APPROVAL SHEET

Title of Thesis: Inferring Autonomic Arousals using Periodic Leg Movements during Sleep

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2018

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ABSTRACT

Title of Thesis: INFERRING AUTONOMIC AROUSALS USING PERIODIC LEG MOVEMENTS DURING SLEEP

Vikramaditya Battina, M.S. Computer Science, 2018

Thesis directed by: Dr. Nilanjan Banerjee, Associate Professor
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Autonomic arousals are closely associated with an increase in heart rate and systemic blood pressure. Frequent arousals might result in cognitive and cardiovascular complications in addition to sleep disorders. To detect these autonomic arousals, subjects undergo polysomnographic(PSG) recording in a sleep lab which is cumbersome and expensive. In this thesis, we study the following hypothesis: certain periodic leg movements during sleep are correlated with significant autonomic arousals. We propose a machine learning technique to predict autonomic arousals from characteristic leg movements. Using a custom designed ankle band our system can detect autonomic arousals with an accuracy of 74%. Our system is the first to use leg movement as a marker for autonomic arousals and be used as an in-home technique to study these arousals.

Inferring Autonomic Arousals using Periodic Leg Movements during Sleep

by

VIKRAMADITYA BATTINA

Thesis submitted to the Faculty of the Graduate School
of the University of Maryland in partial fulfillment
of the requirements for the degree of
Computer Science
2018

ACKNOWLEDGMENT

I would first like to thank my thesis advisor, Dr. Nilanjan Banerjee, Associate Professor at the University of Maryland Baltimore County for his continuous support and motivation while doing research. He steered me in the right direction when I got stuck in any situation.

I would also like to thank sleep analysis expert Dr. Richard P Allen for providing data set, and helping me to define my thesis problem statement and, I would like to thank Dr. Ting Zhu and Dr. Nirmalya Roy for accepting my request and being in the thesis committee.

Finally, I express deepest gratitude to my parents, sister, brother-in-law, and all my friends especially Chetan Sai Kumar, Nikhil Kumar, Manogna Teja and Rashmi Prava Patro for their continuous support and motivation throughout my stay in UMBC.

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Chapter 1

INTRODUCTION

1.1 Sleep and its Significance

The quantity and quality of sleep is significant for one's physical and mental health while it also impacts the quality of life. Sleepiness while doing tasks which need continuous alertness, such as driving, is as dangerous as consuming alcohol during that task. Almost 20 percent of car crashes is due to sleepiness (Medicine *et al.* 2006). While we are asleep, we might be in the REM sleep stage or in the non-REM sleep stage. REM sleep alternates with non-REM sleep, which forms a sleep cycle; there would be 4-5 sleep cycles during our sleep and each sleep cycle lasts for 90 minutes. The Brain behaves utterly different in different sleep stages. During non-REM, the brain would be in an idle state, consuming less energy. Breathing and heart rate are quite regular in this stage. A lower metabolic rate in non-REM sleep helps the brain to repair membranes damaged while one is awake. Brain activity in REM sleep is similar to that in the awake state. REM sleep aids in the regulation of mood and learning. The amount of time you spend in REM sleep reduces with age. The neural activity in REM sleep stimulates the external environment for neural development.

1.2 Autonomic Nervous System

The human nervous system is divided into Central Nervous System(CNS) and Peripheral Nervous System(PNS). The CNS comprises of the brain and spinal cord, whereas the PNS includes nerves from the brain and spinal cord. PNS, which carries nerve signals to CNS, acts like a bus between CNS and the rest of the body. PNS consists of sensory nerves and motor nerves. Sensory nerves transmit nerve impulses to CNS, and from there to effector organs. Motor nerves are divided into the Somatic Nervous System(SNS), and the Autonomous Nervous system(ANS). SNS controls the voluntary actions like moving hands and legs. ANS controls the involuntary actions like heart rate, breathing, blood pressure, body temperature, metabolism, digestion, urination, glands secretion and sexual response. Within ANS, sympathetic nervous system and parasympathetic nervous system are present. The sympathetic nervous system will get activated in a flight or fight situation; for example, when the body gets hot, it secretes sweat to cool the body. The parasympathetic nervous system will perform involuntary actions while the body is at rest; for example, digestion. The sympathetic nervous system and the parasympathetic nervous system complement each other; for instance, the parasympathetic nervous system decreases the heart rate, and the sympathetic nervous system increases the heart rate.

1.3 Period Leg Movements in Sleep

Periodic Leg Movements (PLM) are at least four in number, which have a duration of 0.5 - 10 seconds, with periodicity length of 5 - 90 seconds (Zucconi *et al.* 2006). In general, these PLM occur as a rhythmic extension of the big toe and dorsiflexion of the ankle with occasional flexion at the knee and hip (Pennestri *et al.* 2013a). PLM can occur in awake or sleep, PLM which occur in sleep is referred to PLMS in rest of the document. PLMS are not only limited to RLS and chronic insomnia, but also present in various other

sleep disorders (Coleman Phd, Pollak, & Weitzman). PLMS is also a common problem in people with hypertension, though they do not have any sleep disorder (ESPINAR-SIERRA, VELA-BUENO, & LUQUE-OTERO). (Bastuji & Garca-Larrea) found PLMS and sleep fragmentation are strongly correlated. Sleep fragmentation results in the poor quality of sleep, resulting in daytime sleepiness which affects their quality of life. PLMS is higher in insomniac patients with high nocturnal blood pressure. Medication for PLMS might decrease nocturnal blood pressure (Sieminski & Partinen 2016). In an elderly male population with a higher frequency of PLMSI 30, cardiovascular disease is present with 25 percent confidence (Koo *et al.* 2011). PLMS is a good indicator of cardiovascular disease in patients with kidney disease. PLMSI, number of PLMS per hour, is less in patients who underwent kidney transplantation (LINDNER *et al.*). A study conducted on 382 Restless Leg Syndrome(RLS) patients reports that patients with frequent PLMS (PLMS per hour greater than 35) have the development of Atrial Fibrillation. After taking the treatment for PLMS, there is a reduction in the progression of Atrial Fibrillation (Mirza *et al.* 2013b). In another study on 584 RLS patients, patients with PLMS index higher than 35 have left ventricular hypertrophy (LVH), although they have a similar left ventricular ejection fraction (Mirza *et al.* 2013a).

1.4 Autonomic Arousals

(Bartels *et al.* 2016) defines autonomic arousal (autonomic activation) as an activation of the autonomic nervous system, specifically the sympathetic nervous system, indicated by a rise in blood pressure and heart rate. Most of the PLMS are associated with AASM defined arousal as an abrupt shift in EEG signals and autonomic arousals. (Winkelman 1999) found PLMS are associated with autonomic arousal, even in the absence of AASM-defined arousal, but heart rate elevation was higher when the PLMS were associated with

AASM-defined arousal. Association of PLMS and autonomic arousal might cause daytime hypertension and can lead to cardiovascular related diseases; this explains the reason why PLMS patients are having cardiovascular related diseases as described in section 1.3. Changes in heart rate and blood pressure during PLMS, will be helpful in analyzing the increased risk of cardiovascular related diseases in an elderly. (Gosselin *et al.* 2003).

1.5 Goals and Contribution

As described in section 1.2, 1.4 sleep is very important to lead a quality and healthy life. PLMS associated with autonomic arousals might be a useful marker for potential cardiovascular diseases. To get diagnosed, patients should undergo Polysomnography. Polysomnography(PSG) studies happen in sleep labs or clinics, which are expensive, each night might cost around 700 - 2000 USD, and patients might feel difficult to sleep in an unfamiliar environment, and during PSG several electrodes (approx 27) are attached to his/her scalp, chest, leg and fingertip which might be strange for patients to sleep comfortably.

In this thesis, We study the characteristics of PLMS which are associated with autonomic arousals vs. which are not, and presented an analysis of machine learning classification algorithm to predict PLMS which are associated with autonomic arousal. Four patients underwent PSG recording for one complete night, autonomic arousals were determined from their heart rate derived using EKG data from PSG recording, experts visually score PLMS and leg movements' data collected using custom wearable multisensor leg band called RestEaze band described in section 3.1.

With a system combining of multisensor PLM detection by (Zheng 2018), and prediction of PLMS associated with autonomic arousal, we can diagnose sleep disorders with PLMS at an affordable cost.

