the a posteriori validation of detected sleep spindles and the group-averaged results from the sleep recordings indicate the effectiveness of the proposed method. The rate of false positive in the a-posteriori validation resulted around 5% and thus satisfactory. The evaluation of group averaged maps confirms the central prevalence of the spindles and the application of the method to these sleep recordings has allowed highlighting a mismatch between the topology of spindle amplitude and that of spindle rate.

For the physiological application, the importance of enhancing spindle detection algorithms derives also from the fact that spindles have been growingly attracting the scientists' attention, as they appear to be involved in the offline consolidation phase of learning processes occurring during NREM sleep. In this line, the extraction of several features would allow us to analyze the role of spindles from different perspectives and would provide new and original knowledge on the physiology of sleep. The use of adaptive thresholds would be a great benefit in clinical applications since sleep spindles fade with the severity of several neurological conditions [15], [16].

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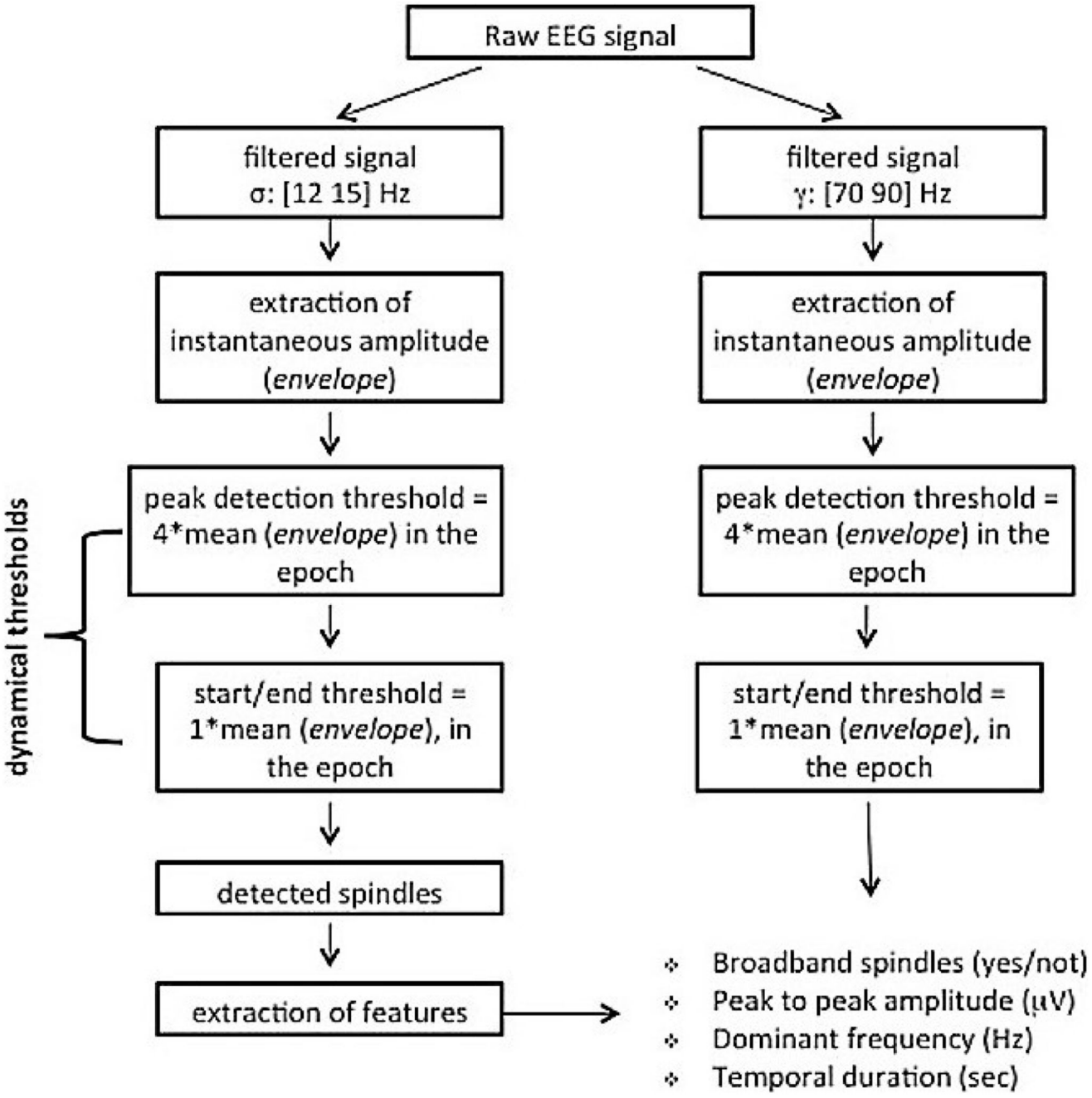

Fig. 1.
Flow diagram of the applied procedure.

