# AN AUTOMATIC METHOD FOR THE STUDY OF REM SLEEP MICROSTRUCTURE

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## ABSTRACT

A method is described for the automatic and quantitative analysis of changes in polysomnographic signals during REM sleep. The implementation of the procedures has been motivated by the remarkable psychophysiological and clinical significance not only of REM sleep per se, but also of its microstructure, given by state variations at frequencies slower than 1 Hz. These procedures provide a segmentation of REM sleep into sub-stages and allow the calculation of quantitative parameters connected with the microstructural properties of REM sleep.

***Index Terms***— Polysomnography, REM sleep, sleep microstructure, slow eye movements, signal segmentation

## 1. INTRODUCTION

In the last decades, polysomnography (PSG) has proved a very useful tool for better understanding brain physiology and for effectively recognizing a large variety of patholo- gies. PSG consists in recording and analyzing a number of different electrophysiological signals, typically including Electroencephalography (EEG), Electrooculography (EOG), Electromyography (EMG), and Electrocardiography (EKG). The use of computer procedures for a quantitative and automatic analysis of PSG signals has constantly increased over the years and can now be viewed as necessary and es- sential. Within the scope of sleep research, the study of the mechanisms and functions of rapid-eye-movement (REM) sleep is certainly among the most significant issues: a basic reason is that this sleep stage is closely connected with a particular state of consciousness, in which the brain, almost completely disconnected from the environment, can gener- ate and live a variety of conscious experiences in the form of dreams. However, the precise terms of the connection between dreaming and REM sleep are currently controver- sial, together with other basic issues, such as: the amount of similarity between consciousness during wakefulness, dur- ing NREM sleep, and during REM sleep; the role of brains- tem activation in the construction of REM mentation; the respective roles of the cholinergic and the dopaminergic system in the neurochemistry of REM sleep; the signific-

ance of changes in connectivity patterns among brain re- gions during sleep (see in particular [1] for a comprehensive review of the current debate about these points).

An important property of REM sleep is that it is far from presenting uniform features, both topographically and tem- porally. In the space domain, interesting phenomena of dis- sociation have been observed, in particular during para- somnias [2, 3] and in patients affected by REM sleep beha- vior disorder. Furthermore, it has been suggested that vivid image experiences during non-REM (NREM) stages can be due to local "covert" REM processes [4].

As regards the time domain, two kinds of experimental data show that marked variations in the PSG signals exist during REM sleep. The first data is the distinction between "phas- ic" and "tonic" epochs [5, 6, 7], the former being characte- rized by distinct oculomotor activity. During phasic REM sleep specific phenomena take place, including: reduction in background alpha activity over occipital regions [8], in- crease in arousal threshold [9], and increase in the motor activity in patients affected by REM sleep behavior disorder [10]. The second kind of data connected with time variations during REM sleep is given by the occurrence of slow eye movements (SEMs), whose frequency range is approximate- ly similar to that of the eye movements that appear before sleep onset and increase over stage 1 [11, 12]. The presence of SEMs, which has been established among the criteria for visual scoring of Stage 1 [13, 14], has recently been studied quantitatively and in detail with regard to REM sleep as well [15, 16, 17].

The aim of our work has been to propose and check a com- prehensive automatic method of quantitative analysis of time variations during REM sleep, focusing on two purpos- es: (a) segmentation into appropriate sub-stages; (b) calcula-tion of parameters able to quantitatively characterize changes in PSG signals.

## 2. METHODS

PSG signals were analyzed which consisted of: 19 EEG traces, derived from electrodes placed on the scalp accord- ing to the 10-20 System, submental EMG, EKG, and two EOG signals, respectively derived from electrode site E1 (about 1 cm above the left outer canthus) and E2 (about 1

cm below the right outer canthus). The reference was given by mastoid electrodes A1 and A2. The frequency ranges for the acquisition were 0.3-64 Hz for the EEG traces, 0.1-64 Hz for the EOG traces, 0.3-64 Hz for the EKG, and 10-64 Hz for the EMG traces. The sampling frequency was 128 Hz.

The implemented procedures were the following:

*Procedure 1*: Calculation of significant frequency-band components of original traces. As for the EEG, the band ranges were the following: delta (from 0.3 to 4 Hz), theta (from 4 to 8 Hz), alpha (from 8 to 12 Hz), beta (from 16 to 32 Hz), and gamma (from 32 to 64 Hz). To detect spindle activity, the EEG activity in the frequency band from 12.5 to 14.5 Hz was also calculated. As for the EOG, two frequency bands were considered for the detection of SEMs and REMs, respectively: in the light of the literature [15, 18, 19],we chose the range from 0.2 to 0.6 Hz for SEMs and the range from 1 to 3 Hz for REMs.

*Procedure 2*: Calculation of time averages of component amplitudes (calculated by Procedure 1) by means of convolutions with rectangular time-windows. The most applied values for the length of the time-windows were 64 s and 2 s. The average over the longer window was connected with lasting, "background" features of the component: its time course generally depended on signal variations related to the succession of stages during sleep. For instance, the average over 64 s of the EEG delta component provided an approximately damped-oscillation graph with maxima corresponding to stage 4, while the average over 64 s of the EEG component connected with the spindles presented marked stable minima corresponding to REM sleep. The shorter window, very differently from the longer one, allowed transient phenomena to be easily recognized.