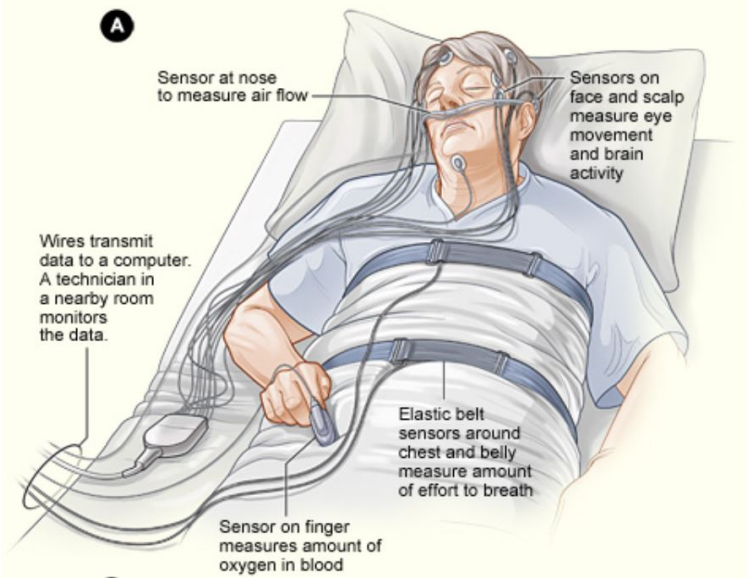


FIG. 1.1: Polysomnography setup of a patient

Retrieved from: (Expert Sleep Medicine)

Chapter 2

RELATED WORK AND BACKGROUND

2.1 Sensors

2.1.1 IMU Sensor

An Inertial Measurement Unit (IMU) (Ahmad *et al.* 2013) is used to measure acceleration, rotation and angular velocity. IMU usually contains Accelerometer, Gyroscope and Magnetometer. The accelerometer is used to measure acceleration and gravitational force; the accelerometer would have up to 3 degrees of freedom(DOF) defined on X, Y and Z axes. A gyroscope is used for measuring angular velocity and rotation. It has up to three degrees of freedom. The magnetometer is an optional sensor in IMU, but generally is used to improve the accuracy of IMU. It has up to three DOF. With the combination of those three sensors, we have up to 9 degrees of freedom. One possible disadvantage of having Magnometer in IMU is that, it would add disturbance when being used in a ferromagnetic environment. Gyroscope would have long run drift issues, and accelerometer is sensitive to fast rotation. Using Kalman filters, we can remove drift issues and sensitivities of Accelerometer and Gyroscope respectively. We need to consider various parameters while choosing the IMU sensor for an application. Below are the few parameters we need to think of:

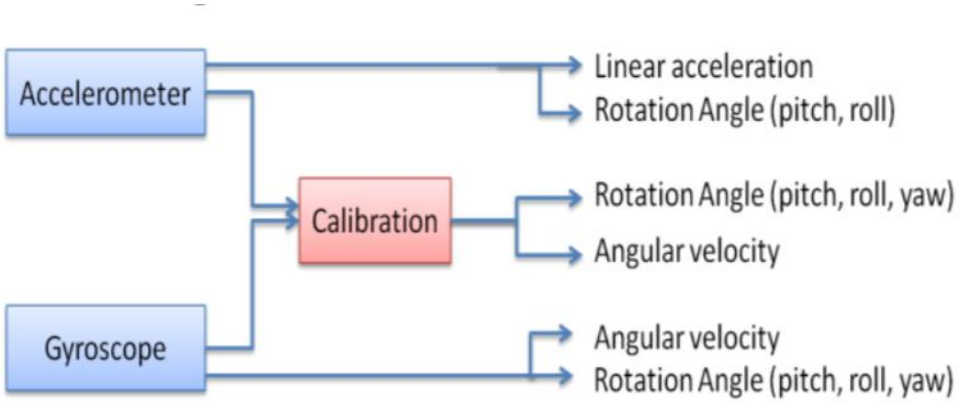


FIG. 2.1: An IMU sensor with accelerometer and gyroscope

Image credit: (Norhafizan *et al.* 2013)

1. Size of IMU sensor, if you are using mobile devices, the sensor needs to be small, whereas in the aircraft, its size doesn't matter.

2. Sampling rate, it is defined as the number of sensor measurements given per sec. For high response rate applications like vehicle navigation, we might need sampling rate up to 200Hz, for other low response rate applications like human movements' detection, 50hz is good enough.

3. DOF is another vital parameter to consider. For position tracking applications, we might need 6 DOF for two sensors and 9 DOF for three sensors; and for movement detection, we might need 6 or 3 DOF.

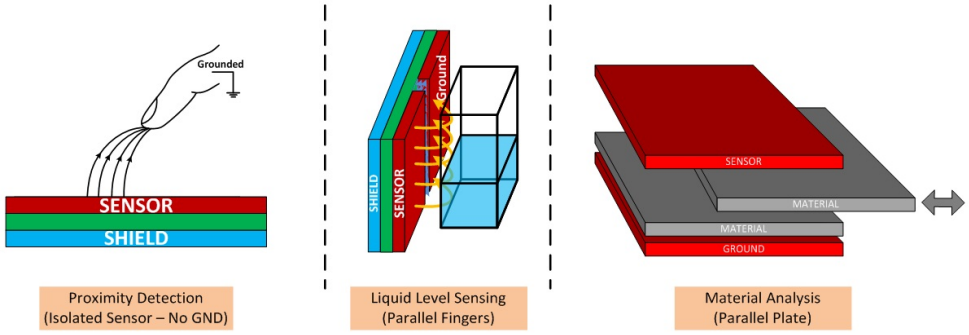


FIG. 2.2: Various Topologies of a capacitive sensor with its applications

Retrieved from: (Wang11 2014)

2.1.2 Capacitive Sensing

A general form of a capacitive sensor consists of two plates separated by a distance, which achieves a capacitance given by equation 2.1

$$C = \frac{\epsilon A}{d} \tag{2.1}$$

From the above equation, it is very clear that capacitance can vary based on area, medium and distance between plates. These are basic parameters for most of the capacitive sensors.

Its low power consumption and temperature insensitivity made it widely acceptable in biomedical and telemetry applications, and its high sensitive nature made a good fit for human gesture recognition, liquid level recognition and material analysis. There are different types of capacitive sensor topologies based on its application, which are described in the figure 2.2.

Human gesture recognition works on the principle of fringe capacitance. Our hand or finger acts as a ground electrode, so when it approaches closer to the capacitive sensor, fringe electric fields stray and cause a change in capacitance. As hand reaches sensor plate,

capacitance increases non-linearly. Insulating shield on the back of the plates helps in reducing electromagnetic inferences.

2.2 PLMS with autonomic arousal

(Siddiqui *et al.* 2007) conducted a study on 8 RLS patients with periodic limb movements disorder. Patients underwent overnight PSG along with continuous monitoring of blood pressure and heart rate. Patients were asked to perform voluntary leg movements which acted as a control for PLMS. Rise in blood pressure(BP) and heart rate(HR) is observed after periodic leg movements when compared to blood pressure and heart rate after voluntary leg movements. PLM in wakefulness, PLMS associated with cortical arousal, PLMS not associated with cortical arousal, and respiratory-related limb movements were specifically focused in this study.

A placebo-controlled and double-blinded study was carried out by (Cassel *et al.* 2016) on 89 idiopathic RLS patients, to assess the relation of periodic limb movements and nocturnal blood pressure(BP). Patients underwent two overnight PSG recordings. In the first night, patients were adapted to sleep in the sleep centers, and (Cassel *et al.* 2016) used first night patients' data if second-night data got corrupted. In this study, if the slope of linear regression line on five consecutive heartbeats ≥ 2.5 then it is considered as a BP elevation. A large number of systolic BP elevations and diastolic BP elevations were observed with periodic limb movements.

(Pennestri *et al.* 2013b) did a research in which they compared the increase in HR and BP associated with PLMS, between healthy subjects and RLS patients. This analysis revealed the rise in HR and BP in both the groups, but that change was significant in RLS patients when compared to that in healthy patients.

(Pennestri *et al.* 2007) conducted a study to assess changes in HR and BP occurred

during PLMS, with or without EEG arousal, in RLS patients. They observed that changes in BP were more significant in PMLS with EEG arousal when compared to that in PLMS without EEG arousal. They also concluded that these variations in BP during sleep might contribute to cardiovascular diseases in RLS patients.

In all the above studies, they didn't consider the classification of PLMS associated with and without autonomic arousals. To address this, we performed a machine learning analysis in this study.

Chapter 3

SYSTEM DESIGN

Patients underwent an overnight sleep study in the sleep lab at Johns Hopkins hospital with the following procedure as described in this chapter.

We can broadly divide the system design of this study into the following components:

1. RestEaze System
2. PSG Recording

3.1 RestEaze System

RestEaze system is an in-home sleep monitoring system. Nowadays, in order to diagnose sleep disorders like RLS and insomnia, too much revenue is spent by people on each sleep lab study. In the sleep lab, patients might feel uncomfortable as several electrodes are being attached to their body. The patient has to sleep in a strange environment, which is a kind of discomfort for him/her. RestEaze system provides sleep analysis in an affordable, convenient and comfortable way. RestEaze system identifies the leg movements and the sleep position using which, it gives sleep quality indices such as sleep position detection,

PLMS per hour, general leg movements during sleep(GLMs) per hour and sleep efficiency value.

