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**Exploration of algorithms of
automatic detection of sleep
microstages (of
morphology of cycling alternating
pattern (CAP) on Non-REM sleep)**

Iordanis Tentsoglidis

SID: 3308170025

SCHOOL OF SCIENCE & TECHNOLOGY

A thesis submitted for the degree of

Master of Science (MSc) in Data Science

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Abstract

The last decades the explosion in diverse domains of IT technology so in hardware as in software set new horizons for further research in many fields or defined from the ground whole new scientific disciplines. Bioinformatics and biomedicine definitely took advantage of tech explosion. As a consequence, sleep medicine is one of those new research areas that arose. This study tries to reproduce, extend and optimize state of the art technics for automatic sleep microstructure analysis. Especially focuses on the Cycling Alternating Pattern (CAP) and the detection of a CAP's prominent feature, the A-phase. An algorithm is reproduced according to state of the art techniques and experimental approaches are tested to classify records between Non A-phase and A-phase events achieving 91% accuracy, 75% sensitivity and 91% specificity. As the results are competitive compared to other studies employing the same dataset (Physionet CAP Sleep database), it is believed that the applied techniques could contribute to sleep research.

Iordanis Tentsoglidis

Date

07/12/2018

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Abbreviations

(REM) Rapid Eye Movement
(CAP) Cycling Alternating Pattern
(NCAP) Non-CAP event
(PSG) Polysomnography
(EEG) electroencephalogram
(EOG) Electrooculography
(EMG) Electromyography
(EKG) Electrocardiogram
(PSD) Power Spectral Densities
(LDA) Linear Discriminant Analysis
(AUC) Area Under the Curve
(AASM) American Academy of Sleep Medicine
(OSA) Obstructive Sleep Apnea
(SFS) Sequential Feature Selection
(TEO) Teager Energy Operator

Contents

ABSTRACT	3
CONTENTS	6
1 INTRODUCTION	10
1.1 HISTORY.....	10
1.2 IMPORTANCE OF SLEEP	11
2 SLEEP ANALYSIS	12
2.1 POLYSOMNOGRAPHY	12
2.2 LINKS BETWEEN PSG AND SLEEP DISORDERS	15
2.3 SLEEP STAGES.....	16
2.4 CYCLING ALTERNATING PATTERN (CAP).....	19
2.4.1 Cap history	19
2.4.2 Cap definition	20
2.4.3 A-Phase Morphology.....	28
3 RELATED WORK	32
3.1 RELATIVE STUDIES AND SCARCITY	32
3.2 FEATURE PROPOSALS.....	35
4 MATERIALS AND METHODS	37
4.1 PHYSIONET SLEEP CAP DATABASE	37
4.2 FEATURES.....	40
5 RESULTS	45
5.1 EXPERIMENTAL APPROACHES.....	45
5.2 EXPERIMENTAL QUESTIONS AND ANSWERS	46
5.3 HYPER PARAMETERS	49
5.4 SEMI-AUTOMATED MODEL	49
5.5 COMPARING RESULTS WITH SIMILAR STUDIES	50
6 CONCLUSIONS AND FUTURE WORK	51

REFERENCES	52
APPENDIX.....	57

List of Figures

Figure 1: Number of sleep research publications per year.....	11
Figure 2: The EOG shows the horizontal movements of the eyes	13
Figure 3: The ECG capture the limb movement	14
Figure 4: The EMG captures the activity of the muscles.....	14
Figure 5: The EEG csptures the electrical activity of the brain	15
Figure 6: Physiological changes in a volunteer during the various sleep states in a typical 8-hour sleep period. The duration of REM sleep increases from 10 minutes in the first cycle to up to 50 minutes in the final cycle; note that slow-wave (stage IV) sleep is attained only in the first two cycles	18
Figure 7 The distribution of sleep stages for healthy adult.....	18
Figure 8: An example of cyclic alternating pattern (CAP) in sleep stage 2. The box outlines a CAP cycle (C) composed of a phase A (A) and the following phase B (B). Bioplolar EEG derivations using international electrode placement; top 6 channels from top to bottom: FP2–F4,F4–C4,C4–P4,P4–O2,F8–T4,T4–T6; bottom 7 channels from top to bottom: FP1–F3,F3–C3,C3–P3,P3–C1,F7–T3,T3–T5,F2–C2; OCULOG: Oculogram, EKG: Electrocardiogram.	20
Figure 9: Arousal preceded and followed by sleep	21
Figure 10: Delta burst in slow wave sleep. Top 4 channels: Bioplolar parasagittal EEG derivation of the right side similar to top 4 channels in fig.8 .C4–A1: C4 connects to left ear (A1); EOG: Electrooculogram; EMG: Electromyogram; EKG: Electrocardiogram.	22
Figure 11: Sequence of vertex sharp transients during the transition from stage 1 to stage 2 sleep. Top 4 channels: Bipolar parasagittal EEG derivation on the left side similar to channels 8, 9, 10, 11 from above; C3–A2: C3 connected to right ear (A2).....	23

Figure 12: K-complex sequences associated with spindles in stage 2 sleep. Top 5 channels: EEG derivation as in Fig. 10	23
Figure 13: Polyphasic burst in stage 2 sleep. Top 5 channels: EEG derivation as in fig. 10	24
Figure 14: K-alpha complex in stage 2 sleep. Top 5 channels: EEG derivation as in fig.11	24
Figure 15: Intermittent alpha rhythm in stage 1 sleep.....	25
Figure 16: Arousal preceded and followed by sleep.	26
Figure 17: The percentage of CAP rate and NCAP rate over the over-night sleep	27
Figure 18: Phase A subtypes. The dotted spots indicate the fast low-amplitude portion of the phase A. EEG derivation as in fig. 12	29
Figure 19: Isolated phase A black spot box preceded and followed by a low-voltage, mixed frequency EEG background for 60 s.....	30
Figure 20: A CAP sequence (between black arrows) associated with a transition from non-REM to REM sleep. EEG derivation as in Fig. 12.	31
Figure 21: Electrode positions according to the 10-20 system. Odd numbered electrodes are positioned over the left hemisphere, whereas even numbered ones are placed over the right hemisphere. Fp=frontopolar, F=frontal, C=central, T=temporal, O=occipital, A=auricular.....	38

List of Tables

Table 1: Bioelectrical signals and its characteristic.....	13
Table 2: Percentage of sleep durance on each stage.	19
Table 3: Number of papers in respective publisher.....	32
Table 4: Features ordered respective to the SFS selection	36
Table 5: Evaluating metrics values for various groupings under 900 estimators of Extra trees classifier and training only on Non A-phase versus A-phase classes but testing on respective grouping.....	46

Table 6: Evaluating metrics values for various groupings under 900 estimators of Extra trees classifier. Train and test applied on the same grouping.....	47
Table 7: Results using oversampling technique	47
Table 8: Evaluation metrics for various values of estimators parameters of Extra trees ensemble model. For the value of 900 estimators the model returned the combination of highest values.....	49
Table 9: Comparing results with similar studies	50

1 Introduction

1.1 History

The perpetual endeavor of humanity to explain and even take under control the unknown functionalities of sleep began even from its primary years. Sleep constituted a vital part of life surrounded by mysteries and myths within an effort to explain something such important and undefined at the same time. Consequently, many ancient population worship sleep as a god and they used to personify it. We come across such instances in ancient Greece and Roman Empire under the names of Hypnos and Somnus. But, as it is aforementioned, it was not until the last century that sleep research rocketed by the rapidly upgrowth of technology. Advanced medical tools and computing made it possible for scientists to accomplish the interpretation of the electrophysiological activity of the brain during sleep and elaborate researches on the domain by developing technics and standards to better understand and study sleep. In the mid of the 4th decade of 20th century the first scientific sleep classification took place by Loomis et(Williams, Karacan, & Hirsch, 1974),(Baxter, Hastings, Law, & Glass, 2008)) and later in 1953 after systematic investigation of sleep Aserinsky and Kleitman defined the classification of sleep into two main phases. But it was not before 1968 where Rechtschaffen and Kales (fA Rechtschafffen, A. Kales., 1968) published the most prominent landmark of scientific research on the domain in the century and set the foundations for describing the process of human sleep by providing a manual of sleep classification. This manual introduced the rules for the scoring of sleep in normal human adults and it was based on Kleitman classification. It identifies five different stages: one REM stage and four non-REM stages. These standards were widely accepted and defined the stages of sleep as they are known until present. Additional, it was the only paper that was widely accepted from the scientific community of the domain for almost half a century until the research around sleep evolve and confront the need for further more specialized and objective standards (Novelli, Ferri, & Bruni, 2010). The latest advances on sleep standards and terminology introduced by the year 2007 from American Academy for Sleep Medicine (AASM). Those updates included changes in terminology, proposed instruction for EEG

derivations, definition of a new sleep stage the “movement time” and the merging of stage 3 and 4 into one stage named N3 (Novelli et al., 2010).

1.2 Importance of Sleep

Although the importance of sleep in human health and its effects on everyday life are evident, there are several studies that validate or challenge it (Cirelli & Tononi, 2008) and attempt to investigate the importance of sleep (Cirelli & Tononi, 2008) as well as primary causes and relations between sleep and its effects on human body. Some of them are addressed, in highlighting the importance of sleep and providing with guidelines as an attempt of improving quality of life (Mukherjee et al., 2015), while others are investigating the relation between amount and quality of sleep with certain diseases such as Stroke, Cardiovascular diseases, Obesity, Coronary heart disease, Dyslipidemia, Depression, Diabetes, Hypertension or general with mortality (Jike, Itani, Watanabe, Buysse, & Kaneita, 2018) finding indications for linkage between long sleep duration and adverse health outcomes.

Due to huge impact of sleep in humans, there were always efforts to decode functional mechanisms of sleep but it is only the last century that researchers possessed the appropriate tools by technological innovations to penetrate deeper into sleep functions. After that, they achieved to set standards for research (A Rechtschaffen, A. Kales., 1968) and discover relations among sleep and other human aspects such as cognition (Ferri & Bruni, 2013).

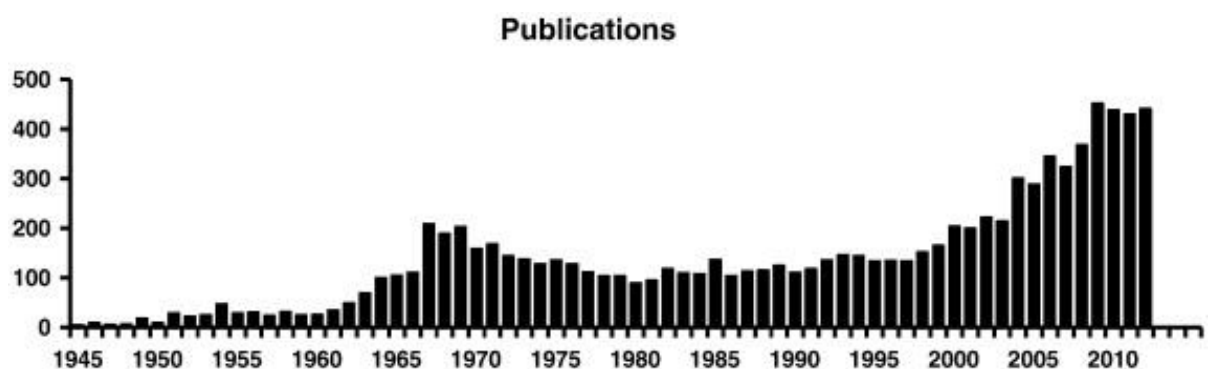


Figure 1: Number of sleep research publications per year

Source: (Ferri & Bruni, 2013)

Although, sleep has been systematically investigated for around 70-75 years, there is an burst on the evolvments on the field the last 10-15 years. The reason is the exponential technological developments so in hardware by the development of faster machines with more and more computational power and advances in technological medical equipment as in software with state of the art Artificial Intelligence methodologies so in advanced management and interface software tools.

2 Sleep Analysis

2.1 Polysomnography

In general, the study of a person's sleep is called polysomnography (PSG). It consist a diagnostic assessment from sleep experts (usually neurologist) on someone's sleep. Experts in order to evaluate a sleep use multiple modals and tools and it take place into specially designed laboratories which carry the necessary equipment. Sleep experts study the outcomes from polysomnography to detect the existence of sleep disorders which could indicate diverse physical or psychological disorders (Bullard, Griss, Greene, & Gekker, 2013). Some of the modes that Polysomnography combines are electroencephalogram (EEG), electroculogram (EOG – detection of eye movements), electromyogram to detect the movements of the muscles of the face or legs, (EMG – to detect muscle activity), and electrocardiogram (ECG or EKG – detection of heart's rate and rhythm). Additional, measures of respiratory function are employed. The most common respiratory measurements are typically pulse oximetry and strain gauges which measure the chest's expansion during breathing.