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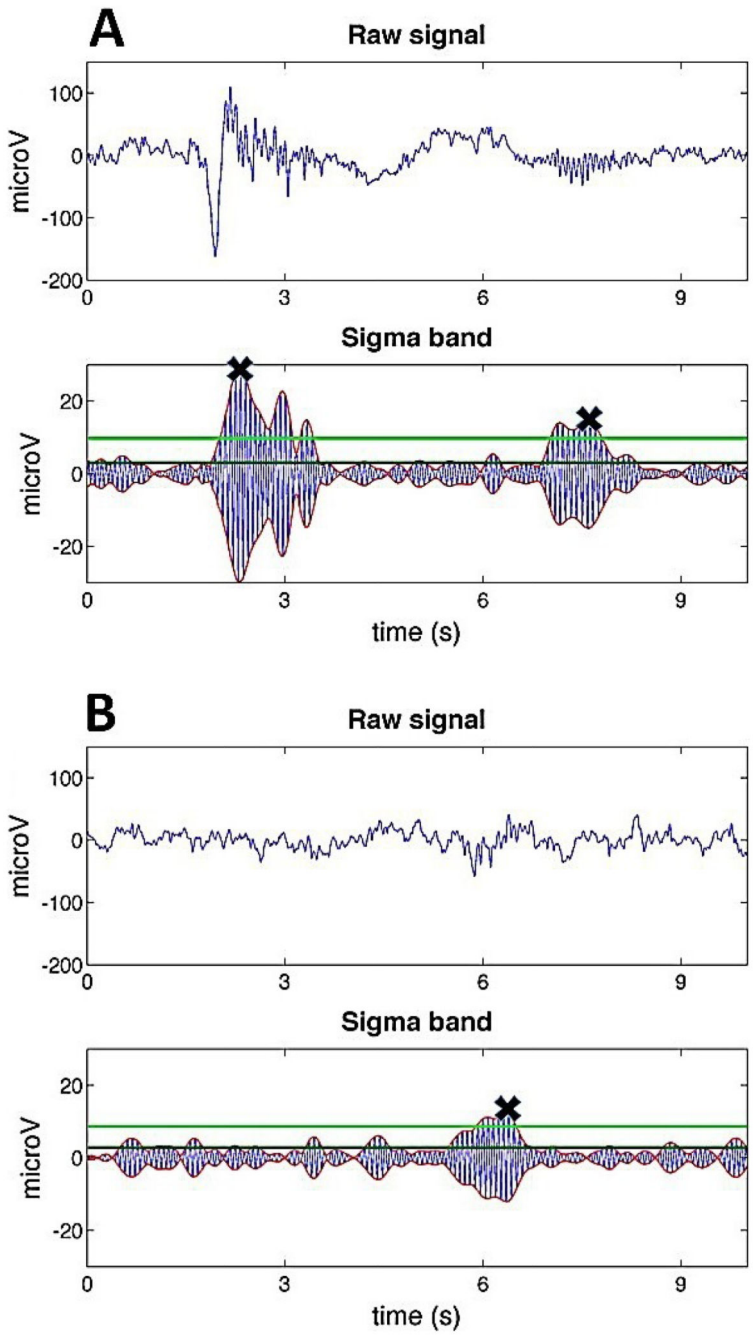

Fig. 2.

Examples of spindle detection based on dynamic thresholds. Each panel has two traces: (top) The EEG signal, filtered in [0.5 – 40*Hz*] as usually seen during visual scoring - (bottom) EEG signal, filtered in [12 – 15*Hz*]. In red, the rectified signal, calculated via Hilbert Transform. In green, lower and upper thresholds. Panel A shows two full-fledged spindles. The first one is following a K-complex, the second one is an temporally isolated one. Both spindles would be recognized by visual scoring of any sleep expert. Panel B show a spindle warped by a slower oscillation and difficult to be identified during visual scoring.

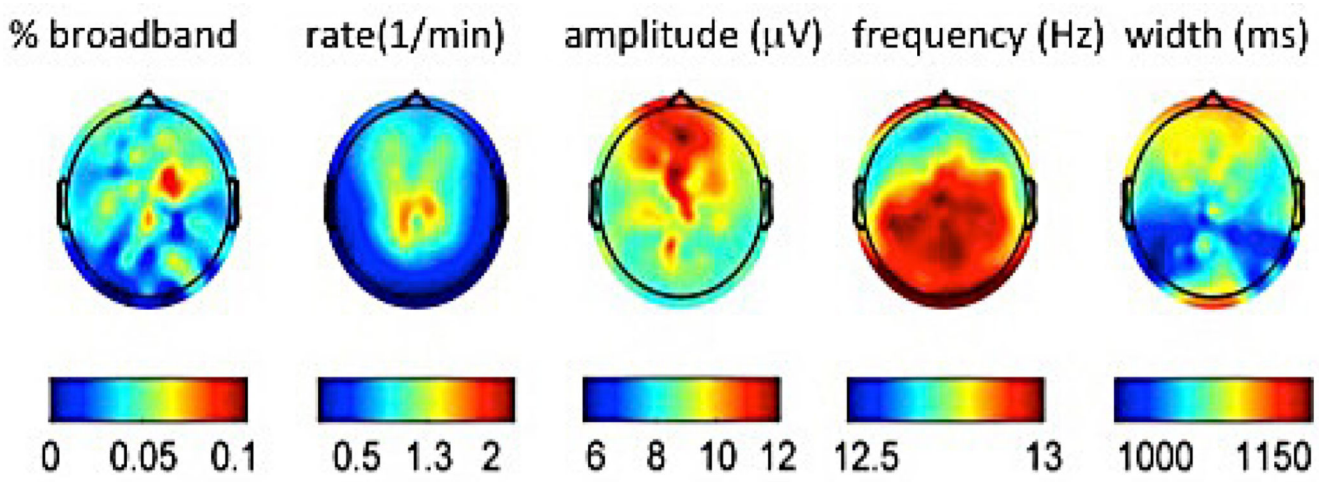

Fig. 3.
Results - Group-averaged topological maps of spindle features.

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Table I

Percentage of False Positive Evaluated on Epochs of 5 Min of Nrem Sleep. For Each Subject, Mean and Standard Deviation Have Been Calculated Over the Epochs.

false positives percentage		
subject	mean	std
s1	0.06	0.04
s2	0.08	0.04
s3	0.04	0.03
s4	0.06	0.04
s5	0.03	0.04
s6	0.06	0.03
s7	0.05	0.02
s8	0.04	0.03