*Procedure 3*: Calculation, as a function of time, of non-dimensional descriptors given by the ratio of the difference between the two averages calculated by Procedure 2 to the average over the longer time-window. Each descriptor was related to a definite signal trace and to a definite frequency band. When the value of a descriptor was equal to zero, the band component amplitude was the same as the background amplitude. When the value of a descriptor was equal to one, the band component amplitude was twice the background amplitude.

*Procedure 4*: Recognition of transient events by the application of two thresholds to the descriptors calculated by Procedure 3 (for reasons of simplicity, we chose zero for the lower threshold and one for the higher threshold) and application of the following criterion for the recognition of epochs characterized by transient increase in band compo- nent amplitude: the descriptor must be greater than the low- er threshold at all instants and must be greater than the high-er threshold at least at one instant (this criterion was applied by Navona et al., [20]). Each recognized epoch was characterized by the following attributes: signal trace, band com-

ponent, peak value of the descriptor, start time, and endtime.

*Procedure 5*: Segmentation of sleep stages into sub-stages by means of queries to a database containing the events recognized by Procedure 4 together with their attributes.

*Procedure 6*: Calculation of two quantitative parameters (mean power and mean spectral frequency) derived from the amplitude average over the shorter window, computed by Procedure 2: these parameters were able to characterize the signal component changes during a constant sleep stage. A third quantitative parameter was given by the percentage of time for each of the sub-stages recognized by Procedure 5.

These procedures were applied to PSG signals obtained from four subjects, whose age range was from 28 to 38 years. Each of them presented four clearly recognizable REM periods.

## 3. RESULTS

The specific purpose of our analysis concerned the study of signal variations during REM sleep. For this reason we only applied our package to REM periods, which were identified by visual scoring and confirmed by the automatic recognition of intervals presenting minimum values of the longer average (over a time-window lasting 64 s) of the component in the frequency band from 12.4 to 14.5 Hz of the EEG traces.

Figure 1 refers to a 1-minute recording during the second REM period of Participant 1, showing six EEG traces and four EOG traces. The alternation between epochs presenting remarkable eye movements and epochs presenting poor eye movements is clearly visible. The difference between slower and faster eye movements is also clear.
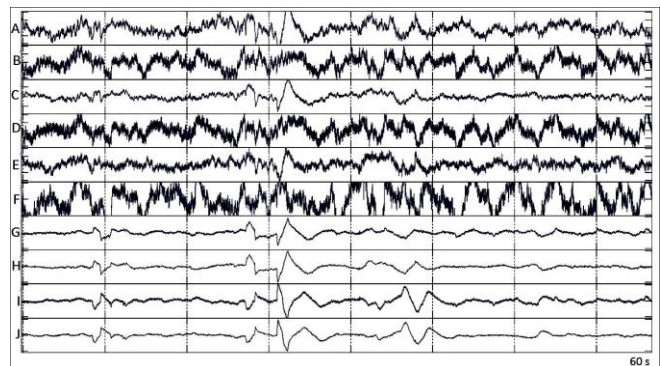


*Figure 1*. Participant 1. Second REM period. From A to F: EEG traces: C3-A3, C4-A1, F3-A2, F4-A1, O1-A2, O2-A1. From G to J: EOG traces: E1-A1, E1-A2, E2-A1, E2-A2. Horizontal scale: 1 minute. Vertical scales: from (-40) to (+40) µV for the EEG traces, and from (-200) to (+200) µV for the EEG traces.
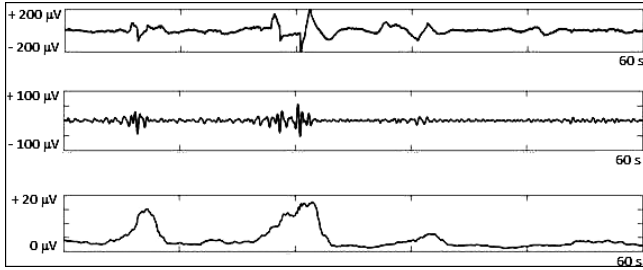
*Figure 2*. Participant 1. Second REM period. From top: E2-A1 EOG trace; its component in the frequency band from 1 to 3 Hz; its amplitude average over a moving win- dow lasting 2 s. Horizontal scale: 1 minute.
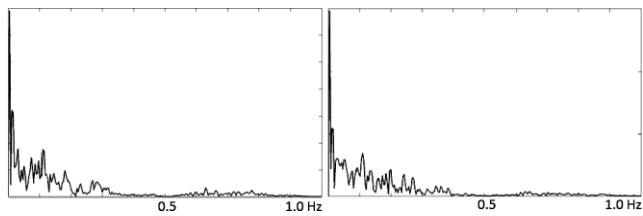