Bio-Electric signals and its origin	Amplitude	Frequency
ECG, Heart muscles	1 to 5 mV	0.05 – 100 Hz
EEG, Brain	0.001 to 0.01 mV	0.5 – 40 Hz
EMG, Muscles	1 to 10 mV	10 to 2000 Hz
EOG, Eye ball movement.	0.01 to 0.1 mV	DC to 10 Hz

Table 1: Bioelectrical signals and its characteristic

Source: (Rahman & Nasor, 2015)

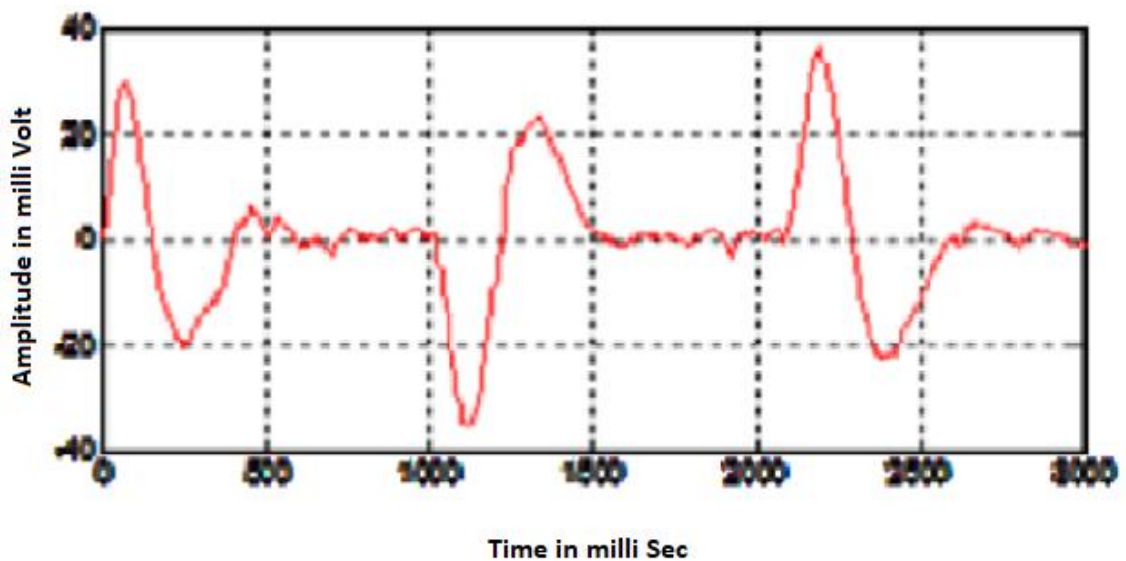


Figure 2: The EOG shows the horizontal movements of the eyes

Source: (Rahman & Nasor, 2015)

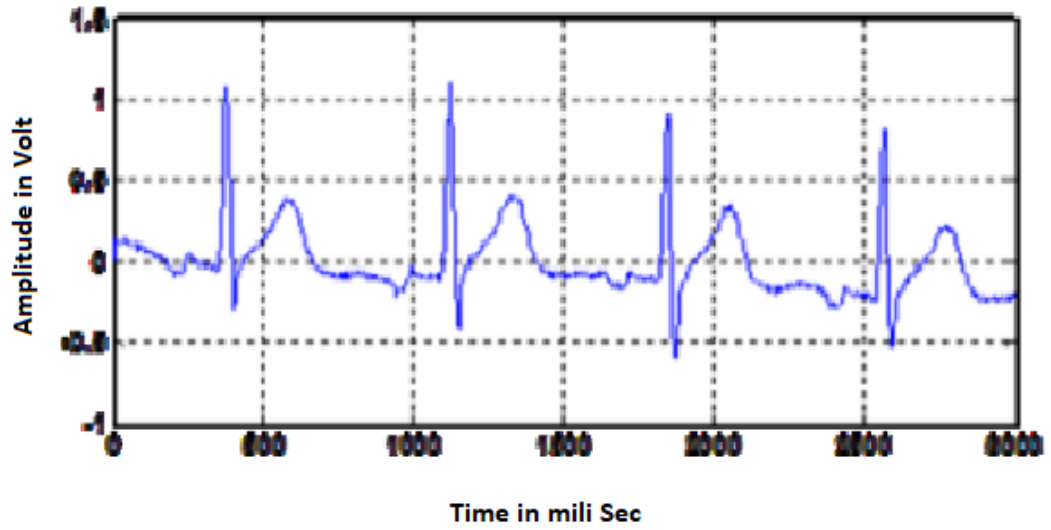


Figure 3: The ECG capture the limb movement

Source: (Rahman & Nasor, 2015)

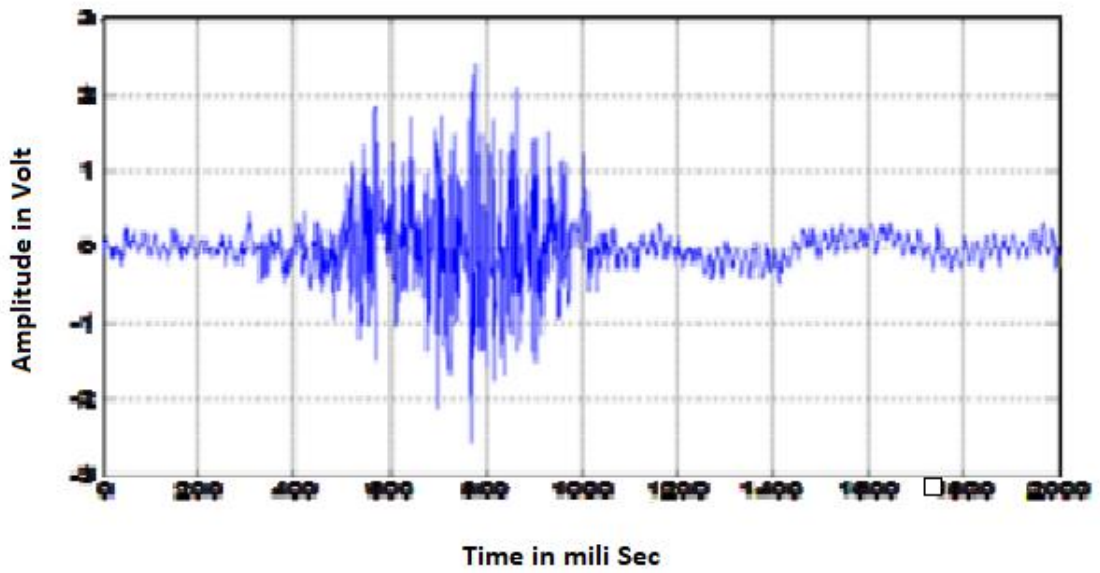


Figure 4: The EMG captures the activity of the muscles

Source: (Rahman & Nasor, 2015)

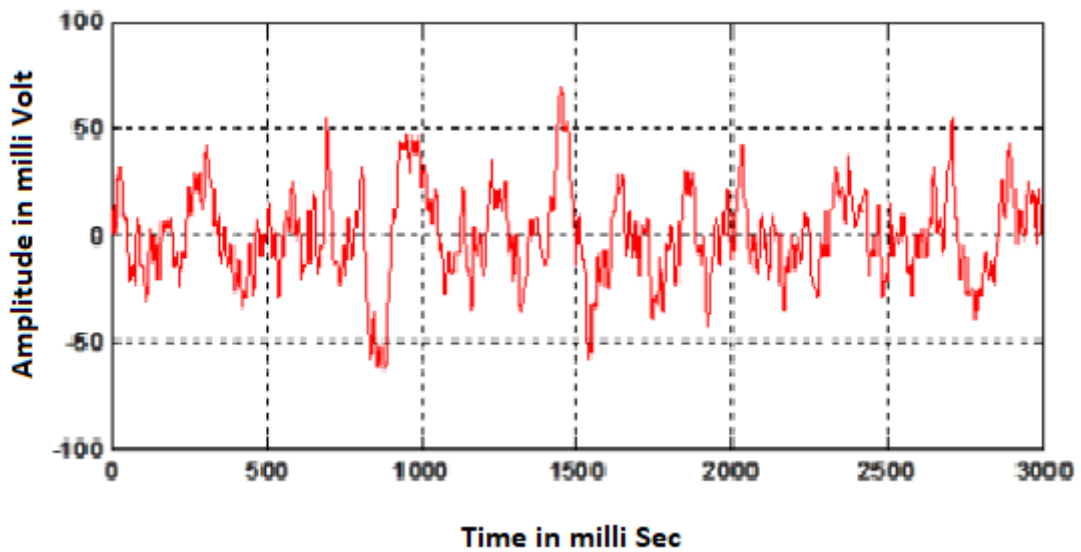


Figure 5: The EEG captures the electrical activity of the brain

Source: (Rahman & Nasor, 2015)

2.2 Links between PSG and sleep disorders

There are several clinical conditions that are related with abnormal indication in PSG. Among them are insomnia, medication (hypnotic drugs e.t.c.), paroxysm epilepsy, comma, Creutzfeldt-Jakob disease, Obstructive sleep apnea (OSA) e.t.c. For this reason there is a growing number of respective studies the last years trying to link specific disorders with sleep microstructure variations and respective medication (Korkmaz, Bilecenoglu, Aksu, & Yoldas, 2018). For instance, it is found that a proportion around 10% of men between 30 to 49 years old are suffering from respiratory sleep disorders, as well as 17% of men between 50 to 70 years old. As far as women are concerned, 3% of women between 30 to 49 years old and 9% between 50 to 70 years old (Peppard et al., 2013). Moreover, in many cases early diagnosis may have vital importance as obstructive sleep apnea (OSA) and many sleep disorders are related with problems in cardiovascular (Bradley & Floras, 2009), neurocognitive and metabolic human systems (Hirshkowitz M, 2008).

2.3 Sleep stages

The characterization of sleep stages is inseparably related with the frequency spectrum of the electroencephalogram. The below standardization of sleep stages was introduced in 1968 by Rechtschaffen and Kales (A Rechtscahffen, A. Kales., 1968) and is widely accepted and used from the scientific community. In order to acquire more insightful information epoching technics are used during the analysis. To clarify, time domain is divided into segments (epochs) of 20-30 seconds and stages are assigned to every segment. Stages are presented in descent order according to their frequency spectrum values which means that the transition from a stage to another usually accompanied with a decrease to the frequency spectrum.

Stage W

It is referred to the awake condition of the brain when eyes are open and active conscious thought exists. This activity is called beta and it is described by high frequency ranging from 15 to 60 Hz and low amplitude ($\sim 30 \mu\text{V}$) activity (Purves et al., 2004). Moreover, relaxed and clam states are characterized by alpha waves which ranging from 8-13 Hz.

Stage 1

Stage 1 usually take place when brain activity proceeds from wakefulness to other sleep stages or could occur during sleep after body movements. It is a drowsy period that characterized from a fall of the frequency values to 4-8 Hz and an increase of amplitude of cortical waves to 50-100 μV which called theta waves.

Stage 2

This is the governing stage of sleep during a physiological nocturnal sleep and is accompanied by descend in the frequency of EEG waves and an increase in their amplitude as well as a further decline on muscles tone. In this stage, we can observe spontaneous bursts of high frequency activity which are known as sleep spindles and high voltage biphasic waves called K-complexes. Sleep spindles possess duration 1-2 seconds and frequency of 10-12 Hz and their cause is the interactions between thalamic and

cortical neurons while K-complexes is believed to rise as a response to any kind of stimuli.

Stage 3

As the sleep deepens, the general brain activity slows down and at stage 3 we can observe 2-4 Hz oscillations with even higher amplitude 100-150 μV . This is considered moderate to deep sleep and less sleep spindles can be observed in this stage.

Stage 4

Stage 4 or slow-wave sleep is the deepest level of sleep and as a consequence it is hard point to awake someone. Here we can come across the lowest frequency spectrum of EEG waves during sleep, around 0.5-2 Hz and high amplitude fluctuations among 100-200 μV which are known as delta waves. Sleep spindles and K-complexes are no more presented in this stage.

During stages 3 and 4, when delta waves activity takes more than 20% of an epoch (i.e. 20 or 30 sec long recording), that epoch is considered as stage 3, when it is more than 50%, as stage 4. A whole cycle is from stage 1 to stage 4 which represents the dominant features of night sleep and called (Non-REM) Non-Rapid Eye Movement sleep with duration around an hour.