As described in figure 3.1, there are four components in RestEaze system which are listed below:

1. Wearable Ankle Bands
2. Mobile Application
3. Web Dashboard
4. Backend Analysis

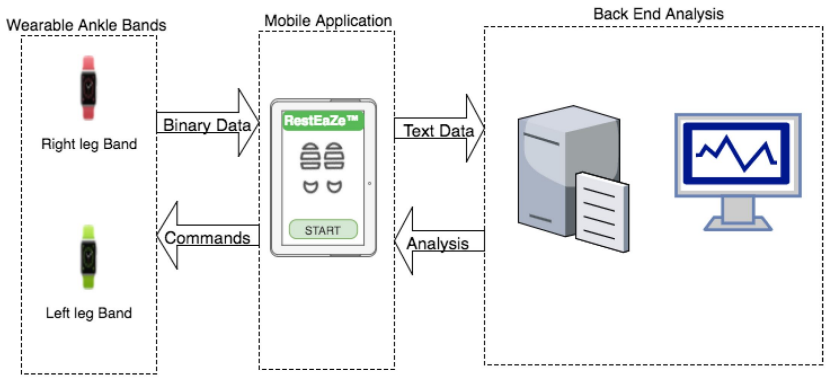


FIG. 3.1: Architecture of RestEaze System

This Image is reprinted from (Utgikar 2017)

3.1.1 Wearable Ankle Bands

Patients can wear this ankle band on left/right leg or both the legs. This wearable band is a multisensor band with three capacitive sensors and an IMU sensor with a three-axis accelerometer, a three-axis gyroscope, and a three-axis magnetometer. The band also has

a Bluetooth module and a flash chip to store data. Using Bluetooth module, it can receive commands and send data to any Bluetooth enabled devices like smartphones, tablets and PCs. These bands are manufactured with different sizes for kids and adults. When there

FIG. 3.2: RestEaze band

is flexion in the foot, the distance between capacitive sensors and the foot gets increased which causes a change in capacitance. The change in capacitance helps to identify the PLM, as most of the PLMs are associated with flexions in the foot. Accelerometer and Gyroscope helps to identify general leg movements and in finding the orientation of leg movements which in turn, aids in sleep position detection. To get an accurate sensor reading, one has to wear ankle band properly.

This band sends leg movement data at 25Hz and it would either work in streaming mode or caching mode. In streaming mode, it sends data to the smartphone application, and in caching mode, it stores the data in flash chip and can be further uploaded to a smartphone application. Before every use, the band has to be calibrated to get an accurate

reading by placing it on a flat surface.

3.1.2 Mobile Application

RestEaze mobile application has calibrate, start and stop buttons to interact with the band. Calibrate button helps to calibrate the capacitive sensors. Start button creates a new session and that session ends when we hit the stop button. The metadata file for each session has calibration offset values, start time and stop time values. In RestEaze mobile application, we can set the application to work either in streaming mode or caching mode. RestEaze mobile application also provides statistics of sleep during a single night or over a period of nights with varying trends. Statistics would be like sleep start time, sleep end time, PLMS per hour, General Leg movements during sleep(GMLS) per hour, sleep efficiency value and, a chart on GLMS and PLMS.

3.1.3 Web Dashboard

Web dashboard provides keen insights on a person's sleep. It offers advanced analysis of leg movements and more number of metrics with great visualization.

3.1.4 Backend Analysis

Uploaded data from the smartphone application is stored in the form of text files. Every user's data is stored in a folder named with his/her user id. The data will be captured in a file with that date, which is then stored in his/her folder on a daily basis and, there will be a separate file for each band. This data is further processed to obtain sleep analysis as shown in the figure.

Session Creation Each session will be saved in different files. For example, when a RestEaze mobile application starts recording from the night till morning, which is the usual

sleep time for a person. Then, raw data of the leg band is stored in two files because data is stored based on the dates as explained in the introduction of this section. Though data is stored in different files, they will have the same session id. The session creation pass extracts each session, making it easy for analysis.

Interpolation While sending data from the band to RestEaze mobile application, some of the Bluetooth packets might get dropped due to connection issues or might be due to data integration issues. So, effective sampling rate might not be 25 Hz. Linear interpolation on missing values will give 25Hz sampling rate. It would be easy to handle data on left leg band and right leg band simultaneously.

3.2 RestEaze in Sleep Study

There is a small variation in the RestEaze band in the in-home setting and in the sleep lab study as shown in figure 3.4. In sleep lab study, RestEaze is used along with PSG so that we can get a very appropriate synchronization between RestEaze sensor signals and PSG signals like EEG, EKG and EMG otherwise, analysis might be erroneous. Synchronization based on timestamps or video, might be prone to error. So same physical signal is inserted in both the RestEaze band and PSG. This physical signal is a pseudo-random square wave. As there is same signal in the RestEaze band and PSG, synchronization between RestEaze and PSG signals will be easy and accurate. However, to compare the entire signal, it would take more time, as data for overnight sleep would be huge. So we only compare five continuous square waves to do synchronization.

3.3 PSG Recording

In the sleep lab, patients underwent overnight PSG recording, which included eight electroencephalogram(EEG) electrodes (M1, C3, C4, M2, O1, O2, F3, F4), (upper, lower left, lower right) chin electromyogram(EMG), peripheral capillary oxygen saturation(Spo2), two electrooculography(EOG) electrodes (E1, E2), left and right leg EMG on tibialis, Electrocardiography(EKG) for heart rate, respiratory-related signals, snoring, left and right leg sync signal which is described in 3.2

In above signals, we are interested in EKG signal to measure autonomic arousals, EEG signals for sleep stage scoring, EMG on tibialis for PLM scoring and, sync signal for synchronization of RestEaze and PSG signals. The sync signal is recorded at 1000Hz and remaining EEG, EKG and EMG signals are recorded at 500Hz.

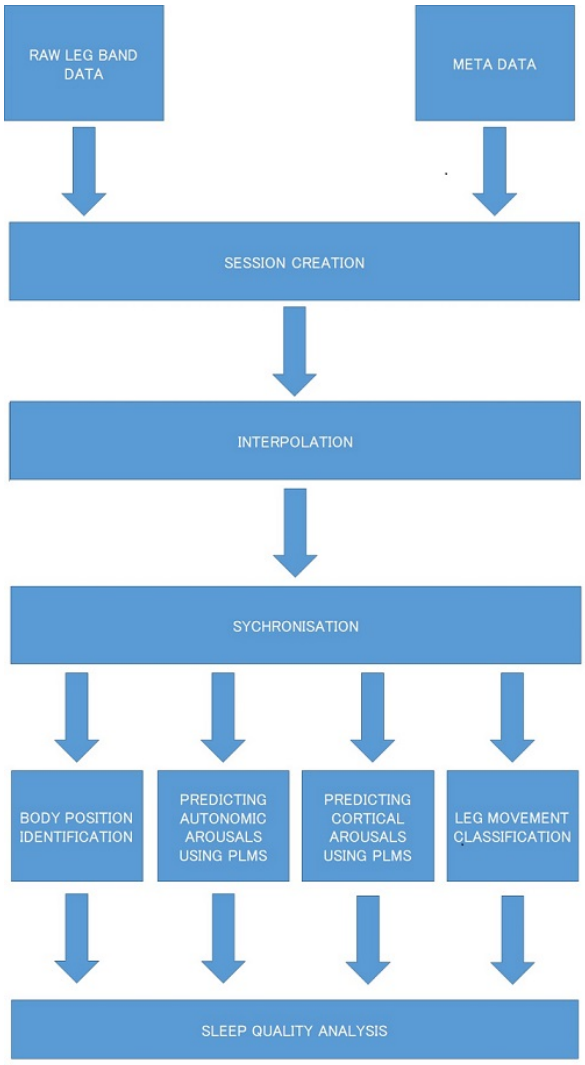


FIG. 3.3: Various Steps in RestEaze Backend Analysis

FIG. 3.4: Sleep lab RestEaze band with Sync Signal

Chapter 4

DATA DESCRIPTION AND PREPARATION

In previous chapter, we illustrated an experimental system design on how we are collecting data for our research. In this chapter, we will describe the dataset used in this research and its preparation in terms of

1. Subjects with their sleep disorder.
2. How we scored PLM, sleep stages and autonomic arousals.
3. Preprocessing on the data of RestEaze wearable band.