*Figure 3*. Participant 1. Fourth REM period. Absolute value of the Fourier Transform of the amplitude average over 2 s of the SEM component (at the left) and of the REM compo- nent (at the right) of the E2-A1 EOG trace. The Fourier Transforms have been calculated over an epoch lasting 256 s. Horizontal scale: 1 Hz. The vertical scales have been normalized to the respective maximum values. The quantita- tive parameters derived from these spectra were:
Central frequency of SEM amplitude variations: 224 mHz;
Central frequency of REM amplitude variations: 206 mHz;
Mean power of SEM amplitude variations: 119 $\mu V^2 s^{-1}$;
Mean power REM amplitude variations: 20.8 $\mu V^2 s^{-1}$.

| 0-6 s | Poor eye movements |
|---|---|
| 6-12 s | REMs |
| 12-20 s | Poor eye movements |
| 20-29 s | REMs |
| 29-32 s | Poor eye movements |
| 32-39 s | SEMs |
| 39-45 s | Poor eye movements |
| 45-53 s | SEMs |
| 53-60 s | Poor eye movements |

*Table 1*. Segmentation of the REM epoch of Figures 1 and 2 into three sub-stages, respectively presenting: poor eye movements; selective enhancement of SEMs; enhancement of REMs.

|  | Segmentation Times | | Segmentation Percentages | |
|---|---|---|---|---|
| Neither SEMs nor REMs | 2:31 | | 59.0 % | |
| Only SEMs | 0:46 | | 18.0% | |
| Only REMs | 0:18 | 0:59 | 7.0 % | 23% |
| Both REMs and SEMs | 0:41 | | 16.0% | |
| *Total* | *4:16* | | *100 %* | |

*Table 2*. Participant 1. Fourth REM period. Parameters cha- racterizing the segmentation of the 256-s epoch considered for the calculation of the Fourier Transforms of Figure 3.

Figure 2 relates to the E2-A1 EOG trace (top graph) during the same one-minute epoch as Figure 1. The central graph shows the faster component (from 1 to 3 Hz), and the bot- tom graph shows its amplitude averaged over the shorter time-window.

Table 1 presents the results of the segmentation procedure into three sub-stages with regard to the REM epoch of Fig- ures 1 and 2: an immediate visual correspondence exists between these results and the EOG signal.

Figure 3, which concerns an epoch lasting 512 s during the fourth REM period, shows the spectral properties of the variations in REMs and SEMs, as given by the amplitude averages over the shorter time-window.

The corresponding quantitative parameters related to the segmentation of the same epoch are reported in Table 2.

## 4. DISCUSSION

A number of different criteria for segmentation and classifi- cation of polygraphic signals have been proposed in the last decades (for a review, see Chapter 56 of [21]), starting from the pioneering autoregressive model proposed by Bodens- tein and Praetorius ([22]). We chose to apply a modified version of the method described in [20] because of its ma- thematical and conceptual simplicity and its effectiveness in analyzing the microstructure of NREM stages [23].

The above described procedures have allowed a quantitative study of PSG changes during REM epochs to be performed. They have offered both a new form of segmentation of REM sleep and the introduction of parameters able to quantitative- ly characterize the microstructure of REM sleep.

The clinical usefulness of this method derives from the high significance of REM sleep with regard to both psychophysi- ology and pathology. In particular, if quantitative PSG pro- vides remarkable tools for the diagnosis and prognosis of disorders of consciousness (see, e.g., [24]), this is especially true for REM sleep, which is characterized by a very partic- ular state of consciousness.

The study of variations in the properties of eye movements during REM sleep appears to be connected with important issues in the current debate about consciousness and about disorders of consciousness. In particular:

(a) The thalamocortical intrinsic loop active during REM sleep [25] appears to be specifically active during phasic REM sleep [26].

(b) The observation of lower thresholds for acoustic stimuli during tonic REM sleep has been interpreted as a reduction of vulnerability [9], a point connected with survival under an evolutionary perspective.

(c) During phasic REM sleep a control mechanisms for the manifestation of elaborate or violent behavior has been observed in patients affected by REM sleep behavior disorder [10].

(d) The progressive decrease of SEM activity during stage 2 in the course of the night supports the potential of SEMs as markers of the homeostatic process of sleep regulation [17].

(e) The amplitude of REMs and SEMs changes slowly (frequencies < 1 Hz): these frequencies are often considered as significant with regard to memory functions and consciousness. Recently, the oscillating properties of REM sleep have been described using both EEG and BOLD signals by Chow et al. [27], who found that activity in the sensorimotor and heteromodal association cortices alternated in multisecond periods.

(f) SEMs are remarkably present both in REM sleep, which is closely connected with the phenomenon of dreaming, and in Stage 1, during which hypnagogic hallucinations occur. A significance of SEMs with regard to properties of sleep mentation can therefore be conjectured.

Future research will aim to fully exploit the quantitative parameters which the method allows to be obtained. Comparisons will be performed between different REM stages of the same night, between different subjects, and especially between different forms of neurological pathologies, in particular disorders of consciousness. Further research will also address the study of the autonomic system function during the various REM sub-stages, by focusing on the correlations between the EKG and the other PSG signals.

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