Non-Rapid Eye Movement (REM) sleep

The level of deep sleep is followed by a quite different state the REM (Rapid Eye Movement) sleep. The sequence of descending frequency is reversed so this stage is characterized by low-voltage, high-frequency activity. This fact is similar to the EEG activity of an awake person. The REM sleep usually lasts around 10 minutes before it returns to the non-REM sleep stages. As previous, in this second round of non-REM sleep we can observe slow-wave sleep, but generally this cycling does not continue respectively all night. The sequence REM - non-REM sleep occurs around 4-5 times every night and its duration widens through the night. In general, the duration of REM sleep also fluctuates depending on age. For instance, newborn possess the record of REM sleep duration as it takes 8 hours, while it lasts 2 hours at a 20 years old person and only 45 minutes to people at the age of 70 years.

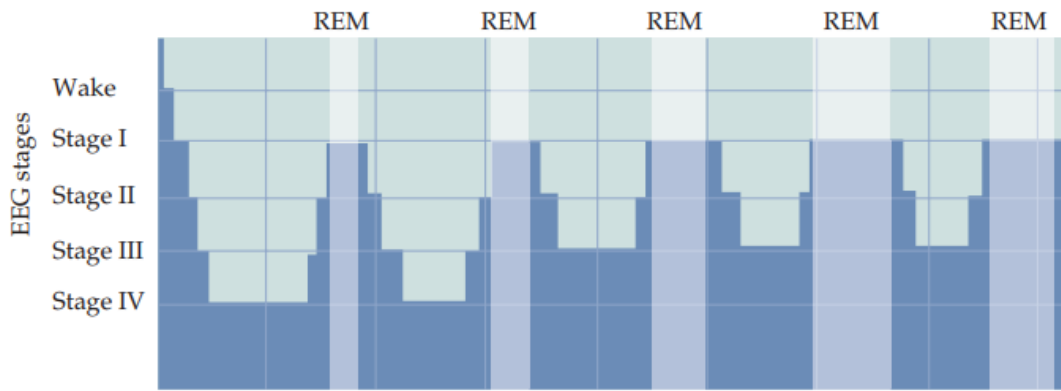


Figure 6: Physiological changes in a volunteer during the various sleep states in a typical 8-hour sleep period. The duration of REM sleep increases from 10 minutes in the first cycle to up to 50 minutes in the final cycle; note that slow-wave (stage IV) sleep is attained only in the first two cycles

Source: (Purves et al., 2004).

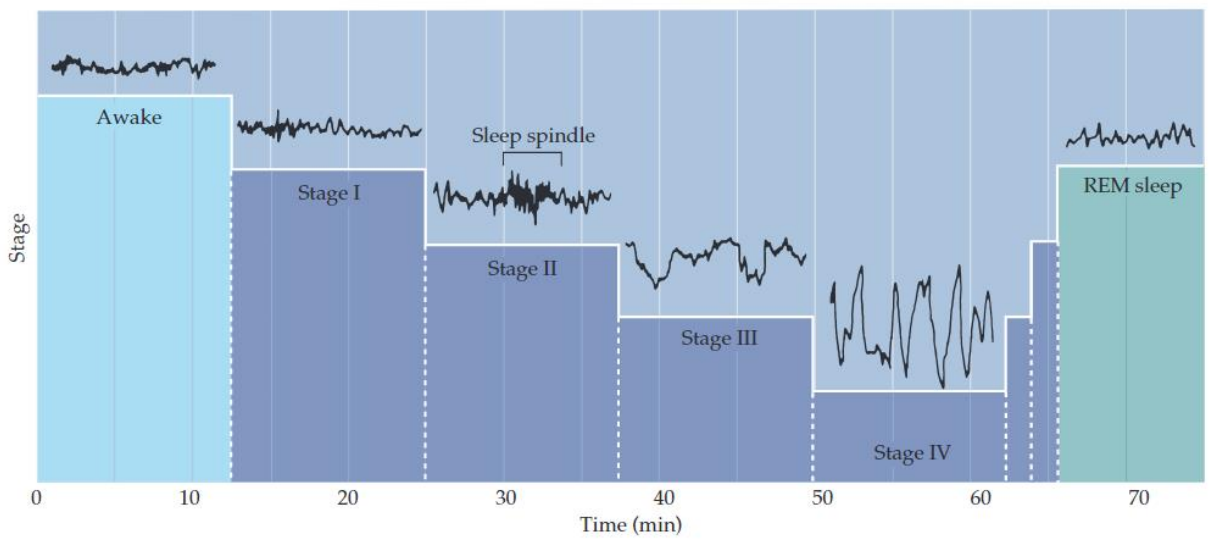


Figure 7 The distribution of sleep stages for healthy adult.

Source: (Purves et al., 2004)

Stage 1	5-10 %
Stage 2	45-60 %
Stages 3 & 4	20-25 %
REM	20-30 %

Table 2: Percentage of sleep duration on each stage.

Source: (Purves et al., 2004)

2.4 Cycling Alternating Pattern (CAP)

2.4.1 Cap history

Due to the presence of CAP in pathologic conditions, researchers hypothesized that it would be also present (including CAP features of its arousals) in normal subjects as well. Based on this hypothesis the research of Terzano in 1985 marked a new era around sleep research. The results of this research are presented in the paper “The cyclic alternating pattern (CAP) as a physiological component of normal NREM sleep” (M. G. Terzano et al., 1985). The following years studies and workshops around the topic made the use of CAP more and more popular and consolidated it as a necessary tool for sleep research. Later during the decade of 1990-2000 several studies were addressed to the clinical applications of CAP, as variations in CAP rate could indicate patients with sleep disorders such as periodic limb movements, epileptic disorders, sleep apnea syndrome and clinical insomnia (Mario Giovanni Terzano & Parrino, 1993). In 2007, American Academy of Sleep Medicine (AASM) modified Rechtschaffen and Kales standards and introduces scoring rules in order to simplify the process of sleep staging.

2.4.2 Cap definition

Studying EEG we can observe repetitive electrophysiological events (Mario Giovanni Terzano et al., 2001). Such events last few seconds and are characterized by steep fluctuations in frequency and amplitude of the signal. In order to define and describe these events, experts use three parameters: the repetitive element (which defines Phase A of a CAP cycle) and is recognized by recurring EEG features, the intervening background (which defines Phase B of a CAP cycle) which is distinguished as the interim of the repetitive elements and the period or cycle which is defined as the total time of a phase A and a Phase B and it describes the recurrence rate.

A very important periodic EEG activity called CAP (Cycling Alternating Patterns) endure from 2 to 60 s and is composed by the sequence of a Phases A and the following Phase B. This sequence composes a cycle fig.10 and can be detected through any of s1, s2, s3, s4 stages of sleep. Temporary events that intensely differentiate from background activity in frequency and amplitude and usually occur in non-REM sleep characterize A-phase and help to detect it.

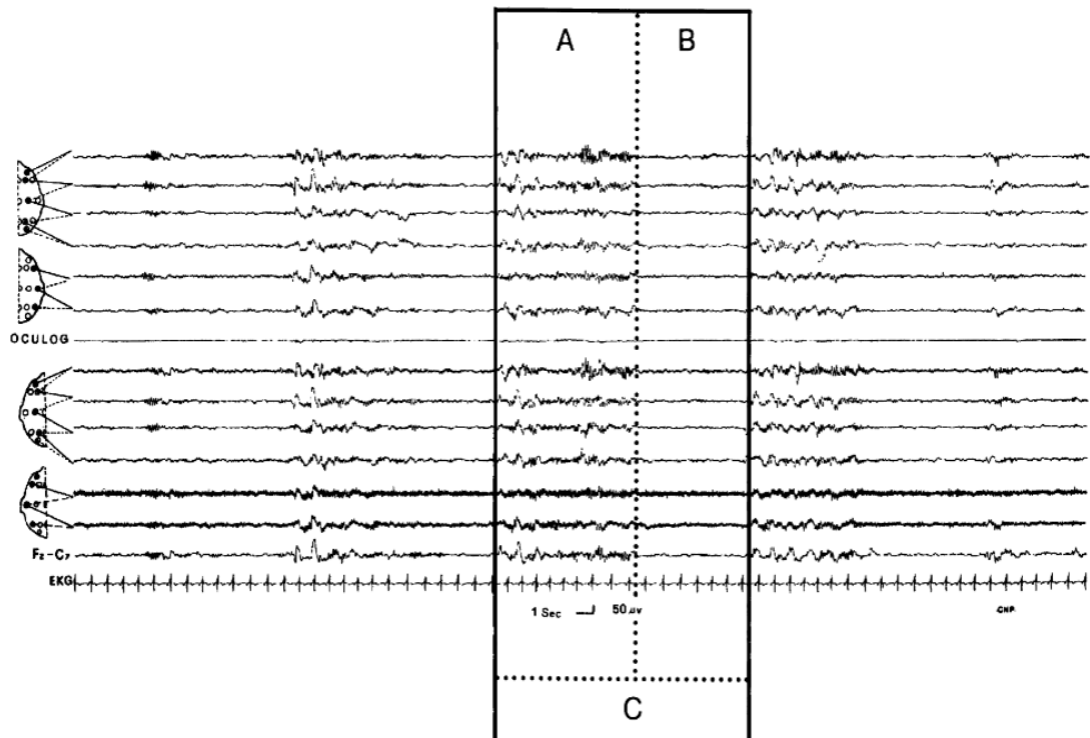


Figure 8: An example of cyclic alternating pattern (CAP) in sleep stage 2. The box outlines a CAP cycle (C) composed of a phase A (A) and the following phase B (B). Biopolar EEG derivations using international electrode placement; top 6 channels from top to bottom: FP2-F4, F4-C4, C4-P4, P4-O2, F8-T8, T8-T4

T4,T4-T6; bottom 7 channels from top to bottom: FP1-F3,F3-C3,C3-P3,P3-C1,F7-T3,T3-T5,F2-C2; OCULOG: Oculogram, EKG: Electrocardiogram.

Source: (Mario Giovanni Terzano et al., 2001)

According to (Mario Giovanni Terzano et al., 2001) the cyclic alternating pattern (CAP) is a periodic EEG activity of non-REM sleep. CAP is characterized by sequences of transient electrocortical events that are distinct from background EEG activity and recur at up to 1 min intervals.” Sleep pathophysiologies and disorders could be detected by the occurrence of CAP, but CAP sequence does not always implies the presence of a disorder. Into this succession of electrological events there are distinct patterns called CAP cycles which are divided into A and B phases. A CAP cycle always begins with phase A and afterwards follows B.

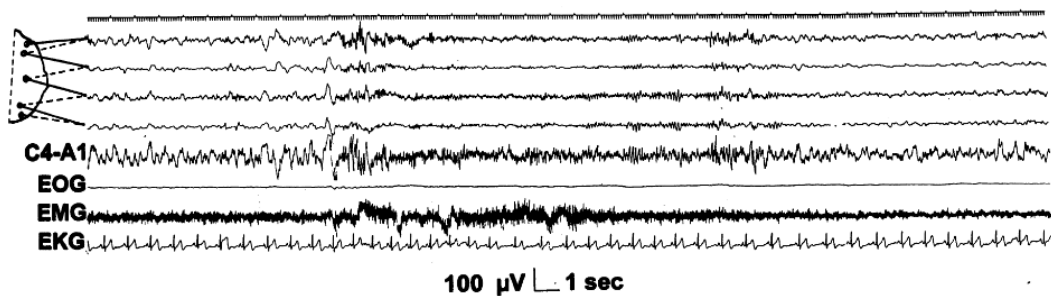


Figure 9: Arousal preceded and followed by sleep

Source: (Mario Giovanni Terzano et al., 2001)

EEG distinguished A-phase activities

During A-phases could be observed the following EEG events:

- Delta bursts
- Vertex sharp transients
- K-complex sequences with or without spindles
- Polyphasic bursts
- K-alpha
- Intermittent alpha
- EEG arousals

Delta bursts

In the frequency bandwidth a sequence of two or more waves with range from 0.5 to 4Hz and amplitude at least 1/3 higher than the background activity defines the appearance of Delta bursts. It is probable to be present deep in stage 2 and they are observed very often in stages 3 and 4. They are distinguished from the background activity of stages 3 and 4 as they exhibit a trend of lower frequency fig 12.