4.1 Extraction of Data From EDF

At the end of the previous chapter, we said all PSG data is captured in the form of EDF files, and the RestEaze band data in the form of CSV for each leg. Using (Teunis van Beelen) code, we extracted 'pandas' (python supported package) compatible csv files (header.csv, signals.csv, data.csv) from a patient's EDF file.

Header.csv file contains patient id, description of the patient, date and time of the data collection, and duration of the data collection. Signals.csv has the information of signals like EEG, EKG, EMG and Spo2 collected during PSG. Each of these signals has metadata such as index of that signal in the data.csv file, sampling frequency, units of signal, physical

Subject	Age	Sex	Disorder
PED002	16	female	ADHD
RZ0015	60	female	insomnia
RZ0016	69	female	RLS
RZ0017	35	female	RLS

Table 4.1: Subject information

limits and digital limits of that signal. Each column in the data.csv file has actual signal data.

4.2 Subjects

Four patients underwent one overnight sleep study as discussed in chapter 3. The doctor at Johns Hopkins selected regular patients who are getting treated. Patients RZ0015, RZ0016, and RZ0017 are adult patients, and PED002 is a pediatric patient. As discussed in chapter 1, PLM are associated with sleep disorder like RLS, insomnia and ADHD which these patients have. RZ0016, RZ0017 has RLS, RZ0015 has insomnia, and the PED002 patient has ADHD. All of these patients are female. We collected data for various other patients as well. We are unable to use those data for multiple reasons such as data is missing and capacitive railing issues of the capacitive sensor. The complete details of these patients are shown in table 4.1

Patient ID	Awake	REM sleep	Non REM sleep	Total PLM
PED002	142	19	100	261
RZ0015	10	7	13	30
RZ0016	190	60	109	359
RZ0017	93	9	119	221

Table 4.2: Number of PLMs across all sleep stages

4.3 PLM scoring

A Well-trained technician in sleep lab scored all PLM. He/She used multiple data sources like video capturing during sleep, EMG signal in PSG, and accelerometer sensor values in RestEaze wearable band to score these PLM.

Table 4.2 provides details on the number of PLMs scored for each subject, across all sleep stages. In this research, we are considering PLMs which occurred in non-REM sleep only. From the table 4.2, we can observe that RLS and ADHD patients have more number of leg movements compared to that of insomniac patient. Figure 4.1 shows the distribution of PLM.

4.4 Sleep Stages Scoring

Sleep stages are calculated using EEG signal by a well-trained technician. He/She took 30-sec window for the EEG signal and classified into various sleep stages such as awake, REM sleep, non-REM sleep stage1, non-REM sleep stage2, and non-REM sleep stage3. In our analysis, as we focused only on non-REM sleep, all different stages in non-REM sleep are combined into non-REM sleep stage. Using the information of these sleep

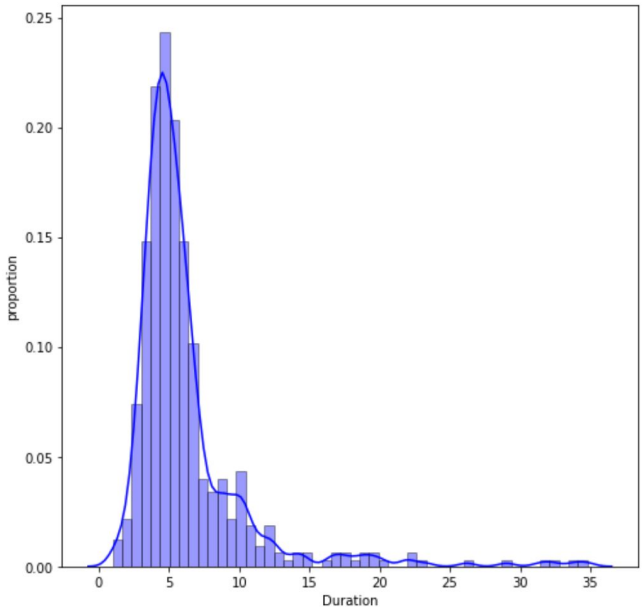


FIG. 4.1: Distribution of duration of PLMs. We considered PLMs which occured in non-REM sleep for patients RZ0015, RZ0016, RZ0017, and PED002

stages, we can extract PLMs and autonomic arousals occurred in non-REM sleep stage.

Table 4.3 and 4.4 show each subject's amount of sleep during different sleep stages. Figure 4.2 shows the sleep cycle of patient 17.

4.5 Autonomic Arousals

To find autonomic arousals, we need to find HR, systolic blood pressure(SBP) and diastolic blood pressure(DBP) elevations. We fitted a linear regression line on five consecutive heartbeats. If the slope of the linear regression line is greater than or equal to 2.5, then it is considered as HR, SBP and DBP elevations. The slope ≥ 2.5 is equivalent to $\geq$ 2.5 mm Hg / beat to beat interval(Bauer *et al.* 2016).

As we are interested only in non-REM sleep, for every non-REM sleep stage interval, we measured heart rate. We found R-peaks in EEG signal to determine heart rate and, the

Patient ID	Awake	REM sleep	Non REM sleep	Total sleep
PED002	1hr 43min	54min 30sec	6hrs 3min	8hrs 41min
RZ0015	58min 30sec	1hr 10min 30sec	5hrs 51min 30sec	8hr 30sec
RZ0016	4hr 42min	1hr 30sec	2hr 17min 30sec	8hrs
RZ0017	2hrs 11min 30sec	35min	4hrs 14min 30sec	7hrs 1min

Table 4.3: Each subject duration of sleep across all sleep stages.

Patient ID	Stage 1	Stage 2	Stage 3
PED002	16min	4hrs 14 min	1hr 33 min
RZ0015	1hr 42min	42min	3hr 27min 30sec
RZ0016	42 min 30sec	16min	1hr 19min
RZ0017	34 min 30sec	17min 30sec	3hrs 22min 30sec

Table 4.4: Duration of sleep across all sleep stages in non-REM sleep.

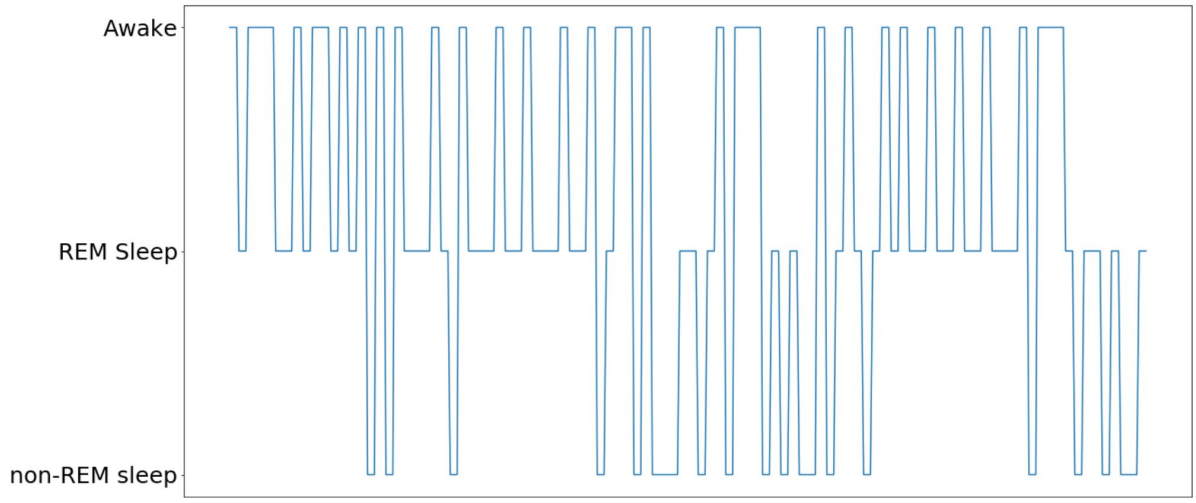


FIG. 4.2: Sleep cycle of patient 17 for the first hour

process of finding R-peaks is described in section 4.5.2.

Once we found heart rate, we did a linear regression fit on five consecutive heartbeats. If the slope of linear regression fit is ≥ 2.5 and R square score ≥ 0.5, then it is considered as a HR, SBP and DBP elevation. If we find HR elevation, then we take a 20 sec HR, SBP and DBP elevation window starting from 7 sec before, and 13 sec after the first heartbeat. In those five heartbeats, this 20-sec window is said to be elevation window. If PLM overlaps within the 20-sec window, then that PLM is associated with autonomic arousals. If we did not find HR elevation, then we will slide five consecutive heart beats window by one heartbeat, and we will repeat the same. Detailed pseudo-code for finding autonomic arousals is defined in algorithm 1.