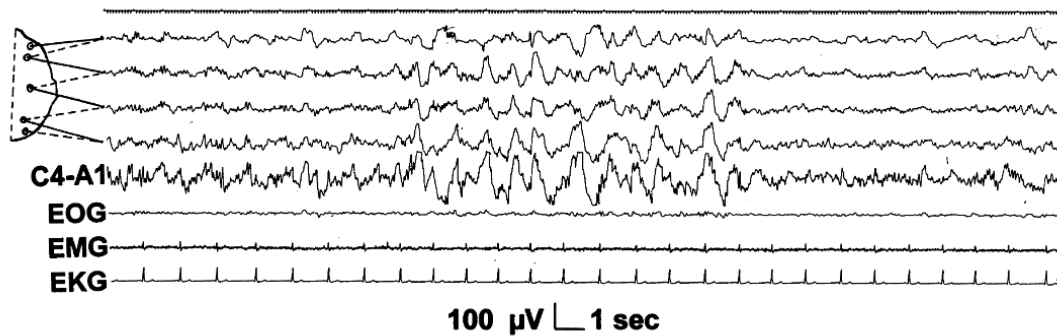


Figure 10: Delta burst in slow wave sleep. Top 4 channels: Bioplolar parasagittal EEG derivation of the right side similar to top 4 channels in fig.8 .C4-A1: C4 connects to left ear (A1); EOG: Electrooculogram; EMG: Electromyogram; EKG: Electrocardiogram.

Source: (Mario Giovanni Terzano et al., 2001)

Vertex sharp transients

Vertex sharp transients are EEG potentials which lasts from 50 to 250 ms, with mutable amplitude (up to 250 µV) and they are more intense at central vertex areas. At least two repetitive potentials in a sequence with duration at least two second form vertex sharp transients and they are often observed at the transition between stage 1 and stage 2.

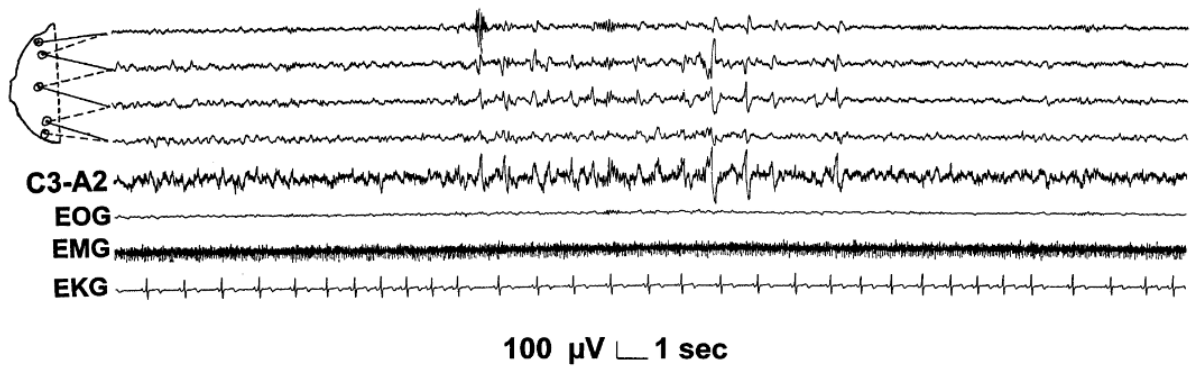


Figure 11: Sequence of vertex sharp transients during the transition from stage 1 to stage 2 sleep. Top 4 channels: Bipolar parasagittal EEG derivation on the left side similar to channels 8, 9, 10, 11 from above; C3-A2: C3 connected to right ear (A2).

Source: (Mario Giovanni Terzano et al., 2001)

K-Complexes sequences

A bi-/triphasic pattern composed of a preceding rapid negative component which is followed by a slower positive wave, is called K-Complexes. A sequence of at least two successive K-Complexes form a K-Complexes sequence. It is possible that a sleep spindles may intervene or follow a K-Complex. A K-complexes sequence lasts at least 2 seconds as each one K-complex lasts from 0.5 to 2 seconds. Sequences of K-complexes can be observed at 2, 3 and 4 sleep stages.

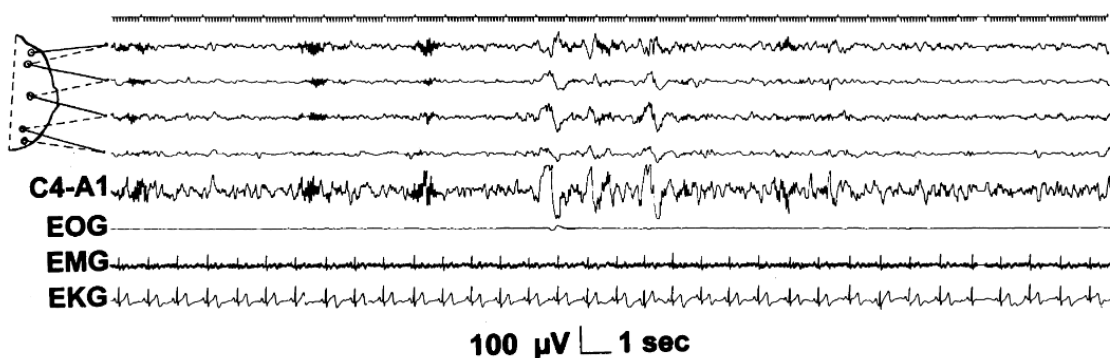


Figure 12: K-complex sequences associated with spindles in stage 2 sleep. Top 5 channels: EEG derivation as in Fig. 10

Source: (Mario Giovanni Terzano et al., 2001)

Polyphasic bursts

Clusters of high-voltage delta waves mixed with theta, alpha or beta rhythms, called Polyphasic Bursts. At least two delta peaks can be found in Polyphasic bursts. They are observed mainly in stage 2, especially before the onset of REM sleep but they can also be found stages 3 and 4.

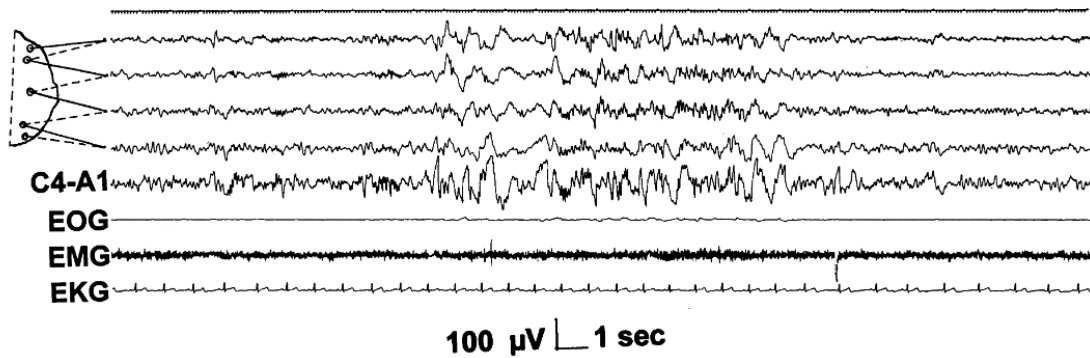


Figure 13: Polyphasic burst in stage 2 sleep. Top 5 channels: EEG derivation as in fig. 10

Source: (Mario Giovanni Terzano et al., 2001)

K-alpha

A K-complex instantly followed by an alpha burst shape a K-alpha and endures at least 2 seconds.

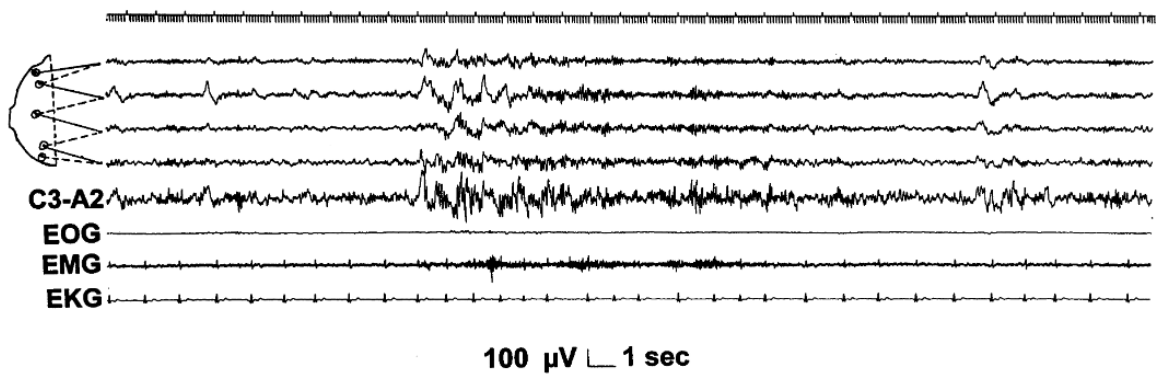


Figure 14: K-alpha complex in stage 2 sleep. Top 5 channels: EEG derivation as in fig.11.

Source: (Mario Giovanni Terzano et al., 2001)

Intermittent alpha

Another feature that is mostly recording from occipital areas is intermittent alpha and it is usually prominent from posterior derivations. At beginning of sleep, the rhythm of alpha, tends to spread anteriorly. Afterwards, at stage 1 it is divided into intermittent sequences and gradually disappears as the sleep proceeds. Alpha rhythm before it becomes extinct it is probable to present fluctuations such as raise in amplitude and reduction in frequency. Except from the beginning of sleep, intermittent alpha may occur during REM sleep and every time that stages happens during the whole length of sleep.

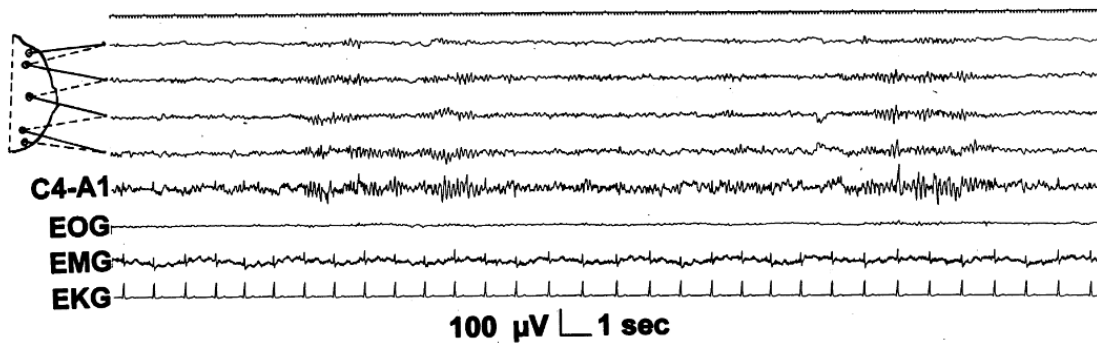


Figure 15: Intermittent alpha rhythm in stage 1 sleep.

Source: (Mario Giovanni Terzano et al., 2001)

EEG Arousals

Abrupt frequency changes from slower to faster rhythms (theta, alpha, beta, excluding spindles) that interfere sleep for time periods more than 3 seconds called EEG Arousals.

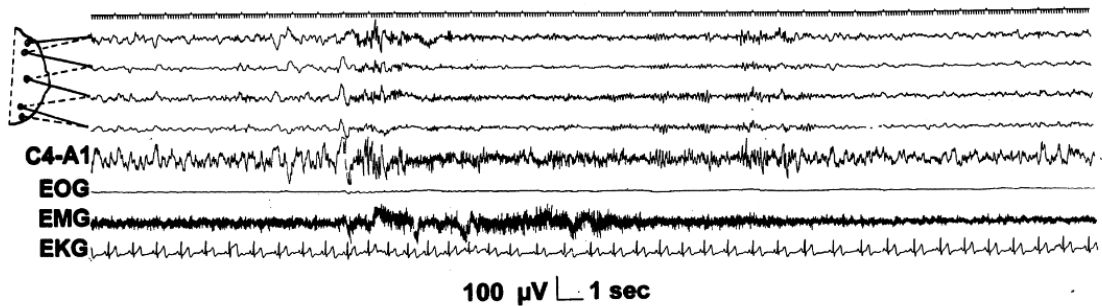


Figure 16: Arousal preceded and followed by sleep.

Source: (Mario Giovanni Terzano et al., 2001)

CAP & CAP Rate

Research on sleep microstructure have proven that the principle role of CAP in sleep is generation and disruption of sleep macrostructure (Halász, Terzano, Parrino, & Bódizs, 2004). As a consequent, CAP can be used to signify instability of sleep.

According to (Mario Giovanni Terzano & Parrino, 1993):

CAP: "Phasic NREM State Characterized by Controlled Ups and Downs of Vigilance, Muscle Tone, and Vegetative Activities"

CAP Rate: "Polysomnographic Parameter That Measures the Instability of Vigilance During NREM Sleep"

The normal values of CAP and as a consequence of CAP rate, diverse through different ages. As it is mentioned in (Mario Giovanni Terzano & Parrino, 1993), CAP rate is mostly present in very young or quite old ages as in newborns it approaches almost 100% and in normal people over 60 years old could reach the proportion of 50%. In mid ages, for instances in young adults Cap rate holds about 25% of total sleep and in middle aged about 38%.

These observations allow sleep experts to recognize the cases where a subject suffers from some kind of disorder. Intense deviation from the expected normal values of the proportion of CAP rate over total length of sleep could indicate the presence of disorder and lead to further investigation.

Except from the presence of disorder there several parameters that can affect CAP rate. Among them, noise can destabilize even normal individual's sleep, previous absence of sleep or medication. For instance, insomniac patients CAP rate could reach levels of over 60% but this level could drop dramatically by the use of hypnotic drugs.

Non-CAP (NCAP)

The absence of CAP pattern for more than one minute is characterized as Non Cap (NCAP) conditions. A secluded A-phase with no A phase before or after for more than a minute is characterized as Non-CAP

All the above, are parameters that a sleep expert has to take into consideration before reach to a diagnosis.

Parting of Two EEG Patterns of NREM Sleep

$$\frac{\text{CAP rate}}{\text{total CAP time}} \times 100; \approx 25-45\% \text{ (age-dependent range)}$$

$$\frac{\text{NCAP rate}}{\text{total NCAP time}} \times 100; \approx 55-75\% \text{ (age-dependent range)}$$

Figure 17: The percentage of CAP rate and NCAP rate over the over-night sleep

Source: (Mario Giovanni Terzano & Parrino, 1993)

2.4.3 A-Phase Morphology

Additional, experts classify A-phases into three sub-phases A1, A2, and A3 where some of them have quite different characteristics between them. Some features that are quite characteristic among them are the mutual proportion of high-voltage slow waves (EEG synchrony) and low-amplitude fast rhythms (EEG desynchrony) during whole A-phase.

A1 phase

The most prevalent EEG activity is EEG synchrony and when it occurs then EEG desynchrony resides at most 20% of the whole A-phase duration. Into A1-phase, K-complex sequences, vertex sharp transients, polyphasic bursts with 20% of EEG desynchrony are observed.

A2 phase

During this subtype EEG desynchrony covers 20-50% of the A-phase and slow and fast rhythms can be observed. Polyphasic bursts with more than 20% and less than 50% of EEG desynchrony are included in this subtype.

A3 phase

The most prevalent feature in EEG activity is rapid low-voltage rhythms with half of phase A covered by EEG desynchrony. Samples of this subtype could be among K-alpha, EEG arousals, and polyphasic bursts with half of EEG desynchrony. Additional, an event of a movement artifact though a CAP sequence is assigned to A3 phase.

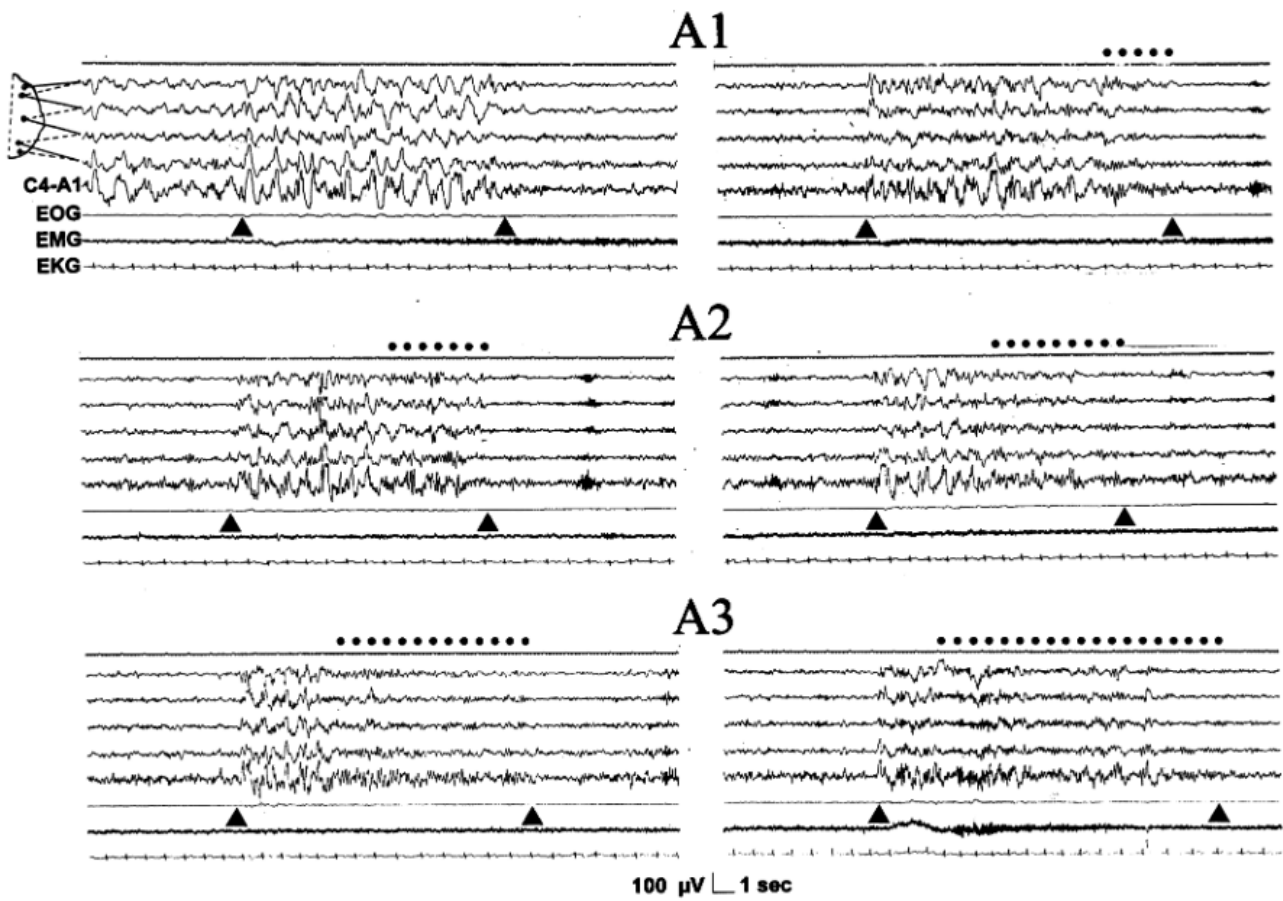


Figure 18: Phase A subtypes. The dotted spots indicate the fast low-amplitude portion of the phase A. EEG derivation as in fig. 12

Source: (Mario Giovanni Terzano et al., 2001)

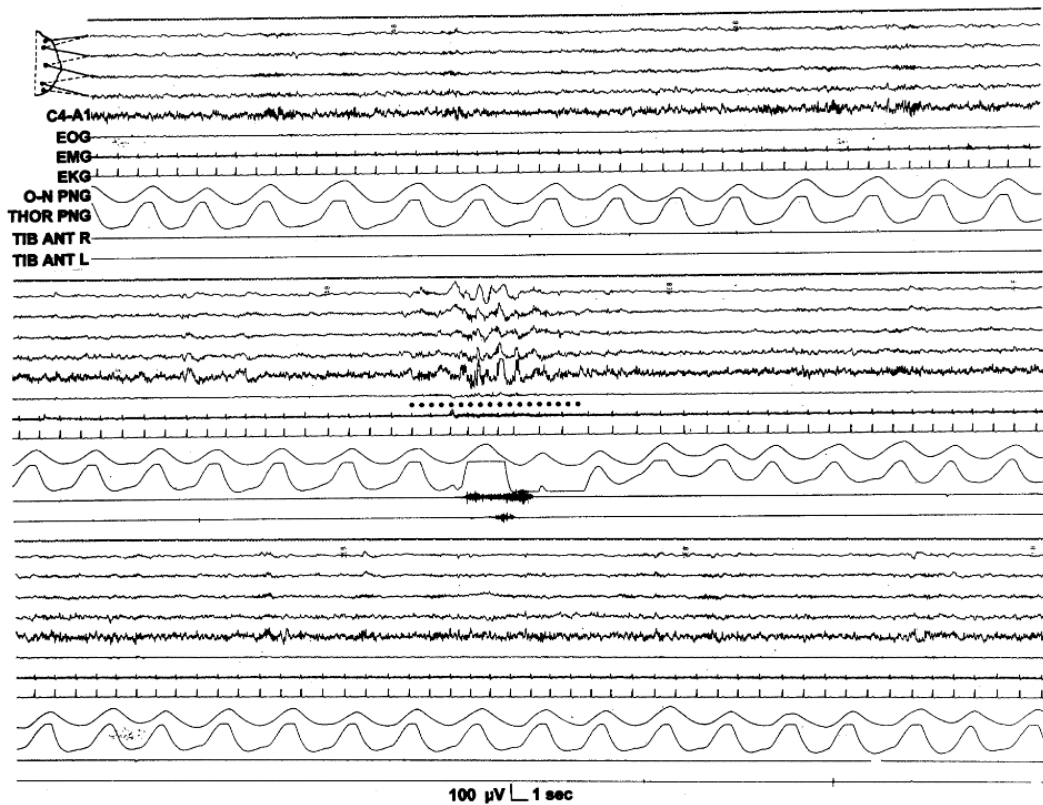


Figure 19: Isolated phase A black spot box preceded and followed by a low-voltage, mixed frequency EEG background for 60 s.

Source:(Mario Giovanni Terzano et al., 2001)

A-phase in REM sleep

Under normal conditions, it is not expected to come across A-phases presence during REM sleep. In the case that they exist they are formed from desynchronized events as a REM sleep's prominent feature is lack of synchronization. Instead it is common that A-phase precede REM sleep and end exactly before the beginning of REM stage. A-phase events in REM characterized by fast low-amplitude rhythms with average distance between them 3 to 4 minutes. However, the existence of a disorder could be highlighted by such events. For instance, sequence of A-phase events with intervals among them less than 1 minute can produce CAP sequence in REM sleep and that may indicate sleep apnea presence.

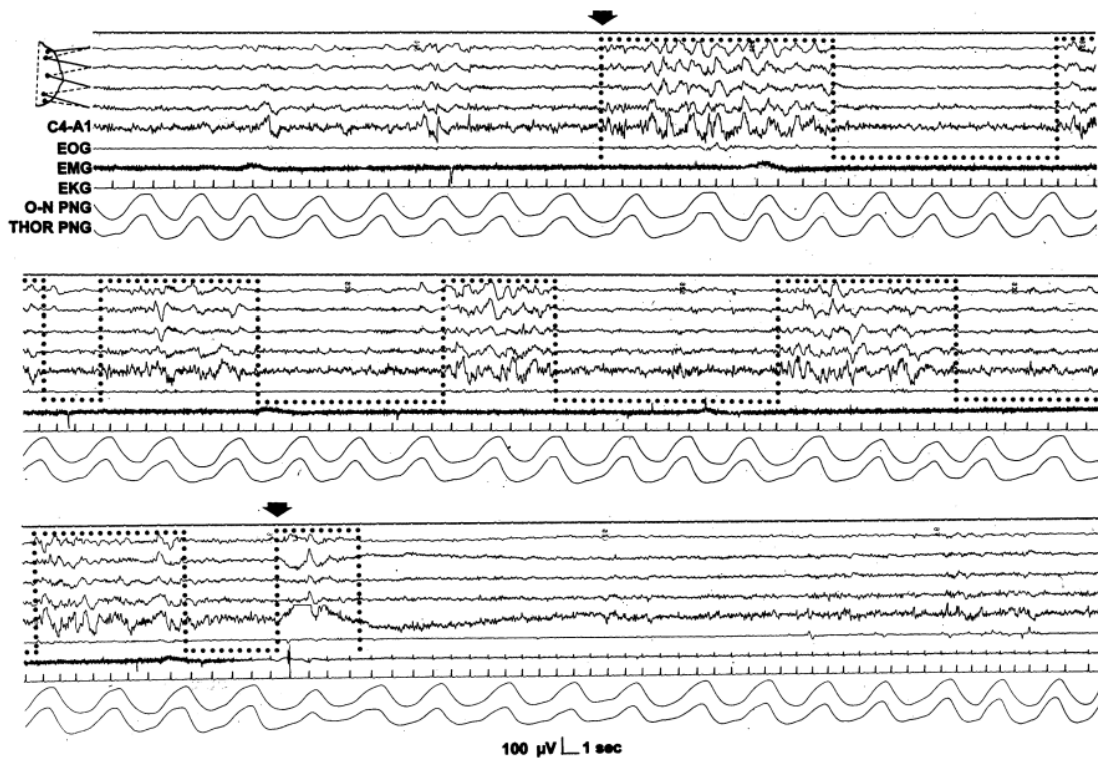


Figure 20: A CAP sequence (between black arrows) associated with a transition from non-REM to REM sleep. EEG derivation as in Fig. 12.