The total number of autonomic arousals and how many of them are associated with PLM, is shown in table 4.5. As described in section 1.4, autonomic arousals which are associated with PLM have higher HR elevation when compared to that which are not associated with PLM, and we can observe the same in figure 4.3. To plot this figure 4.3, we took the 20-sec elevation window, and created a linear interpolation of 200 samples and,

Patient ID	Autonomic Arousals assoc with PLM	Autnomic arousals not assoc with PLM
PED002	71	206
RZ0015	3	8
RZ0017	35	43
RZ0016	32	84

Table 4.5: Autonomic arousals which are associated with PLMs, and which are not

took an average of the elevations accordingly.

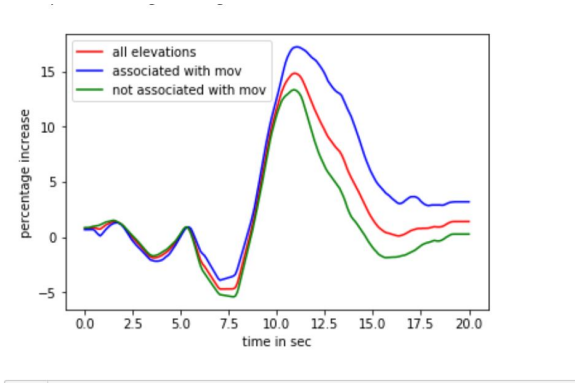
4.5.1 R square score

R square score is a statistical measure to evaluate how well a linear regression model fits the data. In General, R square value is between 0 and 1. R square value 1 says the model is perfect fit and 0 says the model is a bad fit. In (Bauer *et al.* 2016), they did not consider R square value. R square value is very beneficial, as we are finding R-peaks using an automated algorithm. Due to the artifacts, false R-peaks might get detected, and might result in a bad fit of the linear regression model with slope ≥ 2.5.

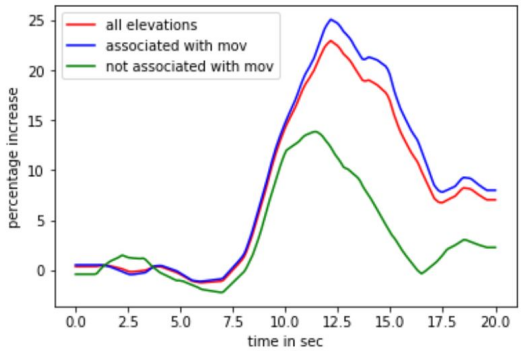
Figure 4.7 shows R-peaks of RZ0017 data, R square of first 5 beats is 0.98 and, there are no wrongly detected peaks, but if you observe figure 4.8, R square score of that figure is 0.45 and you can clearly see that there is wrongly detected peak, which is highlighted in black circle.

4.5.2 Finding R-peaks

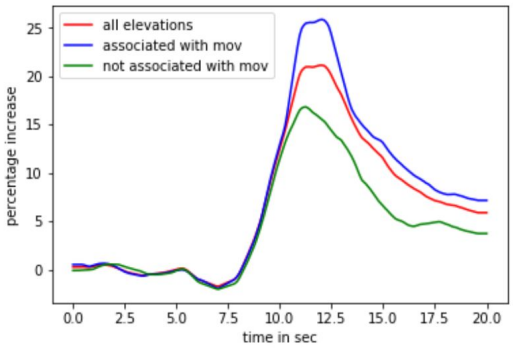
To calculate heart rate, we need to find R-peaks in QRS complex. Initially, we tried BioSPPy package, a python based framework, which worked good for adult patients (RZ0015, RZ0016, RZ0017), but failed to find the right R-peaks in PED002, due to its negative QRS complex, small QRS complex and noise. So we found another implementation(Jami, Pekkanen) of R-peaks based on non-linear transformation and gaussian differ-



(a) HR elevation of PED002



(b) HR elevation of RZ0017



(c) HR elevation of all patients

FIG. 4.3: HR elevation of Autonomic Arousals for all subjects, red color is for HR elevation of all autonomic arousals, blue color is for HR elevation of autonomic arousals which are associated with PLM and, green color is for HR elevation of autonomic arousals which are not associated with any PLM

Algorithm 1 Finding autonomic arousals

Input: EKG, ekg signal
Input: $non-REM\_intervals$ non-REM sleep intervals
Output: $Autonomic\_arousals$ autonomic arousals in non-REM sleep intervals

```
autonomic_arousals = []
for all interval in non − REM_intervals do
  ekg_signal = EKG[interval]
  r_peaks = find_rpeaks(ekg_signal)
  heart_rate, heart_rate_timestamps = calculate_heartrate(r_peaks)
  index = 0
  while index < heart_rate.size() do
    five_heart_beats = heart_rate[index : index + 5]
    slope, r2_score = linear_regression_fit(five_heart_beats)
    if slope >= 2.5 AND r2_score > 0.5 then
      autonomic_arousals.append(heart_rate_timestamps[index])
      {skip 13 sec from here, not 13 heart beats}
      index = skip_13_secs(index, hear_rate, heart_rate_timestamps)
    else
      index = index + 1
    end if
  end while
end for
return autonomic_arousals
```

entiator(Kathirvel *et al.* 2011).

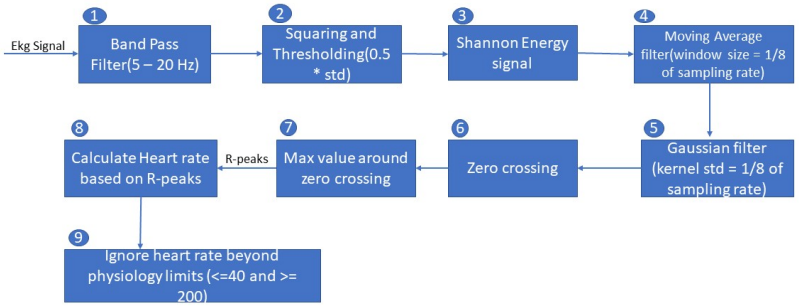


FIG. 4.4: Block Diagram for finding Heart Rate

This image adapted from (Kathirvel *et al.* 2011)

In this algorithm, there would be different stages, as shown in figure 4.4. In stage 1, we pass through bandpass filter of 5Hz and 20Hz, low pass filter to remove drifts in EKG signal due to respiration, and high pass filter to remove noise due to muscle artifacts. In stage 2, squaring was done to avoid QRS detection issues for negative QRS complex, but squaring doesn't help to find smaller and wide QRS complex. So they used new non-linear transformation as shown in stage 3, 4 and 5. In stage 6, we found zero crossing which includes positive and negative zero crossing. To find R-peaks, we need to find maximum value around zero crossing. We tried different window sizes, around zero crossing, a window size of 1/4h of sampling rate worked well for PED002, and a window size of 1/2th of sampling rate worked well for adult patients (RZ0015, RZ0016, RZ0017). Then in stage 8, we found heart rate based on R-peaks, i.e. based on below formula shown in Figure 4.5. However, due to wrong peak detection, we might get heart rate beyond our physiological limits, i.e.¿ 200 and ¡ 40 beats per minute, So we dropped those heart rates.

$$60/((rpeaks[i+1] - rpeaks[i])/sampling_rate)$$

FIG. 4.5: formula for finding rate from R-peaks

Figure 4.6 shows R-peaks in the PED002 signal, and Figure 4.7 shows R-peaks in the RZ0017 signal. We can observe different QRS complex between PED002 and RZ0017 EKG signal.