Automatic Sleep Staging (Computer assisted CAP scoring)

Manual Visual Analysis of polysomnography and CAP scoring from sleep experts is a slow procedure, requires a lot of time, high cost and specialization. These are the major obstacles of large scale application of CAP scoring with large datasets for research and for fast clinical results. Consequently, the use of computational services could help community to overpass such kind of drawbacks (Ferri et al., 2005).

3 Related work

3.1 Relative studies and scarcity

In this chapter, some papers related to this project are analyzed. It will be described the data, the leads, the features and the methods that were used in each project as well as it is mentioned the percentage accuracy of each work.

It is only the last years that Automatic sleep microstructure analysis started to attract scientific community's interest. As a consequence, there is a scarcity on respective studies. The following results imply indication of this state. Searching through some of the most renowned scientific publishers the queries ("sleep" AND "microstructure") and ("CAP" AND "sleep"), they returned:

	IEEE	ACM	SPRINGER
"sleep" AND "microstructure"	20	4	2
"CAP" AND "sleep"	40	2	12

Table 3: Number of papers in respective publisher

Among 15 relative technical studies only 3 use the same renowned Physionet database:

- a) "A machine learning model for identifying CAP in the sleeping brain" (Chindhade, Alshi, Bhatia, Dabhadkar, & Menon, 2018)
- b) " Automatic Detection of A phases for CAP classification" (Fabio Mendonça, Fred, Mostafa, Morgado-dias & Ravelo-garcía, 2018)
- c) "Automatic detection of cyclic alternating pattern" (Fábio Mendonça, Fred, Mostafa, Morgado-Dias, & Ravelo-García, 2018)

Mentioned that all 3 of them are recently conducted as they are released in 2018. The study "A machine learning model for identifying CAP in the sleeping brain" (Chindhade, Alshi, Bhatia, Dabhadkar, & Menon, 2018) used 16 healthy subjects. The EEG lead that was used is F2-F4. A binary logistic regression classifier was used to classify the EEG data into phase A and non-phase A. The maximum obtained accuracy was 58% with the optimum values of Stride and Window at 1276 and 1536 respectively.

(Fabio Mendonça et al., 2018), (Fábio Mendonça et al., 2018) used 14 subjects, 9 males and 5 females, both healthy and patients, with ages between 23-78 years old. The EEG leads that we used are C4-A1 or C3-A2. The feature set that was used in the analysis was consisted by 11 features, which were: The average power, standard variation, Shannon entropy, autocovariance, log-energy entropy, Teager energy operator (TEO) and Power Spectral Density (PSD) in the delta, theta, alpha, sigma and beta bands. In the first (Fabio Mendonça et al., 2018) work, linear discriminant analysis (LDA) was used and achieved a mean accuracy percentage of 75%. In the second (Fábio Mendonça et al., 2018) work, 9 classifiers were used: Logistic regression (LR) with 76% accuracy, Classification Tree (CT) with 70%, Ensemble of decision trees (ET) with 70%, SVM with 72%, Feed Forward NN (FFNN) with 79%, Cascade Forward NN (CFNN) with 76%, k-means Clustering (kMC) with 78%, kNN with 72% and Self organizing map (SOM) with 67% accuracy.

(Navona et al., 2002) employed 10 healthy male subjects, from 22 to 32 years old. The EEG leads that were used were F4-C4. They used five frequency band descriptors, one for each of the EEG leads and thresholds for classification. The maximum achieved accuracy was 77%.

Similar to (Navona et al., 2002) work is (Barcaro et al., 2004) but instead they used 5 male and 5 female subjects with the age ranging from 22 to 29 years old. Their approach achieved 83.5% accuracy.

Another approach was by (Mariani et al., 2011) , 8 healthy subjects were used, 4 males and 4 females, with ages between 23 and 45 years old. The EEG leads that were used were C3-A2 or C4-A1 sampled in 100Hz. The macrostructure stages of wake and REM sleep were excluded from the analysis. The following features were computed: band descriptors (low delta, high delta, theta, alpha, sigma and beta), Hjorth activity in the low

delta and high delta bands and lastly the differential variance of the EEG signal. The accuracy varied from 59.89% (sigma band) to 72.44% (differential EEG variance).

In (Mariani et al., 2012) 8 healthy subjects were used, 4 males and 4 females, with ages from 29 to 42 years old. The EEG leads that were used were C3-A2 or C4-A1, with 100 Hz sampling frequency. The wake and REM sleep stages were also excluded from the analysis. The features that were used were the five band descriptors (delta, theta, alpha, sigma and beta bands), Hjorth activity (3s windows) in the delta band and the EEG variance (1s windows). Four classifiers were used: the linear discriminant that got a mean accuracy of 84.9%, support vector machines (SVM) with 81.9%, adaptive boosting (AdaBoost) with 79.4% and a 3-layer artificial neural network with 81.5%.

(Mariani et al., 2010) in another work of theirs, used 4 healthy subjects. The EEG leads that they used were C3-A2 or C4-A1. The wake and REM sleep stages were excluded from the analysis. Six band descriptors (low delta, high delta, theta, alpha, sigma and beta), Hjorth activity in the low delta and high delta bands and the differential variance of the raw EEG signal were computed. A 3-layer artificial neural network was used for classification that achieved an average accuracy score equal to 81.55%.

Mendez et al. (2015) used 10 healthy subjects, 5 males and 5 females, with ages from 25 to 45 years old. The leads that were used were C3 or C4 in 100Hz or 128 Hz sample rate. The k nearest neighbors (kNN) classifier was used to find the best features or set of features in order to get the higher accuracy. The onset accuracy ranged from 85-91% and the offset accuracy ranged from 79-86%.

(Largo, Munteanu, & Rosa, 2005), used the fast discrete wavelet transform algorithm (DWT) with sampling frequency at 128 Hz. The features that were used were the five band descriptors (delta, theta, alpha, sigma and beta) but they also separated the delta band (0.5-4 Hz) into three sub-bands (0.5-1; 1-2; 2-4 Hz). The concordance that was achieved by the genetic algorithm in this project was 81.1%

In (A. C. Rosa, Parrino, & Terzano, 1999) were used 4 healthy subjects, 2 males and 2 females, with a mean age of 43.75 +/- 2.1 years. The EEG lead C4-A1 was used. The well-known band descriptors were also used in this approach (delta, theta, alpha and sigma activities). For classification, they are using a state machine rule based decision system. The mean correctness that was achieved was 89.8%

(Karimzadeh, Seraj, Boostani, & Torabi-Nami, 2015) used 8 subjects, 4 healthy and 4 patients. The C4-A1 EEG leads were used, with signal sampling at 512 Hz. The following conventional features were used in the analysis: Frequency band features, Hjorth activity for the delta band and differential variance. Three types of classifiers were used in this work: Linear Discriminant Analysis (LDA), Support Vector Machines (SVM) and K-Nearest Neighbors (KNN).

3.2 Feature proposals

In some papers, the researchers tried many different features or set of features and concluded that a smaller number of specific features could also work in a faster and more efficient way. In this section we are presenting each paper's proposals of significant features.

(Mariani et al., 2011) computed nine descriptors, the six band descriptors (low delta, high delta, theta, alpha, sigma and beta), Hjorth activity in the low delta and high delta bands as well as the differential variance of the EEG signal. By using ROC curve they found out that both band descriptors, hjorth activity and the EEG differential variance are all capable descriptors for obtaining good accuracies. Band descriptor mean accuracies were: 59.90% in sigma band, 63.01% in beta band, 64.41% in alpha band, 66.49% in theta band, 68.73% in low delta band, 69.19% in high delta band. The Hjorth activities' mean accuracies were: 70.74% in low delta activity and 71.53% in high delta activity. Finally, the EEG differential variance had an accuracy of 72.44%. (Mariani et al., 2011) also proposes the elimination of the low delta descriptor and the low delta activity, as they could be replaced with the respective in the high delta band. Alternatively, useful could be a single band descriptor and a single activity descriptor for the whole delta band (0.5-4Hz). (Hjorth activity was the best feature.)

(Mendez et al., 2016) used the following features: mean, standard deviation (std), skewness, kurtosis, energy, Lempel–Ziv complexity, delta band power, theta band power, alpha band power, beta band power, sample entropy, Tsallis entropy and fractal dimension. But the features that frequently exist in the best feature sets were the energy, the beta band and the delta band, in this order.

Mendoça et al. (2018) created a list of features order respective to sequential feature selection (SFS) that they applied to their model, the list is the following:

Features	Order
PSD Beta	1
Average Power	2
PSD Theta	3
Teager Energy Operator	4
Standard Variation	5
PSD Alpha	6
PSD Sigma	7
Shannon Entropy	8
Log-energy Entropy	9
Autocovariance	10
PSD Delta	11

Table 4: Features ordered respective to the SFS selection

Source: (Fabio Mendonça et al., 2018)

As mentioned in the paper, using the 3 first components achieved the best results with variance of 78%.

(Karimzadeh et al., 2015) proposed the following features that are not used in the state-of-the-art implementations: Shannon entropy, Spectral entropy, Sample entropy, Tsallis entropy, Higuchi Fractal Dimension (HDF), Kolmogorov entropy and band features with Kolmogorov entropy. Tables II and III show each feature and the respective accuracy values for each classifier, both for healthy subjects and patients.

4 Materials and Methods

4.1 Physionet Sleep CAP database

The dataset employed for this research acquired from Physionet CAP Sleep database and it consists of signals recorded at the Sleep Disorders Center of the Ospedale Maggiore of Parma in Italy. The overall number of polysomnographic recordings in the Cap Sleep Database is 108 and they are classified into 16 recordings from normal subjects as well as from patient subjects with the following disorders: 2 subjects with bruxism, 9 with insomnia, 5 with Narcolepsy, 40 with Nocturnal frontal lobe epilepsy, 10 with Periodic leg movements, 22 with REM behavior disorder and 4 with Sleep-disordered breathing. The format of the files is edf (European Data Format) and consists of 3 EEG channels (F3 or F4, C3 or C4 and O1 or O2, referred to A1 or A2) or more, 2 Electrooculography (EOG) channels, Electromyography (EMG) of the submentalis muscle, bilateral anterior tibial EMG, respiration signals and Electrocardiography (EKG or ECF). Physionet CAP sleep database provide additional information about the gender and age of the subjects as well as additional traces in agreement with the 10-20 international system (Fp1-F3, F3-C3, C3-P3, P3-O1 and/or Fp2-F4, F4-C4, C4-P4, P4-O2).

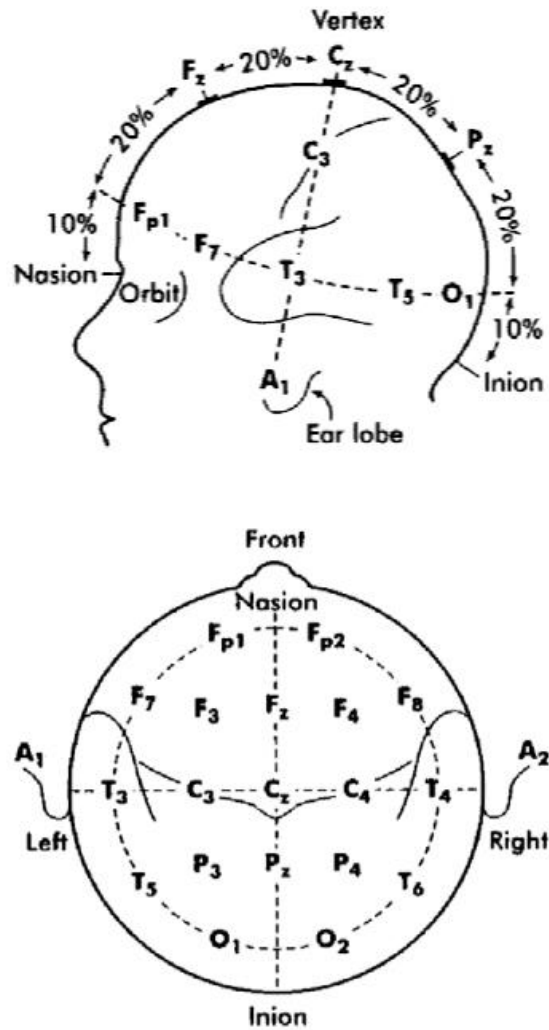


Figure 21: Electrode positions according to the 10-20 system. Odd numbered electrodes are positioned over the left hemisphere, whereas even numbered ones are placed over the right hemisphere. Fp=frontopolar, F=frontal, C=central, T=temporal, O=occipital, A=auricular.

Furthermore, annotations files, from sleep experts educated at Sleep Center, are provided. Those files are in .txt format and contain information about:

- Sleep stages (W=wake, S1-S4=sleep stages, R=REM, MT=body movements)
- Body position (Left, Right, Prone, or Supine)
- Time of the day [hh:mm:ss]
- Event (the A-phase type or the sleep stage)
- Duration (seconds)
- Location (the signal(s) in which the event can be observed)

The scoring process for sleep stage is in agreement with (A Rechtschaffen, A. Kales., 1968) and the respective for sleep microstructure in agreement with the Atlas of rules of (Mario Giovanni Terzano et al., 2001).

Dataset

For the purpose of the current research, were employed only normal subjects and three traces C4-P4, F4-C4, C4-A1. Those traces are among the most common in literature as they are considered to contain bigger amount of information than others. Moreover, 6 subjects were chosen due to lack of those traces in all normal subjects of the database.

Preprocessing

Initially, the EEG recordings for all selected subjects were sampled at 512Hz, they were resampled at 100Hz sampling frequency and they were filtered by a band pass filter from 0.3 to 40Hz with the programming environment Mat-lab (The Mathworks Inc.). A CAP cycle lasts from 2 to 60 seconds, for this reason windows of 2 seconds (the minimum CAP cycle length) were extracted. Windows of less than 2 seconds aborted as a choice because 2 is the shortest length of CAP phase and windows not more than 2 seconds selected in order to capture more abrupt changes in shortest sale. Additional, these windows are overlapping with a step of 1 second in order to have much more instances and to extract insights in a more microscopic scale.

The whole dataset including all 6 full night sleep recordings is composed by 180624 instances where 159787 are out of A-phase events and 20837 belong to A-phase types. In the second type of classification that conducted in this study the 20837 instances are divided into 2336 instances of A-phase onsets, 16165 instances of events clearly into A-phase and respective to onsets 2336 instances of A-phase offsets. The previous analysis implies that around the 88% of instances of the whole dataset is compiled by out of A-phase instances which means indicates great class imbalance in the dataset. In order to overcome the class imbalance obstacle an oversampling technique called SMOTE was applied (Chawla, Bowyer, Hall, & Kegelmeyer, 2002) with the Tomek link method to clean data and eliminate noise (Tomek Ivan 1992).

4.2 Features

A feature set containing the most common features (diverse metrics, complexity and frequency measures) in the literature utilized to extract meaningful insights from the dataset. This feature set applied to each window of 2 seconds with 1 second overlapping and a new dataset with the values of the features emerged. The metrics include:

- Power Spectral Densities (PSD) (low delta, high delta, theta, alpha, sigma, beta)
- Average Power
- Standard Deviation
- Kurtosis
- Skewness
- Log-energy entropy
- Shannon entropy
- Sample entropy
- Tsallis entropy
- Higuchi Fractal dimensions
- Hjorth parameters: activity, mobility, complexity
- Peak number

Power Spectral Densities

Power spectral densities include the delta, theta, alpha, beta-gamma bands of frequencies. Each one of them range in different frequency range and they are useful to define quantitatively diverse states of the brain according to the power of frequency of the EEG activity (Myers, Li, & Curry, 2017). Different densities correspond to different brain states which characterize respective sleep states and as a consequent they are useful to classify them.

Low-delta band (ranging 0.5-2 Hz)

High-delta band (ranging 2-4 Hz)

Theta band (ranging 4-8 Hz)

Alpha band (ranging 8-12 Hz)

Sigma band (ranging 12-15 Hz)

Beta band (ranging 15-25 Hz)

For instance, delta waves are prominent characteristic of A1-phase, rapid with high frequency EEG waves which belong to high alpha or beta bands indicate phases A2 and A3. For every single window and each band, after applying Fourier Transform, turning from time domain into frequency domain, the average energy in the frequency range is computed. Below are presented many of the complexity measures:

Standard deviation

$$\text{std} = \left(\frac{1}{N} \sum_{n=1}^N (s(n) - \bar{s})^2 \right)^{\frac{1}{2}}$$

Skewness

$$\text{skewness} = \frac{\frac{1}{N} \sum_{n=1}^N (s(n) - \bar{s})^3}{\left(\frac{1}{N} \sum_{n=1}^N (s(n) - \bar{s})^2 \right)^{\frac{3}{2}}}$$

Kurtosis

$$\text{kurtosis} = \frac{\frac{1}{N} \sum_{n=1}^N (s(n) - \bar{s})^4}{\left(\frac{1}{N} \sum_{n=1}^N (s(n) - \bar{s})^2\right)^2} - 3$$

Sample entropy (SampEn)

In time series (such as signals) SampEn provides insights about the underlying complexity of the process by measuring the regularity of them (Moorman, 2018). Suppose we have the patterns among data that remain similar for m observations, the logarithmic probability of these patterns to remain similar on the next incremental comparisons with longer patterns is employed to quantify the regularity. The higher the values of Sample entropy are the higher the complexity in the data is as well as it implies higher randomness which makes the data less predictable. Consider a N length time series $y = [x(1), x(2), \dots, x(N)]$. Let's define $N-m+1$ sub-sequences of the form $y_m(i) = [x(i), x(i+1), \dots, x(i+(m-1))]$, with constant m . The likelihood that two subsequences match for m points $B_i^m(r)$ and the probability of match for $m+1$ points $A_i^{m+1}(r)$, where r is the tolerance for accepting matches, give the SampEn, defined as the average of these probabilities over the $N-m+1$ subsequences:

$$\text{SampEn}(m, r) = \left| -\ln \left(\frac{A^{m+1}(r)}{B^m(r)} \right) \right|$$

For the purposes of this experiment SampEn was computed for $m=2$ and $m=5$ (as it was observed high variance for both values) and $r=0.25$. The time window on which SampEn was applied was 2 seconds which means 200 instances and according to (Moorman, 2018) for instances greater than 100 SampEn is largely independent of record length.

Higuchi Fractal dimensions

Higuchi Fractal dimensions feature was calculated respective to (An, Time, We, & The, 1988) study. As most of the features it was computed on 200 instances and the mathematical formula which it was based on is:

$$L_m(k) = \frac{1}{k} \cdot \left[\left(\sum_{i=1}^{\lfloor \frac{N-m}{k} \rfloor} |X(m + i \cdot k) - x(m + (i - 1) \cdot k)| \right) \cdot \frac{N - 1}{\lfloor \frac{N-m}{k} \rfloor \cdot k} \right]$$

X represents the time series and N the total number of instances in X. The sum (after normalization) of absolute differences in ordinates of pairs of points with distance k is symbolized by $L_m(k)$. $L(k)$ symbolize the average of the k values $L_m(k)$ for $m=1, 2, \dots, k_{\max}$ and least squares linear best-fitting procedure computes the value of fractal dimension, and the angular coefficient of the linear regression of the log-log graph of $L(k)$ versus k, with $k= 1, 2, \dots, k_{\max}$. In this experiment based on (Klonowski, 2007), the value for k_{\max} was 8.

Tsallis entropy

Tsallis entropy emerge from the following formula:

$$Ts(q) = \frac{\sum_{j=1}^N (p_f(j) - p_f(j)^q)}{q - 1}$$

q: can be positive

It represents the probability distribution of the signal and according to (Dandan Zhang et al., 2011). Tsallis entropy is the same as Shannon entropy when $q \rightarrow 1$. According to (Mendez et al., 2016) two values for selected in order to acquire information specific for rare and frequent events.

Shannon entropy

With entropy metrics we can measure uncertainty. When it comes to EEG signals it signifies the level of chaos in a system (Dalglish et al., 2007). It is non linear and it attempts to calculate the degree of randomness in time series (McCranie et al., 2011).

Let X be a set of finite discrete random variables $X = \{ x_1, x_2, \dots, x_m \}$, $x_i \in \mathbb{R}^d$, Shannon entropy, $H(X)$, is defined as (Kannathal, Choo, Acharya, & Sadasivan, 2005):

$$H(X) = -c \sum_{i=0}^m p(x_i) \ln p(x_i)$$

Log-energy entropy

$$H_{\text{LogEn}}(x) = - \sum_{i=0}^{N-1} (\log_2(p_i(x)))^2$$

Hjorth Parameters

Hjorth Parameters include activity, mobility and complexity. Respectively they are calculated by the following formulas:

$$\text{Activity} = \text{var}(x(t))$$

$$\text{Mobility} = \sqrt{\frac{\text{Activity} \left(\frac{dx(t)}{dt} \right)}{\text{Activity}(x(t))}}$$

$$\text{Complexity} = \frac{\text{Mobility} \left(\frac{dx(t)}{dt} \right)}{\text{Mobility}(x(t))}$$

Activity is translated as the power of the signal, mobility as the mean frequency and complexity brings into comparison the signal with the pure sine wave and returns how similar they are (Hamida, Ahmed, & Penzel, 2016).

Time sequence

Additional, in order to capture sequence characteristic of EEG behavior during time, 4 previous and 4 next instances added to every instance. In other words, these features provide with insights for 8 seconds before and 8 second after each instance as every row corresponds to 2 seconds.

5 Results

5.1 Experimental Approaches

The contribution of this survey is the introduction of three approaches. First the time sequence feature which add insight about the fluctuation of the signal's values through time. Second, the train-test on different classes, train only on instances out of A-phase versus into A-phase but during testing those two classes include the onsets and offsets instances as described in the following chapter. Third, the grouping of the four classes out of A-phase, A-phase onset, into A-phase, A-phase offset into two classes out of A-phase with A-phase offset and into A-phase with A-phase offset.

Obstacles

It is really hard to compare diverse models and for this reason there is a scarcity on such reviews. Some reasons are the following:

- Different datasets
- Diverse PSG channels

- Various evaluation methods
- Different expert's scoring

Below are analyzed the results from the combination of the experimental approaches. The feature set were extracted from each one of the three traces C4-P4, F4-C4, C4-A1. For the evaluation of the results a 10 fold cross validation technique were used so all the indices (accuracy, sensitivity, specificity and AUC) are averaged. The term sensitivity in this study represents the number of instances that predicted and actually belong to A-phase over the number of all instances that truly belong to A-phase, the true positive rate of predicting A-phases. Respectively, specificity, depicts the number of instances that predicted and actually belong to non A-phase events over the number of all instances that truly belong to non A-phase events.

5.2 Experimental questions and answers

- Which classes to use even for the binary classification of Non A-phase versus A-phase events. To be clear, for the specific type of classification we could define 4 types of events, out of A-phase, A-phase onset, into an A-phase, A-phase offset. The question is what grouping of two groups out of the 4 classes to choose.

Grouping on testing	Accuracy	Sensitivity	Specificity	AUC
Non A-phase/offset vs A-phase/onset	0.91	0.74	0.914	0.59
Non A-phase vs rest	0.897	0.74	0.9	0.58
A-phase vs rest	0.918	0.64	0.925	0.59
Non A-phase/onset vs A-phase/offset	0.9	0.65	0.91	0.577

Table 5: Evaluating metrics values for various groupings under 900 estimators of Extra trees classifier and training only on Non A-phase versus A-phase classes but testing on respective grouping.

- How the model would operate if we train it using the two classes that contain only totally out of A-phase and totally into A-phase respectively. But test it in different classes, for

instance, the two classes would contain out of A-phase and onsets (first class) versus into A-phase and offsets (second class). Fig. 27 (above) presents the results from different train/test class sets and fig.28 (below) presents the results from train/test on same class sets. It is obviously that train/test on different class sets perform better, especially in sensitivity metric.

Grouping on training and testing same	Accuracy	Sensitivity	Specificity	AUC
Non A-phase/offset vs A-phase/onset	0.899	0.6	0.91	0.587
Non A-phase vs rest	0.886	0.59	0.9	0.58
A-phase vs rest	0.91	0.57	0.92	0.56
Non A-phase/onset vs A-phase/offset	0.897	0.57	0.9	0.556

Table 6: Evaluating metrics values for various groupings under 900 estimators of Extra trees classifier. Train and test applied on the same grouping.