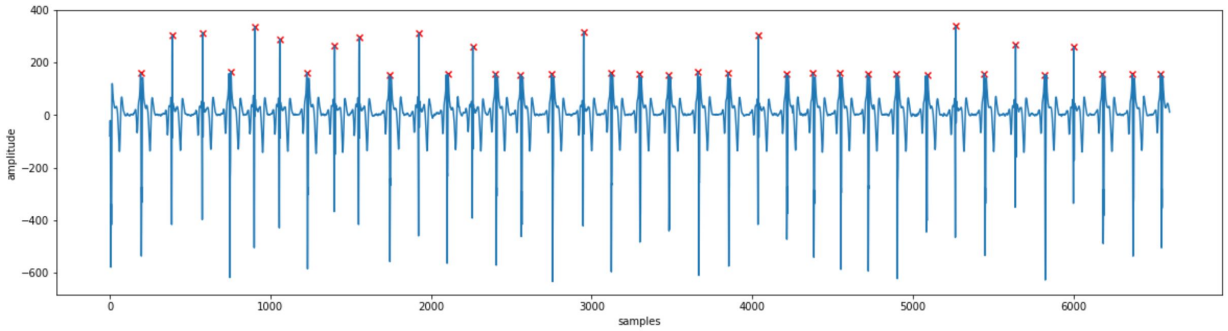


FIG. 4.6: R-peaks detection for subject PED002

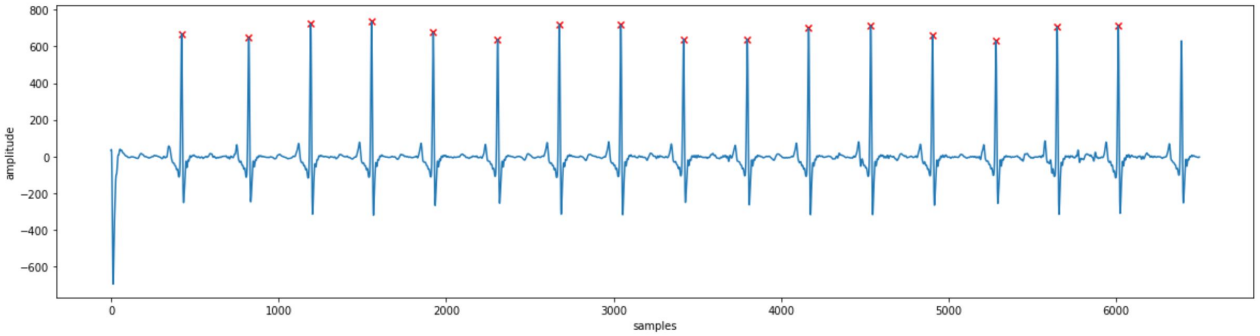


FIG. 4.7: R-peaks detection for subject RZ0017, and R square value for first five beats is 0.98

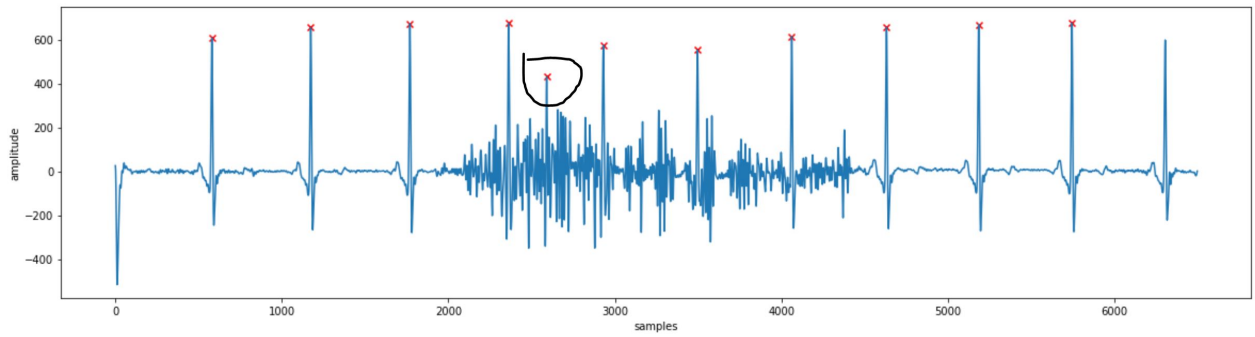


FIG. 4.8: R-peaks detection for subject RZ0017, and R square value for first five beats is 0.45. Black circle has wrongly detected R-peaks

4.6 Filtering Sensor Values

As we are using accelerometer, gyroscope, and capacitive sensor for leg movements, these sensor values might have baseline error, drift issues and noise due to the environment around it. So we need to do bandpass filter on this sensor values to exclude those issues.

The bandpass filter is a combination of low pass and high pass filter. In Figure 4.9, we see that capacitive sensor baseline value is non-zero. In that, accelerometer sensor has a drift due to the gravity component and because of that, it is hard to find the intensity of leg movements, though the gravity component helps in finding roll and pitch. The gyroscope also has a slow drift issue, due to which we might get incorrect results. For all the above reasons, we need to do a high pass filter on these sensor values. And also, a low pass filter will help to remove noise in the signal. However, for the accelerometer to calculate roll and pitch, we need to do only low pass filter.

We used an order four Butterworth bandpass filter with 0.6 - 10 Hz. Along with bandpass filter, we also did a low pass filter of 10 Hz on the accelerometer. This low pass filtered accelerometer signal is used for calculating roll and pitch. Figure 4.10 shows bandpass filtered data.

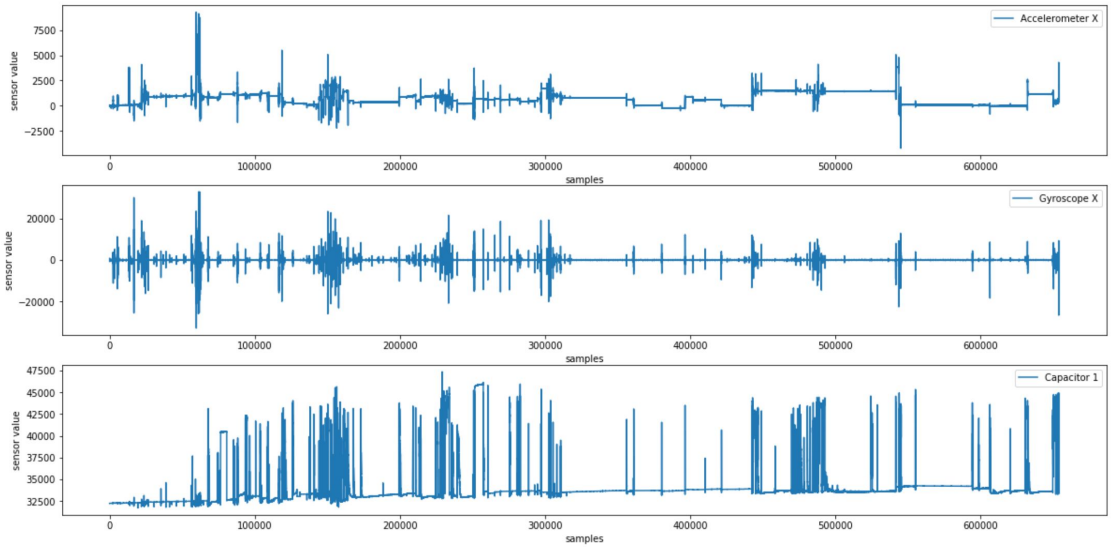


FIG. 4.9: Raw Accelerometer-X, Gyroscope-X, and Capacitive-1 sensor values of RZ0017

Patient ID	PLM with Autonomic Arousal	PLM without Autonomic Arousal
PED002	54	18
RZ0015	3	10
RZ0017	35	84
RZ0016	42	67

Table 4.6: Number of PLMs found in the RestEaze wearable band with Autonomic Arousal, and without Autonomic Arousal.

4.6.1 PLMs in Wearable band data

Some part of Wearable band data for PED002 got corrupted for unknown reasons. So we are able to find IMU sensors data for only 71 leg movements out of 100 scored PLMs of PED002 . For other patients, we are able to find Wearable band data for all scored PLMs.

4.7 Machine Learning Features

In this section, we will explain what sensor values/signals were used to determine features and what all features were calculated based on those signals.

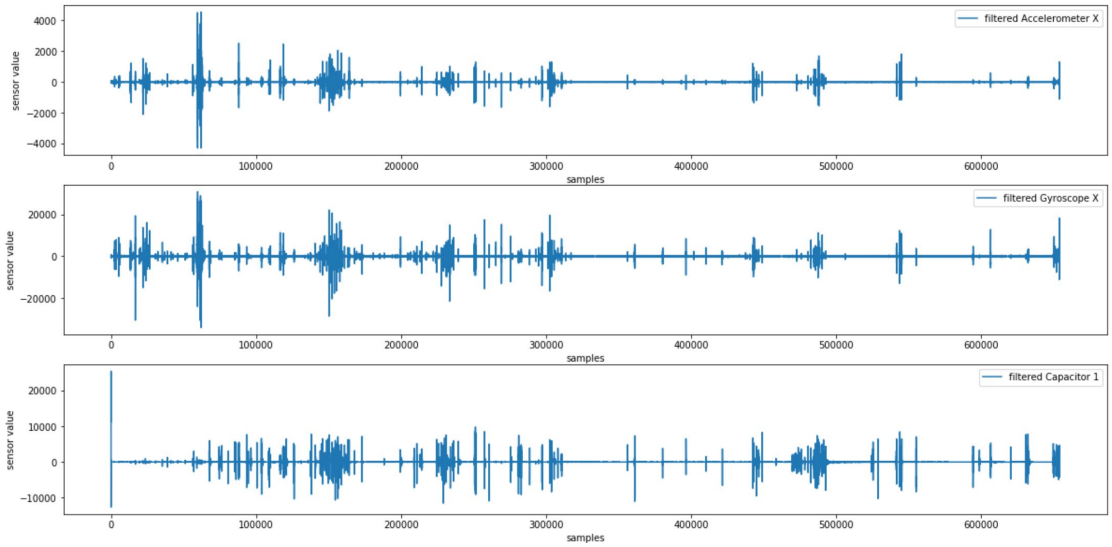


FIG. 4.10: BandPass Accelerometer-X, Gyroscope-X, and Capacitive-1 sensor values of RZ0017

4.7.1 Sensor values used for Features

We used below sensor values to calculate features.

1. Bandpass filtered gyroscope signal on X, Y, and Z axes which give orientation info and angular velocity.

2. Bandpass filtered signal of all three capacitors which captures information of flexions in the foot.

3. RMS value of bandpass filtered accelerometer X, Y and Z axes signal which provides information on general leg movements, and intensity of those movements.

4. Low pass filtered accelerometer X, Y, and Z axes to calculate roll and pitch values.

4.7.2 Features based on Sensor Values

For each PLM, we calculated time domain and frequency domain statistical features for signals described in section 4.7.2. For frequency features, we used FFT algorithm to convert the time domain signal to the frequency domain signal. We ignored the DC component while calculating statistical features in the frequency domain. Table 4.7 shows the list of statistical features. In addition to statistical features in the frequency domain, we also determined the frequency at which there is maximum and minimum power.

Using low pass and bandpass filtered accelerometer signals, we calculated roll and pitch values, given in equation 4.1 and 4.2 respectively where G_x, G_y, and G_z respectively correspond to gravitational acceleration along X, Y, and Z axes. Gravitational acceleration is calculated by subtracting bandpass filter value from lowpass filter value.

4.7.3 Features based on PLM

In addition to the features based on sensor values, we also calculated PLM features such as duration of PLM, relative time at which PLM occurred, number of PLMs happened before/after 10 seconds of the corresponding PLM, and the time duration of closest PLM which occurred before/after the PLM.

$$roll = \tan\text{inverse}\,\frac{G_y}{G_x} \tag{4.1}$$

$$pitch = \tan\text{inverse}\,\frac{-G_x}{\sqrt{G_y^2 + G_z^2}} \tag{4.2}$$

Features
Mean
Standard Deviation
Sum
Max Value
Min Value
Skewness
Kurtosis

Table 4.7: Statistical Features

Chapter 5

MACHINE LEARNING ANALYSIS AND CONCLUSIONS

In this chapter, we will go through the machine learning analysis and conclusions drawn from it. In this research, all machine learning algorithms are performed using scikit-learn. It is a library which provides machine learning packages for Python programming language. We evaluated the support vector classifier algorithm with polynomial kernel and RBF kernel, and random forest classifier. Table 5.1 shows random forest classifier outperformed support vector classifier based on cross-validation accuracy and test accuracy values.

For the random forest, we didn't do any preprocessing, but for support vector classifier we did standard deviation scaling across all features. In the rest of this chapter, PLMs which are associated with autonomic arousals are referred to as the positive class, and which are not associated with autonomic arousals are referred to as the negative class. In this chapter we will focus on machine learning analysis using random forest classifier.

Algorithm	CrossValidation Accuracy	Test Accuracy
SVM Poly kernal	65	64
SVM Rbf kernel	64	62
Random Forest	71	74

Table 5.1: Different Machine Learning with their cross validation accuracy and test accuracy

5.1 Machine Learning Analysis

5.1.1 Random Forest

Random Forest Classifier(Breiman 2001) is an ensemble of decision trees. In ensemble algorithms, a lot of weak classifier results would be aggregated to form a strong predictor. Generally, aggregation would be either by majority vote or weighted average. Each weak classifier would be trained on a subset of training data with replacement; usually, this technique is known as bootstrap aggregating or bagging. Random forest, in addition to bagging, would take a random subspace of feature set.

Decision tree suffers from overfitting and high variance. Random forest reduces this overfitting and high variance by aggregating results from various decision trees which are built on different training samples, and feature space.

Moreover, while using Random Forest, we don't need to focus much on data preprocessing like scaling, normalization, and transforming. It is also resistant to outliers. Another important factor is that Random Forest reveals how much important a feature is, when compared to other features, which is very important while concluding information from results.

Patient ID	PLM with Arousal	PLM Without Arousal	Total Samples
RZ0017	70	168	238
RZ0016	84	134	218
RZ0015	6	20	26
PED002	106	36	142

Table 5.2: Final Data Set per patient

	Number of Samples	Percentage in Data
PLM with Autonomic Arousal	266	43
PLM without Autonomic Arousal	358	57

Table 5.3: Final Data Set based on classes

5.1.2 Significant Features

A complete list of features is described in section 4.7. Using Extra Tree classifier feature importance metric, we concluded 25 significant features which are listed in Table 5.6. We calculated features for both left leg and right leg RestEaze wearable band. We stacked both left and right leg features, due to which size of the data got doubled. The final data set is shown in Tables 5.2, 5.3 and Figures 5.1, 5.2

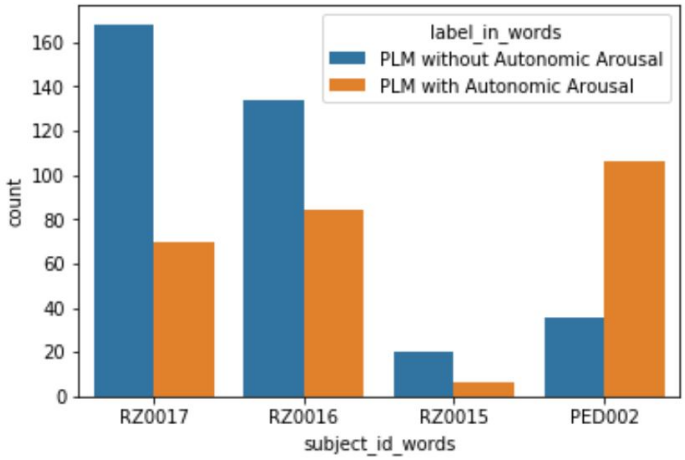


FIG. 5.1: Graphical Representation of Data in Table 5.2

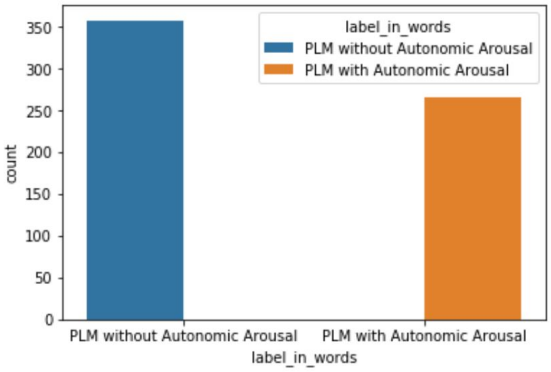


FIG. 5.2: Graphical Representation of Data in Table 5.3

	Negative class	**Positive class**	**Total Samples**	**Ratio of Negative/Positive**
Training	286	213	499	1.34
Testing	72	53	125	1.36

Table 5.4: Train and Test Split distribution

5.1.3 Train and Test Data Split

We split the entire data set into training set and testing set with 80:20 data split. The ratio of positive/negative samples in those two sets remains the same as that in the entire data set. Table 5.4 shows information about the data splitting.

5.1.4 Cross Validation

We performed 5 fold cross-validation on the training set. While performing cross-validation, we did hyper-parameter tuning which included the following parameters:

1. **Number of estimators** - This says the number of decision trees in the random forest. List of values used 3,4,5,10, 15, 20, 25.

2. **Criterion** - it is used to specify whether to use 'gini' or 'entropy' to split the data.

3. **Maximum depth** - this specifies maximum depth of each decision tree up to which

it can grow. List of values used 2,4,6,9,10.

4. **Minimum samples to split** - this specifies minimum number of samples required to split. List of values used 2,3,4,6,8,10.

5. **Minimum samples in leaf** - this specifies the minimum number of samples to be present in the leaf node. List of values used 3,4,5,6,8.

Table 5.5 shows the combination of the above-listed hyper parameters for which we got the best possible cross-validation accuracy.

Random Forest classifier also provides importance of every feature. Figure 5.3 shows the same.