- Class imbalance is really a problem? Below are presented the results with the best hyper parameter and best grouping on testing but additional an oversampling technique was applied to the dataset. The technique called SMOTE employs Tomek links method for cleaning the data and remove the noise (Tomek Ivan 1992).

Grouping on testing	Accuracy	Sensitivity	Specificity	AUC
Non A-phase/offset vs A-phase/onset	0.88	0.46	0.94	0.72

Table 7: Results using oversampling technique

Fig.29 The results from best model including the oversampling technic Smote with Tomek Links.

It seems that oversampling did not help to further improve results as the sensitivity dropped from 75% to 46%.

After several experiments with all the combination of the modes that the above question produce, the best results are presented:

- (I) Classification between Non A-phase and A-phase. No oversampling technique were used. The results are accuracy 0.91%, sensitivity 0.75%, specificity 0.914. In the specific experiment applied a technique where train and test applied on different classes. To

clarify, the model were trained only in two events. Those that are totally out of A-phase and totally into an A-phase leaving aside events that belong in onsets or offsets but they were tested in the following two classes:

- a. The first class contains events out of A-phase and events that belong to offsets.
- b. The second class contains events that are into an A-phase and events that belong to the onsets.

The classifier employed to achieve the highest outcomes was Extra trees ensemble classifier with hyper parameter of the estimator variable equal to 900.

(II) Classification between Non A-phase and A-phase. In this experiment we trained and test the model in the same set of classes, without oversampling technique:

- a. The first class contains events out of A-phase and events that belong to offsets.
- b. The second class contains events that are into an A-phase and events that belong to the onsets.

The produced results are accuracy 0.91%, sensitivity 0.70%, specificity 0.92.

We can observe a decrease in sensitivity than method (I).

Training only in out of A-phase events versus A-phase, operates better but it wasn't a surprise because of the nature of the data in the classes. This means, that offsets possess quite similar characteristics with out of A-phase events as well as onsets possess quite similar features with into A-phase events.

5.3 Hyper parameters

Estimators	Accuracy	Sensitivity	Specificity
120 estimators	0.91	0.724	0.915
150 estimators	0.89	0.73	0.9
500 estimators	0.91	0.745	0.914
700 estimators	0.91	0.745	0.914
850 estimators	0.91	0.7499	0.914
900 estimators	0.91	0.74	0.914
950 estimators	0.91	0.7498	0.914
1000 estimators	0.91	0.746	0.914
1300 estimators	0.91	0.748	0.914
1500 estimators	0.897	0.75	0.9

Table 8: Evaluation metrics for various values of estimator’s parameters of Extra trees ensemble model. For the value of 900 estimators the model returned the combination of highest values.

5.4 Semi-automated model

Another experimental approach is an assisted classification. This approach includes the ground truth of sleep stages S1, S2, S3, REM and the model possesses previous knowledge of the current sleep stages. As a result the model has to be trained and classify every instance if it belongs to Non A-phase or A-phase. In this direction the model achieved classification accuracy 92%, sensitivity 83% and specificity 92%.

5.5 Comparing results with similar studies

Comparing the results of this experiment (best results from method (I)) with the results of relative studies over the same dataset from Physionet sleep Cap database:

	Accuracy % A-phase vs Non A-phase	Model/Method	Sensitivity %	Specificity %	AUC
(I)	58 %	Logistic Regression	-	-	-
(II)	79 %	Feed-forward neural network	76 %	80 %	77 %
(III)	75 %	LDA	78 %	74 %	-
This study	91 %	Extra trees classifier (900 estimators)	74 %	91.4 %	59 %

Table 9: Comparing results with similar studies

- (I) "A machine learning model for identifying CAP in the sleeping brain" (Chindhade, Alshi, Bhatia, Dabhadkar, & Menon, 2018)
- (II) " Automatic Detection of A phases for CAP classification" (Fabio Mendonça, Fred, Mostafa, Morgado-dias, & Ravelo-garcía, 2018)
- (III) "Automatic detection of cyclic alternating pattern" (Fábio Mendonça, Fred, Mostafa, Morgado-Dias, & Ravelo-García, 2018).

6 Conclusions and future work

The sleep microstructure analysis constitutes a problem with wide range of parameters. For this reason, it demands a lot of work and there are many aspects of the problem that have to be taken into consideration. For instances, throughout literature there is a diversity on the datasets on which the various experiments are applied, as well as there are many different sleep experts who apply the annotations (variety of sleep experts means different results due to subjectiveness factor). In addition, through literature, we can observe that in different datasets, best accuracy is achieved by diverse classifiers and methods. This could mean that sleep records from various subjects may be quite different. As a consequence, for further advances in the domain, it could be beneficiary the use of some baseline datasets. On those datasets, experts could compare the diverse state of the art models and every experiment would be more measurable.

Manual scoring is a quite demanding task (as it includes scoring on signals from a whole night sleep) and entails the subjective factor of every scorer. For those reasons, there is a high proportion of scoring disagreement between experts when analyzing the same records. This percentage ranges between 69% to 78% according to (Agostinho C Rosa & Lopes, 2006). Until present, the various studies focus on developing models to imitate the sleep expert's annotations including the subjective factor. This means that models ignore a portion of objectivity, of ground truth. From this hypothesis derive two new addresses. The first one is to try to extend our models by developing technics to enclose the subjective factor of contextually scorer. The second, is to try to direct link records and relative metrics on them, with sleep subjects either healthy or patient. To clarify what I mean, in a way, there exists three poles, the first is the records, the second the sleep standards and rules and the third is the sleep expert (accompanied with his subjectivity). The second pole, the sleep standards and rules, function as intermediate between the other two poles. The main idea of this direction is to bypass the intermediate pole and directly link the rest two. This could be feasible through advanced unsupervised technics which would try to specify patterns in both poles and discover connections between them.

An other direction could be to an automated sequence of classifications. For instance, instead of classifying whole dataset with one model into an extended class set like { stage 1, stage 2, stage 3, stage 4, REM stage, Non A-phase, A1 phase onset, into A1 phase, A1

phase offset, A2 phase onset, into A2 phase, A2 phase offset, A3 phase onset, into A3 phase, A3 phase offset }, which would be ideally if we could achieve very high accuracy, we could apply a sequence of classification where each classification would be based in the previous classification. Firstly, we could train a state of the art model to classify into sleep stages s1, s2, s3, s4, REM, afterwards uses the outcome from the previous classification as feature for the next classification between non A-phases and A-phases. Then, again use the outcome from the previous classifications as feature for the next and classify between the A-phases types (A1, A2, A3).

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APPENDIX

Machine learning python code

```
import pandas as pd

import numpy as np

from sklearn.metrics import accuracy_score

from sklearn import metrics

from sklearn.ensemble import ExtraTreesClassifier

#import imblearn

#from imblearn.over_sampling import SMOTE

#from imblearn.under_sampling import TomekLinks

#from imblearn.combine import SMOTETomek

#from imblearn.under_sampling import ClusterCentroids

#from imblearn.under_sampling import RandomUnderSampler

#from xgboost import XGBClassifier

''' Load data'''

data = pd.read_csv('MLdataset')

''' Remove the feature stges from the semi automated model '''

data=data.drop(['stages'],axis=1)
```

```
''' Built the time sequence feature '''
```

```
limit = 4
```

```
step = len(data.columns)-2
```

```
data11 = pd.DataFrame(data.iloc[limit-1:-limit-1,:-2].values) # 1 before
```

```
data12 = pd.DataFrame(data.iloc[limit+1:-limit+1,:-2].values,columns=list(range(len(data.columns)-1,len(data.columns)-1+step))) # 1 front
```

```
data21 = pd.DataFrame(data.iloc[limit-2:-limit-2,:-2].values,columns=list(range(len(data.columns)-1+step,len(data.columns)-1+2*step))) # 2 before
```

```
data22 = pd.DataFrame(data.iloc[limit+2,:-2].values,columns=list(range(len(data.columns)-1+2*step,len(data.columns)-1+3*step))) # 2 front
```

```
data31 = pd.DataFrame(data.iloc[limit-2:-limit-2,:-2].values,columns=list(range(len(data.columns)-1+3*step,len(data.columns)-1+4*step))) # 3 before
```

```
data32 = pd.DataFrame(data.iloc[limit+2,:-2].values,columns=list(range(len(data.columns)-1+4*step,len(data.columns)-1+5*step))) # 3 front
```

```
data=data.iloc[limit:-limit,:-2].join([data11,data12,data21,data22,
```

```
data31,data32,data.iloc[limit:-limit,-2:]])
```

```
''' Encode the stage feature from the semi automated model '''
```

```
#import category_encoders as ce
```

```
#
```

```
#encoder = ce.OneHotEncoder(cols=['stages'])
```

```
#data = encoder.fit_transform(data)
```

```

""" Fill Nan values with zero """

data = data.replace(np.inf, 0)

data = data.replace(np.nan, 0)

""" Define the classifier """

clf1 = ExtraTreesClassifier(n_estimators=900, max_depth=300,
                            min_samples_split=2, random_state=0, verbose=3, n_jobs=4)

""" Start the loop for the 10 fold cross validation """

sensitivity=[]

specificity=[]

AUC=[]

accuracy=[]

prev=0

for limit in range(round(len(data.targets)/10),len(data.targets),round(len(data.targets)/10)):

    """ Define train and test for every fold """

    X_train = data.drop(list(range(prev,limit)),axis=0)

    data1=X_train

    y_train = data.drop(list(range(prev,limit)),axis=0)

    y_train = y_train.targets

    data1.targets=y_train

    xtest = data[prev:limit]

    xtest = xtest[xtest.columns[:-1]]

```

```
ytest = data[prev:limit]
```

```
ytest = ytest.targets
```

```
''' Define the train classes on Non A-phase(c0) vs A-phase(c2)'''
```

```
c0=data1.loc[data1['targets'] == 'c0']
```

```
#c1=data1.loc[data1['targets'] == 'c1']
```

```
c=data1.loc[data1['targets'] == 'c2']
```

```
#c3=data1.loc[data1['targets'] == 'c3']
```

```
data1 = pd.concat([c0,c])
```

```
data1 = data1.sample(frac=1)
```

```
X_train = data1[data1.columns[:-1]]
```

```
y_train = data1.targets
```

```
nl=[]
```

```
for i in y_train:
```

```
    if i != 'c0':
```

```
        nl.append('c')
```

```
    else:
```

```
        nl.append('c0')
```

```
y_train=nl
```

```
''' Grouping Non A-phase with A-phase offsets vs A-phase with A-phase onsets'''
```

```
nl=[]
```

```

for i in ytest:
    if i == 'c0':
        nl.append('c0')
    elif i == 'c1':
        nl.append('c')
    elif i == 'c2':
        nl.append('c')
    elif i == 'c3':
        nl.append('c0')
ytest=nl

prev=limit

''' Train the classifier'''
clf1.fit(X_train, y_train)

''' Oversampling technique SMOTE '''
# smt = SMOTETomek(ratio='auto')
# X_smt, y_smt = smt.fit_sample(X_train, y_train)
#
# clf1.fit(X_smt, y_smt)

''' Predict '''
y_pred=clf1.predict(xtest)

```

```

""" Compute evaluating metrics accuracy, sensitivity, specificity, AUC"""
accuracy.append(accuracy_score(ytest, y_pred))
# print('accuracy',accuracy_score(ytest, y_pred))
##s=pd.Series(y_predclf1)
##s.unique()

confusion = metrics.confusion_matrix(ytest, y_pred,labels=['c','c0'])
print(confusion)

##pd.DataFrame(ytest).groupby(0).size()

TP = confusion[0][0]
FP = confusion[0][1]
FN = confusion[1][0]
TN = confusion[1][1]

sens = TP/(TP+FN)
spec = TN/(TN+FP)

sensitivity.append(sens)
specificity.append(spec)

from sklearn.metrics import roc_auc_score

```

```

nl=[]

for i in ytest:
    if i != 'c0':
        nl.append(1)
    else:
        nl.append(0)

ytrue=nl

nl=[]

for i in y_pred:
    if i != 'c0':
        nl.append(1)
    else:
        nl.append(0)

y_scores=nl

auc = roc_auc_score(ytrue, y_scores)

AUC.append(auc)

confusion = metrics.confusion_matrix(ytrue, y_scores,labels=[1,0])

import statistics as st

print('accuracy',st.mean(accuracy))

print('sensitivity',st.mean(sensitivity))

print('specificity',st.mean(specificity))

```

```
print('AUC',st.mean(AUC))
```