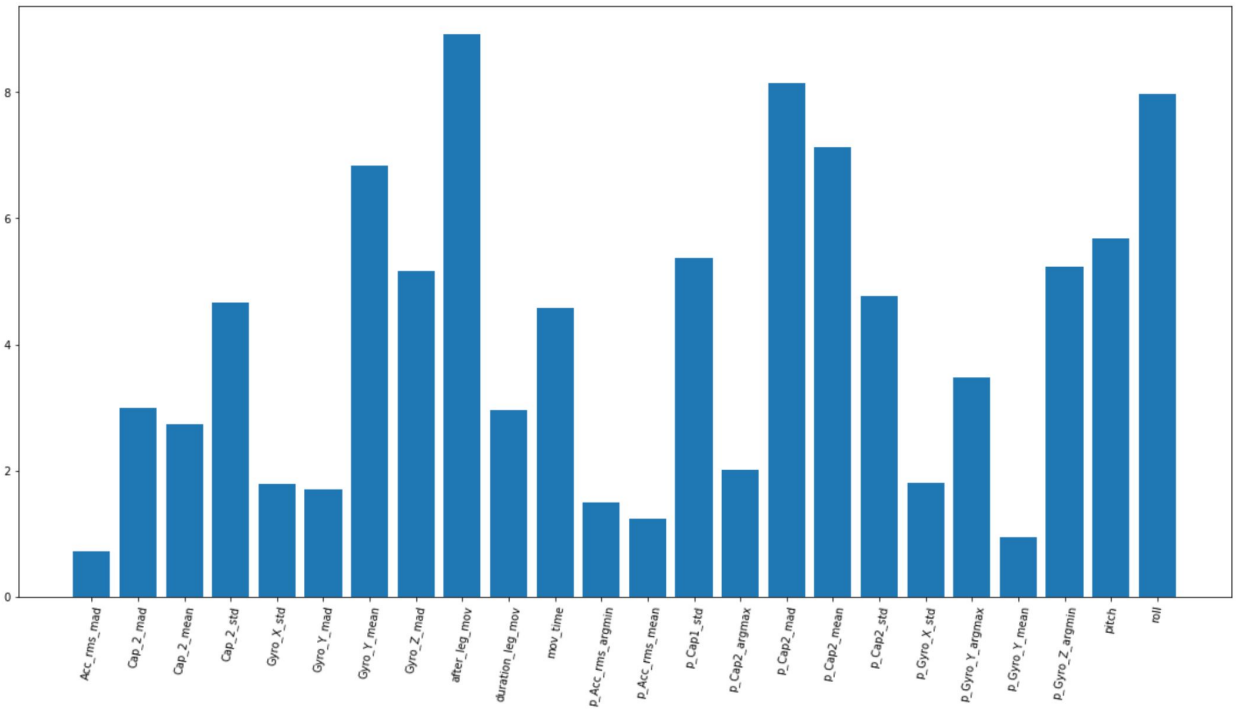


FIG. 5.3: Importance of Features

The data set is nearly balanced, so we considered accuracy as a metric. The accuracy

Hyperparameter	value
criterion	gini
maximum depth	9
Minimum samples in leaf	3
Minimum samples to split node	2
number of estimators	20

Table 5.5: Combination of Hyper parameters of Random Forest for which we got best possible cross-validation accuracy.

of each fold in the cross-validation are [71%, 69% , 80% , 70%, 66%], amounting to an average accuracy of 71%.

5.1.5 Test Accuracy

We achieved a testing accuracy of 74%, all other metrics like precision, recall and f1-score are shown in table 5.7. And a detailed confusion matrix of test data is shown in figure 5.4

5.2 Conclusion

PLMs associated with autonomic arousals are very significant to be considered in sleep analysis because these might lead to cardiovascular disease, and may cause daytime hypertension. We used four patients' sleep data who underwent overnight sleep lab study along with RestEaze system. We achieved 74% accuracy on predicting autonomic arousals using PLMs. We evaluated support vector and random forest classifier and, found that random forest model works better on the given dataset.

From figure 5.3 we can observe that features such as roll, duration of closest PLM, time and frequency domain features such as standard deviation, mean of capacitor two signal, and mean of gyroscope Y-axis signal are very important. Less significant features are

Feature Name	Description
Acc_rms_mad	Sum of values in Accelerometer RMS signal
Cap_2_mad	Sum of values in Capacitor 2 signal
Cap_2_mean	Mean of Capacitor 2 signal
Cap_2_std	Standard Deviation of Capacitor 2 signal
Gyro_X_std	Standard Deviation of Gyroscope X axis signal
Gyro_Y_mad	Sum of values in Gyroscope Y axis signal
Gyro_Y_mean	Mean of Gyroscope Y axis signal
Gyro_Z_mad	Sum of values in Gyroscope Z axis signal
after_leg_mov	Duration of closest PLM
duration_leg_mov	Duration of the PLM
mov_time	Relative time at which movements happened
p_Acc_rms_argmin	Frequency of Accelerometer RMS at which it has minimum power
p_Acc_rms_mean	Mean of Accelerometer RMS at Frquency domain
p_Cap1_std	Standard Deviation of Capacitor 1 signal in frequency domain
p_Cap2_argmax	Frequency of Capacitor 1 signal at which it has maximum power
p_Cap2_mad	Sum of Capacitor 1 signal in frequency domain
p_Cap2_mean	Mean of Capacitor 1 signal in frequency domain
p_Cap2_std	Standard Deviation of Capacitor 1 signal in frequency domain
p_Gyro_X_std	Standard Deviation of Gyroscope X axis signal in frequency domain
p_Gyro_Y_argmax	Frequency of Gyroscope Y axis at which it has maximum power
p_Gyro_Y_mean	Mean of Gyroscope Y axis signal in frequency domain
p_Gyro_Z_argmin	Frequency of Gyroscope Z axis at which it has minimum power
roll	Roll is calculated based on Accelerometer
pitch	Pitch is calculated based on Accelerometer

Table 5.6: List of significant Features used for machine learning analysis.

Class	Precision	Recall	F1-score	Support
PLM with out Autonomic Arousal	0.75	0.83	0.79	72
PLM with Autonomic Arousal	0.73	0.62	0.67	53
avg/total	0.74	0.74	0.74	125

Table 5.7: Classification Report on Testing Data.

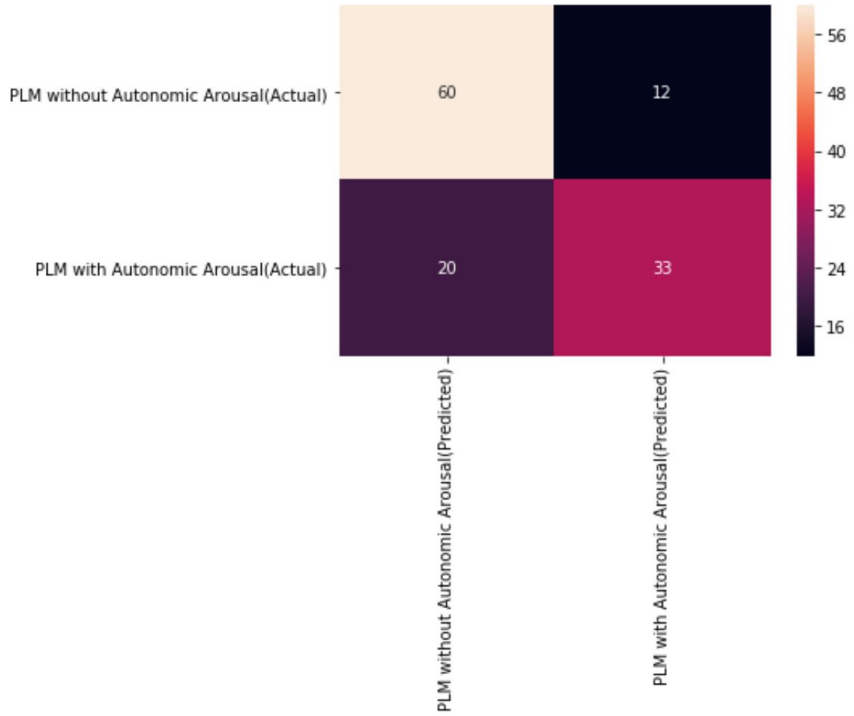


FIG. 5.4: Confusion Matrix for Test Data

time domain accelerometer RMS features such as sum and frequency domain accelerometer RMS such as mean and arg of minimum frequency.

From the above analysis on feature importance, we can conclude flexions in the foot(captures by capacitor signal) and orientation of legs(captures by Gyroscope, roll, and pitch), i.e., sleep position, might be the important factors to determine autonomic arousals based on PLMs.

Chapter 6

FUTURE WORK

In this research, we used PLMs scored by a technician, which is partially an automated process. We can use (Zheng 2018) work on detecting PLMs on RestEaze band data, and we can completely automate the detection of autonomic arousal using PLMs.

Computed autonomic arousals can be evaluated by an expert technician to get cleaner and perfect data.

By using large dataset, we can use wavelet transform, along with standard features on the time domain and frequency domain. Also for large datasets, we can use more sophisticated algorithms such as Deep Neural Network.

By having multiple nights' data of the same patient, we can personalize arousal detection using PLMs by studying the leg movement patterns particular to a patient.

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